DIET PILL (AMPHETAMINES) TRAFFIC, ABUSE AND REGULATION

HEARINGS

BEFORE THE

SUBCOMMITTEE TO INVESTIGATE JUVENILE DELINQUENCY

OF THE

COMMITTEE ON THE JUDICIARY UNITED STATES SENATE

NINETY-SECOND CONGRESS

FIRST SESSION

PURSUANT TO

S. Res. 32

SECTION 12

INVESTIGATION OF JUVENILE DELINQUENCY IN THE UNITED STATES

"INVESTIGATIVE HEARINGS ON THE EFFICACY OF AMPHETAMINES FOR THE SHORT-TERM TREATMENT OF OBESITY AND THE RELATED ISSUE OF PRODUCTION QUOTAS."

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U.S. GOVERNMENT PRINTING OFFICE

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"INVESTIGATIVE HEARINGS ON THE EFFICACY OF AMPHETAMINES FOR THE SHORT-TERM TREATMENT OF OBESITY AND THE RELATED ISSUE OF PRODUCTION QUOTAS"

MONDAY, FEBRUARY 7, 1972

U.S. SENATE,
SUBCOMMITTEE TO INVESTIGATE JUVENILE DELINQUENCY
OF THE COMMITTEE ON THE JUDICIARY,
Washington, D.C.

The subcommittee (composed of Senators Bayh, Hart, Burdick, Kennedy, Cook, Hruska, Fong, and Mathias), met, pursuant to notice, at 10:10 a.m., in room 2228, New Senate Office Building, Senator Birch Bayh (chairman), presiding.

Present: Senator Bayh.

Also present: Mathea Falso, staff director and chief counsel; John M. Rector, deputy chief counsel; Michael A. Nemeroff, assistant counsel; William C. Mooney, investigator; Mary K. Jolly, chief clerk; Nancy L. Smith, research assistant; B. Elizabeth Marten, personal secretary to the staff director and chief counsel; Cheryl A. Wolf, assistant chief clerk; Lance Ringel, and Archie Lovell, interns; Stanley Ebner for Senator Hruska; Dorothy Parker for Senator Fong; Betty A. Webb for Senator Cook, and Ronald Meredith for Senator Burdick.

Senator BAYH. We will convene our hearings this morning.

I would like to make a brief statement relative to the meeting and the purpose of our testimony here today.

We meet today to hear testimony on the efficacy of amphetamines for the short-term treatment of obesity and the related issue of production quotas established for these dangerous substances.

Last July this subcommittee held several days of hearings on S. 674, a bill to establish tighter controls over the manufacture and distribution of amphetamines and amphetamine-like substances. We heard considerable evidence of diversion and abuse of these drugs, including widespread abuse among young people. Shortly after these hearings the Bureau of Narcotics and Dangerous Drugs imposed tighter controls on the amphetamine-like substances accomplishing through administrative procedures the objectives of S. 674. On December 4, 1971, acting on the recommendations of the Surgeon General, BNDD proposed a production quota amounting to a 40 percent reduction in amphetamine and methamphetamine production.

According to a Food and Drug Administration order of August 8, 1970, labeling of amphetamines and methamphetamines must reflect that their medical usefulness is limited to three uses. These are (1) narcolepsy (a rare sleeping illness); (2) hyperkinesis (minimal brain dysfunction in children manifesting itself in hyperactivity); and (3) obesity. Prescription of amphetamines and metamphetamines for appetite control is to be limited to short-term treatment. It has been estimated that less than 1 percent of all prescribed amphetamines are for the first two indications. Thus, if amphetamines were limited to the treatment of narcolepsy and hyperkinesis, the amount of these dangerous substances required to meet the Nation's medical and scientific needs would be substantially lower than that established by the proposed December quota.

This subcommittee, the Congress and the public at large are all too familiar with the horrors of amphetamines—"speed"—abuse, and the "speed" culture the subject of our earlier hearings. Unfortunately, accounts of the destructiveness of these dangerous substances are common.

The medical consequences of abusing amphetamines can be disastrous. National Institute of Mental Health studies indicate that regular users of these drugs develop a tolerance and must take increasingly larger doses to achieve the desired effect. When an abuser attempts to withdraw from the drug, he experiences acute psychological withdrawal symptoms. To ease the agony of "coming down" from his high, he may turn to heroin or barbiturates. This completes the cycle of drug abuse from which he may never escape.

The diversion of amphetamines from legitimate channels of distribution to the illicit market has been well documented. This is not a phenomenon of the past. Last month, BNDD reported the seizure of more than 1 million dosage units of the amphetamine, Bifetamina. The only medical indication for this product is as a short-term adjunct in the treatment of obesity.

The abuse of diet pills is significant and widespread. A recent study by the New York State Narcotic Addict Control Commission reported the following:

(1) Pep pills, amphetamines, and amphetamine-like compounds are the most abused drugs in the State. More than half the users in New York State obtained them without prescriptions—although the law clearly prescribes that prescriptions must be obtained.

(2) Some 222,000 people regularly use diet pills and 19 percent of them are obtained without a prescription.

(3) Of the estimated 222,000 regular users, an additional 46,000 (20.8 percent) obtain at least part of these drugs without a legal prescription.

One is forced to conclude that diversion and the widespread availability of diet pills contributes significantly to the growing abuse of amphetamines in this country.

It is interesting to note that the same euphoric effect which induces youths and others into the cult of the "speed freaks" is reportedly also responsible for the short-period appetite suppression attributed to amphetamines in obesity treatment. As a result of the

stimulation or "high" provided by amphetamines an individual's drive toward overeating is modified. However, even when the appetite is artificially suppressed by pills, researchers have found that the average weight loss is 6.75 pounds during the period of treatment prescribed.

Now, I must admit that I am particularly concerned about the extent to which people remain dependent on these diet pills long after the several week period of indicated treatment has elapsed. How many unsuspecting individuals who turn to these pills as diet aids run the risk of developing tolerance to these drugs and eventual amphetamine dependency?

Various studies and data indicate that many citizens in this country are concerned about their weight. This is a common phenomenon. This subcommittee is endeavoring to determine whether amphetamine treatment for weight problems is perpetuating—indeed, propagating a "speed" culture with problems significantly worse than the problems of obesity.

None of us on the committee profess to be experts. We hope that our witnesses can give us some expert testimony on the extent to which the effort to control weight, and the abuse of drugs prescribed therefor, has aided and abetted the amphetamine—"speed"—culture The decision on the efficacy of amphetamines, methamphetamines and amphetamine-like substances for the treatment of obesity will have significant effects on the availability of these widely abused drugs. If this use is curtailed it appears that far fewer such drugs will be legitimately produced, diverted, and abused. For these reasons I am particularly interested in the testimony of our witnesses this morning. I will include in the record at this point the text of the subcommittee's enabling resolution Senate Resolution 32.

(The document was marked "Exhibit No. 1" and is as follows:)

92D CONGRESS
1ST SESSION

S. RES. 32

[Report No. 92–11]

IN THE SENATE OF THE UNITED STATES

FEBRUARY 1 (legislative day, JANUARY 26), 1971

Mr. MCCLELLAN (for Mr. EASTLAND), from the Committee on the Judiciary, reported the following resolution; which was referred to the Committee on Rules and Administration

FEBRUARY 19 (legislative day, FEBRUARY 17), 1971

Reported, under authority of the order of the Senate of February 19 (legislative day, February 17), 1971, by Mr. CANNON, with amendments

MARCH 1 (legislative day, FEBRUARY 17), 1971

Considered, amended, and agreed to

RESOLUTION

Authorizing additional expenditures by the Committee on the Judiciary for inquiries and investigations.

Resolved, That, in holding hearings, reporting such hearings, and making investigations as authorized by sections 134(a) and 136 of the Legislative Reorganization Act of 1946, as amended, in accordance with its jurisdiction under rule XXV of the Standing Rules of the Senate, the Committee on the Judiciary, or any subcommittee thereof, is authorized from February 1, 1971, through February 29, 1972, for the purposes stated and within the limitations imposed by the following sections, in its discretion (1) to make expenditures from the contingent fund of the Senate, (2) to employ personnel, and (3) with the prior consent

of the Government department or agency concerned and the Committee on Rules and Administration, to use on a reimbursable basis the services of personnel of any such department or agency.

SEC. 2. The Committee on the Judiciary, or any subcommittee thereof, is authorized from February 1, 1971, through February 29, 1972, to expend not to exceed $3,861,300 to examine, investigate, and make a complete study of any and all matters pertaining to each of the subjects set forth below in succeeding sections of this resolution, said funds to be allocated to the respective specific inquiries and to the procurement of the services of individual consultants or organizations thereof (as authorized by section 202 (i) of the Legislative Reorganization Act of 1946, as amended) in accordance with such succeeding sections of this resolution.

SEC. 3. Not to exceed $325,500 shall be available for a study or investigation of administrative practice and procedure, of which amount not to exceed $2,000 may be expended for the procurement of individual consultants or organizations thereof.

SEC. 4. Not to exceed $778,100 shall be available for a study or investigation of antitrust and monopoly, of which amount not to exceed $5,000 may be expended for the

procurement of individual consultants or organizations thereof.

SEC. 5. Not to exceed $228,500 shall be available for a study or investigation of constitutional amendments.

SEC. 6. Not to exceed $280,000 shall be available for a study or investigation of criminal laws and procedures. amount not to exceed $3,000 may be expended for the procurement of individual consultants or organizations thereof.

SEC. 7. Not to exceed $210,000 shall be available for a study or investigation of criminal laws and procedures.

SEC. 8. Not to exceed $9,500 shall be available for a study or investigation of Federal charters, holidays, and celebrations.

SEC. 9. Not to exceed $243,500 shall be available for a study or investigation of immigration and naturalization.

SEC. 10. Not to exceed $259,400 shall be available for a study or investigation of improvements in judicial machinery.

SEC. 11. Not to exceed $620,000 shall be available for a study or investigation of internal security, of which amount not to exceed $3,900 may be expended for the procurement of individual consultants or organizations thereof.

SEC. 12. Not to exceed $308,300 shall be available for a study or investigation of juvenile delinquency, of which amount not to exceed $5,800 may be expended for the procurement of individual consultants or organizations thereof.

SEC. 13. Not to exceed $140,000 shall be available for a study or investigation of patents, trademarks, and copyrights.

SEC. 14. Not to exceed $59,900 shall be available for a study or investigation of national penitentiaries.

SEC. 15. Not to exceed $155,000 shall be available for a study or investigation of refugees and escapees.

SEC. 16. Not to exceed $63,600 shall be available for a study or investigation of revision and codification.

SEC. 17. Not to exceed $180,000 shall be available for a study or investigation of separation of powers between the executive, judicial, and legislative branches of Government, of which amount not to exceed $14,800 may be expended for the procurement of individual consultants or organizations thereof.

SEC. 18. The committee shall report its findings, together with such recommendations for legislation as it deems advisable with respect to each study or investigation for which expenditure is authorized by this resolution, to the

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Senate at the earliest practicable date, but not later than February 29, 1972.

SEC. 19. Expenses of the committee under this resolution shall be paid from the contingent fund of the Senate upon vouchers approved by the chairman of the committee.

Our first witness this morning is Dr. Charles C. Edwards, Commissioner of the Food and Drug Administration, Public Health Service, Department of Health, Education, and Welfare.

Dr. Edwards, we appreciate very much your taking the time to examine this problem with us. You bring some of the expertise that the committee is anxious to hear.

Dr. Edwards. Thank you, Mr. Chairman. We do appreciate the fact that we are meeting with you this morning to discuss this extremely important problem.

I would like to begin first by introducing my colleagues, if I may. On my immediate left is Dr. Elmer Gardner, who is the Director of our Division of Neuropharmacological Drug Products, and on his immediate left is Dr. Barrett Scoville, the Deputy Director of that Division. And on my right is Mr. Peter Barton Hutt, the General Counsel for the Food and Drug Administration.

STATEMENT OF CHARLES C. EDWARDS, M.D., COMMISSIONER OF FOOD AND DRUGS, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE; ACCOMPANIED BY ELMER A. GRADNER, M.D., DIRECTOR, DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, BARRETT SCOVILLE, M.D., DEPUTY DIRECTOR, DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, AND PETER BARTON HUTT, GENERAL COUNSEL, FOOD AND DRUG ADMINISTRATION, HEW

Dr. Edwards. Mr. Chairman, as I said, we are pleased to have this opportunity to appear before you today and discuss the amphetamine quotas and the safety and efficacy of amphetamines and other appetite suppressants.

The Food and Drug Administration has strongly supported placing stringent controls on the amphetamines.

Our drug abuse control program began in February of 1966. In the first 2 years of the program, before this responsibility was transferred to the Department of Justice, we carried out over 2,000 criminal investigations, more than 1,300 arrests were made, and about 300 criminal cases were completed. We made, in addition, approximately 1,100 accountability investigations resulting in 108 civil seizures of depressant and stimulant drugs. Nearly 600 million dosage units of these drugs were removed from the marketplace because no accurate records as required by the law were kept by manufacturers.

More recently we have taken certain broader actions which have been pivotal, I believe, in allowing us to control amphetamines far better at present than they were controlled in the past.

As you mentioned, first we published a significant regulation in 1970 limiting the medical use of amphetamines and declaring them new drugs. The amphetamines, having been marketed prior to 1938 and the passage of important amendments to the Federal Food, Drug, and Cosmetic Act, had been considered "grandfathered" and not subject to the efficacy provisions of the Drug Amendments of

1962. Among other things, this "grandfather" status made it administratively difficult to obtain necessary information on safety and efficacy.

Basing our conclusions in part upon opinions of expert reviewing groups, we published a Statement of Policy and Interpretation on August 8, 1970, announcing that because the drugs had come to be used in a number of new ways since 1938, and because there were questions of efficacy as well as safety, the amphetamines must now be subjects of approved new drug applications. This policy statement was the administrative key opening the way to the comprehensive review of the amphetamines which is now going on.

The policy statement had two important corollaries. First, it required relabeling the drugs with strict and explicit cautionary material and with limitations on the uses of the drugs to three conditions; narcolepsy, minimal brain dysfunction, and as adjunctive therapy in obesity. This deleted a number of questionable indications, such as depression, for which the drugs had been used.

Senator Bayh. Excuse me, Doctor. Does this apply to the "grandfathered" amphetamine drugs as well?

Dr. Edwards. Yes; this applied across the board.

Senator Bayh. Across the board?

Dr. Edwards. Across the board.

This labeling also limited use of the amphetamines in obesity to short-term use and so worked to eliminate prolonged, repeated, unsafe or questionably effective use of the drug for this condition.

The second corollary of the policy statement was that new drug applications were to be submitted by the manufacturers within 1 year and must contain clinical data to support the permitted indications. Eighty-five applications have been submitted, and I shall come to our review of these later.

Another recent major action in respect to the amphetamines was their transfer from schedule III to schedule II of the Comprehensive Drug Abuse Prevention and Control Act.

As you know, schedule III places only limited controls on the drugs listed in it, while schedule II involves narcotic-type restrictions. These restrictions include special order forms, separate recordkeeping, nonrefillable presecriptions, yearly manufacturing quotas, and export-import permits.

When the Comprehensive Drug Abuse Act was passed in 1970, only parenteral methamphetamine was placed in schedule II. In March of 1971, I signed a memorandum recommending that all amphetamines be placed in schedule II.

After the question had been thoroughly discussed within the Department of Health, Education, and Welfare, this recommendation was transmitted to the Bureau of Narcotics and Dangerous Drugs, thus accomplishing what we believe is the greatest single measure in reducing misuse and abuse of the amphetamines.

If you will look at the chart here, Mr. Chairman, at your right and my left, I believe you will agree that the impact of rescheduling has been profound. Here, up until May 1971, prescriptions were being filled and refilled at a rate of about 1.6 million per month.

But, on May 26, 1971, the notice proposing rescheduling of the amphetamines was published in the Federal Register. We can only speculate on the cause for the peak in May and June, but it does appear as if some people were stocking up for the drought ahead. Here, on July 7, the notice of rescheduling became final.

The precipitous drop in prescribing continues until October, at which time the effect of rescheduling appears to have reached its maximum for the near future.

Our most recent action involving the amphetamines was our recommendation in collaboration with the National Institute of Mental Health in setting quotas for the 1972 manufacture of the drugs. As you know, the Bureau of Narcotics and Dangerous Drugs had asked for an estimate of medical and scientific needs for the amphetamines for the coming year to aid them in setting quotas.

As noted in the BNDD regulations, the Director of the Bureau of Narcotics and Dangerous Drugs takes HEW recommendations into account. However, in establishing quotas, he also relies on such factors as total new disposal of the drugs by all manufacturers during previous years, current trends in disposal of the drugs, actual or estimated inventories of the drugs and projected demands for such drugs.

We decided to use previous production of amphetamines as a point of departure in estimating the need for these drugs. There is no doubt that using past production figures is not a fully satisfactory way to estimate medical needs. The alternative to this would ideally be based on an accurate estimate of patients who require amphetamines. At the present time, however, such an estimate appears even more unsatisfactory than the use of production figures for several fundamental reasons.

Senator Bayh. Well, Doctor, I might suggest, that it appears to me that your own charts on prescription rates raise serious questions about the validity of past production as a standard for estimating medical need, particularly in view of the precipitous decline in amphetamine prescriptions filled in the relatively short period since HEW has adopted your earlier recommendations and the recommendations urged by this committee. How can you assess future medical need without considering the byproducts of rescheduling, such as more conscientious prescribing by physicians?

Dr. Edwards. First of all, let me make it clear that this information on the precipitous drop in the number of prescriptions has just recently become available to us; our initial estimate for the quota was made before we had this information. We have therefore changed, or are in the process now of changing, our recommendation to the Department.

Senator Bayh. As a layman, I urge you to make this recommendation. You do not have to be an M.D. to understand what these statistics indicate. A little logic should suffice in this case.

Dr. Edwards. As I say, our statistics just became available within the month. Since that time we have made the recommendation, or are in the process of making the recommendation, in consultation with BNDD, to reduce the quota by another 30 percent.

Senator BAYH. I only raise this, because in your statement you indicate that although you are not fully satisfied, previous production will be used as a point of departure. You are starting with an inflated point of departure.

Dr. EDWARD. Well, I think there is no question that it was inflated, but we did not have any other way at that point in time to start. But I think with this new data that is being accumulated, as we move along, we can provide better answers, as I say later in my statement. We are looking at all of the central nervous system stimulating drugs that are used for this problem of obesity.

Senator BAYH. Good. In my opinion the evidence that you have presented reaffirms the need for production controls. My concern is that such controls be reasonable and yet firm enough to accomplish their purpose. We should not be satisfied with anything less.

Dr. EDWARDS. You are certainly 100 percent correct.

Senator BAYH. Please proceed.

Dr. EDWARDS. I would certainly agree with you.

First, unfortunately, we do not have reliable figures for the incidence or prevalence of narcolepsy and of minimal brain dysfunction or hyperkinetic disorders in children. Most experts will agree that figures occasionally quoted are educated guesses at best. They range from 900,000 to 3 million and more for minimal brain dysfunction and from 25,000 to over 1 million for narcoleptics.

Senator BAYH. Excuse me. How can we obtain reliable data on the extent of these illnesses?

Dr. EDWARDS. I think we can do a far better job than we have done in the past, Mr. Chairman, but these are both difficult figures to get, because the diagnosis is a difficult one. Different people have different criteria for the development of this particular diagnosis. As a result, good, hard figures are always going to be a little on the soft side—if I can use that word. But we can do much better than we have done.

Senator BAYH. What steps are being taken to provide more certainty or accuracy on the incidents of these diseases?

Dr. EDWARDS. Just that NIMH has tried to support studies to get better incident or prevalence figures for hyperkinetic disorders in children. They are always trying to obtain better, proven figures. But I think the problem is not so much one of carrying on further surveys but one of getting better consensus in the field about the diagnostic criteria.

Senator BAYH. The hyperkinetic use, as I recall from earlier hearings, is a matter of concern too many who feared that these drugs were being used merely to sedate Johnnie or Susie so they could not aggravate their teachers. I have been concerned that these drugs may become an all too easy "solution" for behavior problems which are really caused by hunger, poor teaching, overcrowded classrooms, lack of understanding by parents and teachers and other nonmedical causes. Are you studying the extent to which these drugs are prescribed for problems other than the minimal brain dysfunction indication?

Dr. GARDNER. That is part of it. It is recognized that at least in some instances the drug is not prescribed properly. However, when closer diagnosis is made, the amphetamines as well as Ritalin are very valuable in the treatment of this condition. We have to be careful not to discard this whole therapeutic approach.

Senator BAYH. I am certainly not suggesting that. I do not know where you draw the line, but we have had witnesses who have testified that sometimes these drugs are used only to sedate a child, not to deal with his or her other problems.

Dr. EDWARDS. I think that in the treatment of obesity, Mr. Chairman, this type of therapy has been abused. It is also abused some in these other conditions but not to the extent as obesity. I think one of the main reasons it has been abused is because frequently the criteria of diagnosis have not been well enough developed. It has been used as a crutch rather than as a real therapeutic agent.

Senator BAYH. Is anyone at FDA or NIMH—attempting the redefine the criteria for diagnosis and thereby prevent nonindicated use of amphetamines for these school children?

Dr. EDWARDS. We have a report which I would like to submit for the record which goes into some of the background on it. It is a report developed by the Department of Health, Education, and Welfare, of the Conference on the Use of Stimulant Drugs in the Treatment of Behavior of Disturbed Young School Children.

(The report was marked "Exhibit No. 2" and is as follows:)

Exhibit No. 2

REPORT OF THE CONFERENCE ON THE USE OF STIMULANT DRUGS IN THE TREATMENT OF BEHAVIORALLY DISTURBED YOUNG SCHOOL CHILDREN

INTRODUCTION

On January 11-12, 1971, the Office of Child Development and the Office of the Assistant Secretary for Health and Scientific Affairs, Department of Health, Education, and Welfare, called a conference to discuss the use of stimulant medications in the treatment of elementary school-age children with certain behavioral disturbances. In convening the conference, the Office of Child Development was aware of public concern about the increasing use of stimulant medications (such as dextroamphetamine and methylphenidate) in treating so-called hyperkinetic behavior disorders. Were these drugs--so widely misused or abused by adolescents and adults--truly safe for children? Were they properly prescribed, or were they used for youngsters who, in fact, need other types of treatment? Is emphasis on medications for behavior disorders misleading? Might this approach tempt many to oversimplify a complex problem, leading to neglect of remedial social, educational or psychological efforts on the part of professionals, parents, schools and public agencies?

In order to clarify the conditions in which these medications are beneficial or harmful to children, to assess the status of current knowledge, and to determine the best auspices for administering these drugs to children, a panel of fifteen specialists was invited to meet in Washington. The panelists were from the fields of education, psychology, special education, pediatrics, adult and child psychiatry, psychoanalysis, basic and clinical pharmacology, internal medicine, drug abuse and social work. The panel's task was to review the evidence of research and experience and to prepare an advisory report for professionals and the public.

This report briefly outlines the general nature of behavioral disorders in children and then focuses on those disorders that are being treated with stimulant medications. It discusses appropriate treatment and the concerns voiced by the public and media. Finally, the report examines the role of the pharmaceutical industry, professionals, and the news media in publicizing stimulant drugs for children and outlines the glaring gaps in needed research, training and facilities.

BEHAVIOR DISORDERS OF CHILDHOOD

A wide range of conditions and disabilities can interfere with a child's learning at home and in school, his socialization with peers, and his capacity to reach his maximum development. Social deprivations and stress at home or school may retard optimal development. Mental retardation, the more rarely occurring childhood autism and psychosis, and other such disabilities may cause serious problems. Some difficulties arise because of clearly definable medical conditions such as blindness, deafness or obvious brain dysfunction. Some are associated with specific reading or perceptual defects, and others with severe personality or emotional disturbance.

Such dysfunctions are known to require careful evaluation, thoughtfully planned treatment employing a variety of methods on the child's behalf, and conscientious monitoring of remedial treatments. Individualized evaluation and treatment is important for any childhood behavior disorder. There are appropriate occasions for use of medications such as tranquilizers and anti-depressants in some children with these disorders. For over three decades, stimulant

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Sponsored by the Office of Child Development and the Office of the Assistant Secretary for Health and Scientific Affairs, Department of Health, Education, and Welfare, Washington, D. C., January 11-12, 1971.

medications have been selectively used for children under medical supervision. We now focus upon issues related to the current use of these drugs.

"HYPERKINETIC DISORDERS"

The type of disturbance which has evoked misunderstanding and concern has many names. The two most familiar--neither entirely satisfactory--are "minimal brain dysfunction" or, more commonly, "hyperkinetic behavioral disturbance." There is no known single cause or simple answer for such problems. The major symptoms are an increase of purposeless physical activity and a significantly impaired span of focused attention. The inability to control physical motion and attention may generate other consequences, such as disturbed mood and behavior within the home, at play with peers, and in the schoolroom.

In its clear-cut form, the overt hyperactivity is not simply a matter of degree but of quality. The physical activity appears driven--as if there were an "inner tornado"--so that the activity is beyond the child's control, as compared to other children. The child is distracted, racing from one idea and interest to another, but unable to focus attention.

INCIDENCE OF HYPERKINETIC DISORDERS

This syndrome is found in children of all socioeconomic groups and in countries throughout the world. A conservative estimate would be that moderate and severe disorders are found in about 3 out of 100 elementary school children--an estimate that would vary somewhat in different communities. More males than females are affected, as is true in a number of childhood ailments. Children so afflicted are generally of normal or superior intelligence. A significant number so diagnosed have special learning or reading disabilities, in addition to the major symptoms. A near majority are reported to have had behavioral problems since infancy. There is a smaller group of more severely afflicted children upon whom most studies have focused; they may show increased clumsiness and a variety of physical symptoms. Thus, some of the children show hyperactivity and reduced attention which ranges in degree from mild to severe, with or without associated physical signs or special learning impairments; some have complex behavioral and personality problems, as well as special learning and reading difficulties, along with the major hyperkinetic symptoms.

CAUSES OF HYPERKINETIC DISORDERS

We know little about definitive causes. The disorder has been ascribed to biological, psychological, social or environmental factors, or a combination of these. There is speculation that the core set of symptoms--those affecting control of attention and motor activity--may have their origin in events taking place before the child is born, or during the birth process, or they may be related to some infection or injury in early life. The neurological and psychological control of attention is an important but incompletely researched topic, as are the nutritional, perinatal and developmental factors. Thus, in many instances, it is not yet possible even to speculate as to original causes.

THE COURSE OF HYPERKINETIC DISORDERS

Usually, the excessive activity and attentional disturbances are less apparent after puberty. Specialists citing experience and some fragmentary research data believe that treatment enables many to lead productive lives as adults, while severely afflicted children who remain untreated may be significantly at risk for adult disorders. Extensive research is still required on these points. Because the ages of 5 to 12 are crucial to the child's development and self-image, treatments which permit the child to be more accessible to environmental resources are warranted and useful.

DIAGNOSIS OF HYPERKINETIC DISORDERS

In diagnosing hyperkinetic behavioral disturbance, it is important to note that similar behavioral symptoms may be due to other illnesses or to relatively simple causes. Essentially healthy children may have difficulty maintaining attention and motor control because of a period of stress in school or at home. It is important to recognize the child whose inattention and restlessness may be caused by hunger, poor teaching, overcrowded classrooms, or lack of understanding by teachers or parents. Frustrated adults reacting to a child who does not meet their standards can exaggerate the significance of occasional inattention or restlessness. Above all, the normal ebullience of childhood should not be confused with the very special problems of the child with hyperkinetic behavioral disorders.

The diagnosis is clearly best made by a skilled observer. There unfortunately is no single diagnostic test. Accordingly, the specialist must comprehensively evaluate the child and assess the significance of a variety of symptoms. He considers causal and contributory factors--both permanent and temporary--such as environmental stress. He distinguishes special dysfunctions such as certain epilepsies, schizophrenia, depression or anxiety, mental retardation or perceptual deficiencies. The less severe and dramatic forms of hyperkinetic disorders also require careful evaluation. Adequate diagnosis may require the use not only of medical, but of special psychological, educational and social resources.

TREATMENT PROGRAMS

The fact that these dysfunctions range from mild to severe and have ill-understood causes and outcomes should not obscure the necessity for skilled and special interventions. The majority of the better known diseases--from cancer and diabetes to hypertension--similarly have unknown or multiple causes and consequences. Their early manifestations are often not readily recognizable. Yet useful treatment programs have been developed to alleviate these conditions. Uncertainty as to cause has not prevented tests of the effectiveness of available treatments, while the search for clearer definitions and more effective kinds of therapy continues. The same principles should clearly apply to the hyperkinetic behavior disorders.

Several approaches now appear to be helpful. Special classes and teachers can be directed to specific learning disabilities and thus restore the confidence of the child who experiences chronic failure. Modification of behavior by systematic rewarding of desired actions has been reported to be useful in some children. Elimination of disturbing influences in the family or classroom through counseling may often tip the balance, and a happier child may show improved control and function.

There will be children for whom such efforts are not sufficient. Their history and their examination reveal symptoms of such a driven nature that skilled clinicians undertake a trial of medical treatment. Medicine does not "cure" the condition, but the child may become more accessible to educational and counseling efforts. Over the short term and at a critical age, this can provide the help needed for the child's development.

Stimulant medications are beneficial in only about one-half to two-thirds of the cases in which trials of the drugs are warranted. The stimulant drugs are considered to be the first and least complicated of the medicines to be tried. Other medications--the so-called tranquilizers and anti-depressants--are generally reserved for a smaller group of patients. Without specialized medical therapy, the consequences for these children of their failure to manage--even in an optimal environment--are clearly very severe. In such cases, the aim is not to "solve problems with drugs," but to put the severely handicapped child in a position to interact with his environment to the extent that his condition permits.

Response to stimulant medication cannot be predicted in advance. Fortunately, the issue can be resolved quickly. When stimulants are given in adequate doses, a favorable response--when it occurs--is fairly rapidly obtained and is unmistakably the consequence of the drug. Thus, if an adequate test of pharmacotherapy (a few days or weeks) produces only doubtful benefits or none at all, treatment can be promptly terminated. The physician will,

of course, adjust dosage carefully to assure an adequate therapeutic trial. It would be tragic to deprive a child of a potentially beneficial treatment by inattention to dose. Thus, it is clear that not all affected children require medication and that of those who do, not all respond.

When the medication is effective, the child can modulate and organize his activities in the direction he wishes. The stimulant does not slow down or suppress the hyperkinetic child in the exercise of his initiative. Nor does it "pep him up," make him feel high, overstimulated, or out of touch with his environment. Much has been made of the "paradoxical sedative" effect of stimulants in such children. The term is inappropriate. Although their exact mechanism of action is not known, stimulants do not provide a chemical straitjacket. They do not act as a sedative. Rather, they appear to mobilize and to increase the child's abilities to focus on meaningful stimuli and to organize his bodily movements more purposefully.

The hoped-for secondary consequences are better peer relationships, improved self-image, and pleasure in acquiring competencies. Any coexisting dysfunctions--such as special perceptual and learning handicaps--must not be left unattended, simply because pharmacotherapy is available and sometimes helpful. Similarly, personality and psychological problems, social and family problems, may require continued attention.

During drug treatment, the dosage may require shifting to minimize unwanted effects, of which the major ones are loss of appetite and insomnia. Drug treatment should not and need not be indefinite, and usually is stopped after the age of 11 or 12. Frequently, following a sustained improvement over several months or a year or so, drugs may be discontinued, as during a vacation period. Drug-free intervals can be prolonged as observers assess the child's condition.

The decision to use drug treatment thus depends on the commitment to diagnose and to monitor the response to treatment in the best traditions of medical practice. When there is informed parental consent, parents, teachers and professionals can collaborate in organizing and monitoring treatment programs.

CONCERNS RAISED BY THE PUBLIC AND THE NEWS MEDIA

We will now turn to various concerns about hazards and abuses when stimulant medications are used for children. For example, concern has been expressed that the medical use of stimulants could create drug dependence in later years or induce toxicity. This subject touches on the rights of the child to needed treatment, as well as risks to both the child and the public, and requires continued intensive scrutiny.

1. Does the medication produce toxicity?

One should not confuse the effects of intravenous stimulants and the high dosages used by drug abusers with the effects or the risks of the low dosages used in medical therapy. In the dosage used for children, the questions of acute or chronic toxicity noted in the stimulant abuser are simply not a critical issue. Unwanted mental or physical effects do rarely appear in children; cessation of therapy or adjustment of dosage quite readily solves the problem.

2. Is there a risk of drug dependency in later years?

Thirty years of clinical experience and several scientific studies have failed to reveal an association between the medical use of stimulants in the pre-adolescent child and later drug abuse. Physicians who care for children treated with stimulants have noted that the children do not experience the pleasurable, subjective effects that would encourage misuse. They observe that most often the child is willing to stop the therapy, which he views as "medicine." Thus, the young child's experience of drug effects under medical management does not seem to induce misuse. The medical supervision may "train" him in the appropriate use of medicines.

When adults are given stimulants--or even opiates--for time-limited periods under appropriate supervision and for justifiable reasons, there is relatively little misuse. Similarly, in treating epilepsy, barbiturates have been given from infancy to adulthood without creating problems of dependency or abuse.

It is not ordinarily the drug which constitutes abuse but the way in which a drug and its effects are used and exploited by an individual. There are indeed adolescents who, in varying degrees and for varying periods of time, either misuse or dangerously abuse stimulants. They experiment with the effects of excessive dosages to create excitement, to avoid sleep, to defy constraints, and to combat fatigue and gloom. It should be noted that these drugs are not commonly prescribed to children after the age of 11 or 12, when the actual risks of such experimentation or misuse might possibly become more significant.

Alter monitoring of drug use at any age is a part of sensible medical practice. With such precaution and with the available evidence, we find minimal cause for concern that treatment will induce dangerous drug misuse. To the contrary, there are very good reasons to expect that help, rather than harm, will be the result of appropriate treatment.

3. Are there safeguards against misuse?

There are some sensible steps, in addition to medical control, that guard against possible misuse. The child should not be given sole responsibility for taking the medication. He usually need not bring the drug to school. The precautions that surround the medicine cabinet--whether antibiotics, aspirins, sedatives or other medications are present--should be applied. Many such medicines, when misused, can be more dangerous to health and life than even the stimulant drugs. No child in the family should have access to medications not prescribed for him. These are general precautions comprising a part of the child's education in the "etiquette of the medicine cabinet."

4. Do stimulants for children create a risk for others?

The panel agrees that stimulant drug abuse is seriously undesirable and not infrequently dangerous, although views vary on the scope of the problem and the number of actual casualties. Experts also agree that far more stimulants are prescribed for adults than are medically needed and far more are manufactured than prescribed. Overprescription of any medication is deplored, whether or not it is liable to abuse. The question is whether the availability of stimulants for a very few of the childhood behavior disorders threatens the public health.

The prescribed dosage for an individual child constitutes an insufficient quantity to supply the confirmed abuser of stimulants with the amounts he requires. It is also true that illicitly manufactured stimulants are quite readily available and abused in this country. We must weigh the advantages of having appropriate medication available against the dangers of withholding treatment from a child who can clearly benefit from it. We doubt that prescriptions for the children who benefit from stimulants will require the manufacture of excessive and dangerously divertible supplies. With sensible precautions, there is at present no evidence justifying sensational alarm, either about the safety of the individual child who can benefit from therapy or about the safety of the general public.

5. Does medication handicap the child emotionally?

It is sometimes suggested that treated children may not be able to learn normal responses and master adjustments to the stresses of everyday life. These fears are understandable but are not confirmed by specialists who have experience with the conditions and the situations in which medications are properly used. For the correctly diagnosed child, these medications--if they work at all--facilitate the development of the ability to focus attention and to make judgments in directing behavior. Such children can acquire the capacity to tolerate and master stress. The medications, in these circumstances, help "set the stage" for satisfactory psychological development.

The hyperkinetic behavioral disturbance is a form of disorganization that creates great

stress in the afflicted child. The use of therapeutic stimulants for this disturbance should not be equated with the misuse of medication aimed at allowing a normal child or adult to avoid or escape the ordinary stresses of life.

6. What are the rights of the parents?

Under no circumstances should any attempt be made to coerce parents to accept any particular treatment. As with any illness, the child's confidence must be respected. The consent of the patient and his parents or guardian must be obtained for treatment. It is proper for school personnel to inform parents of a child's behavior problems, but members of the school staff should not directly diagnose the hyperkinetic disturbance or prescribe treatment. The school should initiate contact with a physician only with the parents' consent. When the parents do give their approval, cooperation by teachers, social workers, special education and medical personnel can provide valuable help in treating the child's problem.

STIGMATIZING THE MEDICINES AND CHILDREN, AND THE ROLE OF PUBLIC EDUCATION

A child who benefits from stimulants or other psychotropic medications should not be stigmatized; his situation is no different from that of the child who benefits from eyeglasses. It is unjust to stigmatize a child in later life, when competing in various situations (applying for college, employment or organization memberships), by labeling him early in life as "stupid," an "emotional cripple," a "drug-taker," or by any other kind of unjustified and unfortunate stereotype.

Nor should the medicine be stigmatized. Where bad practices prevail--and a number of complaints have been called to our attention--these practices should be squarely dealt with. This is not only a responsibility of physicians and educators, but also of the news media. Yet indignation must be tempered with perspective and scrupulous respect for the facts. An informed and understanding public can foster the growth and development of children, and these public attitudes may lead to the development of more refined and better-delivered health services. Either bad practices or exaggerated alarm can threaten the availability of medical resources for those who critically need it. This has happened before in the history of valuable medicines, and it can take years to repair the damage.

THE PROMOTION OF DRUGS BY INDUSTRY AND THE MEDIA

Pharmaceutical companies producing stimulants or new medications which may become useful for hyperkinetic disorders have a serious obligation to the public. These medicines should be promoted ethically and only through medical channels. Manufacturers should not seek endorsement of their products by school personnel. In the current climate, society can best be served if industry refrains from any implicit urging that nonspecialists deal with disorders and medications with which they are unfamiliar. Professionals and the news media can play useful roles by not pressing for treatments in advance of their practical availability.

THE DELIVERY OF SPECIAL HEALTH CARE: A DILEMMA

Our society has not as yet found complete solutions to the problem of the delivery of special health care. When available treatments cannot be confidently and appropriately delivered by physicians, they are perhaps best withheld until such treatments can be provided--especially with milder dysfunctions. This is not to say that severely afflicted hyperkinetic children should not or cannot receive available medical treatment. But until systems of continuing professional education and ready access to consultants are financed and perfected, some judgment about the pace at which unfamiliar treatments can be widely fostered is required. Finally, we must recognize that it is not only the scarcity of trained personnel, but factors such as poverty and inadequate educational facilities which prevent accessibility to individualized treatment.

THE NEED FOR SKILLS AND KNOWLEDGE

In preparing this report, the Committee was repeatedly struck by our lack of information in many crucial areas. The facts are that children constitute well over half our population, but receive a disproportionately low share of skilled research attention. We have noted the difficulties in arriving at accurate methods of diagnosis and the importance of launching careful longitudinal and follow-up studies. The investigation of causal factors lags. Such factors as perinatal injury, environmental stress or the development of the neurological and psychological controls of attention require study. Variations in different socioeconomic and ethnic groups must be considered in order to arrive at better definitions of behavior properly regarded as pathological. All such research efforts would have aided us in assessing the numbers of affected children and in recommending designs for more effective treatment programs.

Clinical pharmacologists have repeatedly found that drugs may act differently in children than in adults. To use medicines of all kinds effectively in children, more specialists must be trained in drug investigation--pharmacologists who can develop basic knowledge about the action of drugs in the developing organism. There is the obvious need for better and more precisely targeted drugs for the whole range of severe childhood behavior disorders. This requires intense research and training efforts. Such efforts provide the means for developing, testing and delivering better treatment programs. There is a similar need for research in the techniques of special education and also a need to make these techniques available to children who can benefit. It would appear to be a sound Federal investment to conduct such research and training.

In summary, there is a place for stimulant medications in the treatment of the hyperkinetic behavioral disturbance, but these medications are not the only form of effective treatment. We recommend a code of ethical practices in the promotion of medicines, and candor, meticulous care and restraint on the part of the media, professionals and the public. Expanded programs of continuing education for those concerned with the health care of the young, and also sustained research into their problems, are urgently needed.

Our society is facing a crisis in its competence and willingness to develop and deliver authentic knowledge about complex problems. Without such knowledge, the public cannot be protected against half-truths and sensationalism, nor can the public advance its concern for the health of children.

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I would not want to speak specifically to what NIMH is doing. Of course, we are constantly looking at prescription drugs to tighten up on the labeling and the indications for use of these drugs. I think that is our major responsibility in this area. The educational aspect of it, that goes toward or is aimed at the medical profession is, I think, probably more the responsibility of the National Institute of Mental Health. I know they do have some programs, but I would not want to speak specifically to their programs.

Senator Bayh. As I recall, last summer, when Deputy Dr. Simmons represented you before this committee, he said that FDA was going to relabel Ritalin and require that it be used only as an adjunct to an overall program to meet the needs of the child. Has that been done yet?

Dr. Gardner. That relabeling is being completed now. We have met with the company over some period of time and have developed a better labeling format which is mostly aimed at advising the prescribing physician to try other forms of therapy before relying on drug thereapy. It advises further on the length of time that this kind of therapy should be attempted and to discontinue the drug after a period of time, to determine whether or not the child still needs medication.

Senator Bayh. Would you provide us with a report on this relabeling endeavor?

I would like to examine the difference between the old label and the proposed label.

Dr. Edwards. We will provide you, Mr. Chairman, right away, with both the old labeling and the new labeling on Ritalin.

(A copy of the new package insert for Ritalin and a copy of the old package insert for Ritalic was marked "Exhibit No. 3" and is as follows:)

Exhibit No. 3

Final Labeling—Ritalin Hydrochloride (Methylphenidate Hydrochloride USP) Tablets

DESCRIPTION

Ritalin is a white, odorless, fine crystalline powder, solutions of which are acid to litmus. It is freely soluble in water.

ACTIONS

Ritalin is a mild central nervous system stimulant.

The mode of action in man is not completely understood, but Ritalin presumably activates the brain stem arousal system and cortex to produce its stimulant effect.

INDICATIONS

Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social)

Special Diagnostic Considerations

Specific etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

The characteristic signs most often observed are: chronic history of short attention span, distractibility, emotional lability, impulsivity and moderate to severe hyperactvity; specific learning disabilities; perceptual-motor impairments; minor neurological signs and abnormal electroencephalograms. The diag-

nosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these signs. Drug treatment is not indicated for all children with MBD. Appropriate educational placement is essential and psychological or social intervention may be necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

Mild Depression

Apathetic or Withdrawn Senile Behavior

Narcolepsy

CONTRAINDICATIONS

Marked anxiety, tension, and agitation are contraindications to Ritalin, since the drug may aggravate these symptoms. Ritalin is contraindicated also in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS

Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established.

Sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available. Therefore, patients requiring long-term therapy should be carefuly monitored.

Ritalin should not be used for severe depression of either exogenous or endogenous origin.

Ritalin should not be used for the prevention or treatment of normal fatigue states.

There is some clinical evidence that Ritalin may lower the convulsive threshold in patients with prior history of seizures, with prior EEG abnormalities in absence of seizures, and, very rarely, in absence of history of seizures and no prior EEG evidence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. In presence of seizures the drug should be discontinued.

Use cautiously in patients with hypertension.

Drug Interactions

Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors.

Human pharmacologic studies have shown that Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydrantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramie, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy

Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence

Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chonic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS

Patients with an element of agitation may react adversely ; discontinue therapy if necessary.

Periodic CBC and platelet counts are advised during prolonged therapy.

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ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity; anorexia; nausea; dizziness; palpitations; headaches; dyskinesia; drowsiness; skin rash; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy.

In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently. Toxic psychosis has been reported.

DOSAGE AND ADMINISTRATION

Adults

Administer orally in divided doses 2 or 3 times daily, preferably thirty to 45 minutes before meals. Dosage will depend upon indication and individual response.

Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. Patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

Children with Minimal Brain Dysfunction (6 years and over)

Start with small doses (*eg*, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Daily dosage above 60 mg is not recommended. If improvement is not observed after appropriate dosage adjustments over a one month period, the drug should be discontinued.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Ritalin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

OVERDOSAGE

Signs and symptoms of acute overdosage, resulting principally from overstimulation of the central nervous system and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis and dryness of mucous membranes.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. If signs and symptoms are not too severe and the patient is conscious, gastric contents may be evacuated by induction of emesis or gastric lavage. In the presence of severe intoxication, use a carefully titrated dosage of a *short-acting* barbiturate *before* performing gastric lavage.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis or extracorporeal hemodialysis for Ritalin overdosage has not been established.

HOW SUPPLIED

Tablets, 20 mg (peach scored); bottles of 100 and 1,000.

Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1,000 and Strip Dispensers of 100.

Tablets, 5 mg (pale yellow); bottles of 100, 500 and 1,000.

Ritalin Hydrochloride (Methylphenidate Hydrochloride USP) Tablets

DESCRIPTION

Ritalin is a white, odorless, fine crystalline powder, solutions of which are acid to litmus. It is freely soluble in water.

ACTIONS

Ritalin is a mild central nervous system stimulant.

The mode of action in man is not completely understood, but Ritalin presumably activates the brain stem arousal system and cortex to produce its stimulant effect.

INDICATIONS

Ritalin is indicated for the treatment of mild depression.

Ritalin is indicated as an aid to general management in the treatment of minimal brain dysfunction in children, which often manifests itself in the form of hyperkinetic behavior.

Ritalin is indicated in the treatment of drug-induced lethargy produced by tranquilizers, barbiturates, antihistamines, and anticonvulsants.

Ritalin is also useful in the treatment of apathetic or withdrawn senile behavior.

Ritalin is indicated in the treatment of narcolepsy.

CONTRAINDICATIONS

Marked anxiety, tension, and agitation are contraindications to Ritalin, since the drug may aggravate these symptoms. Ritalin is contraindicated also in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS

Ritalin should not be used for severe depression of either exogenous or endogenous origin.

Because the drug may mask normal fatigue states induced by overexertion, it should not be used to increase mental or physical capacities beyond physiological limits.

Ritalin should be administered with caution to patients with a history of seizures, since it may lower the convulsive threshold.

Use cautiously in patients with hypertension.

Ritalin is not recommended for children under six years, since safety and efficacy in this age group have not been established.

Drug Interactions

Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors.

Human pharmacologic studies have shown that Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobardital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy

The safe use of this drug in pregnant women or during lactation has not been established. Therefore, the benefits must be weighed against the potential hazards.

Animal studies using low dosages in the rat revealed no adverse effects on reproduction.

Drug Dependence

Ritalin should be given cautiously to emotionally unstable patients, particularly those with a history of drug dependence (including alcoholism), since such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the basic personality disturbances involved.

PRECAUTIONS

Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC and platelet counts are advised during prolonged therapy.

Long-term administration of Ritalin to children should be accompanied by repeated medical follow-up including appropriate laboratory tests, since much remains to be learned about the effects of long-term Ritalin therapy on child health and development.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other adverse reactions: hypersensitivity reactions, anorexia, nausea, dizziness, palpitations, headache, dyskinesia, drowsiness, skin rash. Blood pressure and pulse changes, both up and down, may occur; tachycardia may be observed more frequently in children than in adults. A few instances of angina and cardiac arrhythmia have occurred. Abdominal pain and weight loss during prolonged therapy have been reported and may occur more frequently in children.

DOSAGE AND ADMINISTRATION

Administer orally in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Dosage will depend upon indication and individual response.

Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. The few patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

In children with minimal brain dysfunction, as an aid in general management, start with small doses (*eg*, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Daily dosage above 60 mg is not recommended. Paradoxical aggravation of symptoms or other adverse effects are indications to reduce dosage or, if necessary, to discontinue the drug.

OVERDOSAGE

Signs and symptoms of acute overdosage, resulting principally from overstimulation of the central nervous system and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis and dryness of mucous membranes.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. If signs and symptoms are not too severe and the patient is conscious, gastric contents may be evacuated by induction of emesis or gastric lavage. In the presence of severe intoxication, use a carefully titrated dosage of a *short-acting* barbiturate *before* performing gastric lavage.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis or extracorporeal hemodialysis for Ratalin overdosage has not been established.

HOW SUPPLIED

TABLETS, 20 mg (peach); bottles of 100 and 1000.

TABLETS, 10 mg (pale green): bottles of 100, 500, 1000 and Strip Dispensers of 100.

TABLETS, 5 mg (pale yellow); bottles of 100, 500 and 1000.

Senator BAYH. Let me and my staff know if you feel this labeling goes far enough. Perhaps the committee could be helpful to you in this respect. We would like to have your expert judgment on this matter.

Dr. EDWARDS. We will do that.

(The extent to which labeling is sufficient subsequently supplied for the Record was marked "Exhibit No. 4" and is as follows:)

EXHIBIT No. 4

EXTENT TO WHICH LABELING IS SUFFICIENT

The labeling does adequately reflect current medical knowledge. Of course, if more detailed or specific directions for use become necessary, or if required for some other reason, the package insert will again be revised.

Senator BAYH. The report that you have submitted, is that the March 1971 Freedman report?

Dr. EDWARDS. Yes.

Dr. GARDNER. Yes.

Dr. EDWARDS. Moving on to the obesity problem, the number of obese people is also subject to a certain range of estimates, but approximately 30 million Americans between 21 and 65 years of age are at least 20 percent overweight.

Second, there is not a clear-cut concensus on which of these patients should be treated with any stimulant drugs, and of those who need drugs, which patients might benefit from alternative stimulant drugs rather than the amphetamines.

Third, the critical question of the appropriateness of amphetamines as adjuncts in programs of weight reduction has not been resolved. We did not believe that we should abruptly alter medical practice in this respect without thorough evaluation of all data on its usefulness and hazards. Further, we wished to be as certain as possible about the efficacy and abuse potential of other central nervous system stimulants widely used in the treatment of obesity.

Even allowing for interim use of the amphetamines as weight reducers, we did conclude that the quotas of the amphetamines should be smaller than the amounts used and distributed in previous years. First, in a number of instances medical societies have resolved that its members restrict the use of amphetamines. Thus, in certain localities, medical practice itself would lead to a reduction in the use of amphetamines.

Second, the new recordkeeping requirements would decrease diversion of the drug from legitimate channels. The Bureau of Narcotics and Dangerous Drugs has estimated this diversion at somewhat less than 20 percent.

Further, we estimated that the very important nonrefillable prescription aspect of the amphetamine rescheduling should have a significant impact on the prescribing practices of American physicians. We have been gratified that this has in fact occurred, as evidenced by the prescription figures which I have mentioned earlier, and they are on the chart.

Senator BAYH. Excuse me, Doctor. What is the percentage of decline?

Dr. GARDNER. It is about 60 percent.

Senator BAYH. How can the Bureau of Narcotics and Dangerous Drugs estimate the diversion at somewhat less than 20 percent when you have a 60 percent decrease over that chart study period?

Dr. GARDNER. This describes prescription practices. By diversion I believe they meant diversion immediately into illicit use; whereas,

this reflects also what might be called "medical misuse," both in terms of prescription practices and patients going from one doctor to another doctor for prescriptions to get filled.

Senator BAYH. Well, now, II and III both require prescriptions; right?

Dr. EDWARDS. Right. You mean Schedule II and Schedule III?

Senator BAYH. Right. A prescription would be required for Ritalin or any amphetamine whether it was on II or III?

Dr. GARDNER. But on Schedule II, the prescription would have to be rewritten each time. It would not be refillable, and that is the main difference between the two schedules.

Senator BAYH. Schedule II requires more caution and security.

Do you have any evidence that doctors prescribe Schedule III drugs with less care and concern than Schedule II drugs?

Dr. GARDNER. Yes, I believe that is so, just as prescriptions for morphine decreased considerably when it was scheduled. The need to refill necessitates rewriting a prescription each time and makes the doctor much more alert to what he is doing.

Senator BAYH. At least, a doctor is aware that a patient who may have had a prescription 2 months ago is still on that treatment?

Dr. GARDNER. And the pharmacist, too.

Senator BAYH. Well, the pharmacist has knowledge everytime he fills a prescription, does he not?

Dr. GARDNER. Just the connotation of Schedule II makes a great deal of difference both to the physician and the pharmacist; it makes also for closer recordkeeping. They know that there is going to be, because of closer recordkeeping, much more surveillance than would be the case with other schedules.

Senator BAYH. How many doctors would agree that the 60 percent decrease indicates that many physicians have heretofore not been properly practicing medicine?

Dr. EDWARDS. There is no question that this reflects not only the moving into Schedule II but it also reflects, I think, the educational program that has been carried on by the various congressional groups, by the medical profession itself, and by others—any number of groups. I think there is no question that this has had a major role to play, as well as there is no question that the drug was massively overused.

Returning to my prepared statement: Taking these factors into account, in the relatively short time we had to consider the problem, we decided as an initial estimate that the medical needs for amphetamines would be decreased by 40 percent. We included in our recommendation a provision that if we became aware of further evidence, we were prepared to recommend changes and further reductions. The quota we proposed was less than one-third the amount of amphetamines which manufacturers themselves had requested to produce.

The analysis of prescription trends which we have made since the quotas were first proposed indicates that the proposed quotas can reasonably be further revised downward. The exact figure is still under consideration, but we anticipate that it will be considerably lower.

Senator BAYH. Pardon me. You are saying that this additional information will permit you to lower the 40 percent reduction?

Dr. EDWARDS: We are recommending, Mr. Chairman, to the Department that the quota be reduced by another 30 percent.

Senator BAYH. Another 30 percent?

Dr. EDWARDS. In other words, we are talking about 70 percent as the reduction in the overall production.

Senator BAYH. And the manufacturers are requesting three times the amount of your original recommendation?

Dr. EDWARDS. Dr. Gardner, can you speak to that?

Dr. GARDNER. Yes.

Their request was for three times the amount that would have been available with just the 40 percent reduction.

We are now talking about a total of 70 percent reduction or 30 percent of the amount that was produced in 1971.

Senator BAYH. Are they requesting considerably more than they produced last year?

Dr. GARDNER. That is right.

Dr. SCOVILLE. I just wanted to say, to be fair to the manufacturers, that they were instructed to add a 50 percent on for inventory when they made out these estimates. Some of them privately said that they were not quite sure why they needed to do that.

Senator BAYH. Who requested this?

Dr. SCOVILLE. They were instructed. This is a new procedure, Mr. Chairman, and when the firm representatives, I understand, went down to BNDD to fill out their forms, they requested more than they had produced in 1971, there is no doubt about that, but the figure was further inflated by a 50 percent inventory allowance which was tacked onto their estimates.

Senator BAYH. Well, who suggested the 50 percent inventory allowance?

Dr. SCOVILLE. I believe they were instructed by BNDD representatives to use that figure, sir.

Senator BAYH. There is no current inventory? Are you suggesting that the cupboard is bare?

Dr. SCOVILLE. It seems peculiar to me, Mr. Chairman, I must say, because the cupboard is not bare.

Dr. EDWARDS. This is strictly, as you know, a responsibility of the Bureau of Narcotics. Our responsibility was to try as best we could to estimate the medical and scientific use and need for this particular drug.

Senator BAYH. Well, I realize the sensitive position you are in, you have responsibilities different than those of BNDD. As I recall, BNDD is supposed to be the agency primarily responsible for protecting us from dangerous drugs. This kind of a laissez-faire attitude is unsatifactory. If BNDD recommends that industry crank in an additional 50 percent as part of the production quota the whole purpose of production controls is defeated. It is a charade.

Dr. EDWARDS. I cannot comment as to this particular figure that Dr. Scoville mentions. I do know Mr. Ingersoll in the Attorney General's office has been interested in our bringing our recommendation

down to its lowest level. So, I think that their attitude is, in general, very healthy towards this whole problem.

Senator Bayh. Did you consider current reserves when you recommended the 40 percent reduction?

Dr. Edwards. No. Our basic responsibility is to estimate the actual need. It had nothing to do with what was held in reserve or anything else, but the actual medical and scientific need for the particular year, the year 1971, and for 1972.

Senator Bayh. It seems to me that that is what controls is all about.

Dr. Edwards. That is right.

Senator Bayh. To crank in an additional 50 percent factor, as we discussed a minute ago, and then act as if the cupboard is empty is not being as accurate as we should be.

Please continue Dr. Edwards.

Dr. Edwards. In the long run, production quotas for amphetamines will depend on whether the drugs continue to be used in obesity, since that is the commonest use.

This, in turn, depends upon our review of the 85 new drug applications submitted last fall and placing them in the context of data on the efficacy and abuse potentials of alternative obesity agents.

FDA reviewers have been handicapped by a fundamental problem, that of establishing acceptable criteria for reviewing these drugs. Simultaneous with the publication of the August 1970 statement, our reviewers began drawing up guidelines for testing and determining the efficacy of drugs used to treat obesity. Several drafts of guidelines were prepared.

We felt an obligation to validate our standards with members of the scientific and medical community. In February of 1971, we invited a number of prominent experts in the treatment of obesity, in nutrition, and in drug testing to review our guidelines and to serve as an ad hoc committee to settle upon generally acceptable criteria of efficacy. Although the committee generally agreed that anorectic agents are of potential value in treating obesity, the committee could not reach more than a minimal consensus as to how long drugs should be tested and as to how much weight loss should be induced by their use in order to declare them useful in the treatment of obesity.

Because of our concern over the need to develop what we consider to be adquate efficacy criteria for this widely used class of drugs, we asked the chairman of the ad hoc advisory group to present the problem to a second advisory committee later in the year. This was done, again without conclusive consensus.

We were thus confronted with a problem in evaluating new drug application for the most important member of a therapeutic class of agents. The potential usefulness of these agents in treating obesity was fairly widely accepted, but experts could not agree upon criteria for defining that usefulness.

Senator Bayh. Excuse me, doctor. Were they able to agree upon the dangers prevalent in the excessive use of these drugs?

Dr. Edwards. I am sure they could.

Dr. Gardner might want to comment on that. He was with this committee.

Dr. Gardner. They could. The dangers were fairly obvious and have been obvious, Mr. Chairman. But at the same time the question is whether or not these drugs are effective at all in obesity and if they are to establish that and to know which drugs among the many will be effective. If we eliminate all of the drugs for treating obesity, then we are faced with another problem. At times we would have a potentially serious condition without any totally effective therapeutic regimen. We do not want to go from one extreme to the other.

Senator Bayh. Yes. In the study, are you exploring solely the use of amphetamines in treating obesity?

Dr. Gardner. No. In fact——

Senator Bayh. Are there other drugs that provide the same general kind of therapeutic effect?

Dr. Gardner. Yes, there are. Many of these, and perhaps all of these, have abuse potential. We are faced with the need to establish at least some balance between the efficacy of these drugs for treating obesity and the risk in terms of abuse potential.

Senator Bayh. What are some of the alternatives? The British Medical Association, and the British Health Service 3 or 4 years ago, I believe in 1968, endorsed fenfluramine as an alternative for obesity treatment.

Dr. Gardner. Fenfluaramine. That is one drug that is supposedly less of a stimulant. That is not really well established. There are others such as Tenuate, Preludin, Ionamin, Pre Sate, all of which, although they have not necessarily been abused, may have abuse potential. If widely available these drugs could possibly be as abused as the amphetamines. It is this kind of prediction that we are in a sense forced to make in deciding which of the drugs should be available for the treatment of obesity.

I might mention that at least in one country, Sweden, when an attempt was made to restrict one drug, other drugs such as Preludin and, to a lesser degree, Tenuate, were abused. The whole class of drugs used for the treatment of obesity might all have abuse potential and if available widely enough might very well be abused.

Senator Bayh. There is no question that there is a decided tendency to substitute. This is why we wanted a reclassification of Preludin and Ritalin. Now that we have accomplished that they will be subjected to the same controls and safeguards as the more traditional amphetamines. This was not the situation that existed in Sweden.

Dr. Gardner. Not initially.

Senator Bayh. Preludin became the drug of choice, because it was not subjected to the same kind of controls as the amphetamines?

Dr. Gardner. That is right.

Senator Bayh. I understand that A. H. Robins has filed an application for the approval to market fenfluramine in the United States.

Is this the kind of an acceptable substitute that the British apparently think it is? What is your position on this?

Dr. GARNDER. We are not sure about that yet, Mr. Chairman. That is one of the drugs we are evaluating, along with the others, in looking at this whole class.

Senator BAYH. Is fenfluramine ever prescribed by doctors in the United States?

Dr. GARDNER. No, it has not been marketed yet in this country. It is still in an investigation stage.

Senator BAYH. Do you have any information as to whether it is an adequate substitute?

Dr. GARDNER. We have some information, but, as I said, we are not certain yet that this, in fact, is less of a stimulant and would have less abuse potential. That is something we are looking into.

Senator BAYH. What effort has been made to study the data relied on by the British?

The British Medical Association and the British Health Service which are, rather substantial authorities both claim that this agent can be used to treat obesity without stimulant effects or danger of drug dependence. Are you discrediting these studies?

Dr. GARDNER. Not necessarily, but I do not think that this would be all of the evidence we would want to receive to make a decision. There are people in this country who are not in total agreement with their conclusion that this is not a stimulant drug. It is a depressant drug at certain dosage levels and appears to be a stimulant drug at other dosage levels, which would be contrary to what the British had decided.

Senator BAYH. How long has fenfluramine been under review at FDA?

Dr. GARDNER. I am not sure when the application was submitted. It had been withdrawn, and the application is being looked at again along with all of the other drugs to see whether, as we have said, this would be an effective substitute.

Senator BAYH. I am not pushing this particular drug but inasmuch as the British seem to feel we could substitute it without the negative effects——

Dr. EDWARDS. I think the important thing here, Mr. Chairman, is twofold. First, we are not necessarily in agreement—and I am not speaking as one of the authorities—with the British findings. Second, we are not sure that any of these drugs are any good in terms of really efficacious use in treating obesity. Our point, the point I make in this next paragraph, is that we came to the conclusion that you cannot look at just one of the central nervous system stimulating drugs, used for the treatment of obesity. You have to look at them all, and that is what we are trying to do now. We hope within the next month or two to have this completed.

Senator BAYH. Within the next month or two?

Go head. Excuse me, doctor.

Dr. EDWARDS. As I said, our reviewing division then decided that the soundest course to follow was to review all important studies for all agents of this class, and, then, on the basis of this review establish what the optimal standards for efficacy testing can reasonably

be. Once these standards were established, the amphetamines would be measured against them in respect to efficacy in weight reduction programs.

At the same time other reviewers have been carrying out a similar program in assessing the abuse potential of the nonamphetamine central nervous system stimulant drugs currently available. Here, too, the job is difficult, for universally accepted methods for ranking drugs according to their central nervous system abuse potential have not been developed as has been done for evaluating narcotics. In evaluating these drugs, a pivotal question will be whether the amphetamines possess greater abuse potential than these other agents.

The reviews involve 13 single entities; 116 new drug applications for these entities in various formulations and combinations; approximately 225 studies containing 10,000 subjects. All of this comprises 766 volumes of data. Because of the extent of the review project, computer support has been developed to analyze the some 225 studies under our consideration.

Consultant advice has been sought not only from experts in the treatment of obesity but from experts in the fields of drug dependence, neuropharmacology, psychiatry, and drug regulation in the United States, Canada, and Sweden. A timetable has been worked out with a June 1 deadline for completion of the study and initiation of appropriate action including quota recommendations by July 1.

Our reviewers have done preliminary reviews in a number of what appear to be the best studies for amphetamines and alternate antiobesity products. The amount of average weight loss which the drugs have contributed appears to have been small and to have been shown for only short periods of time, particularly when compared with such important variables as diet, counseling, motivation, and the influence of a conscientious physician. At the same time, there are patients in each study who did benefit substantially in that they experienced significant weight loss.

Our approach may be to label the drug for short-term use in obesity only for those patients who do not respond to other treatment, and who do respond to this form of treatment during a short-term trial. We should keep in mind that this pertains to all central nervous system stimulant anorexigenics, not only the amphetamines; although not all have been actually abused, all do have, we believe, abuse potential.

Ideally, an antiobesity drug would restore fat people to normal weight so that they would stay there. No drug we know of offers such promise and this standard does not appear resonable. We do hope to be able in our review to define how much weight loss, over how long a period, obese people can expect.

Senator Bayh. Would you provide us with a list of the substances in this class?

Dr. Edwards. We can give you a total list of all of the drugs that we have that would categorize in this class.

(The list later supplied for the record was marked "Exhibit No. 5" and is as follows:)

Exhibit No. 5

LISTING OF THE PRINCIPAL APPETITE SUPPRESSANT DRUGS

1. amphetamine
2. methamphetamine
3. dextroamphetamine
4. benzphetamine
5. phentermine
6. phenmetrazine
7. phendimetrazine
8. chlorphentermine
9. diethylpropion

The following combinations are examples of those that contain central nervous stimulants in combination with other CNS drugs, with sedatives, or with ingredients having other pharmacologic actions. There are many variations of these combinations:

10. methamphetamine, phenobarbital
11. methamphetamine, amphetamine, dextroamphetamine
12. dextroamphetamine, meprobamate
13. amphetamine, dextroamphetamine
14. dextroamphetamine, butabarbital
15. methamphetamine, pentobarbital
16. dextroamphetamine, amobarbital
17. dextroamphetamine, prochlorperazine
18. dextroamphetamine, secobarbital
19. dextroamphetamine, phenobarbital
20. dextroamphetamine, amphetamine, amobarbital
21. amphetamine, dextroamphetamine, methaqualone
22. amphetamine, dextroamphetamine, riboflavin
23. amphetamine, phenobarbital
24. amphetamine, amobarbital
25. methamphetamine, amobarbital, homatropine methylbromide
26. amphetamine, dextroamphetamine, methamphetamine, desoxyephedrine
27. dextroamphetamine, amphetamine, butabarbital

Senator Bayh. Is there any way now of ascertaining in advance which patients are liable to have the significant weight loss over a short period of time and maintain that significant loss?

In studying this problem, it seems to me if you establish more accurate criteria which would limit the number of persons treated by these drugs, that we would accomplish a great deal.

Has any attention been given to this?

Dr. Edwards. If I could, I would like to have Dr. Scoville speak to that point.

Dr. Scoville. Mr. Chairman, what you propose is what would be highly desirable. Unfortunately, up to now, even though experts all agree that we would like to know beforehand and not afterwards who is going to benefit, they also seem to agree right now that you cannot pinpoint the man who will benefit without giving him a therapeutic trial.

Senator Bayh. In other words, you cannot say "Any man who has blue eyes and wavy blond hair and is between 5 feet 2 inches and 5 feet 4 inches automatically classifies for use of the drug?" It is not that easy?

Dr. Scoville. It is not that easy, Mr. Chairman. We do hope that when we have got the analysis completed, with this mass of data

that is available, that we might be able to predict a little more, for example, that people must be 25 or 30 percent overweight if they are going to get significant benefit from the drug.

Dr. EDWARDS. I think, Mr. Chairman that we have moved into an area, in which, for the first time, a really hard look is being taken at this problem of efficacy. I am sure that in the next few months some far more meaningful information as to the efficacy of these drugs, and some specific information you have requested as to who will benefit most and who will not, will be forthcoming. We do not have it now, but I am reasonably optimistic that some of it is going to be available.

Senator BAYH. You say that within the next month or 2 this study will be completed?

Dr. EDWARDS. Well, we have said, for giving us some leadtime, we have set June 1 as our date, but we hope to have it completed before that.

Senator BAYH. You will make that information available to us?

Dr. EDWARDS. We certainly will.

Senator BAYH. At least on an off-the-record basis when it is available to you.

Dr. EDWARDS. This will be public information. I think it will do a great deal, and that is why we want to look at some of the new drug applications in the context of the total class of drugs and not just independently. It is not a matter of our not being interested in these new drug applications but we do not feel we should be looking at one alone but as a part of the total picture.

I repeat that ideally, an antiobesity drug would restore fat people to normal weight so that they would stay there. No drug we know of offers such promise and this standard does not appear reasonable. We do hope to be able in our review to define how much weight loss, over how long a period, obese people can expect. In other words, what the person taking this medication can expect from the medication. We also would like to pinpoint the sort of overweight people who will best benefit from these drugs, and to compare drug effect with the effects of the variables previously mentioned. Our indepth statistical, computer-assisted review should be revealing in these comparisons.

We shall then balance efficacy against risk. Risk involves the innate toxicity of these drugs when taken over weeks or months. It also involves the misuse of these drugs in inappropriate conditions. And the third aspect of risk is a public health factor involving the illegal or street use of the drugs by people who haven't received them by prescriptions.

We cannot responsibly make a decision about amphetamines without considering the impact it might have on the prescribing, diversion, availability, and abuse of other central nervous system stimulants as happened in Sweden, as Dr. Gardner mentioned, following the restrictions on the use of amphetamines. An initial step was taken when we recommended the transfer of Preludin and Ritalin, the drugs most widely abused in Sweden, into schedule II. The transfer became effective in October 1971. However, we believe it

necessary to consider not merely these two compounds but the whole therapeutic class.

In view of the abuse potential of the appetite control drugs, it is conceivable that if there is no greater average weight loss induced by these drugs than noted in our preliminary review, consideration should be given to the elimination of the use of all central nervous system stimulants, including the amphetamines, in all cases of obesity other than those in which these drugs produce a meaningful weight loss. The practicing physician would have to exert caution in deciding for which patients these drugs would be appropriate. These drugs might be reserved for other indications in which their benefits are more nearly unique and necessary. If this conclusion is reached, no similar drugs could be marketed for treatment of obesity in the future until the manufacturers have unequivocally established to our satisfaction by animal and human testing that the drugs are devoid of the mood-elevating, stimulant, and dependence-producing properties which have made amphetamines and related drugs a public health problem today.

Thank you, Mr. Chairman. We would be delighted to answer any other questions you or your staff might have.

Senator Bayh. Well, in looking at the amphetamine abuse problem, would it be your judgment that the bulk of amphetamine abuse is of drugs whose sole medical indication is as an adjunct in the short-term treatment of obesity?

Dr. Edwards. Do you ask if I believe that is the basis for the bulk of the misuse of the drug?

Senator Bayh. Yes.

Dr. Edwards. I think, without question, that it is in the treatment of obesity.

Now, I think that probably the greatest abuse has been not in the short-term treatment but in continuing it over a long period of time. In other words, the chronic use of the amphetamines in the treatment of obesity.

Senator Bayh. Are you saying that the problem could be treated on a short-term basis with the right kind of continuing medical care and attention but that often it drags on to the point that it then becomes an abuse?

Dr. Edwards. That is right.

Would you like to speak on that, Dr. Gardner?

Dr. Gardner. We are really dealing with two kinds of problems. One is what might be called medical misuse where it is either overprescribed or overutilized by a patient who would go to different doctors. The other is really an abuse in the sense of street use where the drug may be diverted from, either medical misuse but also from other sources, such as theft from pharmacies, illegal manufacture, et cetera. That may be a very different kind of problem.

Senator Bayh. Is there anything that FDA can do to insure that this amphetamine type of drug is used only as an adjunct to a total program of weight reduction?

Dr. Edwards. We have to, Mr. Chairman. Obviously, ultimately, the final, and key factor, is the practicing physician. I think we

have a responsibility to provide the practicing physician with all the currently available information on the drug. In the final analysis the physician is the one who has to write the prescription. I think we have tightened it up as much as we can in terms of placing it in the class that it is now in, class II. I think from here on out we are going to rely very heavily upon the medical profession in treating it the way it should be treated and using it the way it should be used.

Senator BAYH. Is there any way of determining what portion of the 60 percent decrease is attributable to a change in the doctors' approach?

Dr. SCOVILLE. Some of that drop, Mr. Chairman, is explained by the nonrefillable aspect of the schedule II drugs.

Senator BAYH. Is the decline a temporary phenomenon?

Dr. SCOVILLE. Mr. Chairman, it might be temporary if we do not follow along with the quota.

In other words, if the quota were left too high allowing a potential increase in prescriptions, there are some who feel that the decrease would, in fact, be as you suggest, a temporary phenomenon.

Senator BAYH. Would you explain that, doctor? I understand that you feel that perhaps the bulk of that decrease is because the attending physician is more carefully prescribing these drugs. Now, if that is the case, why would the availability of twice as much of this drug on the market, in the cupboard so to speak, result in a shift to former prescription trends? It would seem that the stricter controls would cause the doctors to reexamine at regular intervals the efficacy of continuing the treatment. Is there evidence to suggest that when there is an amphetamine surplus, that doctors are going to continue to use these drugs when they are not actually required?

Dr. EDWARDS. No.

Senator BAYH. Am I making myself clear?

If this is the case, it suggests the possibility that an overabundance of these drugs is associated with widespread medical misuse and perhaps illicit trade.

Dr. EDWARDS. I do not think, Mr. Chairman, that we suspect this will move back up. I think the problem is: Will it stay right where it is or will it continue down even further? And we believe that—I think the point that Dr. Scoville was making—if the quota is left where it is now, there is a good likelihood that it would stay right where it is right now. But if the quota is brought down even further with, of course, an improved educational program, we have reason to believe that this line will drop even more.

Senator BAYH. I strongly concur that quotas are important in this particular area. I think they should be reasonable, not inflated by a 50 percent reserve when these drugs are already stockpiled. I am trying to account for the dramatic decline. It seems the quota would deal with the illicit channel; that by tightening down on supply you make it more difficult for these drugs to be stolen and diverted through illicit channels.

Dr. EDWARDS. Correct me, Dr. Scoville, if you disagree, but I do not think that we are suggesting that this drop by some 60 percent has little if anything to do with the quota per se. It is due primarily

to the fact that it was made a schedule II drug, so every prescription, every one, is nonrefillable, and I think it was due to an awareness on the part of some of the responsible elements of the medical profession and the societies, in pleading to their members and recommending strongly that amphetamines not be overused. I think these are the two ingredients that have brought about this drop and not the quota per se, because there are still plenty of amphetamines to be had. There is no shortage of amphetamines, and there will not be any shortage of amphetamines in my judgment even after it is cut another 30 percent.

Senator BAYH. Would you give us a breakdown of the figures on page 5 of your statement. You indicate that approximately 30 million Americans between 21 and 65 years of age are at least 20 percent overweight; 30 million! How many of these 30 million suffer from simple obesity, caused by an excessive caloric intake?

Dr. EDWARDS. I do not know just to what degree we can break it down. We will try to break it down as best we can. I suspect that certainly the bulk of those 30 million would be the kind that just eat too much. But we will try to break this down as best we can.

Do you have any breakdown in it right now?

Dr. SCOVILLE. No.

Senator BAYH. Will you provide this data to the committee?

Dr. EDWARDS. We will provide that for the record.

(Information subsequently submitted for the record was marked, "Exhibit No. 6" and is as follows:)

Exhibit No. 6

NUMBER OF AMERICANS 20% OR MORE OVER THEIR BEST WEIGHT (MILLIONS)

Metropolitan Life Insurance Company, using data from their 1960 Statistics Bulletin and the 1969 census figures has provided the following information:

Age group	Males	Females
20 to 29	1.6	1.7
30 to 39	2.7	2.8
40 to 49	3.8	5.0
50 to 59	3.4	4.9
60 to 64	1.1	.6

Ordinary obesity (i.e. 20 percent over best weight), as opposed to extreme obesity, is quite common and the only immediate cause is excessive caloric intake. This exogenous factor, however, is most often combined with an endogenous factor (i.e. disturbed psychological mechanism). Thus, compulsive eating may serve as an outlet for frustrations caused by diminished physical attractiveness, decreased family responsibilities, emotionally upsetting hormonal changes, etc. Factors such as these may be responsible for their being more "over-weight" women than men in the 40–49 and 50–59 age groups.

Senator BAYH. What percentage of the 30 million are taking amphetamine-type drugs? Do we know that?

Dr. SCOVILLE. Mr. Chairman, I think some of the best data are in Dr. Chambers, New York State survey, which you quoted.

(Information subsequently submitted for the record was marked, "Exhibit No. 7" and is as follows:)

EXHIBIT No. 7

NUMBER OF THE 30 MILLION THAT ARE ON AMPHETAMINE TYPE DRUGS

The percentage of the 30 million on amphetamine-type drugs, indications for the use of these drugs include narcolepsy, minimal brain dysfunction in children and anti-obesity. The number of narcoleptics in the United States has been estimated to be 25,000 to 1,000,000 while for minimal brain dysfunction the figures mentioned range between 900,000 and 3,000,000. Since there were 9,500,000 *new* prescriptions for amphetamines last year, 66.9 percent of them were for anti-obesity.

Dr. GARDNER. There are two surveys that are adequate on the kinds of people taking amphetamines or stimulant drugs. One of these was conducted by Dr. Chambers, and another by Dr. Balter of NIMH. It is still difficult to know which of the people with obesity would take these drugs—or what percentage of the people with obesity are actually using these drugs versus people taking them who are not obese. We certainly know there are many people on drugs who are not obese.

Senator BAYH. You do not know how many amphetamine-type prescriptions are filled in the treatment of obese people?

Dr. GARDNER. No.

Senator BAYH. Will the studies you are presently conducting develop this data?

Dr. EDWARDS. Not really, no. You see, one of the problems, Mr. Chairman, is that you cannot prove, and I cannot tell you, how much of this drug is being misused in the treatment of depression and conditions like that. It is at least temporarily a mood-elevating drug. However, the diagnosis does not have to be shown on a prescription; merely how the drug is to be used. So, the prescription per se would not give us the kind of information that you, I, and all of us, would like to have.[1]

[1] NUMBER AND PERCENT OF USE OF AMPHETAMINES AND RITALIN N.D.T.I.—12 MONTHS ENDING MAR. 31, 1971

[Amounts in thousands]

Disease or disorder	Code	Subcode	All amphetamines		Ritalin	
			Number	Percent	Number	Percent
Nonendocrine obesity [1]	38	287	11,615	84	52	2
Mental disorders (total)	05		566	4	843	40
Primary childhood behavioral disturbances		324	148	(2)	293	(14)
Neurotic depressive reaction		314	99		141	(7)
Nervousness, debility	16	790	121	1	233	11
Disease of C.N.S. sense organs	06		(2)		248	12
Circulatory disorders	07		(2)		217	10
Medical-surgical aftercare	18	Y10	(2)		116	5
All other uses			1,572		421	20
Total uses			13,874	100	2,130	100

[1] Weight reduction.
[2] Not listed and very small or zero.

APPENDIX

A Brief Description of N.D.T.I. (National Disease and Therapeutic Index):

N.D.T.I. is a nationally recognized and widely used record of the complete daily activities of representative physicians. The physicians are selected to represent adequately their respective places in the universe of physicians and for two designated days each quarter each physician writes down his entire record

of patient activity. He identifies the patient's sex, age and other characteristics, designates the diseases or condition which he is treating and specifies what drugs he has used to treat the patient and how and where they were used. The designation of disease or condition follows the World Health Code designations of diseases. In addition to describing what the diagnosis was and what drugs were used, the physician also designates the desired action or the reason for using the drug.

Senator Bayh. Well, you have been very kind. There are some other areas that I would like to explore, but we can do that in written form and not take more of your time today. We are anxious to get this information Doctor, so that our staff can review it.

Dr. Edwards. Well, we will have this information for you just as soon as we have it in a presentable form.

Senator Bayh. Thank you, Doctor, and gentlemen.

Dr. Edwards. Thank you.

(Dr. Edwards' prepared statement is as follows:)

Prepared Statement of Charles C. Edwards, M.D., Commissioner of Food and Drugs, Public Health Service, Department of Health, Education and Welfare

Mr. Chairman and Members of the Subcommittee: I am pleased to have the opportunity to appear before you today to discuss the amphetamine quotas and the safety and efficacy of amphetamines and other appetite suppressants.

The Food and Drug Administration has strongly supported placing stringent controls on the amphetamines.

Our Drug Abuse Control program began in February of 1966. In the first two years of the program, before this responsibility was transferred to the Department of Justice, we carried out over 2,000 criminal investigations, more than 1,300 arrests were made, and about 300 criminal cases were completed. We made, in addition, approximately 1,100 accountability investigations resulting in 108 civil seizures of depressant and stimulant drugs. Nearly 600 million dosage units of these drugs were removed from the marketplace because no accurate records as required by the law were kept by manufacturers.

More recently we have taken certain broader actions which have been pivotal, I believe, in allowing us to control amphetamines far better at present than they were controlled in the past.

First, we published a significant regulation in 1970 limiting the medical use of amphetamines and declaring them new drugs. The amphetamines, having been marketed prior to 1938 and the passage of important amendments to the Federal Food, Drug, and Cosmetic Act, had been considered "grandfathered" and not subject to the efficacy provisions of the Drug Amendments of 1962. Among other things, this "grandfather" status made it administratively difficult to obtain necessary information on safety and efficacy.

Basing our conclusions in part upon opinions of expert reviewing groups, we published a Statement of Policy and Interpretation on August 8, 1970, announcing that because the drugs had come to be used in a number of new ways since 1938, and because there were questions of efficacy as well as safety, the amphetamines must now be subjects of approved new drug applications. This policy statement was the administrative key opening the way to the comprehensive review of the amphetamines which is now going on.

The policy statement had two important corollaries. First, it required relabeling the drugs with strict and explicit cautionary material and with limitations on the uses of the drugs to three conditions: narcolepsy, minimal brain dysfunction, and as adjunctive therapy in obesity. This deleted a number of questionable indications, such as depression, for which the drugs had been used.

This labeling also limited use of the amphetamines in obesity to *short-term* use and so worked to eliminate prolonged, repeated, unsafe or questionably effective use of the drug for this condition.

The second corollary of the policy statement was that new drug applications were to be submitted by the manufacturers within one year and must contain

clinical data to support the permitted indications. Eighty-five applications have been submitted, and I shall come to our review of these later.

Another recent major action in respect to the amphetamines was their transfer from Schedule III to Schedule II of the Comprehensive Drug Abuse Prevention and Control Act.

As you know, Schedule III places only limited controls on the drugs listed in it, while Schedule II involves narcotic-type restrictions. These restrictions include special order forms, separate recordkeeping, nonrefillable prescriptions, yearly manufacturing quotas, and export-import permits.

When the Comprehensive Drug Abuse Act was passed in 1970, only parenteral methamphetamine was placed in Schedule II. In March of 1971, I signed a memorandum recommending that *all* amphetamines be placed in Schedule II.

After the question had been thoroughly discussed within the Department, this recommendation was transmitted to the Bureau of Narcotics and Dangerous Drugs, thus accomplishing what we believe is the greatest single measure in reducing misuse and abuse of the amphetamines.

If you look at this chart, I believe you will agree that the impact of rescheduling has been profound. Here, up until May 1971, prescriptions were being filled and refilled at a rate of about 1.6 million per month. Here, on May 26, 1971, the notice proposing rescheduling of the amphetamines was published in the *Federal Register*. We can only speculate on the cause for the peak in May and June, but it does appear as if some people were stocking up for the drought ahead. Here, on July 7, the notice of rescheduling became final.

The precipitous drop in prescribing continues until October, at which time the effect of rescheduling appears to have reached its maximum for the near term.

Our most recent action involving the amphetamines was our recommendation in collaboration with the National Institute of Mental Health in setting quotas for the 1972 manufacture of the drugs. As you know, the Bureau of Narcotics and Dangerous Drugs had asked for an estimate of medical and scientific needs for the amphetamines for the coming year to aid them in setting quotas.

As noted in the BNDD regulations, the Director of the Bureau of Narcotics and Dangerous Drugs takes HEW recommendations into account. However, in establishing quotas, he also relies on such factors as total new disposal of the drugs by all manufacturers during previous years, current trends in disposal of the drugs, actual or estimated inventories of the drugs and projected demands for such drugs.

We decided to use previous production of amphetamines as a point of departure in estimating the need for these drugs. There is no doubt that using past production figures is not a fully satisfactory way to estimate medical needs. The alternative to this would ideally be based on an accurate estimate of patients who require amphetamines. At the present time, however, such an estimate appears even more unsatisfactory than the use of production figures for several fundamental reasons.

First, unfortunately we do not have reliable figures for the incidence or prevalence of narcolepsy and of minimal brain dysfunction or hyperkinetic disorders in children. Most experts will agree that figures occasionally quoted are educated guesses at best. They range from 900,000 to 3 million and more for minimal brain dysfunction and from 25,000 to over 1 million for narcoleptics.

The number of obese people is also subject to a certain range of estimates, but approximately 30 million Americans between 21 and 65 years of age are at least 20 percent overweight.

Second, there is not a clear-cut consensus on which of these patients should be treated with any stimulant drugs, and of those who need drugs, which patients might benefit from alternative stimulant drugs rather than the amphetamines.

Third, the critical question of the appropriateness of amphetamines as adjuncts in programs of weight reduction has not been resolved. We did not believe that we should abruptly alter medical practice in this respect without thorough evaluation of all data on its usefulness and hazards. Further, we wished to be as certain as possible about the efficacy and abuse potential of other central nervous system simulants used in obesity.

Even allowing for interim use of the amphetamines as weight reducers, we did conclude that the quotas of the amphetamines should be smaller than the amounts used and distributed in previous years. First, in a number of instances

medical societies have resolved that its members restrict the use of amphetamines. Thus, in certain localities, medical practice itself would lead to a reduction in the use of amphetamines.

Secondly, the new recordkeeping requirements would decrease diversion of the drug from legitimate channels. The Bureau of Narcotics and Dangerous Drugs has estimated this diversion at somewhat less than 20 percent.

Further, we estimated that the very important nonrefillable prescription aspect of the amphetamine rescheduling should have a significant impact on the prescribing practices of American physicians. We have been gratified that this has in fact occurred, as evidenced by the prescription figures which I have mentioned earlier.

Taking these factors into account, in the relatively short time we had to consider the problem, we decided as an initial estimate that the medical needs for amphetamines would be decreased by 40 percent. We included in our recommendation a provision that if we became aware of further evidence, we were prepared to recommend changes and further reductions. The quota we proposed was less than one-third the amount of amphetamines which manufacturers themselves had requested to produce.

The analysis of prescription trends which we have made since the quotas were first proposed indicates that the proposed quotas can reasonably be further revised downward. The exact figure is still under consideration, but we anticipate that it will be considerably lower.

In the long run, production quotas for the amphetamines will depend on whether the drugs continue to be used in obesity, since that is the commonest use.

This in turn depends upon our review of the 85 new drug applications submitted last fall and placing them in the context of data on the efficacy and abuse potentials of alternative obesity agents.

FDA reviewers have been handicapped by a fundamental problem, that of establishing acceptable criteria for reviewing these drugs. Simultaneous with the publication of the August 1970 statement, our reviewers began drawing up guidelines for testing and determining the efficacy of drugs used to treat obesity. Several drafts of guidelines were prepared.

We felt an obligation to validate our standards with members of the scientific community. In February of 1971, we invited a number of prominent experts in the treatment of obesity, in nutrition, and in drug testing to review our guidelines and to serve as an ad hoc committee to settle upon generally acceptable criteria of efficacy. Although the committee generally agreed that anorectic agents are of potential value in treating obesity, the committee could not reach more than a minimal consensus as to how long drugs should be tested and as to how much weight loss should be induced by their use in order to declare them useful in the treatment of obesity.

Because of our concern over the need to develop what we consider to be adequate efficacy criteria for a widely used class of drugs, we asked the chairman of the ad hoc advisory group to present the problem to a second advisory committee later in the year. This was done, again without conclusive consensus.

We were thus confronted with a problem in evaluating new drug applications for the most important member of a therapeutic class of agents. The potential usefulness of these agents in treating obesity was fairly widely accepted, but experts could not agree upon criteria for defining that usefulness.

Our reviewing division then decided that the soundest course to follow was to review all important studies for all agents of this class, and then on the basis of this review establish what the optimal standards for efficacy testing can reasonably be. Once these standards were established, the amphetamines would be measured against them in respect to efficacy in weight reduction programs.

At the same time other reviewers have been carrying out a similar program in assessing the abuse potential of the nonamphetamine central nervous system stimulant drugs currently available. Here, too, the job is difficult, for universally accepted methods for ranking drugs according to their central nervous system abuse potential have not been developed as has been done for evaluating narcotics.

In evaluating these drugs, a pivotal question will be whether the amphetamines possess greater abuse potential than these other agents.

The reviews invlove 13 single entities; 116 new drug applications for these entities in various formulations and combinations; approximately 225 studies containing 10,000 subjects. All of this comprises 766 volumes of data. Because of the extent of the review project, computer support has been developed to analyze the some 225 studies under consideration.

Consultant advice has been sought not only from experts in the treatment of obesity, but from experts in the fields of drug dependence, neuropharmacology, psychiatry, and drug regulation in the United States, Canada, and Sweden. A timetable has been worked out with a June 1 deadline for completion of the study and initiation of appropriate action including quota recommendations by July 1.

Our reviewers have done preliminary reviews in a number of what appear to be the best studies for amphetamines and alternate antiobesity products. The amount of average weight loss which the drugs have contributed appears to have been small and to have been shown for only short periods of time, particularly when compared with such important variables as diet, counseling, motivation, and the influence of a conscientious physician. At the same time, there are patients in each study who did benefit substantially in that they experienced significant weight loss.

Our approach may be to label the drug for short-term use in obesity only for those patients who do not respond to other treatment, and who do respond to this form of treatment during a short-term trial. We should keep in mind that this pertains to all central nervous system stimulant anorexigenics, not only the amphetamines; although not all have been actually abused, all do have abuse potential.

Ideally, an antiobesity drug would restore fat people to normal weight so that they would stay there. No drug we know of offers such promise and this standard does not appear reasonable. We do hope to be able in our review to define how much weight loss, over how long a period, obese people can expect. We also would like to pinpoint the sort of overweight people who will best benefit from these drugs, and to compare drug effect with the effects of the variables previously mentioned. Our in-depth statistical, computer-assisted review should be revealing in these comparisons.

We shall then balance efficacy against risk. Risk involves the innate toxicity of these drugs when taken over weeks or months. It also involves the misuse of these drugs in inappropriate conditions. And the third aspect of risk is a public health factor involving the illegal or street use of the drugs by people who haven't received them by prescriptions.

We cannot responsibly make a decision about amphetamines withhout considering the impact it might have on the prescribing, diversion, availability, and abuse of other central nervous stimulant drugs. We will do everything in our power to prevent the occurrence in the United States of the widespread abuse of other central nervous system stimulants as happened in Sweden following the restrictions on the use of amphetamines. An initial step was taken when we recommended the transfer of Preludin and Ritalin, the drugs most widely abused in Sweden, into Schedule II. The transfer became effective in October 1971. However, we believe it necessary to consider not merely these two compounds, but the whole therapeutic class.

In view of the abuse potential of the appetite control drugs, it is conceivable that if there is no greater average weight loss induced by these drugs than noted in our preliminary review, consideration should be given to the elimination of the use of *all* central nervous system stimulants, including the amphetamines, in all cases of obesity other than those in which these drugs produce a meaningful weight loss. The practicing physician would have to exert caution in deciding for which patients these drugs would be appropriate. These drugs might be reserved for other indications in which their benefits are more nearly unique and necessary.

If this conclusion is reached, no similar drugs could be marketed for treatment of obesity in the future until the manufacturers have unequivocally established by animal and human testing that the drugs are devoid of the mood-elevating, stimulant, and dependence-producing properties which have made amphetamines and related drugs a public health problem today.

I will be happy to answer any questions you may have.

(Additional questions submitted to the Food and Drug Administration were marked "Exhibit No. 8," their response was marked "Exhibit No. 9" and is as follows:)

Exhibit No. 8

FEBRUARY 17, 1972.

DR. CHARLES C. EDWARDS,
Commissioner, Food and Drug Administration,
Rockville, Md.

DEAR DR. EDWARDS: As you recall, on February 7, 1972, at the Subcommittee's hearing on amphetamines, I mentioned that my staff had several additional inquiries and requests regarding amphetamine-obesity treatment. I would appreciate your responses to or compliance with the following:

(1) What is the therapeutic value of short-term amphetamine treatment for obesity, a condition requiring long-term treatment?

(2) Does the FDA have a program similar to the consumer product safety program which aims to educate the public on the dangers and limited usefulness of amphetamines? If not, would FDA agree to undertake such an endeavor?

(3) A number of the anti-obesity drugs are compounds of amphetamine substance and other ingredients such as barbiturates or vitamins: (i) Are these more costly compounds more or less effective than pure amphetamine or methamphetamine in the short-term treatment of obesity? (ii) Are these combination drugs more dependence prone than pure amphetamine or methamphetamine? (iii) What is the National Academy of Science's opinion of the effectiveness of these combinations? Do you concur in their opinion? If not, why?

(4) Please submit FDA Efficacy Reports and Evaluations of the obesity drugs cited—Certain Anoretic Drugs—August 8, 1970, 35 Fed Regis, No. 154.

(5) Please provide a list of all NDA drugs with abuse potential that FDA has referred to the Attorney General as required by 201 (F) of the Controlled Substances Act.

I am certain that your testimony will be a valuable contribution to our inquiry and I look forward to your appearance before the Subcommittee. If you have any questions, please refer them to Ms. Mathea Falco, Staff Director and Chief Counsel, or John M. Rector, Deputy Chief Counsel at (202) 225-2951.

Sincerely,

BIRCH BAYH,
Chairman.

Exhibit No. 9

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,

PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
Rockville, Md., March 28, 1972.

HON. BIRCH BAYH,
Chairman, Subcommittee to Investigate Juvenile Delinquency, Committee on the Judiciary, U.S. Senate, Washington, D.C.

DEAR SENATOR BAYH: Commissioner Edwards has asked us to reply to your February 17 letter announcing a hearing (since postponed) and requesting certain information about barbiturates and amphetamines.

Mr. John Rector of your staff has indicated that the Subcommittee would like to have our answers on the amphetamine questions, the barbiturate information to follow. Accordingly, the following information on amphetamines is submitted:

(1) What is the therapeutic value of short-term amphetamine treatment for obesity, a condition requiring long-term treatment?

This can best be answered after completion of FDA's comprehensive review of the problem. As indicated by Dr. Edwards in his testimony before the Subcommittee to Investigate Juvenile Delinquency on February 7, 1972, the deadline for completion of this study has been set at June 1, 1972, with action to be initiated on July 1.

(2) Does the FDA have a program similar to the consumer product safety program which aims to educate the public on the dangers and limited usefulness of amphetamines? If not, would FDA agree to undertake such an endeavor?

By virtue of the structure and function of FDA, much of the drug education is directed toward the physician. Education of the consumer for this drug area is partially the function of the National Institute of Mental Health, which has prepared and widely distributed material to the general public concerning the dangers and limited usefulness of amphetamines. Copies of these and similar brochures as well as a bibliography of publications available from the National Clearinghouse for Drug Abuse Information are included with this report. FDA does sponsor some educational programs directed to consumers and these are usually of a broader scope and generally involve subjects not covered by programs of other agencies.

(3) A number of the anti-obesity drugs are compounds of amphetamine substance and other ingredients such as barbiturates (or vitamins). (i) Are these more costly compounds more or less effective than pure amphetamine or methamphetamine in the short-term treatment of obesity? (ii) Are these combination drugs more dependence prone than pure amphetamine or methamphetamine? (iii) What is the National Academy of Science's opinion of the effectiveness of these combinations? Do you concur in their opinion? If not, why?

Amphetamines have been evaluated as "Effective, but . . ." by the NAS/NRC as anorectic agents in obesity. The combination anti-obesity drugs (e.g. amphetamines plus anti-anxiety compounds) were judged to be only "possibly effective" because there is absence of positive controlled studies. Basic studies were considered necessary to clarify the issue of their effectiveness. Certain studies were carried out, and are being evaluated in the comprehensive review of the amphetamines; more precise answers to your questions will be available upon completion of the evaluation. Dependence liability relative to "pure" amphetamines will also be evaluated.

(4) Please submit FDA Efficacy Reports and Evaluations of the obesity drugs cited—Certain Anorectic Drugs—August 8, 1970, 35 *Federal Register*, No. 154.

The NAS/NRC drug efficacy study reports on the eight combination drugs cited in the *Federal Register* on August 8, 1970, are submitted with this report.

(5) Please provide a list of all NDA drugs with abuse potential that FDA has referred to the Attorney General as required by 201 (F) of the Controlled Substances Act. Triclofos, which is a hypnotic agent and a congener of chloral hydrate.

Please let us know if we can be of further assistance.

Sincerely yours,

GERALD F. MEYER,
Director, Office of Legislative Services.

QUESTION (2) AMPHETAMINES—EDUCATIONAL MATERIALS DISTRIBUTED BY NATIONAL INSTITUTE OF MENTAL HEALTH

WHAT IS A STIMULANT?

Stimulants are drugs, usually amphetamines, which stimulate the central nervous system. They induce a transient sense of well-being, self-confidence, and alertness. They are used to combat fatgue, curb appetite, and reduce mild depression.

The stimulants include cocaine, amphetamine (Benzedrine, "bennies"), dextroamphetamine (Dexedrine, "dexies"), and methamphetamine ("speed" or "crystal"). Stimulants are also known as "uppers" or "pep pills." Mild stimulants include coffee, tea, and caffeine.

HOW DO AMPHETAMINES WORK?

Research has shown that these compounds resemble the natural body hormones, epinephrine and norepinephrine. As a result of this similarity, these drugs can act directly, by mimicking the natural hormones, in their effects on nerve endings, and/or indirectly by causing increased release of the natural hormone. Whichever the case, the amphetamines stimulate certain areas of the nervous system which control blood pressure, heart, respiratory, and metabolic rates, all of which are increased. Appetite is markedly decreased and the senses are hyperalert. The body is in a general state of stress as if it were extremely threatened or expecting a violent fight. The amphetamines artificially intensify and prolong such stimulation, keeping the body in a state of tension for prolonged periods of time.

WHAT ARE THE MEDICAL USES OF AMPHETAMINES?

Amphetamines were synthesized for medical purposes in the 1920's in a search for chemicals that would constrict blood vessels. They were first used to treat colds because they shrink the nasal membranes and give temporary relief to "stuffy" nasal passages. More effective drugs with fewer side effects are now used for this purpose. Amphetamines are now mainly

prescribed for narcolepsy (overwhelming episodes of sleep during normal waking hours), depression, and to control appetite. Physicians also prescribe them to ward off fatigue during dangerous and prolonged tasks. Paradoxically, these drugs are sometimes used in the treatment of hyperactive children with certain behavioral disorders.

WHAT IS THE EXTENT OF AMPHETAMINE USE?

Amphetamines are available in all countries where Western medicine is practiced. In the U.S., approximately one-fourth of all medical prescriptions for mood-altering drugs are for stimulants, mainly amphetamines.

Half of the legally manufactured supply of amphetamines is estimated to find its way into illegal channels for non-prescribed use. Amphetamines are also produced in black-market laboratories. Although the exact number of amphetamine abusers is not known, the use of enormous quantities of amphetamines has drastically increased. Quantities of amphetamines are also used without supervision for weight reduction or to keep awake over prolonged periods.

WHAT ARE THE ROUTES TO STIMULANT ABUSE?

Overuse of amphetamines may start in the physician's office, where doses are prescribed for depression, lethargy, or obesity, and subsequent supervision is inadequate. Most cases, however, originate in illicit channels where drugs are sold indiscriminately to such customers as truck drivers who want to stay awake during long hauls, or teenagers and young adults looking for kicks.

Amphetamines were in widespread use long before their abuse potential was recognized. Limiting them to use only by prescription did not end their misuse. Today their abuse is a major medical and social problem.

HOW ARE AMPHETAMINES TAKEN?

Amphetamines are usually swallowed in the form of capsules or tablets. Crystal methamphetamine and cocaine can be inhaled or "snorted." They can also be injected into veins, in which case the effects are much more rapid and intense.

WHAT ARE THE TYPES OF STIMULANT ABUSE?

Until recently there have been chiefly two types of abusers. One included the sporadic user who occasionally takes the drug to exert himself beyond his physiological limits. He may want to stay awake, to drive, excel in an athletic contest, or cram for an examination. This type of abuse rarely leads to difficulties, but it may. Instances of death during athletic contests have been traced to amphetamine use.

A second type of abuse is taking moderate amounts to "keep going," to "feel high," or to counteract the depression that occurs when an attempt is made to stop the drug. "Spree" or "binge" abusers use the drug in social settings for "kicks." Heavy users of this type may use 75-100 mg. per day (the average is 15-30 mg.) for long periods. These individuals are likely to become drug dependent.

Since 1967, a new type of abuse has developed, which involves repeated injections of massive doses intravenously. This type of amphetamine use produces practically the same effect as cocaine. Such users are called "speedfreaks" or "methheads."

WHAT ARE THE EFFECTS OF AMPHETAMINE USE?

In ordinary amounts the amphetamines provide a transient sense of alertness, wakefulness, well-being, and mental clarity. Hunger is diminished, and short-term performance may be enhanced in the fatigued person. The drugs may increase the heart rate, raise the blood pressure, produce palpitation (throbbing heart), and rapid breathing, dilate the pupils, and cause dry mouth, sweating, and headache.

But these drugs create a dependence upon them, as tolerance increases rapidly, requiring higher and higher doses to obtain the original effect. Usually, if the drug is stopped for a week or so, the body becomes sensitive to amphetamines as before. If use continues, however, a person can become psychologically dependent on the drug in a few weeks. The sense of power, self-confidence, and exhilaration artificially created by amphetamine use is so pleasant, and the fatigue and depression that follow discontinuance are so severe, that the user is heavily tempted to revert to the drug.

WHAT ARE THE EFFECTS OF "SPEED"?

When amphetamines are taken intravenously in large amounts, an ecstatic "high" occurs which ebbs in a few hours. To regain the high, reinjection is necessary. This cycle can go on for days until the user is physically exhausted. Shakiness, itching, and muscle pains are common. A person on amphetamines has a tendency to talk rapidly and volubly, and to pace around or perform other stereotyped acts. He appears oversensitive to stimuli, and may be jumpy and anxious. A mood of apprehension or panic may develop.

Heavy amphetamine users and "speedfreaks" become physically debilitated and suffer from malnutrition. With no desire for food or sleep, they lose weight and become careless about personal hygiene. They become susceptible to infections, such as viral hepatitis, caused by a dirty needle. There is evidence of liver damage from high doses. Brain cell damage has also been reported.

Social and moral deterioration also occur with heavy users. They tend to become impulsive, irritable, unreliable, and unstable. Behavior may become assaultive and unpredictable. Of all drug abusers, "speedfreaks" most resemble the cocaine user, whose behavior was largely responsible for the term "dope fiend." "Speedfreaks" invariably become suspicious of those around them, and in extreme cases suffer from paranoid delusions of being threatened or the object of a plot. Schizophrenia-like disturbances resulting from prolonged, heavy use may last for several months after the drugs are discontinued. The depression into which heavy amphetamine abusers fall when they come down from their high ("crash") is extremely severe. Suicide during such moods is known. Lethargy, fatigue, muscle pains, ravenous hunger, and mental depression are the chief symptoms when the drugs are discontinued. Some scientists regard these as stimulant withdrawal symptoms indicating a true physical dependence.

"Speed" can occasionally kill, from accidents resulting during paranoid delusions, homicidal rages, or through injections with contaminated substances. Death from overdose in the tolerant individual, however, is uncommon. Most frequently, the deterioration of personality, judgment, and health resulting from continued use of "speed" leaves the "speedfreak" in a limbo, neither physically dead nor physically alive.

WHAT KINDS OF PERSONS ARE LIKELY TO ABUSE STIMULANTS?

Medical experts believe that heavy amphetamine abusers usually suffer from some form of psychic instability which existed before the drug was tried. Such persons use stimulants to help them deal with prob-

lems of living and their emotional inadequacies. This type of person is frequently apathetic, without energy, and depressed—unable to feel or enjoy the natural "turn-ons" or "highs" that others find in normal experience. Frequently he is unable to relate easily to others. Young persons who are discouraged and hopeless and without the ability to form warm interpersonal relationships may come to rely on stimulants for the transient sense of power, self-confidence, and well-being they create.

WHAT CAN BE DONE ABOUT THE "SPEED" PROBLEM?

Elimination of the large-scale illicit sources of supply of amphetamines, and tighter regulation of legitimate production are part of the answer. In addition, the consequences and complications of using amphetamines indiscriminately must be made known as widely as possible. It seems likely that only the most disturbed persons will become involved in the "speed" scene if the known effects of taking this drug are properly disseminated.

For those who do become drug-dependent, skilled treatment is needed. Doctors should carefully supervise patients for whom they prescribe amphetamines.

WHAT ARE THE PENALTIES FOR ILLEGAL POSSESSION?

These drugs are legally available only on a doctor's prescription. New Federal schedules recently enacted by Congress replace penalties for illegal possession established under the Drug Abuse Control Amendments of July 15, 1965. Under this new legislation, the Comprehensive Drug Abuse Prevention and Control Act of 1970, illegal possession is punishable as follows: for a first offense, imprisonment of up to 1 year and/or a maximum $5,000 fine. Unlawful distribution or possession with intent to distribute may bring up to 5 years' imprisonment and/or a maximum $15,000 fine and a required 2-year special parole term (except that cocaine is subject to stiffer penalties because it is legally considered a narcotic). Involvement in a continuing criminal enterprise carries a penalty of from 10 years to life imprisonment, and a maximum $100,000 fine and forfeiture of profits from and interests in the enterprise that is in violation of the Act, if it is a first offense. For a second or subsequent offense, penalties are doubled. A person who is at least 18 who distributes amphetamines illegally to a person under 21 years of age is subject to imprisonment and/or fine twice that otherwise authorized.

WHAT ABOUT AMPHETAMINE ABUSE IN OTHER COUNTRIES?

Other countries besides the U.S. have had outbreaks of amphetamine abuse. After World War II, these drugs were widely available in Japan without prescription. At one time it was estimated that between 500,000 and one million persons were regular users. About 5 percent of adults in some of the larger cities of Japan were amphetamine dependent. This epidemic was eventually controlled through the elimination of sources of supply and increased regulatory measures.

Serious amphetamine abuse problems exist in Great Britain. Sweden even banned medical use of these drugs, except for those few cases approved by a special commission. Despite this cutoff of legitimate supplies, the problem continues.

WHAT ARE TREATMENT APPROACHES?

Because compulsive drug abuse, particularly the intravenous injection of speed, is a comparatively recent phenomenon, few appropriate treatment and rehabilitation services exist. Most formal drug treatment programs in the U.S. are designed primarily for narcotic addicts. However, today informal drug treatment clinics are springing up in communities where the drug problem is particularly acute, and community mental health centers are beginning to develop services for the young drug abuser.

Treatment of the "speedfreak" is very difficult. Like heroin users, persons who have broken the habit often relapse. Both medical and psychiatric help may be needed. Because compulsive drug abuse is usually related to a breakdown in human relationships, a considerable amount of social and psychological support is required.

One of the more effective treatment approaches is group therapy, in which recovered ex-users interact with users. Those who have come through the speed scene are trusted, and their counsel is likely to be accepted by those who wish to stop the destructive use of drugs. Such groups provide a substitute for the drug-using groups to which these persons formerly related, and provide supportive help. Such groups also open up opportunities for self-exploration and learning to trust and relate to others, which is important in personality reconstruction.

WHAT RESEARCH IS BEING DONE?

The National Institute of Mental Health, part of the Health Services and Mental Health Administration of the Department of Health, Education, and Welfare, is the Federal agency primarily responsible for research in drug adiction and abuse. The program is focused within the Center for Studies of Narcotic and Drug Abuse.

Extensive animal and clinical studies are being conducted to uncover the underlying mechanism through which stimulant drugs act on the body and nervous system. Techniques to analyze changes that may occur in nerves, cells, and muscles as a result of chronic heavy use, and to detect the presence of drugs in the body are being developed. New drugs and methods for treating over-use are being sought.

In addition, the NIMH is supporting a number of surveys to determine the extent of use of these drugs among various population groups. Behavioral scientists are studying the complex causes of drug abuse so that this problem can be better understood. Research and demonstration programs are underway to develop more effective approaches to its solution through education, prevention, and rehabilitation.

COCAINE

Cocaine is a substance derived from the coca bush, a plant that grows in the uplands of Bolivia, Peru, and Chile. It has been used for centuries by Andean Indians who rely on its anti-fatigue and anti-hunger effects to sustain them through a life of toil and deprivation in the rarefied atmosphere.

In the Western world, cocaine was at one time used medically as a local anesthetic; however, at present, effective synthetics have been developed, without the unfavorable side effects of cocaine. It was also a drug of abuse at the turn of the century.

Today cocaine ("snow") has begun to reappear on the U.S. drug scene. In large doses, it produces violent stimulant, hallucinatory, and ecstatic effects. Overdoses are not rare and cause death from cardiac or respiratory arrest.

The favorite methods of taking cocaine are by "snorting" and injection. It is frequently mixed with heroin ("speedball") to provide a smoother "high." The effect is much shorter than that produced by "speed" but is similar otherwise. The body does not develop tolerance, but marked psychic dependence results. As with amphetamines, severe depressions occur as the drug's effects wane, impelling the abuser to continue its use.

Chronic use results in nausea, digestive disorders, loss of weight, insomnia, skin abscesses, and occasional convulsions. Prolonged sniffing perforates the septum of the nose. Paranoid delusions, with auditory and visual hallucinations, occur. The mental disturbances often trigger compulsive, violent anti-social acts. Under the proposed new penalty structure, penalties for possession or sale of cocaine are the same as those for the narcotics.

National Clearinghouse for
Drug Abuse Information
P.O. Box 1701
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SEDATIVES

SOME QUESTIONS AND ANSWERS

WHAT ARE THE SEDATIVE DRUGS?

Sedative drugs are manufactured for medical purposes to reduce tension and anxiety, to treat certain psychosomatic disorders, and to induce sleep. Certain sedatives are used in the treatment of epilepsy.

The barbiturates, made from barbituric acid, are by far the largest group of sedatives. The first sleep-producing barbiturate was synthesized in 1903. Today there are over 50 commercial brands on the market.

The barbiturates vary in duration of action. They range from the very fast-acting thiopental (Pentothal) which can be used as an anesthetic, to moderately fast-acting pentobarbital (Nembutal) and secobarbital (Seconal), to the slow-acting phenobarbital (Luminal).

The barbiturates, especially the short-acting ones, may lead to heavy abuse. Without careful medical supervision to avoid habituation, increasing doses are used to produce the desired effect, and physical dependence occurs.

On the street, the sedatives are called "goofballs," "sleepers," and "downers." They appear in a variety of colored capsules or tablets. Seconals are called "red devils," Nembutals are "yellow jackets," Tuinals are "rainbows," and Amytal capsules are "blue angels."

Besides the barbiturates, other sedatives that may be abused inclued glutethimide (Doriden), chloral hydrate, bromides, and certain minor tranquilizers such as meprobamate (Miltown, Equanil), and chlordiazepoxide (Librium).

HOW DO BARBITURATES WORK?

The principal response elicited by barbiturates is a depression of the central nervous system. They act upon the cerebral centers and interfere with the passage of impulses in the brain. They appear to affect the enzyme processes by which energy is acquired, stored in the protoplasm of the cells, and utilized. They depress brain function, and in large doses depress the brain centers responsible for maintaining the rhythm of respiration.

WHAT ARE THE EFFECTS OF THE BARBITURATES?

The barbiturates exert a powerful sedating action on the central nervous system. Properly prescribed and taken as directed in small doses, they relieve tension and anxiety. In larger doses (three or four times as much) they produce drowsiness and sleep. They are also used medically for such psychosomatic conditions as high blood pressure, peptic ulcer, spastic colitis, and other psychophysiologic disorders.

Increasing use of barbiturates quickly produces tolerance, which means that more is required to produce the desired effect, leading to the strong desire to continue taking barbiturates in progressively larger amounts. Addiction to 50 or more sleeping pills a day has been reported. Those who take excessive amounts of barbiturates usually go into a coma. However, in persons used to taking large doses, instead of producing drowsiness or sleep, barbiturates may produce restlessness, excitement, and even delirium, resembling the excitation of the alcoholic. Persons intoxicated with barbiturates may appear to be inebriated, and may be mistaken for "drunks." Their coordination is poor, their speech is slurred, they become irritable, confused, and unsteady of gait. Ability to accomplish skilled, precise tasks is lost. Judgment, perception, and memory are impaired. In extreme cases, disorientation, aggressive behavior, hallucinations, and paranoid delusions may develop.

Barbiturates are frequently used in conjunction with amphetamines, often to induce sleep after the amphetamine "jag" is over. Alternatively, amphetamines may be taken to counteract the barbiturate "hangover." This results in a chemical attempt to regulate the sleep-waking rhythm which often ends in failure.

Although the two types of drugs have opposite actions, some persons become dependent on both barbiturates and amphetamines because of their combined effect. Instead of completely neutralizing a "downer," an "upper" may not only take the edge off the jittery excitement, but also may create a pleasant, mood-elevating effect, leading to habitual swallowing of large quantities of some combination of amphetamines and barbiturates.

HOW WIDELY ARE THESE DRUGS USED?

According to statistics, 178,000,000 prescriptions for mood-changing drugs were filled by U.S. pharmacies in 1967. Of these prescriptions, about 65 percent were for sedative drugs (31 percent for barbiturates and other sedatives and hypnotics, 34 percent for minor tranquilizers). Most of these prescriptions went to some 30,000,000 adult Americans.

While the majority of these drugs are legally used for medical purposes, an unknown but large quantity of barbiturates also enters illegal channels. Recent estimates indicate that of all the barbiturates manufactured in the United States more than half was diverted to illicit use. A good share of the "goofballs" being distributed today on the black market are capsules that were legally manufactured, but found their way into illicit channels by theft, exportation and reimportation from a foreign country, hijacking, and indiscriminate sales to unauthorized persons.

WHO ARE THE SEDATIVE ABUSERS?

Persons who are tense and anxious, or who have trouble with insomnia, may become overinvolved with sedatives and come to depend on them. Those who get in the habit of using these pills routinely may find

themselves using increasingly large amounts. The largest group of persons prescribed barbiturates and tranquilizers have been adults over 20, principally those in the 40-59 age group. However, today they are also being used more and more frequently by teenagers who find them in the family medicine cabinet or obtain them from black market sources.

Many cases of barbiturate or tranquilizer misuse begin in the physician's office. A doctor may fail to adequately examine the basis of complaints for his patient's symptoms, or may overprescribe pills, or permit multiple refills of the prescription without his supervision to assure they are being properly used.

Heroin addicts may take barbiturates to supplement or substitute for their preferred drug. Amphetamine users who become jittery may take them to ease their tension.

HOW DANGEROUS ARE BARBITURATES?

The barbiturates are highly dangerous when taken without medical supervision. Because they are commonly prescribed by doctors, many people mistakenly consider them safe to use freely and carelessly. They are not. Death may result from use of barbiturates, either from overdose or sudden withdrawal.

A common mode of suicide with drugs is with sleeping pills. Some 3,000 barbiturate suicides occur each year. Accidental deaths, due to taking a larger number of pills than intended, are not uncommon.

Death can also occur when a number of barbiturate capsules are swallowed by someone intoxicated with alcohol. These drugs act as synergists and are additive in their effects. Coroners have found a number of instances in which the barbiturate and alcohol levels in the blood were insufficient to produce death, but the combination did.

A regular, heavy user who has built up tolerance to the drug, and requires large amounts to obtain the desired effect, suffers withdrawal symptoms when the drug is suddenly stopped. The severe withdrawal state resembles delirium tremens. The user is agitated, restless, may have muscle cramps, nausea, and convulsions. In addition, he may see things that are not there, and have delusional, confused thoughts.

The treatment of chronic barbiturate intoxication consists of the slow decrease of the drug under medical supervision. Sudden barbiturate withdrawal is a serious medical emergency and requires hospitalization. It is more dangerous than heroin withdrawal, and can be deadly.

It has been mentioned that less than lethal doses of alcohol and sleeping pills, taken together, may be fatal. This is also true of combinations of barbiturates with anesthetics, narcotics, or tranquilizers. These drugs act to potentiate, or intensify, each other's effects. They may depress vital functions such as breathing and heart action to the point where they cease. Past a certain point, even persons whose bodies have acquired tolerance to barbiturates risk death from an overdose.

WHAT ARE THE LEGAL CONTROLS?

Like the stimulant drugs, the sedative drugs are available only on prescription. They are controlled by the Comprehensive Drug Abuse Prevention and Control Act of 1970 passed in October 1970. This law controls abuse of the drugs in two ways. It provides for regulating manufacture, distribution, and possession. Thus, all registered manufacturers, processors, and their suppliers, wholesale druggists, pharmacists, hospitals, clinics, public health agencies, and research laboratories must keep accurate records of receipts and outflow. No prescription for a controlled drug older than 6 months can be filled, nor can refills be made more than five times in a 6-month period.

There are also strong penalties for illegal possession and distribution. The new Federal law replaces old penalties for illegal possession and distribution established under previous legislation. Illegal possession is punishable as follows: for a first offense, imprisonment of up to 1 year and/or a maximum $5,000 fine. Unlawful distribution or possession with intent to distribute a barbiturate listed in the five schedules containing drugs with the highest abuse potential may bring up to 5 years' imprisonment and/or a maximum $15,000 fine, and a required 2-year special parole term for a first offense. Involvement in a continuing criminal

enterprise (large scale trafficking) carries a penalty of from 10 years to life imprisonment, and a maximum $100,000 fine, and forfeiture of profits from and interests in the enterprise. For second and subsequent offenses penalties are doubled. A person who distributes barbiturates illegally to someone under 21 years of age is subject, if it is a first offense, to imprisonment and/or fine twice that otherwise authorized.

WHAT CAN BE DONE TO PREVENT AND TREAT BARBITURATE ADDICTION?

Tighter regulations and enforcement of law on the legitimate manufacture and distribution of barbiturates and tranquilizers are part of the answer. Because barbiturates and tranquilizers have sound medical usefulness, physicians must be wary of yielding to the demand of patients for increased amounts when, in fact, they may be manifesting tolerance. Widespread dissemination of information about the dangers of overusing these addictive drugs is essential.

Certain kinds of barbiturate addiction are regarded by many medical authorities as more difficult to cure than narcotic addiction. Withdrawal requires careful medical and nursing supervision. After withdrawal, psychiatric help is frequently needed. Like other drug abusers, the chronic barbiturate abuser usually suffers from inability to cope with the stress of living, and finds facing reality difficult. Considerable social and psychological support, often most successfully provided through group therapy and relating to others who have "kicked the habit," is helpful.

WHAT RESEARCH IS BEING DONE?

The National Institute of Mental Health, part of the Health Services and Mental Health Administration of the Department of Health, Education, and Welfare, is the Federal agency primarily responsible for research on drug addiction and abuse. The program is focused within the Division of Narcotic Addiction and Drug Abuse.

Despite their longtime use, just how barbiturate drugs act on the body, brain, and nervous system is not fully understood. Much remains to be learned about the effects of massive doses. Basic studies are underway to determine the precise mechanism through which the drugs work, and how tolerance develops. New analytic techniques are being applied to assess changes that occur in body organs and cells as a result of chronic heavy use. New drugs and methods to treat over-use and dependence are being sought. Research and demonstration programs are underway to develop more effective approaches to the solution of drug abuse through education, prevention, and rehabilitation.

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WHAT ARE NARCOTIC DRUGS?

The term narcotic refers to opium and to pain-relieving drugs made from opium, such as morphine, paregoric, and codeine. These and other opiates are obtained from the juice of the opium poppy (*Papaver somniferum*). Heroin, Percodan, and Dilaudid are derivatives of morphine. Several synthetic drugs such as Demerol and methadone are also classed as narcotics. Narcotics are widely used in medicine as analgesics which relieve pain and induce sleep.

Heroin, sometimes referred to by such slang terms as "Smack," "Scag," "Horse," "Junk," and "H," is morphine chemically altered to make it some three to six times stronger. Since heroin is the narcotic used by most addicts today, these questions and answers will focus on heroin.

WHAT IS NARCOTIC ADDICTION?

When the abuser of a narcotic gets "hooked"—meaning addicted—his body requires repeated and larger doses of the drug. Once the habit starts, larger and larger doses are required to get the same effects. This happens because the body develops a "tolerance" for the drug.

A second sign of heroin addiction is withdrawal sickness. When the addict stops using the drug, he may sweat, shake, get chills, develop diarrhea and nausea, and suffer sharp abdominal and leg cramps. Modern treatment helps the addict through these withdrawal symptoms. Science now has new evidence that the body's physical addiction may last much longer than previously believed.

There is another kind of drug dependence connected with the use of narcotics. This is known as psychological dependence. The user develops a craving for the drug for emotional reasons. He comes to depend on the drug as a way to escape facing life.

Narcotic use can become even more of an escape than expected. Contaminated injections or unexpectedly high doses caused over 900 deaths in New York City alone during 1969. Over 200 of these were among teenagers.

WHAT ARE THE EFFECTS OF THE DRUG?

Typically, the first emotional reaction to heroin is reduction of tension, easing of fears, and relief from worry. Feeling "high" may be followed by a period of inactivity bordering on stupor.

Heroin is usually sold heavily "cut" or adulterated with milk sugar, quinine, or other materials. Typically it is mixed into a liquid solution and injected into a vein ("mainlining") although it can also be injected just under the skin ("skin popping"), or sniffed through the nose. The latter methods of use are more common among "joy poppers" than confirmed addicts. However, addiction is possible no matter which method is used. Taken in any way, the drug appears to dull the edges of reality. Addicts will relate that heroin "makes my troubles roll off my mind," and "it makes me more sure of myself." As the addict becomes more and more used to the drug, he requires increasing doses to achieve a "high." Eventually, he doesn't even obtain a "high." Instead, he is forced to continue using heroin to avoid the withdrawal sickness. In other words, he now shoots heroin to feel normal.

The drug depresses certain areas of the brain, and may reduce hunger, thirst, and the sex drive. Because addicts do not usually feel hungry, and spend their money for heroin, they can become malnourished and physically depleted. Pneumonia, tuberculosis, and venereal disease occur more frequently in addicts than in the rest of the population. The injection of contaminated material and the use of unsterile syringes and needles cause hepatitis and blood infections that may settle in the brain, heart valves, or spread throughout the body.

Withdrawal symptoms appear in the addicted person within 12 or 16 hours after the drug has been last taken and become progressively worse. After 2 or 3 days they begin to subside, and within a week the "junkie" is free from withdrawal symptoms.

WHO TAKES NARCOTICS?

Studies by the National Institute of Mental Health show that heroin addiction today is found generally among young men of minority groups in ghetto areas. However, heroin usage is spreading to young people of both sexes from more fortunate backgrounds. It is estimated that more than half of the known addicts live in New York State—most of them in New York City. Estimates of the total number of addicts range up to 200,000. Recent figures show that more than half are under 30 years of age, a few as young as 10.

All narcotic addiction in the United States is not limited to the heroin users. Some middle-aged and older people who take narcotic drugs regularly to relieve pain can also become addicted. So do some people who can obtain opiates easily, such as doctors and nurses. They take injections to keep going under pressure, and eventually find themselves locked into narcotic addiction.

WHAT IS THE LIFE OF AN ADDICT LIKE?

The addict will admit that, once "hooked," obtaining a continued supply becomes the main goal of his life. His concentration on getting money and drugs frequently prevents the addict from continuing either his education or his job. His health is often bad. He may be sick one day from the effects of withdrawal, and sick the next from an overdose. Statistics indicate that his life span may be shortened by 15 to 20 years.

He is usually in trouble with his family and in constant threat of trouble with the law. He lives to support his addiction.

DOES ADDICTION LEAD TO CRIME?

Some studies suggest that many of the known narcotic addicts had some trouble with the law before they became addicted. Once addicted, they may become even more involved with crime because it costs so much to support a heroin habit. For example, an addict may have to spend from $25 to $100 to buy his day's supply of heroin.

Most authorities agree that the addict's involvement with crime is not a direct effect of the drug itself, but turning to crime is usually the only way he has of getting that much money. The crimes are nearly always thefts, prostitution, pimping, or "pushing." When the addict is desperate due to withdrawal sickness, he may resort to violence.

WHAT ARE THE LEGAL PENALTIES?

New Federal penalty schedules have been enacted by Congress to replace those established under the Narcotic Control Act of 1956. Under this new legislation, the Comprehensive Drug Abuse Prevention and Control Act of 1970, illegal possession is punishable as follows: for a first offense, imprisonment of up to 1 year and/or a maximum $5,000 fine. Second and subsequent offenses are punishable by up to 3 years of imprisonment and/or a maximum fine of $10,000.

For unlawful distribution of narcotics in the two schedules of highly dangerous drugs, and for possession with intent to distribute, if a first offense, the penalties are imprisonment up to 15 years and/or $25,000 maximum fine, with a 3-year special parole term required. Second and subsequent commissions of this offense are punishable by imprisonment or fine twice that otherwise authorized, and a special parole term of 6 years. The penalties are somewhat lower if the drug appears in Schedules III through V, which includes drugs with less abuse potential. A person who is at least 18 and who gives a narcotic to a person under 21 years of age is subject to imprisonment for up to 30 years for a first offense and 45 years for subsequent offenses and/or a fine twice that otherwise authorized. Those persons involved in continuing criminal enterprise face imprisonment of 10 years to life, and a $100,000 fine and forfeiture of all profits gained from the enterprise. For a second offense, penalties are set at 20 years to life, a $200,000 fine, and forfeiture of profits.

WHAT IS THE TREATMENT FOR ADDICTION?

Medical authorities say that the addict is a sick person. He needs treatment for his personality problems, physical addiction and withdrawal sickness. Then, he needs considerable help to keep him from going back to drug use after his withdrawal.

The most difficult part of his treatment comes after he is out of the hospital. The doctors can help get him off the drug and help to restore his health. But it is harder to keep him from picking up the habit again, for many reasons. Drug-taking may have become his career. His friends may all be addicted. He may have no job skills and his work record is generally poor. He will have great difficulty making a fresh start in life and learning to enjoy existence without drugs.

A number of rehabilitation approaches to the problem of addiction are being tested including ex-addict self-help groups and narcotic substitutes. Rehabilitation means to rebuild—physical, mental, emotional, social, and vocational reconstruction. With many addicts, every aspect of existence will need rehabilitation.

One promising, experimental effort to help addicts is through maintenance on methadone, a narcotic commonly used to treat withdrawal from heroin. When taken regularly, methadone eliminates the craving for heroin as well as its euphoric effects. In some neighborhoods, addicts are maintained on methadone by daily doses administered at a local community clinic. Close supervision is most important, including urine analyses to make sure that the addict is following directions about taking no drug but methadone. Counseling, job retraining, and the building of a new way of life must be combined with methadone maintenance treatment.

Because the rebuilding of a life can take many services and special programs, this opportunity for addicts in the past was very limited. The Narcotic Addict Rehabilitation Act of 1966 gives certain addicts a choice of treatment instead of prosecution or imprisonment, or—if they are not charged with a crime—the right to ask for treatment on their own initiative or on that of a related person. Federal legislation also provides for a complete range of rehabilitation services to be made available to addicts in their own communities.

WHAT IS THE NARCOTIC ADDICT REHABILITATION ACT OF 1966?

The Act provides that:

1. An addict charged with a non-violent Federal offense who elects to be committed for treatment instead of prosecuted for his crime can be committed to the Secretary of Health, Education, and Welfare for examination, treatment, and rehabilitation.

2. An addict after conviction of a Federal offense can be committed to the Attorney General for a treatment period of no more than 10 years, or for the maximum period of sentence that could be imposed for his conviction.

3. An addict not charged with an offense can be civilly committed to the Secretary of Health, Education, and Welfare for treatment upon his own application, or that of a relative or another "related individual."

Care of the addict after his release from the hospital is a key aspect of his treatment. Aftercare programs provide continuing treatment for up to 3 years in the addict's home community. These programs are individually designed to meet his special needs.

The Act (NARA) is administered by the National Institute of Mental Health, Department of Health, Education, and Welfare, and by the Department of Justice.

Communities can also receive Federal support for building or staffing narcotic addict treatment centers for people dependent on narcotics and other drugs who want help. These centers are supported by NIMH grants matched by community or State funds. A full range of treatment facilities are available: hospital care, emergency treatment, and outpatient services with all the special rehabilitative facilities that may be required.

WHAT IS BEING DONE TO LEARN MORE ABOUT ADDICTION?

The Division of Narcotic Addiction and Drug Abuse, National Institute of Mental Health, is the focal point for Federal activities in drug abuse research. The Division operates Clinical Research Centers at Lexington, Kentucky and Fort Worth, Texas. There, scientists are studying patterns of drug use, the nature of addiction, and the psychosocial aspects of the addict. At Lexington, the Addiction Research Center focuses on many basic questions about the process of addiction from the cellular to the human level. New narcotics are screened to prevent highly addictive ones from coming onto the market. The Addiction Research Center is in the forefront in the search for a safe narcotic antagonist which will neutralize the effects of heroin in the body.

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DRUG ABUSE

SOME QUESTIONS AND ANSWERS

What Is a Drug?

A drug is a substance which by its chemical nature has an effect upon the mind or body. Many substances not usually thought of as drugs are included in this definition such as: caffeine, alcohol, nicotine, pollutants, and household chemicals. These are considered drugs because they affect the function of the living organism. However, this publication deals with those drugs commonly referred to as drugs of abuse, including marihuana, hallucinogens, narcotics, amphetamines, and barbiturates.

Why Are Drugs Being Abused Today?

The misuse of drugs is not a new phenomenon. Different types of drug abuse have been present for years in the United States and other countries. The reasons that man has used drugs throughout history are mainly the same reasons for today's non-medical drug use: to ease pain, to stop anxiety, to produce happiness, and to change experience and thought. Many of the reasons that young people and adults use drugs are one and the same: for fun, to make social communication easier, to feel better, to relieve boredom and frustration, to escape from problems, and perhaps to protest.

What Is the "Problem"?

The drug problem is complex. There are few issues which arouse so many emotions as the abuse of drugs. In one respect, the problem is that we are a drug-oriented society and people are using more drugs without understanding their actions.

The problem is also one of people and their feelings and beliefs about drugs. Just as no two people are exactly alike, no two drug users are the same. Many people tend to lump everyone who uses drugs into one category. However, not all drug abusers are at the same level of involvement and distinctions must be made between the various types of users.

The experimenters have tried a drug, most likely marihuana, only a few times often due to curiosity or peer-group pressure. This group does not plan to con-

tinue drug use and their experience is usually not more than an occasional social exposure.

The moderate or social group uses drugs with some regularity; however, drugs have not become the most important factor in their lives.

The chronic users regularly take drugs which have assumed a central role in their life styles. This group consists of a small proportion of all drug users, but they are the ones who are drug dependent.

What Are Some Definitions Associated With Drug Misuse?

Drug dependence—physical or psychological—is a condition which results from chronic, periodic, or continuous use of various chemicals. There are many different kinds of drug dependence according to the type of drug used and each has specific problems associated with it.

Habituation is the psychological desire to repeat the use of a drug intermittently or continuously because of emotional needs. Many individuals come to use drugs habitually to escape from reality or just to feel better.

Addiction is the physical dependence upon a drug. Its definition includes the development of tolerance and withdrawal. As a person develops tolerance he requires larger and larger amounts of the drug to achieve the same effect. Withdrawal occurs when the use of an addicting drug is stopped abruptly and is characterized by a wide range of distressing symptoms such as: diarrhea, vomiting, and cramps. Many drug users develop a compulsion to continue taking a drug to avoid the withdrawal symptoms.

Are All Drugs Harmful?

Many people still seem to think of drugs as magic potions which have only the good effects they seek. However, almost every drug, even those not commonly thought of as drugs of abuse, is potentially dangerous at some dosage level for certain people under some circumstances. Some drugs can also be harmful when taken in dangerous combinations or by very sensitive people in small or ordinary amounts.

The fact that some drugs can bring about beneficial results does not mean that pills will solve all problems. What is needed is a new respect for all drugs. Drugs that affect the mind can have subtle or obvious side effects which may occur immediately or become evident only after long-term, continuous use.

Why Do Drugs Have Such a Wide Range of Effects Upon Different Users?

All drugs have many effects and these vary among individuals, on different occasions in the same individual, with the amount of the drug, and the length of time the drug is used. Many factors not related to the chemical make-up of the drug cause varying effects. These include the expectations of the user, the circumstances or setting under which he takes the drug, and the meaning of drug use to the individual.

Even the same individual taking the same dose of a drug on subsequent occasions may have a completely different reaction. As the drug affects the individual, he becomes more susceptible to the moods of the people around him and the setting in which he takes the drug. These factors can markedly alter the drug's effects.

Where Does a Person Go If He Has a Drug-Related Problem?

A user can ask his family, a friend, physician, or minister to help find the best resource in the community. The family doctor, mental health professionals, or school counselors should be among the first contacted. Some community mental health centers have special drug abuse units; all centers can provide referral to appropriate resources.

What Considerations Could Make an Impact on Our Drug Abuse Problem?

1. A double standard produces a credibility gap. Adults who misuse liquor, tobacco, or other drugs should be judged by the same standards as young people.
2. Children should not be continually exposed to the idea that the stresses of daily life require chemical relief. Respect for all chemicals, especially mind-altering chemicals, should be instilled in people at an early age.
3. Factual information about drugs should be stressed rather than attempts to frighten people.
4. Efforts to detect and apprehend all illegal manufacturers and large-scale traffickers of illicit drugs should increase.
5. Further research in prevention, education, and treatment techniques should be carried out.

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21. _____copies of HOW SAFE ARE OUR DRUGS, FS 13.111:44/2, at 15¢ per copy

22. _____copies of HUNG ON LSD, STUCK ON GLUE, FS 5.228:28010, at 10¢ per copy

23. _____copies of KATY'S COLORING BOOK ABOUT DRUGS AND HEALTH, J 24.2:K 15, at 35¢ per copy

24. _____copies of LEAVING THE DRUG WORLD BEHIND, HE 5.225:25055, at 10¢ per copy

25. _____copies of LSD: SOME QUESTIONS AND ANSWERS, PHS Publication No. 1828, HE 20.2402:L99/971, at 10¢ per copy

26. _____copies of LSD-25: A FACTUAL ACCOUNT, J 24.8:L 99/rep., at 30¢ per copy

27. _____copies of MARIHUANA, FABLES AND FACTS, HE 20.2402:M 33, at 5¢ per copy

28. _____copies of MARIHUANA AND HEALTH, A REPORT TO THE CONGRESS FROM THE SECRETARY, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, HE 20.2402:M 33/3, at $1.50 per copy

29. _____copies of MARIHUANA, REPORT BY THE SELECT COMMITTEE ON CRIME, 91-2:H. rp. 978, at 50¢ per copy

30. _____copies of MARIHUANA: SOME QUESTIONS AND ANSWERS, PHS Publication No. 1829, HE 20.2402:M 33/2/970, at 10¢ per copy

31. _____copies of MENTAL HEALTH MATTERS, DRUG ABUSE, HE 20.2402:D 84/9, at 10¢ per copy

32. _____copies of NARCOTIC ADDICT REHABILITATION ACT OF 1966, HE 20.2402:N 16/966, at 10¢ per copy

33. _____copies of NARCOTIC DRUG ADDICTION, FS 2.22/31:2, at 25¢ per copy

34. _____copies of NARCOTICS: SOME QUESTIONS AND ANSWERS, PHS Publication No. 1827, HE 20.2402:N 16/2/971, at 10¢ per copy

35. _____copies of PASSAGES ON DRUGS FROM BLACK LITERATURE (one each of 15 fliers), PHS Publication No. 2089, HE 20.2402:D 84/11, at 75¢ per set

36. _____copies of PUBLIC SPEAKING ON DRUG ABUSE PREVENTION: A HANDBOOK FOR THE LAW ENFORCEMENT OFFICER, J 24.8:D 84/3, at 30¢ per copy

37. _____copies of RECENT RESEARCH ON NARCOTICS, LSD, MARIHUANA AND OTHER DANGEROUS DRUGS, PHS Publication No. 1961, HE 20.2402:N 16/4, at 20¢ per copy

38. _____copies of RESPECT FOR DRUGS, J 24.8:D 84, at $1.25 per copy

39. _____copies of SEDATIVES: SOME QUESTIONS AND ANSWERS, PHS Publication No. 2098, HE 20.2402:SE 2, at 10¢ per copy

40. _____copies of STIMULANTS: SOME QUESTIONS AND ANSWERS, PHS Publication No. 2097, HE 20.2402:ST 5, at 10¢ per copy

41. _____copies of STRENGTHENED PROGRAMS OF INTERNATIONAL COOPERATION FOR HALTING THE ILLICIT SUPPLY OF DRUGS, S 1.71:244, at 10¢ per copy

42. _____copies of STUDENTS AND DRUG ABUSE, PHS Publication No. 1946, HE 20.2402:D 84/2, at 25¢ per copy

43. _____copies of TASK FORCE REPORT: NARCOTICS AND DRUG ABUSE, ANNOTATIONS AND CONSULTANTS' PAPERS, Pr 36.8:L 41/N 16

44. _____copies of TERMS AND SYMPTOMS OF DRUG ABUSE, J 24.2:D 84/3, at 35¢ per copy

45. _____copies of VOLATILE SUBSTANCES: SOME QUESTIONS AND ANSWERS, PHS Publication No. 2150, HE 20.2402:V 88/3, at 10¢ per copy

46. _____copies of WILD HEMP (MARIHUANA), HOW TO CONTROL IT, A 1.68:969, at 10¢ per copy

47. _____copies of YOU THINK YOU HAVE PROBLEMS, J 24.2:P 94, at 10¢ per copy

48. _____copies of YOUTH REPORTERS DISCUSS "PROBLEM" DRUGS, HE 21.109:2, at 50¢ per copy

49. _____copies of YOUTHFUL DRUG USE, HE 17.2:D 84/2, at 30¢ per copy

50. POSTERS ABOUT DRUG ABUSE:

    A. BROTHER...DON'T PASS IT ON, HE 20.242]:B 79, at 15¢ per copy

    B. DON'T BLOW IT WITH DRUGS, HE 20.2421:D 84, at 15¢ per copy

    C. JOHN WAS OK...UNTIL HIS MOMMA CAUGHT HIM, HE 20.2421:J 61, at 15¢ per copy

    D. IS IT POSSIBLE THAT SOMEONE YOU CARE ABOUT HAS CHANGED FOR NO APPARENT REASON, J 24.2:Is 1, at 15¢ per copy

    E. MISERIA (SPANISH VERSION), HE 20.2421:M 68, at 15¢ per copy

    F. SLAVERY (BLACK VERSION), HE 20.2421:SL 1, at 15¢ per copy

    G. SLAVERY (WHITE VERSION), HE 20.2421:SL 1/2, at 15¢ per copy

    H. THINGS COULD BE WORSE WE COULD BE HUNG UP ON DRUGS, D 2.9:55, at 10¢ per copy

    I. WANTED DEAD OR ALIVE...MARIHUANA, J 24.11:M 33, at 20¢ per copy

    J. WILL THEY TURN YOU ON OR WILL THEY TURN ON YOU, HE 20. 2421:W 66, at 20¢ per copy

51. _____copies of A FEDERAL SOURCE BOOK: ANSWERS TO THE MOST FREQUENTLY ASKED QUESTIONS ABOUT DRUG ABUSE, Pr Ex 13.2:An 8, at 25¢ per copy or $18.75 per hundred copies

52. _____copies of SELECTED DRUG ABUSE EDUCATION FILMS, Pr Ex 13.8:F 48, at 10¢ per copy

53. SELECTED DRUG EDUCATION CURRICULA SERIES:

A. _____copies of BALTIMORE COUNTY BOARD OF EDUCATION, GRADES 6, 9, 12, Pr Ex 13.8:Ed 8, at $1.00 per copy

B. _____copies of FLAGSTAFF PUBLIC SCHOOLS, GRADES K-12 Pr Ex 13.8:Ed 8/2, at 65¢ per copy

C. _____copies of GREAT FALLS SCHOOL DISTRICT NO. 1, GRADE 6, Pr Ex 13.8:Ed 8/8, at $1.25 per copy

D. _____copies of NEW YORK STATE EDUCATION DEPARTMENT, GRADES 4, 5, 6, Pr Ex 13.8:Ed 8/3, at 65¢ per copy

E. _____copies of RHODE ISLAND STATE DEPARTMENT OF EDUCATION, GRADES K-12, Pr Ex 13.8:Ed 8/5, at $1.25 per copy

F. _____copies of SAN FRANCISCO UNIFIED SCHOOL DISTRICT, GRADES K-12, Pr Ex 13.8:Ed 8/7, at $1.75 per copy

G. _____copies of SOUTH BAY UNION SCHOOL DISTRICT, GRADES K-12, Pr Ex 13.8:Ed 8/4, at $1.25 per copy

H. _____copies of TACOMA PUBLIC SCHOOLS, GRADES 6-12, Pr Ex 13.8:Ed 8/6, at 60¢ per copy

54. _____copies of RESOURCE BOOK FOR DRUG ABUSE EDUCATION, PHS Publication No. 1964, Fs 2.22:D 8 4/12, at $1.25 per copy

NOTE: It is recommended that Item No.54 be used in conjunction with the above curricula.

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NATIONAL CLEARINGHOUSE FOR DRUG ABUSE INFORMATION
REPORT SERIES

SERIES 9, No.1 SEPTEMBER 1971

NATIONAL CLEARINGHOUSE FOR DRUG ABUSE INFORMATION
BRIEFING REPORT

The establishment of the National Clearinghouse for Drug Abuse Information was announced in March, 1970 by President Richard M. Nixon in response to the nationwide need for a focal point for accurate and reliable information on drug abuse. The Clearinghouse operates as a central source for the collection and dissemination of drug abuse information within the Federal government and serves as a coordinating information agency for groups throughout the country involved in drug abuse information. The Clearinghouse services diverse groups with varying information needs. Users include physicians, lawyers, pharmacists, teachers, police, government officials, community leaders, concerned individuals, researchers and Federal officials.

The major activities of the NCDAI are distribution of drug abuse information materials, answering of inquiries by mail and phone, referral of specialized requests to appropriate government or private resources, publication of recurring secondary source reference materials and fact sheets, and operation of an up to date and comprehensive computerized information storage and retrieval system. The computer based file provides the data for Clearinghouse resource publications and for response to individual inquiries.

DISTRIBUTION OF GENERAL AUDIENCE DRUG ABUSE INFORMATION MATERIALS

The NCDAI serves as a central distribution point for Federal publications related to drug abuse. Publications of the Bureau of Narcotics and Dangerous Drugs, DOJ, Social and Rehabilitation Service, DHEW, Law Enforcement Assistance Administration, DOJ, and several other agencies are currently being distributed. The Clearinghouse also disseminates information on pertinent films, records, plays, posters, and any other type of material available. The Clearinghouse has developed packets of informational materials suitable for the general needs of the interested and concerned public as well as groupings of publications and films oriented toward a particular topic. The Clearinghouse also provides consultation to groups preparing for a seminar, lecture series, panel discussion or conference in order to assemble the most pertinent and useful materials for the event.

Since its inception, the NCDAI has distributed over 5,000,000 copies of drug abuse publications. The most widely disseminated publication is A FEDERAL SOURCE BOOK: ANSWERS TO THE MOST FREQUENTLY ASKED QUESTIONS ABOUT DRUG ABUSE, produced jointly by the U.S. Departments of Justice; Health, Education, and Welfare; Defense; Labor; and the Office of Economic Opportunity. A Drug Education Curricula Series, produced in cooperation with the Office of Education, is available to educators so that guidelines, representative of various grade levels and communities, for presenting information on drug abuse to students can be shared by schools who are just beginning to implement and develop programs of their own. This series will eventually be replaced by a selected guide to drug education resources, to be developed in cooperation with the Office of Education and other Federal agencies.

Hundreds of films dealing with the issue of drug abuse, have inundated the media and are being provided by their producers to schools and community groups, and the Clearinghouse is involved in several projects concerning the plethora of these films. The Clearinghouse coordinates a loan service for films in cooperation with the National Audiovisual Center. Government films including "The Answer is Understanding", "A Day in the Death of Donny B.", "Are Drugs the Answer?", "Here's Help", "Curious Alice", "What Do Drugs Do?" and other films are available to the public from this collection. Current information on the rental, distribution, and purchase of privately-produced films and films originating from other Federal agencies can be obtained from the Clearinghouse at all times in the form of a listing entitled "Checklist of Recent Films on Drug Abuse."

The NCDAI distributes Selected Drug Abuse Education Films, which is a concise guide to the use of several films on drug abuse. The guide, which is periodically updated, gives pertinent details on how to obtain films for preview, rental, loan or purchase in addition to narrative summaries of content. The film guide also suggests ways to use films in the classroom, appropriate audiences, supplementary materials and ideas for further discussion.

Cataloging and classification is conducted by the Clearinghouse for its film and audio bank of stock scenes on drug abuse. Footage for a complete film bank is continually being added so that broadcasters, filmmakers and other individuals or groups can obtain authentic motion picture or still footage from a comprehensive stockpile.

The NCDAI also publishes "Tune In", a recurring newsletter on drug abuse programming designed to meet the information needs of radio and TV broadcasters. "Tune In" describes broadcasters' activities in the area of drug abuse so that ideas on programs presented on the air, educational television and radio series, or special feature stories can become known to other professionals in the field. "Tune In" features excerpts of evaluations of radio and television materials to facilitate an interchange of program material and ideas among broadcasters.

RESPONSE TO PUBLIC INQUIRIES

The routine distribution of drug abuse publications, in response to public demand, is managed through a complex logistical operation by contractors or staff outside the premises of the Clearinghouse. These requests are usually for specific publications and do not call for any particular expertise in replying. However, the Clearinghouse has already received over 15,000 inquiries which require complex and detailed responses in addition to specialized materials. Inquiries of this nature range from chemists asking for procedures on identifying drugs of abuse in body fluids to community leaders setting up a drug abuse prevention program. These inquiries are received by the Clearinghouse either by mail, visits, direct telephone calls, or through a 24-hour telephone message service.

Specialized inquiries are processed by NCDAI staff members. NCDAI staff maintains close communication with researchers, programs and consultants in the field, and thus remains in touch with change and progress in the drug abuse field. Clearinghouse information specialists have received substantial formal training in drug abuse problems in addition to their prior academic and work experience.

If a request for information requires a thorough search of the literature pertinent to the subject of inquiry, the specialist will utilize the computerized information storage and retrieval system by drawing from either the resource and materials or drug abuse program file. Requests for exhaustive coverage of a topic are processed by completing a computer search and sending the relevant printouts to the inquirer. When the demand for a computer search on a specific topic recurs over a delineated period of time and the subject grows to have a more general audience, the Clearinghouse will publish the most recent and complete version of the search and thereby have it readily available for immediate distribution.

The NCDAI "Selected Reference Series" and "Report Series" are a reflection of these recurring requests for information. The NCDAI "Report Series" is comprised, in part, of a "Drug Series" and a "Modality Series." The "Drug Series" consists of several fact sheets pertaining to individual drugs of abuse for which very little compiled information was previously available. This series is intended for the reader who wishes historical and pharmacological information on, for example, cocaine, methadone, heroin, or mescaline. Each report includes a list of citations from which the issue was prepared.

The "Modality Series" presents various approaches and solutions to drug abuse and drug abuse-related problems. Issues in this series define the concepts inherent in the particular approach being dealt with, and provide examples in the form of descriptions of operating programs. Some issues are Voluntary Action and Drug Abuse: Some Current Highlights; Drug Abuse Treatment and Prevention - Religious Activities and Programs; Methadone Maintenance Programs; and Crisis Intervention: Current Developments.

Other NCDAI "Report Series" concern areas of general interest to people involved in drug abuse activities. For example, one recent issue provides complete information on Federal funding, another entitled Selected Government Materials on Drug Abuse contains abstracts of Federal publications pertaining to drug abuse and yet another describes training opportunities for drug abuse personnel.

The "Selected Reference Series" is a series of bibliographies which are short, representative listings of citations on subjects of topical interest. Each reference series is meant to present an overview of the existing literature but is not meant to be comprehensive nor definitive in scope. For example, some of the reference lists concern the use of drugs by young people, the genetic effects of the drugs of abuse, drug abuse and the military, methadone, and narcotic antagonists.

By observing the frequency of requests for searches of the literature, the Clearinghouse is able to keep attuned to changing information needs, new areas of interest and concern to the public, as well as shifts in currents and trends in the drug abuse field

throughout the country. Development of resource materials is thus tied directly to the demands of the public for topics and types of information.

NCDAI COMPUTERIZED INFORMATION-RETRIEVAL SYSTEM

The NCDAI is the first Federal agency to systematically organize and synthesize the mass of substantive data in the drug abuse field into an operational computerized information storage and retrieval system. The NCDAI system features abstracts or descriptions of books, pamphlets, journal articles, posters, films and other audiovisual materials, as well as descriptions of drug abuse treatment and prevention programs. The system utilizes the IBM developed Document Processing module, an automatic indexing software package available for use with the System 360. The 360/50 enables the increased storage of citations by providing multi-volume access. Searching of the files is initiated by utilization of cathode ray tube and typewriter terminals with printouts of searches accomplished by an off-line high speed printer. This configuration permits direct on-line access to the main NCDAI data base on a time-shared basis by established satellites with compatible terminals.

The NCDAI system is a natural language, whole text processing system which has as its most important feature, the ability to incorporate words appearing in the literature into its vocabulary automatically. The dictionary word entries arise from the most recent literature abstracted or programs described, thereby keeping the entire system updated and free of archaic terms. Searches are formulated by combining the dictionary words into logical statements which retrieve the desired abstracts from the computer.

The NCDAI data base is organized into four main files. First, the Drug Abuse Information Resources and Materials file contains abstracts of documents and audiovisual materials. Scanning of the biomedical, pharmacological, social, and behavioral science literature in addition to more popular and unorthodox publications such as the underground press is conducted on a regular basis. The file contains standard and historically significant works ranging from the LaGuardia Report on Marijuana of 1944 to the Indian Hemp Commission Report of 1893-4, but is essentially composed of the most current studies in the field. The coverage of this file is monitored by comparing its holdings to current materials so that gap areas can be identified and filled.

All computer entries are assigned an indexing code which defines the major subject area within which the document logically falls. Some of these subject areas are: sociocultural aspects of drug abuse; epidemiology; law and public policy; behavioral and physiological effects of drugs; prevention-public education; prevention-public information; psychology; pharmacology; etiology; treatment and rehabilitation and volatile substances. Abstracts can be retrieved by searching on these subject area designations, title, author, year of publication, medium, or by a more complex procedure utilizing Boolean logic.

The NCDAI system is using this computer file to develop an Annotated Bibliography on Drug Dependence and Abuse. The publication will be constructed in a similar fashion to the computer file itself and will categorize references according to the identical major subject areas. The bibliography will be updated intermittently with new versions superseding the former ones. The Annotated Bibliography will be especially helpful to students writing dissertations, law enforcement officials, teachers, or researchers. A preliminary edition, Drug Dependence and Abuse: A Selected Bibliography, has been published and is available on request.

The National Inventory of Drug Abuse Programs file is a comprehensive collection of information on drug abuse programs throughout the country. The demand for searches of this file originates from Federal official program directors, parents in need of consultation, young people looking for treatment situations, teachers starting prevention programs in their schools, or law enforcement officials wishing to set up a training program for their staff. The types of programs described and entered into the computer include treatment, rehabilitation, information, education, training, community action, counseling and supportive programs, law enforcement, prevention and public information programs. Information on programs can be retrieved upon request in many ways including geographic location, type of program, mode of operation, funding source, and sponsoring organization. Each program entry also contains a non-evaluative narrative description written from the materials and reports contributed by the program itself. Included in the narrative description is information on speakers bureaus, staffing services and activities of the program. At the end of each computer entry the materials and publications generated by the program are listed including curricula, pamphlets, annual reports, evaluation studies and films. The entire list of these references is also abstracted and entered into the Drug Abuse Information Resources and Materials file so that they can be retrieved upon request.

The National Inventory of Drug Abuse Programs file is the data base from which the Clearinghouse publication An Annotated Directory of Drug Abuse Programs in the United States will be derived. The Annotated Directory will include several listings of programs according to state, city and type of program as well as narrative descriptions incorporating all the information included in the computer entry for each program. Each drug abuse program is re-surveyed by the NCDAI so as to delete closed-out programs, add newly formed ones, and change outdated information recorded for existing programs. The Annotated Directory will be revised and reissued periodically as new information becomes available.

The Drug Abuse Program Information file includes voluntary action, private, state, regional, county, and local programs with a special portion of the file dedicated to Federal programs. Federal programs can be retrieved through requests for fiscal year starting dates, fiscal year ending dates, contract or grant number, sponsoring Federal agency, or Federal contact for state programs utilizing Federal funds. Narrative descriptions of Federal programs are constructed according to the same principles as non-Federal entries. These descriptions are prepared by participating Federal agencies including the Department of Justice; Department of Defense; Department of Health, Education, and Welfare; Office of Education; Office of Economic Opportunity; Department of Labor; Department of Commerce; and the Department of Agriculture.

The Clearinghouse has completed A Guide to Federal Drug Abuse Programs which lists and describes Federal programs included in the computer data bank. The Guide will be updated continuously.

OUTREACH PROGRAM

The Clearinghouse is currently making presentations on its programs and capabilities in ten cities throughout the country. Following these ten presentations the Clearinghouse will be featured in a closed-circuit TV broadcast designed to reach the education community in thirty-five cities.

NCDAI COMMUNICATIONS NETWORK SYSTEM

The Clearinghouse has initiated its Drug Abuse Information Communications Network System by cooperating with several states and Federal agencies also included in developing information storage and retrieval services. Several agencies are participating in a pilot program to test the network concept, and the system is expected to become a national network of cooperating information centers. States, Federal agencies, and local communities have sent their information specialists to the Clearinghouse for a brief

intensive training course in the techniques of searching and operating the complex of devices employed by the NCDAI staff. Terminals with on-line access to NCDAI information files are established on site for use by the local or state program. The specialists return to their home base of operation with the necessary skills required to operate the terminal and retrieve relevant information.

The type of equipment and training needed for a remote location to obtain access to all 3 NCDAI computer files described above are as follows:

1) Remote location centers would need to rent an IBM 2741 typewriter terminal, teletype terminal, or similar device at a cost to the operating program of approximately $100.00 a month.

2) Phone line cost and installation information would need to be obtained by the local telephone company and the respective hardware vendor.

3) Training of qualified remote location personnel is accomplished at the NCDAI by its technical information staff. Transportation and living expenses during training are provided by the cooperating center.

The conceptual basis of the entire operation rests on the need for the dissemination of information in the drug abuse area and the vast amount of data to be collected and stored. Establishing on-line terminals to the NCDAI data base eliminates duplication of collection and operating efforts and enhances the speed of response-time to individual requests for information. The network concept is presently operating as a test program. Evaluation of the program will determine the extent of expansion of this system to states and major metropolitan areas.

The National Clearinghouse for Drug Abuse Information, operated by the National Institute of Mental Health on behalf of the Federal agencies engaged in drug abuse education programs, is the focal point for Federal information on drug abuse. These Federal agencies are the Department of Justice, Bureau of Narcotics and Dangerous Drugs; Department of Health, Education, and Welfare; Office of Economic Opportunity; and the Department of Defense. The Clearinghouse distributes publications and refers specialized and technical inquiries to Federal, State, local, and private information resources. Inquiries should be directed to the National Clearinghouse for Drug Abuse Information, 5600 Fishers Lane, Rockville, Maryland, 20852.

U. S. GOVERNMENT PRINTING OFFICE : 1972 O - 451-7

QUESTION (4) AMPHETAMINES—NAS/NRC REPORTS ON THE DRUGS NAMED IN THE AUGUST 8, 1970 FEDERAL REGISTER ANNOUNCEMENT

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

Division of Medical Sciences

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number: 11–538 E–01. 2. Date originally approved, April 25, 1961.
3. Rx. 4. Brand Name: Biphethamine-T "12½," Biphetamine-T "20."
5. Applicant's Name and Address: Strasenburgh Laboratories, Div. Wallace & Tiernan Inc., 755 Jefferson Road, Rochester, New York 14623.
6. Quantitative formula:

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.) (milligrams)*
Biphetamine-T "12½":	
Dextro amphetamine	6. 25
Dextro amphetamine	6. 25
Methaqualone	40
ll as cationic exchange resin complexes of sulfonated polystyrene.	
Biphetamine-T "20":	
Dextro-Amphetamine	10
l-Amphetamine	10
Methaqualone	40
ll as cationic exchange resin complexes of sulfonated polystyrene.	

7. Dosage form (tablets, etc.): Biphetamine-T "12½," Black & Green Capsule; Biphetamine-T "20," Black & Red Capsule (2 sizes).
8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.
9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).
10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).) See reverse side.
11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.
12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white). See reverse side.

PANEL ON PSYCHIATRIC DRUGS

Indications

I. Biphetamine-T is indicated for exogenic obesity.

Evaluation: Possibly effective.

Comments: The amphetamines have been evaluated as "Effective, but . . ." as anorectic agents in obesity. The Panel evaluates methaqualone as "Probably effective" as a daytime sedative, similar to such daytime sedatives as barbiturates in the treatment of anxiety. The utility of the combination in the treatment of either condition or both concurrently has not been determined. The drugs might antagonize each other's effects.

In the total absence of positive controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begain to clarify the issue.

A majority of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a

total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight; a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-eating induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

II. Biphetamine-T effects: 10–12 hr of appetite appeasement with mild invigoration and reduction of anxiety.

Evaluation: Possibly effective.

Comments: Inadequate documentation regarding blood levels of the preparation following the use of the sustained-release capsule is available to the Panel; the Panel suggests that further studies be conducted to demonstrate the superiority of the sustained release form to the usual form of administration.

See also comments for Indication I.

Documentation: Clinical experience and judgment of the Panel.

III. Biphetamie-T utilizes as 1:3 ratio of levoamphetamine to dextroamphetamine. This ratio has been shown to have better anorectic activity than the dextroform alone.

Evaluation: Possibly effective.

Comments: Documentation in support of this assertion is inadequate.

Documentation: Clinical experience and judgment of the Panel.

General comments

The Panel suggests the deletion from the package insert of the following unsupported statement: Both the appetite-curbing action of Biphetamine and the calming action of Tuazole (methaqualone) are released simultaneously at a predictable rate.

The Panel suggests the deletion from the package insert of the following statements, which pertain to the individual ingredients of the combination and not necessarily to the combination; these statements should be so phrased that they do not imply that the same individual action occurs with the combination, unless such action can be demonstrated:

Tuazole (methaqualone) has been shown to be a potent and effective calming agent with a low order of toxicity.

Tuazole (methaqualone) has several qualities of both short-acting barbiturates and mephenesin.

As a calming agent, Tuazole (methaqualone) is desirable and lends itself ideally to prolongation through ionic release from its resin complex. These properties make Tuazole ideal for decreasing the hyperactivity associated with amphetamine therapy in some patients.

Approved by Daniel X. Freedman, *Chairman.*

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL
Division of Medical Sciences

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number: 9–946 E–01.
2. Date Originally Approved: April 16, 1956.
3. Rx.
4. Brand Name: DU-ORIA.
5. Applicant's Name and Address: B. F. Ascher & Co., Inc., 5100 East 59th Street, Kansas City, Missouri 64130.
6. Quantitative Formula:

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc. (milligrams)*
Methamphetamine Hydrochloride	10. 0
Reserpine	. 25

7. Dosage Form (tablets, etc.): Tablets.
8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.
9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white). See labelling attached (Exhibit A).
10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).) (Exhibit B).
11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.
12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white). Exhibit C—description of unpublished clinical test of DU-ORIA Tablets and *in vivo* test of sustained release of methamphetamine from DU-ORIA.

PANEL ON PSYCHIATRIC DRUGS

Indications

I. In obesity and weight reduction, in conjunction with prescribed diet, Du-Oria curbs appetite and reduces the tendency to snacking due to tension and nervousness.

Evaluation: Possibly effective.

Comments: Amphetamines have been evaluated as "Effective, but . . ." by the Panel as anorectic agents in obesity. Reserpine has been evaluated as "Possibly effective" as an antianxiety agent; the dose of reserpine used in this combination is so low, however, as to be probably ineffective. If the reserpine does have an effect, the utility of the combination in the treatment of either condition, or both concurrently, has not been determined. The drugs might antagonize each other's effects.

In the total absence of positive controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begin to clarify the issue.

A majority of the Panel evaluated the sympathomimetic stimulants as

"Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight; a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-easting induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

II. Du-Oria is useful also as an adjunct in some cases in which nervousness, tension, and irritability are combined with feelings of depression, anxiety, and lassitude.

Evaluation: Ineffective.

Comments: Reserpine has been evaluated by the Panel as "Possibly effective" as an antianxiety agent, but in this low dosage is considered to be probably ineffective as an antianxiety agent. In addition, there is no evidence for the claimed biphasic effect of this combination as stated in the indication.

Documentation: Clinical experience and judgment of the Panel.

General comments

Inadequate documentations regarding blood levels of the preparation following the use of the sustained-release capsule is available to the Panel; the Panel suggests that further studies be conducted to demonstrate the superiority of the sustained release form to the usual form of administration.

Approved by Daniel X. Freedman, *Chairman.*

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

Division of Medical Sciences

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number: 12-371 E-01. 2. Date Originally Approved: June 30, 1960. 3. Rx.

4. Brand Name: Prelu-Vite®.
5. Applicant's Name and Address: Geigy Chemical Corporation, Ardsley, New York 10502.
6. Quantitative Formula:

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.)*
Phenmetrazine hydrochloride	25 mg.
Vitamin A	2,000 USP units.
Vitamin D	200 USP units.
Thiamin mononitrate, U.S.P	2.0 mg.
Riboflavin U.S.P	2.0 mg.
Niacinamide U.S.P	20.0 mg.
Calcium pantothenate	3.0 mg.
Pyridoxine hydrochloride U.S.P	1.0 mg.
Vitamin B_{12} (cobalamin concentrate)	.5 mcg.
Ascorbic acid	37.5 mg.
Iron (from ferrous fumarate)	5.0 mg.
Calcium (from dicalcium phosphate)	140.0 mg.
Phosphorus (from dicalcium phosphate)	108.0 mg.
Iodine (from potassium iodide)	0.1 mg.
Copper (from cupric sulfate)	1.0 mg.

7. Dosage Form (tablets, etc.): Capsules.
8. Route of Adm. (Oral, etc. Where a new drug application covers differen routes of administration, separate forms should be used): Oral.
9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white). Attached.
10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).) Attached.
11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested. None.
12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white). None.

PANEL ON PSYCHIATRIC DRUGS

Indications

1. Preludin (phenmetrazine hydrochloride) is indicated only as an anorexigenic agent in the treatment of the overweight patient.

Evaluation: Effective, but . . .

Comments: Although the vitamins contained in this combination do not appear to enhance or detract from the anorectic effect of phenmetrazine, there does appear to be some clinical rationale for the inclusion of vitamins in a weight-reduction program, although not necessarily in fixed-dosage combinations.

A majority of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of

the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight; a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-eating induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

Approved by Daniel X. Freedman, *Chairman.*

PANEL ON DRUGS USED IN METABOLIC DISORDERS

Indications

I. Aids weight reduction.

May be used in obesity complicated by diabetes, moderate hypertension, or pregnancy.

Evaluation: Probably effective.

Comments: The addition of multi-vitamin and mineral supplements in this combination preparation is considered effective as a dietary supplement. This addition is probably sound, although scientifically unproved. In complete starvation, a requirement does exist. At the recommended dose of one tablet two to three times a day, the dose provided probably is excessive as a dietary supplement.

The biggest problem relates to the effectiveness of phenmetrazine hydrochloride as an appetite depressant. Although there is some lingering doubt in some investigators' minds, most experts will agree that the sympathomimetic amines do have a pharmacologic depresssant effect on appetite, along with all the other effects. These effects must be appreciated by the physician using them and have often resulted in their abandoment. Certainly, dietary restriction without the use of such "crutches" is to be preferred in any weight-reduction program.

Documentation:

1. Appetite depressants; dextro-amphetamine. Med. Letter 2(#3): 11–12, 1960.

2. Fineberg, S. K. Evaluation of anorexigenic agents; studies with chlorphentermine. Amer. J. Clin. Nutr. 11:509–516, 1962.

3. Preludin. Med. Letter 2(#8):31–32, 1960.

General comments

I. Fortunately, exaggerated claims for Preludin over other agents are carefully avoided in the brochure. However, it does use the terms "relative lack" and "rarely" when referring to side reactions, when in reality reported side effects with Preludin run from 40 to 100%. Most of these are mild, but some degree of sympathetic overactivity is to be expected with any of these agents.

II. See the general statement on multiple-vitamin preparations.

General statement on multiple-vitamin preparations

The Panel does not recognize the need for multi-vitamin supplementation in healthy individuals eating an adequate diet. However, it does recognize the

need for multiple-vitamin and-mineral preparations in certain segments of the population. It also recognizes the lack of precise data on which rational formulation can be based. Therefore, it takes the following position toward all such preparations:

1. All should be appropriately labeled as either "supplemental" or "therapeutic."
2. The formulations of supplemental preparations should be based on dietary allowances recommended either by the Food and Nutrition Board of the National Academy of Sciences or by an equivalent body.
3. Any preparations labeled "therapeutic" should be so formulated so that the physician can prescribe adequate therapeutic amounts without the danger of toxicity.
4. They should not contain disproportionate amounts of any nutrient that could be potentially hazardous in the recommended dosage. The recommended dosage and labeling for any fat-soluble vitamin should include proper warning concerning possible toxicity.
5. They should not contain nonessential materials.
6. The Panel favors the use of oral preparations when feasible.

Approved by Don H. Nelson, *Chairman.*

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

DIVISION OF MEDICAL SCIENCES

DRUG EFFICACY STUDY

Form A

(To be submitted in duplicate by applicant)

1. NDA Number: 11–280 E–01. 2. Date Originally Approved: October, 1957. 3. Rx.

4. Brand Name: BAMADEX® Dextro-amphetamine Sulfate with Meprobamate Tablets.

5. Applicant's Name and Address: Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

6. Quantitative Formula

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.)*
Dextro-amphetamine Sulfate	5 mg./tablet.
Meprobamate	400 mg./tablet.

7. Dosage Form (tablets, etc.) Tablets.

8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.

9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).

10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).)

11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.

12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white).

Indications

I. Bamadex Tablets are useful in the management of obesity, to curb appetite, especially in patients presenting associated emotional problems, such as anxiety and tension.

Evaluation: Possibly effective.

Comments: Although amphetamines have been evaluated as "Effective, but . . . " as anorectic agents in obesity, and meprobamate has been evaluated as

"Effective" in the treatment of anxiety, the utility of the combination in the treatment of either condition or both concurrently has not been determined. The drugs might antagonize each other's effects.

PANEL ON PSYCHIATRIC DRUGS

In the total absence of positive controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begin to clarify the issue.

A majority of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight; a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to cub the increased appetite and over-eating induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thron, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

General comments

The Panel suggests that the following statement in the package insert be modified; the following interaction of the two drugs has not been demonstrated: Bamadex combines the anorectic action of dextro-amphetamine sulfate (5 mg) and the tranquilizing action of meprobamate (400 mg).

Approved by Daniel X. Freedman, *Chairman.*

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

Division of Medical Sciences

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number 12–127 E–01.

2. Date Originally Approved: November 6, 1959.
3. Rx.
4. Brand Name: "Appetrol".
5. Applicant's Name and Address: Wallace Laboratories, Cranbury, New Jersey.
6. Quantitative Formula:

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.)*
Meprobamate	400 mg./tablet.
d-amphetamine sulfate	5.0 mg./tablet.

7. Dosage Form (tablets, etc.) Tablets.
8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.
9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).
10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure, Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original form A (blue) and 1 copy to duplicate Form A (white).)
11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.
12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white).

PANEL ON PSYCHIATRIC DRUGS

Indications

I. Appetrol is useful in the management of obesity, to curb appetite, especially in patients presenting associated emotional problems, such as anxiety and tension.

Evaluation: Possibly effective.

Comments: The single reference provided on the combination does not adequately support its use for this indication.

Although amphetamines have been evaluated as "Effective, but . . ." as anorectic agents in obesity, and meprobamate has been evaluated as "Effective" in the treatment of anxiety, the utility of the combination in the treatment of either condition or both concurrently has not been determined. The drugs might antagonize each other's effects.

In the total absence of positive controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begin to clarify the issue.

A majority of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (2–5). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of

the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Batterman, R. C. Sustained-action amphetamine-meprobamate combination for the treatment of abesity. Curr. Ther. Res. 6:447–453, 1964.

2. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

3. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight; a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

4. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-easting induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

5. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

II. Appetrol combination provides an effective appetite depressant and central-nervous-system stimulant, dextroamphetamine sulfate (5 mg), modified by a tranquilizer, meprobamate (400 mg), which helps counteract excessive central-nervous-system stimulation and relieves the anxiety component frequently found in overweight patients.

Evaluation: Possibly effective.

Comments: Same as for Indication I.

Documentation: Same as for Indication I.

General comments

The Panel suggests the deletion from the package insert of the following statements, which pertain to the individual ingredients of the combination and not necessarily to the combination; these statements should be so phrased that they do not imply that the same individual action occurs with the combination, unless such action can be demonstrated:

Meprobamate has been proved effective in the relief of anxiety and tension states and in related conditions.

A modest calorigenic effect and increased physical activity have been reported, with the use of Dextro-amphetamine sulfate.

Dextro-amphetamine sulfate has essentially no effect on the peripheral vascular system, metabolism, or uterine musculature.

Approved by Daniel X. Freedman, *Chairman.*

National Academy of Sciences—National Research Council

Division of Medical Sciences

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number 12–042 E–01. 2. Date Originally Approved: November 5, 1959. 3. Rx.

4. Brand Name: "Eskatrol" Spansule Capsules.

5. Applicant's Name and Address: Smith Kline and French Laboratories, 1500 Spring Garden Street, Philadelphia, Pennsylvania.

6. Quantitative Formula

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.)*
Dextroamphetamine sulfate	15 mg./capsule.
Prochlorperazine as the maleate	7.5 mg./capsule.

7. Dosage Form (tablets, etc.): Capsules.

8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.

9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).

10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).)

11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.

12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white). 1. Clinical Summary from NDA 12-042 which contains information on studies done in 724 patients. "Eskatrol" was shown to be an effective anorectic agent while producing a minimum of side effects. In addition, "Eskatrol" has been shown to be efficacious for the relief of the anxieties and tensions seen in the obese patient.

PANEL ON PSYCHIATRIC DRUGS

Indications

I. Eskatrol Spansule Capsules are indicated in overweight patients, particularly in those who depend on food for psychologic release.

Evaluation: Possibly effective.

Comments: Amphetamines have been evaluated as "Effective, but . . ." in the treatment of obesity. Prochlorperazine is considered to be "Possibly effective" as an antianxiety agent (see Compazine Tablets, Log 1740, comments for Indication I). The utility of the combination in the treatment of either anxiety or obesity, or both concurrently, has not been determined. The drugs might antagonize each other's effects.

In the total absence of positive controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begin to clarify the issue.

A majority of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight; a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-eating induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

II. Eskatrol Spansule Capsules provide daylong control of appetite and help relieve emotional stress associated with overeating and with dieting.

Evaluation: Possibly effective.

Comments: Inadequate documentation regarding blood levels of the preparation following the use of the sustained-release capsule is available to the Panel; the Panel suggests that further studies be conducted to demonstrate the superiority of the sustained release form to the usual form of administration.

Documentation: Clinical experience and judgment of the Panel.

III. The desire to eat is reduced and patients, particularly the so-called "compulsive eaters," feel better and are able to adjust to the weight-reducing program—even for long periods.

Evaluation: Possibly effective.

Comments: The Panel considers the wording of the indication to be excessive and suggests it be modified.

See also comments for Indication I.

General comments

The Panel has additional reservations about this preparation. The package insert does not sufficiently stress that Eskatrol is a short term adjunct, as is pointed up in the literature. The sustained-release form for this combination has not been adequately documented, compared with other dosage forms given at the same dose.

In addition, prochlorperazine is known to stimulate appetite and cause weight gain; the possibility arises that its presence in the combination may detract from the anorectic effect of the amphetamine.

Approved by Daniel X. Freedman, *Chairman.*

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

Division of Medical Sciences

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number: 10–207 E–01. 2. Date Originally Approved September 27, 1956. 3. Rx.

4. Brand Name: Dexserpine "5" Tablets.

5. Applicant's Name and Address: Nysco Laboratories, Inc., 34–24 Vernon Boulevard, Long Island City, New York.

6. Quantitative Formula:

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.) (milligrams)*
Reserpine Alkaloid	0. 1
Dextro-Amphetamine Sulfate	5

7. Dosage Form (tablets, etc.): Tablet.

8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.

9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).

10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to orlginal Form A (blue) and 1 copy to duplicate Form A

(white).) We have no additional information than that submitted with our original application.

11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.

12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white). None.

PANEL ON PSYCHIATRIC DRUGS

Indications

1. Dexserpine "5" is indicated as an appetite depressant in the treatment of obesity.

Evaluation: Possibly effective.

Comments: Amphetamines have been evaluated as "Effective, but . . ." by the Panel as anorectic agents in obesity. Reserpine has been evaluated as "Possibly effective" as an antianxiety agent; the dose of reserpine used in this combination is so low, however, as to be probably ineffective. It the reserpine does have an effect, the utility of the combination in the treatment of either condition, or both concurrently, has not been determined. The drugs might antagonize each other's effects.

In the total absence of positive controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begin to clarify the issue.

A majority of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264–501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle. The mechanism of amphetamine-induced loss of weight: a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-eating induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

Approved by Daniel X. Freedman, *Chairman.*

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

DIVISION OF MEDICAL SCIENCES

DRUG EFFICACY STUDY

Form A—(To be submitted in duplicate by applicant)

1. NDA Number: 12–415 E–01. 2. Date Originally Approved: July 28, 1960.
3. Rx.
4. Brand Name: Delfetased Stedy tabs.
5. Applicant's Name and Address: Eastern Research Laboratories Incorporated, 302 South Central Avenue, Baltimore, Maryland.
6. Quantitative Formula.

Established (Non-Proprietary) Name of Active Ingredients (in order shown on label)	*Amount (per tablet, per ml., etc.) (milligrams)*
Methamphetamine Hydrochloride	30. 00
Amobarbital	120. 00
Cacia	10. 11
Pharmaceutical Glaze	4. 76
Stearic Acid	33. 11
Talc	11. 34
Gelatin	4. 53
Cane Sugar	46. 09
Corn Starch	50. 06
Calcium Carbonate	16. 17
Magnesium Stearate	5. 18
Dicalcium Phosphate q.s	187. 03
S.D.C. Emeral Green Color	. 02
Total	518. 40

7. Dosage Form (tablets, etc.): Sustained Release Tablets.
8. Route of Adm. (Oral, etc. Where a new drug application covers different routes of administration, separate forms should be used): Oral.
9. Therapeutic Claims—Attach 10 labels and 10 package inserts (if used) to original Form A (blue) and 1 copy to duplicate Form A (white).
10. List of literature references most pertinent to an evaluation of the effectiveness of the drug for the purposes for which it is offered in the label, the package insert, or brochure. Approximately 5 to 10 key references are requested, if available. (Attach 10 copies to original Form A (blue) and 1 copy to duplicate Form A (white).)
11. The applicant is invited, if he so desires, to submit any unpublished material that is pertinent to the evaluation of the drug by the Academy—Research Council. This supplementary material should be packaged with Form A (white). A single copy of this material is requested.
12. In this space, please list and describe briefly the supplementary material that is submitted with Form A (white).

PANEL ON PSYCHIATRIC DRUGS

Indications

1. Delfetased Stedy Tabs are indicated for obesity.

Evaluation: Possibly effective.

Comments: Although methamphetamine has been evaluated as "Possibly effective" in the treatment of obesity and amobarbital has a definite effect as a daytime sedative, the use of the combination in either anxiety or obesity, or both concurrently, has not been determined. The drugs might antagonize each other's effects. In the total absence of controlled studies, the combination is evaluated as "Possibly effective." Basic studies, beginning in the animal, of the interaction of the anorectic and tranquilizing effects of the two drugs in this combination are necessary to begin to clarify the issues.

This drug is apparently similar pharmacologically to dextroamphetamine. On the basis of the presumed pharmacologic similarity, it may have a similar effect, although documentation of efficacy of this drug for this indication is meager. There is, however, inadequate direct supporting evidence for its use for this indication. The preferential abuse of methamphetamine, compared with dextroamphetamine, raises some suspicion that it is different pharmacologically

from the parent compound, dextroamphetamine. Additional studies on this compound for this indication are necessary.

A majorty of the Panel evaluated the sympathomimetic stimulants as "Effective, but . . ." as anorectic agents, with the following comment. Sympathomimetic stimulants as a class have been shown to have a generally short-term anorectic action. Anorectic agents suppress appetite. They are not a treatment of obesity in themselves and should be used primarily as an adjunct to a total program of weight reduction for obese patients that includes patient education, motivation calorie restriction, and exercise. The anorectic effect of anorectic agents often plateaus or diminishes after 4–6 weeks (1–4). The dosage of drug must be individually titrated and given at least 1 hr before meals.

Clinical opinion as to the contribution of the sympathomimetic stimulants in a weight-reduction program varies widely. Most studies of these preparations are for short periods. The Panel suggests that controlled studies of the long-term effects of the sympathomimetic stimulants in weight-reduction programs be conducted. These preparations have a significant potential for drug abuse.

A minority of two of the Panel members agreed with the above comment of the majority of the Panel, but evaluated the sympathomimetic stimulants as "Probably effective" as anorexiants. Their reasoning for the "Probably effective" evaluation was that: (a) most studies of these preparations have been for short periods, (b) there is no available evidence that the use of these anorexiant preparations alters the natural history of obesity, (c) there is some evidence that anorectic effects may be strongly influenced by the suggestibility of the patient, and (d) there are reservations about the adequacy of the controls in some of the clinical studies. The minority suggested that controlled studies on the long-term anorectic efficacy of the sympathomimetic stimulants be conducted.

Documentation:

1. Fazekas, J. F. Anorexigenic agents. New Eng. J. Med. 264:501–503, 1961.

2. Harris, S. C., A. C. Ivy, and L. M. Searle, the mechanism of amphetamine-induced loss of weight: a consideration of the theory of hunger and appetite. J.A.M.A. 134:1468–1475, 1947.

3. Kinard, S., L. C. Mills, J. Terrell, and J. H. Moyer. Use of d-amphetamine to curb the increased appetite and over-eating induced by reserpine therapy. J. Amer. Geriat. Soc. 4:1073–1077, 1956.

4. Thorn, G. W., and P. K. Bondy. Obesity, p. 398. In T. R. Harrison, R. D. Adams, I. L. Bennett, Jr., W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, Eds. Principles of Internal Medicine. (5th ed.) New York: McGraw-Hill Book Co., 1966.

II. Delfetased Stedy Tabs are indicated for a completely logical synergistic combination of wide application as a mood normalizer for the common depressed states encountered in every day practice.

Evaluation: Possibly effective.

Comments: The Panel suggests the deletion from the indication of the unwarranted phrase "a completely logical synergistic." The Panel is unaware of any antidepressant activity of amobarbital: the Panel evaluated methamphetamine as "Possibly effective" in the treatment of mild depression. In the absence of any specific controlled documentation in support of the combination's effectiveness, the Panel evaluates Delfetased Stedy Tabs as "Possibly effective," and suggests that additional controlled studies be conducted.

This drug is apparently similar pharmacologically to dextroamphetamine. On the basis of the presumed pharmacologic similarity, it may have a similar effect, although documentation of efficacy of this drug for this indication is meager. There is, however, inadequate direct supporting evidence for its use for this indication. The preferential abuse of methamphetamine, compared with dextroamphetamine, raises some suspicion that it is different pharmacologically from the parent compound, dextroamphetamine. Additional studies on this compound for this indication are necessary.

Controlled studies provide little basis for the use of amphetamines in depressive states. Amphetamines have been used in a wide variety of mood disorders, fatigue, and hard-to-define emotional states. In general clinical experience, the euphoriant and antifatigue effects of these drugs are occasionally useful in self-limited situational crises to hasten the natural recovery of the patient, but not usually in overt depression. The widespread abuse of these drugs, however, stems from these identical properties.

Although possible effects of these drugs in reducing fatigue and increasing euphoria would appear to make them ideal for treating depressive states, in many cases of depression these drugs cause an increase of agitation and tension, rather than an amelioration of the depression. Amphetamines are therefore not the treatment of choice in depressive states, except in self-limited alterations of mood. It is possible that these drugs are effective in some patients, depressed or nondepressed, but the characteristics of patients clinically benefited by amphetamines have not been adequately defined.

The Panel considers these drugs to be possibly effective in the treatment of mild depressive states, as well as for the production of euphoria. The Panel emphasizes that amphetamines are not the treatment of choice for depression, other than as an elevation of mood that is self-limited.

Documentation:

1. General Practitioner Research Group. Dexamphetamine compared with an inactive placebo in depression. Practitioner 192:151–154, 1964.

2. Gottlieb, J. S., and F. E. Coburn. Psychopharmacologic study of schizophrenia and depressions; intravenous administration of sodium amytal and amphetamine sulfate separately and in various combinations. Arch. Neurol. Psychiat. (Chicago) 51:260–263, 1944.

3. Overall, J. E., L. E. Hollister, A. D. Pokorny, J. F. Casey, and G. Katz. Drug therapy in depressions; controlled evaluation of imipramine, isocarboxazide, dextroamphetamine-amobarbital, and placebo. Clin. Pharmacol. Ther. 3:16–22, 1962.

4. Thal, N. Cumulative index of antidepressant medications. Dis. Nerv. Syst. 20:197–206, 1959.

General comments

The Panel suggests the deletion from the package insert of the following vague and unjustified statements:

Delfeta-sed induces a serene outlook without excessive tranquility.

The patient is alert but composed, free from emotional peaks and thoughts with Delfeta-sed.

Delfeta-sed relieves anxiety which is a part of every illness.

In obesity: The dieting obese sometime experience emotional problems as secondary symptoms resulting from restricted food intake: anxiety, depression, irritability and tension. Subjective relief is accomplished with Delfeta-sed.

The mood is altered to promote optimism and impart a cheerful sense of energy and well-being with Delfeta-sed.

The Panel is unaware of any conclusive evidence of superiority of the sustained-release preparations to the usual forms of administration.

Approved by Daniel X. Freedman, *Chairman.*

(Additional questions submitted to John E. Ingersoll were marked "Exhibit No. 10", their response was marked "Exhibit No. 11" and is as follows:)

Exhibit No. 10

FEBRUARY 16, 1972

JOHN E. INGERSOLL, *Director, Bureau of Narcotics and Dangerous Drugs, Washington, D.C.*

DEAR MR. INGERSOLL: During the Subcommittee's February 7, 1972 amphetamine hearing, several questions arose which I believe your Bureau should be able to answer:

(1) What was the total 1971 production of Preludin, in kilograms and dosage units?

(2) What were the total amphetamine and methamphetamine reserves as of December 4, 1971, in kilograms and dosage units?

(3) Was the availability of these stockpiles a factor in the February 8, 1972, recommendation of 80% reduction over 1971 production? Explain?

(4) Did BNDD instruct industry to include a 50% reserve in their 1972 quota requests? If so, explain.

(5) Please explain the discrepancy in the following sets of BNDD production figures.

(a) BNDD figures submitted to Congressman Paul Rogers, February 1, 1972:

	1969	1970	1971 (Est.)
amphetamine	16,548 kg	14,575 kg.	9,356 kg.
(10 mg.)	(1,654,770,100)	(1,457,459,800)	
methamphetamine	8,449 kg.	6,087 kg.	4,926 kg.
(10 mg.)	(844,447,800)	(608,733,200)	

(b) BNDD's Annual Production Survey of Stimulant and Depressant Bulk Chemicals, May 22, 1971, Table II:

	1969	1970
amphetamine	34,474 kg.	27,154 kg.
10 mg.)	(3,447,400,000)	(2,715,400,000)
methamphetamine	11,718 kg.	6,799 kg.
(10 mg.)	(1,171,600,000)	(680,000,000)

I am certain that your testimony will be a valuable contribution to our investigation and I look forward to your appearance before the Subcommittee. If you have any questions, please refer them to Ms. Mathea Falco, Staff Director and Chief Counsel, or John M. Rector, Deputy Chief Counsel, at 225–2951.

Sincerely,

BIRCH BAYH,
Chairman.

Exhibit No. 11

U.S. DEPARTMENT OF JUSTICE,
BUREAU OF NARCOTICS AND DANGEROUS DRUGS,
Washington, D.C., April 5, 1972.

HON. BIRCH BAYH,
Chairman, Subcommittee to Investigate Juvenile Delinquency, Committee on the Judiciary, U.S. Senate, Washington, D.C.
(Attention of Mr. John Rector.)

DEAR SENATOR BAYH: This is in response to your recent request for answers to five questions which you have posed with regard to amphetamine and preludin quotas in your letter of February 16. This information was not previously forwarded inasmuch as the hearing was indefinitely postponed shortly after the receipt of your letter. Each question has been answered in an individual attachment with an appropriate heading.

We shall continue with our preparation of answers to your questions concerning barbiturates for presentation at such times as the postponed hearing is rescheduled.

Sincerely,

JOHN E. INGERSOLL,
Director.

"What was the total 1971 production of Preludin (Phenmetrazine hcl) in kilograms and dosage units?"

In 1971 the Fher Corporation produced 2,455 kilograms of the phenmetrazine base. They converted this to 2,763 kilograms of the salt, phenmetrazine hydrochloride. This was, in turn, formulated into dosage units by Geigy Pharmaceuticals as follows:

25 milligram tablets	51,000,000
50 milligram tablets	19,500,000
75 milligram tablets	45,000,000
Total dosage units	115,500,000

"What were the total amphetamine and methamphetamine reserves as of December 4, 1971, in kilograms and dosage units?"

There was no prior legal reporting requirement; therefore, this information was not available at the time the quotas were set. An investigative program has been formulated to determine this figure by June 30, 1972. This program will consist of visits by BNDD agents to all registered manufacturers of amphetamine products, including those dosage form manufacturers who have received procurement quotas. In addition, we will visit all persons who have been registered in Schedule III as manufacturers of amphetamine and have not applied for procurement quotas or registration as Schedule II amphetamine manufacturers.

These visits will be directed at obtaining a complete determination of the quantity of amphetamine products in stock and in the manufacturing "pipeline". They will also enable BNDD to enforce the new security requirements and ensure that all firms are adequately registered. Those firms that do not comply will be considered as candidates for action against their BNDD registration.

When this information has been compiled, the quotas will be revised to reflect the amphetamine products currently stockpiled.

"Was the availability of these stockpiles a factor in the February 8, 1972, recommendation of 80% reduction over 1971 production?"

The Bureau calculated the 1972 aggregate production quotas by taking 1971 dispositions by domestic manufacturers (excluding 1971 exports) and reducing this by a factor of 70%, which factor was put forth by the Surgeon General of the United States as amount of past production which exceeded legitimate domestic needs under currently accepted medical practice. This computation gave us the estimated 1972 needs for domestic consumption. As a result of the withdrawal of an application of registration to export amphetamines by Pennwalt Corporation, there were no requests for production in 1972 for export purposes. Thus, no quantities were allocated for 1972 export purposes. An additional small quantity was allocated for production for conversion into drugs controlled in other schedules or not controlled under the law.

Upon totaling the estimated 1972 domestic consumption, the quotas needed for 1972 export purposes (none), and the estimates for production for conversion of other drugs, we were able to estimate the 1972 net disposal of amphetamine. This figure was then increased by 50% in order to provide a stockpile for reserves sufficient to last six months. The result was the total estimated gross manufacturing needs in 1972. This was the figure which has been published as the aggregate production quota for 1972.

In allocating this figure among amphetamine manufacturers, existing stockpiles are taken into account. If a manufacturer's existing stockpiles are taken into account. If a manufacturer's individual share of total production is 1,000 kilograms, this is considered his gross quota. The manufacturer must deduct from this quota all existing inventories in order to compute his net quota, that is, the quantity he will be allowed to produce during 1972 in addition to his stocks on hand. In many cases, the net quota will be zero, and there will be no production during 1972 by some manufacturers.

Existing stockpiles are applied against individual manufacturing quotas, and not against the aggregate production quota, in order to distribute quotas fairly. It is possible for one company to have inventories sufficient to supply the entire domestic needs, while another firm has virtually no stocks on hand. If this inventory situation were used to offset the aggregate quota, the first company would be given a monopoly. Instead, we will permit the second firm to produce enough to supply its fair share of the market.

Therefore, it should be understood that actual production of stimulants during 1972 will probably be far less than the aggregate production quota established by the Bureau.

"Did BNDD instruct industry to include a 50% reserve in their 1972 quota requests?"

The application for individual manufacturing quotas requested the manufacturer to estimate his net disposal for 1972 and then to request his quota for 1972. The second item could include up to 50% of his estimated net disposal for inventory reserves. The Bureau did not instruct the industry to include inventory reserves of 50%, but allowed them to include up to this level on their application. The Bureau was able to use this application to evaluate the inventory which was requested by the firms.

A copy of the application form and instructions follow:

APPLICATION FOR INDIVIDUAL MANUFACTURING QUOTA FOR A BASIC CLASS OF CONTROLLED SUBSTANCE

SEE INSTRUCTIONS ON REVERSE

NAME AND ADDRESS OF APPLICANT *(Include no., street, city, state and ZIP code)*

CALENDAR YEAR

NAME OF SUBSTANCE

SCHEDULE NUMBER

BNDD REGISTRATION NO.

BNDD CONTROLLED SUBSTANCE NUMBER

	CURRENT YEAR		1ST PRECEDING YEAR		2ND PRECEDING YEAR	
	Actual Quantity Alkaloids and Salts (Grams)	*Anhydrous Base Content (Grams)*	*Actual Quantity Alkaloids and Salts (Grams)*	*Anhydrous Base Content (Grams)*	*Actual Quantity Alkaloids and Salts (Grams)*	*Anhydrous Base Content (Grams)*
1a. Authorized Manufacturing quota (if any)						
1b. Actual or estimated amount manufactured						
2. Actual or estimated net disposals						
3. Actual or estimated inventory allowance						
4. Actual or estimated inventory as of Dec. 31						

5. Estimated Net Disposal for calendar year for which quota is requested: Grams

6. Quota requested Grams

7. Remarks:

SIGNATURE OF APPLICANT

DATE

TITLE OF APPLICANT

FOR BNDD USE ONLY

APPROVED FOR: GRAMS

APPROVED BY

DATE

BND FORM (AUG 1971) - 189

SUPERSEDES BND-189, (11/69), WHICH IS OBSOLETE.

INSTRUCTIONS (FORM BND 189)

(a) Any person who is registered to manufacture any basic class of a controlled substance listed in Schedule I and II, and who desires to manufacture a quantity of such class, shall apply on Form BND 189, "Application for Individual Manufacturing Quota for a Basic Class of Controlled Substance", for such manufacturing.

(b) A separate application on Form BND 189 must be made for each basic class to be manufactured.

(c) Each applicant will insert the name and address of the registrant, along with the other required information at the top of Form BND 189.

(d) Each applicant shall complete Item Nos. 1, 2, 3 and 4 for the current year and the two preceding years.

(e) The term "net disposal" means the quantity of a basic class of controlled substance sold, exchanged, given away, used in the production of another substance (whether a controlled substance or not), contained in or combined with other substances, or otherwise consumed by or transferred to another person by the registrant during a stated period, less the quantity returned to the registrant by any purchaser and the quantity sold or transferred by the registrant to another registered manufacturer of the same basic class of controlled substance.

(f) The term "inventory allowance" is that amount sufficient to maintain an inventory equal to (1) for current manufacturers, 50 percent of his average estimated net disposal for the current calendar year and the last preceding calendar year; or (2) for new manufacturers, 50 percent of his reasonable estimated net disposal for the next calendar year, as determined by the Director.

(g) Each applicant shall denote his estimated net disposal for the calendar year for which quota is requested in Item 5 and his requested manufacturing quota for the basic class desired in Item 6.

(h) Each applicant may insert any additional factors which he finds relevant to the fixing of his manufacturing quota in Item No. 7, including the trend of (and recent changes in) his and the national rates of net disposal, his production cycle and current inventory position, the economic and physical availability of raw materials for use in manufacturing and for inventory purposes, yield and stability problems, potential disruptions to production (including possible labor strikes) and recent unforeseen emergencies such as floods and fires.

(i) Each application shall be signed by the registrant, if an individual; by a partner, if a partnership; or by an officer of the firm, if a corporation. Another person may sign for the registrant, if proof of authority (e.g., general power of attorney) is on file with BNDD.

(j) Each applicant for a manufacturing quota for a basic class of controlled substance must be filed on or before May 1 of the year preceding the calendar year for which the manufacturing quota is being applied, with the Distribution Audit Branch, Bureau of Narcotics and Dangerous Drugs, Department of Justice, Washington, D.C. 20537.

"Please explain the discrepancy in sets of BNDD amphetamine production figures submitted to Congressman Rogers on February 1, 1972, and those contained in the BNDD Production Survey dated May 22, 1971."

The 1969 and 1970 data for amphetamines and methamphetamines found in Table II of BNDD Annual Production Survey, dated May 22, 1971, was (in the absence of any legal obligation to report to BNDD) collected on a voluntary basis from those firms known to be involved in licit production and importation. The Annual Survey data for the most part is expressed in terms of kilograms of the various salts. These salts such as hydrochloride and sulfate are the forms which are converted directly into the pharmacologically active dosage units.

The data for the same years furnished to Congressman Paul Rogers on February 1, 1972, were derived from legally required BND forms submitted by the firms requesting 1972 manufacturing quotas for these basic classes of controlled substances. These figures are expressed in kilograms of the anhydrous alkaloid or base. The base is convertible to many different salts at varying ratios. (See attachment for list of reciprocals.)

It should be recognized that the two previously mentioned sets of data on the base material and the usable drug salts are not comparable. Moreover, we can only speculate as to the number of dosage units either will finally result in and it is presently more realistic to conclude that a certain number of 10 mg dosage units can be produced from a given amount of the *salts* (as opposed to the base). However, this speculation will not be necessary when in the future persons requesting procurement quotas will be also required to submit exact number of dosage units produced in previous years.

CONVERSION FACTORS FOR AMPHETAMINE, METHAMPHETAMINE AND THE MORE COMMON SALTS IN SCHEDULE II OF THE CSA OF 1970

(1) Substance	(2) To Anhydrous alkaloid	(3) Reciprocal
Amphetamine adipate	0.4896	2.0809
Amphetamine aspartate	.5039	1.9844
Amphetamine phosphate, monobasic	.5797	1.724
Amphetamine phosphate, dibasic	.7339	1.625
Amphetamine resin complex, resinate	.3900	2.564
Amphetamine saccharate	.3915	2.554
Amphetamine succinate	.5339	1.873
Amphetamine sulfate, dibasic	.7339	1.3627
Amphetamine sulfate, monobasic	.5797	1.725
Amphetamine tartrate	.4740	2.110
Methamphetamine hydrochloride	.8035	1.245
Methamphetamine potassium saccharate	.4151	2.409

In making conversions of narcotic salts to their equivalency in anhydrous alkaloids, multiply the quantity of the individual salt by the factor shown in column 2 opposite that particular salt. To determine the quantity of a designated salt which a given quantity of anhydrous alkaloid represents, multiply the quantity of the anhydrous alkaloid by the reciprocal shown in column 3 opposite that particular salt.

Senator BAYH. I would like to make one change in the order of our witnesses. Dr. Edward A. Wolfson, I understand, has a plane to catch.

Dr. Wolfson, if you would come forward now, we will try to make it possible for you to meet your schedule.

Dr. Wolfson is associate professor and vice chairman of the Department of Preventive Medicine and Community Health and director of the Division of Drug Abuse at the New Jersey College of Medicine and Dentistry, Newark, N.J.

I understand, Doctor, you are appearing on behalf of American Public Health Association. We appreciate your taking the time to be with us.

STATEMENT OF EDWARD A. WOLFSON, M.D., M.P.H. ASSOCIATE PROFESSOR AND VICE CHAIRMAN, DEPARTMENT OF PREVENTIVE MEDICINE AND COMMUNITY HEALTH, NEW JERSEY COLLEGE OF MEDICINE AND DENTISTRY, NEWARK, N.J., ON BEHALF OF THE AMERICAN PUBLIC HEALTH ASSOCIATION

Dr. WOLFSON. Thank you, Mr. Chairman. Shall I read this statement now, sir?

Senator BAYH. You may handle it anyway you want. Read it or excerpt it. Proceed as you wish.

Doctor, inasmuch as you do have a scheduled flight we could put your entire statement in the record as if it had been read. You can highlight your principal concerns, and then we can develop it further through dialog.

Dr. WOLFSON. That will be fine, Senator.

At long last there appears to be little or no debate that the central nervous system stimulant group of drugs has an inordinately high abuse potential. I would like to make the point, that there are other stimulants and chemicals such as methylphenidate (Ritalin) and phenmetrazine (Preludin), which neuropharmacologically mimic and parallel the action and abuse potential of the amphetamines. Therefore, we should be discussing this group in its entirety. If we decrease production of one of the stimulants while we retain present production levels of the others, I do not think we are getting to the generic issue, and I raise it for that reason.

I do not believe we have the necessary facts to give a definitive figure on a quota. If we make the assumption that there is some legitimate medical use for short-term treatment for obesity——

Senator BAYH. Well, Doctor, are you, as a physician, making the assumption that there is no legitimate short-term use?

Dr. WOLFSON. No, sir; I believe that there is. Speaking as a practicing physician, and I did practice internal medicine for 12 years. I did use amphetamines, I hope wisely and with judgment. There are instances where the short-term treatment may be quite effective, as an example for excessive weight gains during pregnancy. Excessive weight gains during pregnancy can bring on the risks of not only maintaining the weight after pregnancy but also in hypertension, a difficult delivery et cetera, and difficulty birth delivery itself, and I think in instances such as this, and in the short-term use with selected patients, with hypertension, some cardiacs, and in some diabetics. The anorectics might prove to be quite effective.

To my knowledge, in all of the trials that have been done, whether they have been controlled or uncontrolled using the amphetamine group for a short period of time, they have resulted in more of a weight loss than using a placebo. On the other hand, we have to realize that a trial is a little different than treating a chronic disease. The stimulative effect of the drug itself may have resulted in a bias that the patient was not aware of. As for long-term treatment, I am sure we all agree that obesity is a chronic and lifetime disorder for the most part, and there is no place for the stimulant group.

Senator BAYH. Is it true that those with a cardiac problem or

pregnant who might profit from the use of these pills constitute a very small minority of those who presently use amphetamines?

Dr. Wolfson. I agree, Senator. Historically, the medical profession has demanded the right of medical decisions and is against regulation or intervention. With the stimulants, it is my bias that we have certainly gone beyond that point. Certainly the precedent of regulation has been set with other substances such as the opiates. The weight of medical and/or scientific evidence is that for the average obese patient, who has a chronic problem which is determined by social and psychological factors for the most part, that there is no good indication for the use of the so-called anorectics. However, even assuming that we allow proper medical judgment to use this group of drugs for some of these patients, certainly there is for two much of the amphetamines available. I think perhaps the better way to handle this, at least from my own prospective, is to opt for some type of reasonably strict regulation rather than complete prohibition for the short-term treatment of obesity. If we use a very strict type of regulation, such as I think is going to be done, the majority of patients and society generally will benefit. Physicians are finally becoming aware that this group is every bit as pernicious as the narcotic group in its abuse potential. We sometimes do not look at things very scientifically, I am afraid, and I hope that physicians will become aware that those other substances I mentioned have the same potential dangers.

Senator Bayh. Well, Preludin and Ritalin, of course, have been put on the schedule II, and I understand within the next month or so production controls will be established for these two substances. So, I think your point is well taken. If we cannot see that each of these substances are treated with the same kind of safeguards, we're merely going to shift abuse from one drug to another.

Dr. Wolfson. I am very glad to hear about the controlled production to be placed on these other substances—and I hope on similar others that might follow. Additionally, all of us must realize that chronic and high dosage use of oral amphetamine substances may be every bit as dangerous as mainlining the drug, that is; the "speed" scene. I think many people have not jumped the gap, so to speak, and think of the oral use as being relatively safe, whereas it is the intravaneous use only which is dangerous.

Senator Bayh. Could you expand on that a bit, because I think you are hitting a very important point. And, at least from the standpoint of social acceptability, it is a horrible thing to think about shooting amphetamines. In fact, I was talking, within the last couple of weeks, with the chairman of the board of a major drug company, trying to explore the possible abuse of various products, and that person seemed unaware that any of this substance was being shot intravenously. On the other hand, I suppose there is a higher degree of tolerance or acceptability, as long as they are taken orally. Could you elaborate doctor?

Dr. Wolfson. I think you have just about said it, Senator Bayh. We have accepted the notion, if you will, of "recreational pharmacology"; that is, we accept the use of some chemicals not only because they might relieve pain or other significant symptoms, help us

with a particular diagnostic problem, or with the treatment of disease, but because in some instances the effect is pleasurable. Just think of the favorite American pastime, the cocktail party. This is certainly "recreation through chemistry." In accepting the self-prescribing of substances in our society, it seems to be all right to be using a so-called "legitimate" drug. Going beyond it, what does this legitimate drug do? We know the amphetamines have a fantastic abuse potential. There is much debate as to whether the effect of the amphetamine group is primarily to decrease appetite or whether it has its effect mainly by the euphoria that it might produce, the increased activity, the irritability, or whatever. We apparently accept this, but unfortunately we often get trapped. We think of the drug scene as an outside phenomenon with the "other" people being involved. You know, the "junkie" uses a drug. And we picture the speed scene and the horrors of mainlining amphetamine. But regardless of the route of administration, it is the same drug, and pharmacologically, of course, it does the same thing. The major difference is that initial "rush" or "flash" that occurs when you mainline a drug. Basically, the user of intravenous drugs is using them not only for their pharmacological effect but also for that tremendous rush or so-called organism that he gets during the first few moments. Unfortunately, society does accept the fact that it is permissible to use certain dangerous chemicals orally. We do not accept using intravenous drugs in general and I think we liken it to the mainlining of heroin. Perhaps some think of the "speed" scene as being quite different than the heroin scene, but it is really quite similar. More importantly, we have people caught up with the oral amphetamine scene who have every bit as difficult a problem. Just one example might serve to illustrate. Recently, a chemical model of an acute psychosis has been induced in volunteers by the hourly oral administration of amphetamine in usual doses. Within 24 hours in some patients and within 5 days in every case the acute psychotic episodes were very much like an acute schizophrenia.

Senator Bayh. What is an example of an acute condition?

Dr. Wolfson. Usually it is a paranoid type of schizophrenia. The volunteer initially experiences an initial stimulant effect with the first few doses of medication—and note here I call it a "medication" here and not a drug—that is part of our hang-up—he will be excited and irritable as you might expect with high dosage amphetamine use. And then there seems to be a bit of a lull before the storm, and the person in every instance seems to withdraw into themselves and become rather suspicious. Sometimes, one notes overt, repetitive activity which seems rather unappropriate. He continues to withdraw and perhaps feels that the FBI is after him.

Senator Bayh. Does that require drugs? [Laughter.]

Dr. Wolfson. That is well put. Well, all right. So, his wife is after him or whatever. He might cower in the corner and be completely psychotic at that moment, an absolutely frightening chemical model of psychosis. Fortunately the psychotic effects in the volunteer have been transient, lasting from hours to a few days.

Incidentally, that is one of the reasons, Senator, as a physician I would not like to see an absolute ban on this type of drug. I think

that controlled research of this type could be of tremendous value. Indeed, it might give us some of valuable leads to the chemical control of schizophrenia.

Senator BAYH. What are your thoughts relative to the history and possibility of "diet pill" addiction when used only orally?

Dr. WOLFSON. It is every bit as high, I believe, if the drug is used long enough in high enough dosages. I think this has been well documented.

Senator BAYH. You say "long enough and high enough dosages." What are we talking about, Doctor?

Dr. WOLFSON. We know that tolerance sets in quite rapidly with the amphetamine substances, and that would include the Ritalin, Preludin, et cetera. That is, the effects that the person apparently is looking for requires higher and higher dosages of the drug—very much like with the opiates. Tolerance to amphetamines occurs very rapidly, certainly within a matter of weeks to months. In order to get the increased euphoria, augmented energy, or "high"—or whatever the person needs and is taking the drug for—higher and higher dosages will be used. Sometimes absolutely phenomenal doses are utilized—doses up to perhaps 100 times the dosage that is normally taken therapeutically. When one uses dosages of that magnitude for any period of time, we undoubtedly mimic the situation described in the chemical model of acute psychosis. With "side-effects," you almost wonder if they are indeed side effects or if they are actually the true effects of this particular group of chemicals finally manifesting themselves. As a matter of fact, in Sweden where one of the major drug abuse problems was Preludin, often mainlined, they described a "new" psychiatric entity, "noia" for paranoia, because of the multitude of people who became paranoid with the long term use of the stimulant. Clearly the oral use of high dosages over a long period of time is every bit as pernicious as the intravenous use. People get trapped, they get trapped into the so-called "yo-yo" phenomena or the "ups-and-downs" syndrome. After long term oral stimulant use, many users become irritable and are unable to sleep amongst other symptoms. They often turn to the sedative group of drugs in order to try to control some of these symptoms and thus get trapped into another group of chemicals where dependency, physical and psychological, and tolerance are significant problems. Often higher and higher doses of both groups—the so-called ups and downs are used. This is not to say, obviously, that every nor the majority of patients who use amphetamines or like substances for the control of obesity get into such a bind. As with all drugs, the reasons why a drug is used and the manner in which it is used is equally as important as the drug itself.

Senator BAYH. I notice in describing the kind of individuals and the problems of obesity, you described a rather limited category of people, and, second, you referred only to short term use for diets. This is relatively short term control, a coordinated program involving the use of drugs and a physician's close supervision. Let me ask you to give us your professional opinion. Do you see any long range benefit of amphetamines for weight reduction or control?

Dr. WOLFSON. No. I would certainly agree that if one is to use

this drug for the control of obesity, that 3 to 4 weeks' usage should be a reasonable time. While most of the studies have shown that the amphetamines are somewhat effective in the short term trials, every single study that I am aware of using the chemical over a 2 to 3 months' periods of time, has revealed that the differences between drug and placebo and drug and no drug therapy have smoothed out completely. Amphetamines are not effective at all in the long term treatment of the usual case of obesity. Obesity is a chronic, and, in many instances, a lifetime problem.

Senator BAYH. Thank you, Doctor.

Do you have any further observations or comments?

Dr. WOLFSON. The major principles that I would like all of us to consider are whether society really needs a particular drug, whether or not the drug is effective and whether or not the drug is safe. I do not think the amphetamine-like drugs are safe, I believe they are of only questionable effectiveness in limited situations, and certainly society does not need the vast supplies that it has on hand. We do not need the reserves that we have or that are suggested by some, nor do we need to have nearly as much of these drugs produced each and every year.

Again, I do not know what the exact production figure or the quota should be. I feel that probably 50 percent of production is diverted into the illicit market and that 90 percent of the "legitimate" medical use is used to treat obesity; my guess is that at least 75 percent of that usage is unwarranted, either by the fact that many patients are using amphetamines for longer than 4 weeks, are getting multiple prescriptions from multiple unwary physicians, or are using considerably higher dosages than is safe. Just using those figures, admittedly only educated guesses, my feeling would be that a 10 to 15 percent production would be more than adequate to cover research needs, reserves, and legitimate medical use.

Senator BAYH. Ten or 15 percent?

Dr. WOLFSON. Ten or 15 percent.

Senator BAYH. Not reduction but production?

Dr. WOLFSON. Ten or 15 percent production, a reduction of 85 percent to 90 percent. I also feel that whatever quotas are set, I would hope that the quotas are set in a manner whereby each of the factors is brought into the open; that is, we are decreasing production so much for this reason and so much for another. Only then can other interested parties look at the reduction critically and sensibly and try to study it as I am sure the FDA, NIMH, and HEW are trying to do. And whatever quotas are set, I would hope that an integral part of the judgment would be an understanding that this is an interim quota, and that this would be reassessed after a reasonable period of time. Hopefully, we need not to go through with a completely new legislative process of setting quotas. If in so many months or within 1 year there will be a reevaluation of the various factors that are used to set the quotas, perhaps by then we can have more of the answers to the questions I heard you asking before and more of the answers to the questions that still have not been asked.

Senator BAYH. You mentioned you thought 50 percent was going

through illicit channels. That is significantly higher than the previous witness, Dr. Edwards, assessed. Do you have statistics to substantiate that 50-percent figure?

Dr. WOLFSON. No, sir, no new information or statistics. The only way I got the 50 percent is reading the testimony of the Pepper hearings which were held about a year and a half ago. It appeared this figure of 50 percent was accepted, and I have just used it on that basis. I do not know where that figure comes from.

Senator BAYH. Regarding those pills that are not diverted criminally, is it your judgment that the use of amphetamines for obesity is not the healthiest kind of use?

Dr. WOLFSON. I do not think it is healthy at all. The credibility gap between Government, the pharmaceutical industry, physicians, and the ultimate consumer is really being put to a test here. Hopefully we will not get trapped into accepting a reduction percentage merely because that number might satisfy most people rather than really trying to examine each part of the question that is being factored.

I wish I could be of more help in giving specific figures but I obviously do not have those.

Senator BAYH. That is quite all right. I appreciate your thoughtfulness and the information contained in your testimony. If you have additional thoughts or data I hope you will make them available to the subcommittee.

Dr. WOLFSON. I would be happy to. Thank you, sir.

Senator BAYH. Thank you, Doctor.

(Dr. Wolfson's prepared statement and curriculum vitae is as follows:)

CURRICULUM VITAE, EDWARD A. WOLFSON, M.D., M.P.H.

Home address: 44 Devonshire Place, Glen Rock, New Jersey 07452.
Date of birth: February 4, 1926 New York, New York.
Military service: World War II, U.S. Army, August 1943 to June 1946. Combat Infantryman. Purple Heart.
Education:
A.B. Cornell University, 1948.
M. Nutr. Science, Cornell University School of Nutrition, 1949.
M.D., Cornell University Medical College, 1953.
M.P.H., Columbia Univ. School of Public Health, 1971.
Private practice, Internal Medicine, Paterson, New Jersey, 1957–69.
Honors:
Phi Kappa Phi.
Alpha Omega Alpha.
Who's Who in the East.
Licenses:
New York #75308 July 22, 1954.
New Jersey #15503 May 2, 1956.
Hospital appointments:
Out-patient Physician, New York Hospital, N.Y.C., 1957–67.
Senior Attending in Medicine, St. Joseph's Hospital, Paterson, New Jersey, 1966–71.
Attending in Medicine, Martland Medical Center, Newark, N.J., 1969– .
Consultant to the Dept. of Medicine-Valley Hospital, Ridgewood, New Jersey, 1971– .
Consultant in Community Medicine, St. Joseph's Hospital, Paterson, New Jersey, 1971– .
Consulting Physician, VA Hospital, East Orange, N.J., 1971– .

Diplomate:
- American Board of Internal Medicine, 1961.
- Associate Fellow, American College of Physicians, 1962.
- Fellow, American College of Physicians, 1971.
- Fellow, American College of Preventive Medicine, 1971.

Academic rank:
- Instructor of Medicine, Cornell University Medical College, 1957–67.
- Clinical Instructor of Medicine, College of Medicine and Dentistry of New Jersey/Newark, 1963–69.
- Associate Professor of Preventive Medicine and Community Health, New Jersey Medical School, 1969– .
- Director, Division of Drug Abuse, New Jersey Medical School, 1969– .
- Vice-Chairman, Department of Preventive Medicine and Community Health, New Jersey Medical School, 1971– .
- Associate Professor of Medicine, New Jersey Medical School, 1971– .

Professional organizations:
- American Medical Association.
- American Public Health Association.
- American Society of Internal Medicine.
- New Jersey Gastroenterological Society.
- Pan-American Medical Association.
- World Medical Association.
- Medical Society of the State of New Jersey—
  - Delegate to Annual Convention, 1960– .
  - Council on Public Relations, 1966–68.
  - Chairman, Credentials Committee, 1967.
  - Council on Drug Abuse, 1970– .
  - Committee on Medical Education, Consultant, 1971– .
- Passaic County Medical Society—
  - Program, Chairman, 159–62.
  - Executive Committee, 1968– .
  - Assistant Treasurer, 1968–71.
  - Chairman, Public Health Committee, 1969– .
  - Co-Chairman, Public Relations Committee, 1969–71.
  - Chairman, Environmental and Community Health Programs, 1970–71.
  - Treasurer, 1971– .
  - New Jersey Public Health Association—
    - Executive Committee, 1969–71.
    - Chairman, Drug Abuse Committee, 1969–71.
  - American Association for the Advancement of Science, 1969– .
  - Association of Teachers of Preventive Medicine, 1970– .
  - Academy of Medicine, New Jersey, 1970– .

Community:
- President, Passaic County Heart Association, 1965–66.
- Board of Trustees, New Jersey State Heart Association, 1966–68.
- Research Committee, New Jersey State Heart Association, 1966–69.
- Professional Chairman, Glen Rock Community Chest, 1966.
- Board of Trustees, Passaic Valley Health Facilities Planning Council, 1967–71.
- Member, Mayor's Committee on Drug Abuse, Paterson, N.J., 1969–71.
- Advisor on Drug Abuse to Mayors of Passaic and Fairlawn, N.J., 1970–71.
- Member, Mayor's Narcotic Advisory Council, Newark, N.J., 1971– .

Miscellaneous:
- Director, Institute on Drug Abuse for Educators—Three-week Course, Newark, N.J., June 22–July 10, 1970.
- Steering Committee, Institute for Continuing Medical Education of N.J.
- Elected Member Faculty Council, New Jersey Medical School, 1970–71.
- *Mental Health Advisory Committee* of the Division of Medical Assistance and Health Services for the State of New Jersey, 1970–71.
- Secretary of Faculty Organization, New Jersey Medical School, 1971– .
- Advisory Board of *Contemporary Drug Problems—A Law Quarterly.*
- Editorial Board of *Drug Forum*—The Journal of Human Issues.
- Consultant to Special Action Office for Drug Abuse Prevention (Executive Office of the President), 1971– .

Drug Abuse Task Force for the American Public Health Association, 1971– .

Chairman, Continuing Education Committee, N.J. Medical School, 1970– .

Published articles:

MCDERMOTT, W. et al. Pyrazinamide-Isoniazid in Tuberculosis, *The American Review of Tuberculosis*, Vol. 69, No. 3, March, 1954. (Technical assistance while spending two months medical student elective at Navajo Indian Medical Center, Arizona).

LIPKIN, M., FULTON, L., and WOLFSON, E. A. The syndrome of the hypersensitive xiphoid. *New Eng. J. of Med.* 253:591, October 6, 1955.

EINSTEIN, S. and WOLFSON, E. A. Alcoholism curricula: How professionals are trained. *The Internat. J. of the Addictions*, 5, No. 2:295:312, 1970.

WOLFSON, E. A. Newark, Narcotics and the Medical School. *The Journal of the Medical Society of New Jersey*, 67, No. 5:207–210, 1970.

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WOLFSON, E. A. Section on Drug Addiction. *In:* Grolier International Encyclopedia, Grolier Society, New York, 1971 Edition.

WOLFSON, E. A. Acute Drug Abuse Emergencies. In *Emergency Room Care*, ed. by Spitzer, Oaks, and Mayer. New York. Grune and Stratton.

EINSTEIN, S., QUINONES, M. A., and WOLFSON, E A. Developing a treatment program for the drug abusers: problems and perspectives. *Alcoholism*, Vol. VI, No. 2, 1970.

WOLFSON, E. A., LAVENHAR, M., EINSTEIN, S., QUINONES, M. A. and LOURIA, D. B. A Medical School's Approach to Drug Abuse. (Abstract). *Ann. Int. Med.* May, 1971. (Paper presented to American College of Physicians Annual Meeting, Denver, Colorado, March, 1971.)

WOLFSON, E. A. Medical Tapes by Phone for New Jersey Physicians—

1. The Psychedelic Scene (9 min.) [1]
2. Amphetamines and Barbiturates (9 min.) [1]
3. The Narcotics (8 min.) [1]

WOLFSON, E. A. Alternatives to Methadone. *Hospitals, J.A.H.A.* 45:53–55, 1971.

QUINONES, M. A., WOLFSON, E. A., and EINSTEIN, S. Developing a Drug Abuse Curriculum in the School System. *J. Drug Ed.* 3:235–239, 1971.

WOLFSON, E. A. and LOURIA, D. B.: The Medical Complications of Drug Abuse. *Pediatric Portfolio*. Vol. 1, no. 15, September, 1971.

WOLFSON, E. A., LOURIA, D. B., and EINSTEIN, S. Some Disturbing Aspects of the Drug Scene. *Intern. J. Environ, Studies.* 2:177–182, 1971.

WOLFSON, E. A., and LOURIA, D. B. Prevention of Drug Abuse. *Postgraduate Medicine.* 51: 163, Jan. 1972.

Accepted for 1972 publication:

WOLFSON, E. A. and LOURIA, D. B. Chapter on Marihuana. *In* Drug Abuse: A Text for Teachers. "What—How—When to Teach." Edited by J. Edwards, New Haven.

WOLFSON, E. A. Semantics of the Drug Scene. *Drug Forum.*

WOLFSON, E. A., and LOURIA,, D. B.: Marihuana: Tempest Over Pot. *Contemporary Drug Problems*—A Law Quarterly.

EINSTEIN, S. E., LAVENHAR, M., WOLFSON, E. A., QUINONES, M. A., and MCATEER, G. M.: The Training of Teachers for Durg Abuse Educational Programs: Preliminary Considerations. *Journal of Drug Education.*

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Papers presented:

The Doctor's Role in Drug Abuse. Presented at the *Annual Meeting of the Medical Society of the State of New Jersey*, Atlantic City, N.J., May, 1970.

The Marijuana Myth: Games or Options for the Community. Presented at the *Opening Plenary Session of the International Symposium on Drug Abuse:* Jerusalem, Israel, August 13, 1970.

The Epidemiology of Drug Abuse and the Treatment of Acute Drug Abuse Emergencies. Presented at the *International Congress of Medicine and Surgery* (Pan American Medical Association): Guayaquil, Ecuador, Sept., 1970.

Comprehensive Programs for Drug Addicts. Presented at the *Institute on Hospital and Community Psychiatry* (American Psychiatric Association); Philadelphia, Pennsylvania, September 24, 1970.

Drug Abuse, Essex County and the Medical School. Presented at the *Essex County Medical Society Symposium on Drug Abuse;* East Orange, N.J. January 14, 1971.

Crisis Intervention & Deceptions in the Illicit Drug Market. Presented at the *Annual Meeting of the Medical Society of the State of New Jersey*, Atlantic City, New Jersey, May, 1971.

Alternatives to Methadone. Presented at *American Hospital Association*, Chicago, Illinois, May, 1971.

Drug Abuse in the 1970's. Presented at *10th Annual Pediatrics Symposium*, Mamionedes Hospital, Brooklyn, N.Y., May, 1971.

Semantics and Deceptions in the Drug Scene. Presented at the *Seminar for the New Jersey Judiciary;* Cherry Hill, N.J., September, 1971.

The Epidemiology of Drug Abuse in Suburban New Jersey High Schools. Presented at the *99th Annual Meeting of the American Public Health Association*, Minneapolis, Minnesota, October, 1971.

Confidential Registration of Narcotic Abusers. Presented (by Dr. Mark Quinones) at the *99th Annual Meeting of the American Public Health Association*, Minneapolis, Minnesota, October, 1971.

Doxepin HCl (Sinequan) as an Adjunct to Methadone in Opiate Detoxification. Presented at the *Fifth World Congress of Psychiatry*, Mexico City, November, 1971.

The Role of the Practicing Physician. Presented at the *Fourth National Conference on Methadone Treatment*, San Francisco, California, January, 1972.

The Epidemiology of Drug Abuse, Presented at the *Canadian government Ministry of Health and Welfare meeting on Behavioral Sciences and the Drug Phenomenon.* Montreal, Canada, January, 1972.

Critical Issues and Methadone Maintenance: Treatment, Therapy or What? (Presented by Dr. Stanley Einstein) at the *Fourth National Conference on Methadone Treatment*, San Francisco, California, January, 1972.

Papers accepted:

Crisis Intervention. To be presented at the *American College of Emergency Physicians*, Atlantic City, May, 1972.

Drug Abuse as a Public Health Program. To be presented at the *Second International Symposium on Drug Abuse.* Jerusalem, Israel, May, 1972.

Lecturer or panelist:

Hospitals and medical societies, including—

Stanford Hospital, Conn.
Fort Hamilton VA Hospital, Brooklyn, N.Y.
Upstate Medical Center, Syracuse, N.Y.
Somerset Hospital, Somerville, N.J.
Valley Hospital, Ridgewood, N.J.
St. Francis Community Health Center, Jersey City, N.J.
Overlook Hospital, Summit, N.J.
Passaic County Medical Society, N.J.
Saint Joseph's Hospital, Paterson, N.J.
Princeton Hospital, N.J.
Mercer Hospital, Trenton, N.J.
Hudson County Medical Society, N.J.
St. Barnabas Hospital, Livingston, N.J.

Lecturer or panelist—Continued
Hospitals and medical societies, including—Continued
Chilton Memorial Hospital, Morris Plains, N.J.
Middlesex County Medical Society, N.J.
Bergen County Medical Society, N.J.
Perth Amboy General Hospital, N.J.
Beth Israel Hospital, Newark, N.J.
Mount Carmel Hospital, Columbus, Ohio.
Orange Memorial Hospital, Orange, N.J.
United Hospitals of Newark, Newark, N.J.
Association of Montclair Physicians, Montclair, N.J.
Bergen Pines Hospital, Paramas, N.J.
Colleges and universities including—
Rutgers University, Newark, N.J.
Williams College, Williamstown, Mass.
Lycoming College, Williamsport, Pa.
College of Wooster, Wooster, Ohio.
Columbia Univ. School of Urban Ecology, New York, N.Y.
Douglas College, New Brunswick, N.J.
Newark State College, Union, N.J.
Yale U. School of Epidemiology and Public Health, New Haven, Conn.
Fairleigh Dickinson University, Rutherford, N.J.
Cornell U. Medical School, Department of Pharmacology, guest lecturer.
Miscellaneous—
Annual meeting New Jersey Public Health Association, Oct., 1969.
National Seminar on the Problems of Drugs Among Young People, Institute for Development of Educational Activities, Nov., 1969.
Governor's Conference on Drug Dependence and Abuse, Michigan, Dec., 1969.
Essex County Prosecutor's Narcotic Seminar, April, 1970.
American Chemical Society, Oct., 1970.
American Association of School Administrators, Annual meeting, Feb., 1971.
Command Course on Organized Crime in N.J. for Chiefs of Police, Trenton, N.J., Aug., 1971.
Conference of Municipal Court Justices, Trenton, N.J., Oct., 1971.
Pfizer Faculty, Drug Abuse Institute for Physicians (Trenton, Philadelphia, Atlantic City), 1971.
Drug Abuse Training Institute for the Military, San Antonio, Texas (Co-Director), Nov., 1971.
Workshops for Union County Educational System, Madison, N.J., 1969–71.
Department of Health, Wayne, N.J. Public School System, Newark
State College, New Jersey Mayors Conference, 1969–71.
New Jersey Interfaith Coordinating Council on Drug Education, New Brunswick, N.J., Jan., 1972.
Drug Abuse Institute for Physicians, New Orleans, La., Feb., 1972.
Third Army Alcohol and Drug Abuse Workshop, Fort Gordon, Ga., Feb., 1972.
Drug Abuse Institute for Physicians, Houston, Texas, March, 1972.

Prepared Statement on Use of Amphetamines for Short-Term Obesity Treatment

(By Edward A. Wolfson, M.D., M.P.H.)

I appreciate the opportunity to speak before the Committee, primarily on behalf of the American Public Association but also personally, on the public health issue of the efficacy of amphetamines for the short-term treatment of obesity and the related vital issue of setting lower production quotas. My bias is that the subject of drug dependency and the misuse of a farrago of mind-altering substances is indeed a public health issue. Relevant societal and medical decisions can be derived if we are guided by the principles of a paraphrased World Health Organization definition of health,—that is, not only the absence of disease, but the presence of physical, mental, and social well-being for the entire community as well as for the individual.

At long last there appears to be little or no debate that the central nervous system (CNS) stimulant group of drugs has an inordinately high abuse potential—probably mediated via their sympathomimetic (or adrenaline-like) effects on the higher nervous system centers. There are many authorities who believe that this is the most dangerous of the currently abused psychoactive drugs, yes, more dangerous than the opiates. Clearly the subject of amphetamines needs critical re-evaluation and re-education, education not only of the unaware stimulant users, the pharmaceutical industry, and law makers—but also of the medical profession. Fortunately, physicians today are becoming aware that the amphetamines are more dangerous pharmacologically than the opiates, that the stimulants are indeed "addictive", and that the derivatives initially thought to be harmless are anything but. The recent decrease in prescriptions for amphetamines bear this out. The scientific literature now abounds with well documented examples of the detrimental psychological and physical effects of long-term, high-dosage use of these chemicals. Recently a chemical model of acute psychosis has been induced within 1 to 5 days by the hourly oral administration of average amphetamine dosages to presumably psychiatrically normal volunters each with a previous history of stimulant abuse. Despite this, it is not generally recognized that oral administration of the amphetamines in high doses over long periods is every bit as pernicious as intravenous use. While it is not our task today to reiterate the dangers of the stimulants, it is important that we appreciate that the stimulant problem is not confined solely to the amphetamines. There are other CNS stimulants such as Metrazol that are never abused, probably because of the profound side-effects relative to the low or absent euphorogenic potential. However, there are other chemicals such as methylphenidate (Ritalin) and phenmetrazine (Preludin), which neuropharmacologically mimic and parallel the action and abuse potential of the amphetamines. All of us realize that the so-called "hard" drug in Sweden is the stimulant phenmatrazine, and over the past years there literally has been a Swedish epidemic of abuse of this stimulant, a drug used medically in this country for the treatment of obesity. The amphetamine-type drugs seem to exert their effects and common abuse potential either by releasing norepinephrine (or dopamine) from nerve endings or more likely by its potentiating action. The latter probably occurs by the inhibiting of the re-uptake of the chemical messenger (the norepinephrine) at the synapse. I raise this side issue since the generic issues will not be resolved if we merely decrease production of one agent while maintaining or potentially increasing the production of similar agents.

At the onset, I would like to state that I am unable to nor do I intend to make any dogmatic statements on a definitive quota figure. If we make the assumption that legitimate medical use includes the short term treatment of obesity, then I do not believe anyone can set an absolute figure at this time. But we must resolve the obesity dilemma and then set equations, arriving at quota figures honestly and openly. We must examine policies and figures critically, know what (and how) is being factored, and then have the interim judgments evaluated—and finally re-assessed every 6 months or so. It is far easier, given the known dangers of this group, to merely conclude that there should be a reduction in supply and simply pick a percentage which presumably makes all concerned satisfied—a variation of the numbers game. But what are the amounts necessary for legitimate medical use, research, and scientific needs? What is the ratio of effects vs hazards, gain vs. the dangers for individuals and populations? Understandably, there are variables and unknowns in all of these equations and the suggested answers will depend to a large degree on the subjective input of the one who testifies—the so-called "expert". Does he represent the manufacturer who stands to reap considerable profit in "pushing" trade names and "variations on a theme?" The economic value of sales is substantial. Recall that the patent rights on the basic drug have long expired and that the drug is easily manufactured from inexpensive chemicals. There must be something to this since about 40 drug companies are manufacturing some 60 or more variations—some as their sole product. Perhaps we are being told something by the industry and we ought to listen—namely, that amphetamines must have a low order of effectiveness since so many new variations and combinations are being introduced. To the credit of some, the stimulant line has been discontinued by some producers.

Perhaps the "expert" is a practicing physician who historically demands the right of medical decisions without interference, regulation, or control and who jealously guards high right to prescribe what he deems best for the individual patient. Or we might hear from the representatives of public health who have the primary concern of the health of populations or, finally, the authority in the drug scene who sees and treats the dropouts from a drug-oriented society.

I would sincerely hope that all who testify will attempt to answer the only really relevant questions—does society need the drug, is it effective, and is it safe? The drug is not safe, it is of questionable effectiveness in limited situations, and in all probability society does not require for legitimate use the vast supplies it now unfortunately enjoys. Let me attempt to illustrate the dilemma of perspectives as one who has been a private medical practitioner, who now practices and teaches preventive medicine, and who is intimately involved in the drug scene. I practiced internal medicine for 12 years and on occasion, and I hope with proper judgement and discrimination, used the amphetamines and similar compounds for the short-term treatment of obesity. I concluded then that in some instances these chemicals were efficacious in the short run. A good example of selective and controlled chemical intervention is the importance of controlling weight gain during the self-limited condition of pregnancy where there is a definite risk, in terms of difficult delivery, incidence of pre-eclampsia, and in post-natal maintenance of excessive weight, in the patient who gains excessive weight during the pregnancy. Similarly there might be legitimate indications, assuming proper monitoring, for the short-term use in the cardiac, diabetic, or hypertensive. The dangers in such instances are minimal while the potential gains are substantial. Indeed almost every study using amphetamines, in controlled or uncontrolled trials, has demonstrated that over a four week period, patients taking amphetamines lose weight more readily than patients on placebo or on no medication. A possible problem here is that even in well designed "double-blind" studies, patients may promptly recognize the drug by the stimulant effect and bias may shape the apparent effects of the drug.

Almost all studies over longer periods of time, however, tend to show a wash-out of drug—placebo or drug—no drug differences over a period of 2 to 3 months, and certainly the amphetamines and like substances are not a cure for obesity—a complex, frequently lifetime problem with predominantly social and psychological determinants. And there are those who believe that use of chemicals encourages a "lazy" attitude on the part of many patients who must also contend with a potential "rebound" when the presumed anorectics are stopped. Furthermore, there is a world of difference between a trial demonstrating an effect of a chemical and the actual treatment of a chronic medical problem. Finally, in terms of long-term effects, many believe that some of the lay groups such as Weight Watchers are better able to transform an obese patient into a lean patient and keeping him that way through supportive and diet therapy rather than chemotherapy. In a 1966 paper (London and Schreiber, Annals of Internal Medicine, Vol. 65, page 80) on the use of appetite suppressants in the out-patient treatment of obesity, patients were divided into 6 groups: (1) amphetamines and bi-weekly group discussion, (2) placebo and groups, (3) no medication and groups, and (4), (5), and (6) the same medication or no medication but no group discussions. The six month study revealed that supportive group discussions appeared to be the most important factor.

So let us agree, for we will not resolve the question today, that there is a limited place for the use of amphetamines in the short-term, 3 to 4 weeks only, treatment of selected obese patients by careful, dedicated, and well-trained physicians who are fully cognizant of the drugs' dangers. The real questions here are: (1) how many of such patients and how many of such physicians are-there, and (2) how do we best regulate the obvious and flagrant overuse and sometimes indiscriminate over-prescribing? How many physicians have had the opportunity of observing cachetic and psychotic "speed freaks", how many physicians are conned into providing "diet" pills by persuasive patients, how many physicians are assuaging their own anxieties by giving into their own need to offer something to a patient, and how many do not perceive the roots of obesity as a conflict in social customs and psychological turmoil and perhaps inadvertently give license to the epidemic of self-prescribing of drugs for any and all, imagined or real, social and psychological discomforts? How many

physicians use the sympathominetics only when all reasonable alternatives have been explored?

If, as we are led to believe, approximately 50% of the 8–10 billion dosages are diverted into the illicit market (it would thus seem to me that a reduction of production quotas of at least 50% are warranted on this basis alone) and approximately 90% of the legitimate" medical use is for obesity, then it is inconceivable to me that the remaining 3.6 to 4.5 billion dosages are truly necessary for the short-term use in selected and appropriate obese patients. By my simple arithmetic, that would be enough for about 40 million patients. As Dr. Edison of Salt Lake City has questioned, is not the obvious overuse of stimulants, for obesity or otherwise, really only a reflection of American culture—increased activity, drive, the need to excel, the compulsion to speed? Perhaps we mistake speed for progress.

Most physicians are in favor of the FDA determining whether a drug is efficacious but do not favor, as a matter of principle, of having medical judgment regulated. I would prefer the option of self-regulation or regulation by education rather than legislation—but the stimulant problem is beyond this state. If today the choice were no quotas, the status quo, vs. total restriction or prohibition of the use of the sympathomimetics for the treatment of obesity, I would favor the latter. But I would opt for a form of control through licensing and prescription forms and pharmacy tabulations kept in a manner similar to the opiates. This would not interfere with a physician's decision of how to treat his patient but would certainly make him better aware of the abuse potentials and the significance of what he is doing. The precedence has been set with the restrictions on prescribing narcotics and the scientific justification is equally sound for including the sympathomimetics. Since many local medical societies are asking members to voluntarily curb amphetamines (and I hope, other sympathomimetics) prescriptions for anything other than narcolepsy (irresistible fits of falling asleep), the hyperkinetic syndrome (a behavioral disorder), and in some instances for the short-term treatment of obesity, it appears that organized medicine is eager to cooperate in facing this critical problem. While applauding this voluntary approach, unless nationwide restrictions (indeed, international) are levied and strict production quotas are set, this will not resolve overavailability and may even penalize the knowing physician and the patient who may benefit from a short course on the drug. Through licensing and strict monitoring, the physician—abuser will readily become apparent and in jeopardy of meaningful penalty. Clearly this should have a deterrent effect on any physician who uses the stimulants excessively. For one thing, we should not permit physicians to receive large orders direct from manufacturers or wholesalers.

If one looks at this problem through the eyes of the teacher of Preventive Medicine or one who is involved in he drug scene, the bias is naturally towards exceedingly strict controls of production and over-prescribing. In addition to obesity being a chronic and lifetime problem in most instances, the obese patient often is an orally-dependent person who exhibits an inability to tolerate frustration—yet we attempt to treat this patient with a dependent-producing agent. Parenthetically, there is an anorectic agent available in Europe, fenfluramine, while apparently is quite effective in decreasing appetite but which is not concomittantly a stimulant (actually it may be a mild depressant). Housewives just don't take it, physicians do not prescribe it frequently, and obviously it's not a best seller.

I believe it is time we stopped playing games! Accepting the limited use of the sympathomimetics in narcolepsy and the hyperkinetic syndrome and even for the short-term use in obesity demands profound limitations on availability. Certainly no one believes truck drivers should use them to stay awake and probably lose critical judgement in the bargain, notbody wants to see our athletes resort to stimulants (after all, we regulate horses), and their use in mild depression! How about considering cocaine or low doses of pure LSD, or most certainly cannabis—a far safer pharmacologic agent.

So how do we set a reasonable reduction figure? I emphasize reasonable because token responses will only serve to increase the credibility gap between government—industry—science—medicine—and the ultimate consumer, the public. To begin with, what *is* the diversion figure? With no information to the contrary, I must assume 50% diversion—thus to *begin* with, there should be an international agreement for at least a 50% reduction of production. We are

told that 90% of medical use is for obesity—90% of what? Are we to believe that we do not have production figures from legitimate producers? While regulation of legitimate companies are no problem, illicit and unscrupulous manufacturers should be held legally accountable for the dropouts from the amphetamine scene and dealt with accordingly. As for obesity, allow me an assumption—namely that at least 75% of the use of sympathomimetics is unwarranted medically. We know that many doctors make a business of "reduction through chemistry", many patients use prescribed amphetamines for long periods of time (this should be controlled), some patients obtain multiple prescriptions from unwary physicians, and the principle of tolerance results in many patients using higher doses than are medically safe. If so, I believe that the anticipated medical needs would be no more than 10–15% of present production. I suspect this figure is far too high and should more than adequately cover research needs, reserves, etc. Certainly, research on the model toxic phycosis must continue. In any event, the quota should be based on anticipated legitimate medical needs and not on present production levels.

A built-in re-assessment every 6 months of the factors used in determining the ultimate interim quota should be mandatory. We must reduce the available levels by all available means to those amounts consistent with critical evaluation of all factors at all levels. We require a breakdown in how the final figures are derived and a full explanation of the process so that all seriously concerned with the drug scene can work intelligently on behalf of the public. All sectors and interests should participate more fully in the control of this burgeoning and significant public health problem.

(American Public Health Association's petition to the Bureau of Narcotics and Dangerous Drugs pertaining to annual quotas for manufacture of amphetamine drugs marked "Exhibit No. 12" and is as follows:)

Exhibit No. 12

OFFICE OF CHIEF COUNSEL,
Bureau of Narcotics and Dangerous Drugs,
Washington, D.C.

DEAR SIR: The American Public Health Association wishes to submit the following comments pertaining to annual quotas for manufacture of amphetamine drugs set pursuant to S. 306 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 and printed in 36 Federal Register 23165 (December 4, 1971):

1. The reduction in the proposed aggregate quotas of 40% from last year's production figures for amphetamines is a step in the right direction, but should not, in our opinion, by any means exhaust continued efforts to reduce the production to the limits set by legitimate medical needs. The efforts of groups like ours, concerned with the public health, to comment intelligently on the proposed quotas is somewhat inhibited by the failure to accompany the proposed quotas with a fuller explanation of how they were arrived at. The Federal Register contains a list of criteria considered but gives no hint as to how each criterion was factored into the total equation. We sincerely believe that the Bureau would perform a service to the American people and especially to those in the public health field if it published a breakdown of the way in which the 40% reduction figure was arrived at. As it is, it is difficult to understand and hence evaluate whether that reduction is indeed low enough.

2. Specifically, we remain in doubt as to the factual or scientific basis on which the amount needed for legitimate medical uses was computed. We understand that approximately 90% of the amphetamine prescriptions issued last year were for weight control. Similarly, "An Assessment of Drug Use in the General Population" in New York State published by the Narcotic Addiction Control Commission in 1970 showed that 11.8% of the population interviewed had taken diet pills at least once, and 222,000 were taking them regularly (6 times a month or more); 76.1% of these regular users had legal prescriptions although they tended not to follow the medical regimen prescribed. Most such users were unemployed, female housewives.

There is, of course, severe doubt in the medical profession as to whether amphetamines have any legitimate function to perform in the weight control field.

In its release of August 8, 1970, 35 Fed. Reg. 12652, the Food and Drug Administration discussed the efficacy evaluation of the National Academy of Sciences on the use of amphetamines in weight control as follows:

"The Academy found that such drugs as a class have been shown to have a generally short-term anorectic action. They further commented that clinical opinion on the contribution of the sympathomimetic stimulants in a weight reduction program varies widely, the anorectic effect of these drugs often plateaus or diminishes after a few weeks, most studies of them are for short periods, no available evidence shows that use of anorectics alters the natural history of obesity, some evidence indicates that anorectic effects may be strongly influenced by the suggestibility of the patient, and reservations exist about the adequacy of the controls in some of the clinical studies. There significant potential for drug abuse was also cited."

The American Medical Association Drug Evaluations Chapter 33, p. 267, also states:

"The amphetamines and amphetamine-like drugs are commonly used as adjuncts in the management of obesity. Whether they *should* be used for this purpose has been challenged. Their untoward effects, their tendency to produce psychic dependence, and their evanescent effectiveness in reasonable dosage leave much to be desired.

". . . effective weight reduction and maintenance require an understanding of good nutrition and successful alteration of the underlying psychologic or pathologic factors producing excessive caloric intake.

"Anorexiants can be used as short-term adjuncts in an overall program of weight loss, but their use is appropriate only as long as fat loss continues without undesirable effects, psychic dependence, or need for an increase in dosage. Prolonged use of therapeutic doses or short-term use of large doses of these drugs is almost always followed by fatigue and mental depression.

"The amphetamines are of unequivocal usefulness only in a few conditions. These include narcolepsy and cataplexy; hypersomnia (eg, in Kleine-Levin syndrome); adjunctive use in certain highly selected patients with aggressive psychiatric or neurological disorders (eg, childhood behavioral problems, psychomotor epilepsy, psychopatic personality), all beyond the scope of this discussion; and incapacitating drowsiness occurring in some patients who must take sedating anticonvulsants."

In view of these overriding cautions on the use of amphetamines in obesity control, and of the well recognized abuses in the past in this realm, we think the Bureau should make known the policies and figures upon which it is relying to estimate legitimate need for medical purposes, so that its judgment can be evaluated by other interested groups.

3. We understand that the Food and Drug Administration is currently undertaking a reevaluation of its earlier policy of August 8, 1970, on the short term use of amphetamines in obesity control. Wall Street Journal, December 22, 1971. In addition, we understand that two New York medical groups have submitted data contesting the proposed quotas on the grounds that they should include no amount at all for this use. In view of these developments, we think it would be premature to set the annual quotas proposed without the full input of the ongoing FDA study as well as the information private groups can offer. We believe that the Bureau under Section 306 could set an interim quota for the first quarter of the year so that present over-production would not continue and at the same time it would not be authorizing an unduly high quota for the entire year to come. During the next few months it could then take account of the new FDA study and other input on this problem, before permanent quotas were set.

Again, let us urge the Bureau, as we have done in the past, to explain more fully the basis of its actions in this critical area so that we and others who are sincerely concerned with this problem may work together more intelligently and so that the American people can understand and participate more fully in the control of this public health problem.

4. At this time, APHA would like to reserve its right to participate in any hearings or proceedings that might take place on the proposed quotas.

Sincerely yours,

CHARLES R. HALPERN,
PATRICIA M. WALD,
Attorneys for American Public Health Association.

Senator BAYH. Our next testimony will be presented by four individuals who have had personal experience with the abuse of the amphetamine—diet pills—we are studying. Mr. Richard Hartig, director of Topic House in Prince Georges County, Mary Godo, Gary Doby, and Steven Sharp. If you would come forward now, please.

Mr. Hartig, are you ready? We appreciate very much all of you taking the time to share your thoughts and experiences with us.

STATEMENT OF MR. RICHARD HARTIG, DIRECTOR, TOPIC HOUSE, PRINCE GEORGES COUNTY, MD., ACCOMPANIED BY MARY GODO, GARY DOBY, AND STEVEN SHART

Mr. HARTIG. I am Richard Hartig, the director of the Topic House. It is a drug center in Suitland, Temple Hills, Md. Do you want me to give a brief summary of the house?

Senator BAYH. Please.

Mr. HARTIG. The Topic House means talking over problems in confidence, and it was established about 6 months ago by a group of churches to resolve the drug abuse problem and the addiction problem in the area. It is backed by about eight churches of various denominations and contributions they make to the place.

We have a house, an old house, that we have converted into a drug center. It is not a halfway house. It is a place where we have rap sessions, therapy groups, and speakers, et cetera.

We are connected with the Prince Georges County drug program in that we have a group of young people who are called roving leaders. Mary Godo on my right is one of them. These roving leaders go out into the shopping centers, and out into places where they meet the people their same age in resolving the drug situation today, and by rapping, and by referring them to services, et cetera. We have five of these young people who are paid a minimal salary by the county for 3 hours a day, and they are doing about three to twice as much time, giving time into this problem as really is required of them.

We receive about 40 calls a day into the house relating anywhere from suicides to wanting jobs, et cetera, and giving family relationships and background and everything. We find that most of these problems are drug related.

The two gentlemen on my left have been some of the young men who have been helped by coming to the place, and I think they can give you a little bit of information on drug use and abuses from their own experiences, et cetera.

I might say that we have two hot lines and we are located at 4911 St. Barnabas Road, and we are open from 1 p.m. till 9 p.m. Every Monday and Thursday night, through the auspices of Dr. Wonderlick's guide group, we have psychologists conduct therapy sessions for these young people. They are interviewed on a personal basis, and with the juveniles who are under 18, their parents must consent and take part in these sessions also. If a person is in a bad enough state where they need detoxification or methadone treatment, we can refer them to the county drug treatment center. Most of them, however, have problems that are related, and trips that are not strung

out, or they are original users, and we try to get them into an atmosphere where drugs are not allowed and drugs are not used, and through an educational way, through speakers and et cetera, and particularly through this group therapy get at some of the causes of drug problems today. I understand that the focus today is diet pill or amphetamine abuse. We will be very glad to answer any questions that you might have.

Senator BAYH. Yes. How many people do you treat or counsel at Topic House?

Mr. HARTIG. Well, when they first come in, we give them a form. It is anonymous, and no names are required, and they give us a brief history of their background, not only of home and educational background, but of their drug usage. And then these are generally young people that live in the area, and we get to know them quite well. We encourage them then to come into the place and get into the therapy groups, or schedule drug speakers, and we have a program with movies every Tuesday night. At other times, it is an informal grouping and we have rap sessions and we discuss the problems. We have a doctor, and we are connected with doctors in the community who refer people to us. We are connected with the juvenile services who have young people into the group therapy sessions, and we are connected—well, we are connected with different organizations in the mental health department who, when they have people who have drug problems, basically they refer them to us.

Senator BAYH. Could you tell me, please, how many young people you are treating, or counseling, or rapping with?

Mr. HARTIG. As I mentioned, we receive about 40 calls on the hot line during the day. We have this for approximately 400 face-to-face, one-to-one personal contacts that we have made and dealt with. Anytime during the day, when it is open until closing, you will find from a dozen to two dozen young people in the place, in the house.

Senator BAYH. You have had about 400 in therapy?

Mr. HARTIG. Yes, in the therapy groups. The therapy, group therapy, is on Monday night for people under 18, and there are two groups being conducted by this guide, Dr. Wonderlick's guide therapy group, and they are full. There are about eight people in each group meeting from 7:30 to 8:30 p.m. and 8:30 to 10 p.m. Their parents meet on a separate night. Adult groups meet on a Thursday evening at 6:30 p.m. for an hour and a half, and then another hour and a half, and they have about 10 in each group. Now, these are people who have requested, who have been interviewed personally and I think we are having some good results. These two gentlemen on my left are in these groups, and right now.

Senator BAYH. Could you gentlemen identify yourselves for the record here, please?

Mr. SHARP. Yes. My name is Steve Sharp.

Senator BAYH. Steve Sharp?

Mr. SHARP. Yes.

Mr. DOBY. I am Gary Doby.

Senator BAYH. Mary, why don't you start by telling us exactly how you got involved with Topic, and what you generally try to do. Give us what experience you may have observed relative to the amphetamine diet pill problem we are discussing here.

Miss Godo. Well, I got started in the Topic House by an accident.

Senator Bayh. Could you pull the microphone up closer to you?

Miss Godo. I got started in the Topic House by an accident. I was walking down the road and one of the fellows that works there picked me up hitchhiking. He told me about the place. I had been dealing with drugs for about 8 years. I went there. I cannot say that I was very enthused when I first went there.

Senator Bayh. Could you pull that up closer? My battery in my hearing aid is run down a little. [Laughter.]

Miss Godo. I wasn't very enthused with the program when I first went there because, you know, I kind of just went there to find out what it was like.

Then, after a week or so, I got very deeply involved. I started calling places to find out where you could get help for things like drugs, where you could take people that are on drugs that want to get off drugs, to send them where they will not have any police record. This is the main thing, the reason why most kids will come into the Topic House and other organizations like this, because they do not want a police record.

I started drugs with using marihuana, and I went and used speed, and I——

Senator Bayh. Do not be nervous. This is very helpful to us. Take your time and tell as you see it, as it is.

Miss Godo. Well, I will give you what I feel about it. I think it is doing a really great thing. Myself, I have had lots of girls come to me and talk to me about their problems, and it does seem to me that a lot of people, I mean, a lot of teenagers and adults ought to understand each other, and this is very necessary now.

I will get back. O.K. I started speed, and the kind of speed I did was black beauties,[1] and what was called white cross. I was into this for 6 months, and I was 125 pounds, and I went down to 90 pounds. And it is not as easy stopping, as, you know, like everybody says, well, you can take speed, and you know, you are not addicted.

Senator Bayh. I am not certain I follow what you said. You say you started with marihuana, and then you moved to speed?

Miss Godo. Yeh. I moved to speed through a friend.

Senator Bayh. Pardon me?

Miss Godo. I got on speed through a friend. There was a very heavy set lady who lives around the corner from me, and she used to go to three different doctors and get prescriptions for all three different types of speed.

Senator Bayh. When you talk about speed, are you talking about diet pills?

Miss Godo. Yes.

Senator Bayh. I want to make sure we get our lingos straightened out. To some people speed suggests that you have to shoot it. You were taking these pills orally?

Miss Godo. Yes, I was. She asked me one day if I would like some. I was feeling real down in the dumps, and I did not have like all the sense I guess I should have had, and she said, well, this will perk you up, and I had not had much sleep, so I took one of them

[1] Biphetamine,® see Appendix B, 5(a–e).

and I felt really great. So, I kept coming back to her until she stopped giving them to me, and then a friend that lived next door to me gave me some, and I just went on from there. And then I used to go with an addict who used to sell speed, and that's what introduced me to white cross.

Senator BAYH. You said white cross? What is white cross?

Miss GODO. I am not sure. I just know that it is a diet pill.

Senator BAYH. It is another kind of diet pill?

Miss GODO. Yes.

Senator BAYH. Did you take them?

Miss GODO. Yes; I did.

Senator BAYH. How many pills were you taking a day?

Miss GODO. Anywhere from three to four. It would depend on how many I could get.

Senator BAYH. Three to four?

And how long did you take these diet pills?

Miss GODO. About 6 months.

Senator BAYH. About 6 months? Then what happened?

Miss GODO. I just, I just gave up on them. I was losing weight, and I looked terrible. I looked just like a ghost, and so I just gave them up. When you come down off of them, it is very hard to stop taking them. It is very hard to stop doing them after a while, because you get this—it is like you were all up, and you have all of this energy, and all of a sudden, it hits you in the back of the neck, and you have no energy any more, and you are really tired, and your whole body is aching with pain from taking these.

Senator BAYH. Did you use anything to help you off the high?

Miss GODO. No; I did not. I just did it with myself, and I told myself that it was not good.

Senator BAYH. You did not take any barbiturates to try and balance the speed?

Miss GODO. No. I did go into barbs, though, but I could not take barbs. They were too much for me. I used to get sick, so I tried a couple of times, but it did not work and I could not take them.

Senator BAYH. You got these amphetamines without going to a doctor or without having to present a prescription?

Miss GODO. Yes; I did.

Senator BAYH. Did you buy these pills from the lady next door, or did she give them to you?

Miss GODO. It did not start out that way, but it ended up that way.

Senator BAYH. What does a pill cost?

Miss GODO. Well, you can get—well, the black beauties did not cost me anything.

Senator BAYH. The black beauties? Biphetamine®?

Miss GODO. I did not pay for them. They gave them to me. The white crosses were four for a dollar.

Senator BAYH. Do you live with your parents, Mary?

Miss GODO. Yes; I did. My mother.

Senator BAYH. Was your mother at all concerned when you went from 130 to 90 pounds?

Miss GODO. Well, I was kind of like batted around, and I did not

live at home, you know, all of the time. And I guess, you know, it was just like, gradually, and I did not lose it all at once, and it was just, you know, I started getting very weak, and so I just quit myself, you know. I told her I was using drugs, and I did not tell her —well, it is kind of when you get into it after a while, you kind of want somebody to say, look, I know you are doing drugs and I will help you. I used to leave little hints around, and I knew she knew, because I used to get parsley and put it into a jar and put it up in my closet to look like marihuana, so I would put it up in my closet and she used to find it. And she would think that it was marihuana, but it wasn't, just to leave little hints around. But then, when I found out that I had to do it on my own, I did it on my own.

Senator Bayh. Could you relate any experiences you may have had talking to other young women such as yourself that may have had similar experiences, or more severe experiences than you, with speed?

Miss Godo. Well, a couple of years ago, my girlfriend got almost a complete breakdown from them because her system was just, you know, was built up to taking all of this speed, and then all of a sudden you could not get any and she just, you know, had a complete nervous breakdown.

Senator Bayh. How much speed was she taking a day?

Miss Godo. About eight.

Senator Bayh. How did she get those pills?

Miss Godo. She bought them in the street.

Senator Bayh. On the street?

Miss Godo. Yes.

Senator Bayh. In your community, it is readily available?

Miss Godo. Yes.

Senator Bayh. Were do you generally buy?

Miss Godo. I would rather not say.

Senator Bayh. I will ask the question and you do not have to answer it. Did you have a drug store or somebody on the corner, or was there a regular dealer?

Miss Godo. You can get drugs anywhere you want to if you are looking for them. You can get them. You can find them.

Senator Bayh. Is that the case now?

Miss Godo. Yes; it is.

Senator Bayh. Today?

Miss Godo. Yes; it is. You know, I would like to put one thing on that I know about, and that is a policeman told me that a man was going to an elementary school giving heroin out to the youngsters, free. I think that this has got to be stopped. I mean, you know, elementary school children.

Senator Bayh. A policeman told you that?

Miss Godo. He said that he was going to make an arrest on this guy that was distributing the heroin through the schools.

Senator Bayh. Well, I would hope that he did.

Miss Godo. Well, I do not know if he did or not. I mean, I have not heard from him since then.

Senator Bayh. All right. Gentlemen, why don't you tell us what your experience has been. Steve, do you want to start?

Mr. SHARP. Is there anything basically you want to know about it?

Senator BAYH. You might pull the microphone closer. I would like to know basically what your experience with drugs has been. How you got started? What specifically your experience with speed has been?

Mr. SHARP. Well, I basically got started on it by buying it off the street because, like, basically, you can get any kind of drug you want just down at the street corner, the shopping center, almost any place, and like amphetamines, you know, are just as easy to obtain as barbituates or anything else.

Senator BAYH. Well, did you take the diet pills?

Mr. SHARP. Yes; I have.

Senator BAYH. Could you tell us how you got started with them?

Mr. SHARP. I happened to be in school one day, and a friend of mine had some. I popped a couple. I got them in the street, and I started getting into them.

Senator BAYH. How long did you take speed?

Mr. SHARP. I was not really into speed, you know, except for a couple of months, and then I got out of speed and started going on to other drugs. But, I took like Dexedrine® and barbs and things like that.

Senator BAYH. Are you taking barbs as well as speed?

Mr. SHARP. Well, you know, barbituates came later on.

Senator BAYH. Pardon?

Mr. SHARP. Barbituates came later on, and I started getting the downs after the speed.

Senator BAYH. You took the speed for a couple of months?

Mr. SHARP. Uh-huh.

Senator BAYH. How many pills did you take a day when you were taking speed?

Mr. SHARP. It really varied. If I had them, I was not really addicted to them.

Senator BAYH. What was the most you ever took in 1 day?

Mr. SHARP. About six or seven.

Senator BAYH. About six or seven?

Is it possible to take six or seven and then not take any at all?

Mr. SHARP. It is possible to take it, but you cannot keep it up for quite a few days.

Senator BAYH. Did you switch to barbs after the speed?

Mr. SHARP. Yes.

Senator BAYH. How did all that happen? What was your experience with barbs?

Mr. SHARP. Well, like, you know, I just happened to be at a friend's house, and like, you know, they just happened to throw me on to it, and I started getting into that.

Senator BAYH. How many barbs did you take in a day?

Mr. SHARP. I was taking quite a few of them. I was taking an average of 12 or 15 at times.

Senator BAYH. Twelve or 15 at one time?

Mr. SHARP. Uh-huh.

Senator BAYH. How regular and how often did you take those?

Mr. SHARP. I basically take them in the morning, and in the afternoon and evening.

Senator BAYH. Twelve or 15 each time?

Mr. SHARP. No, not each time. Through the whole day.

Senator BAYH. Over how long a period of time did you follow that course, Steve?

Mr. SHARP. For about 2 or 3 months.

Senator BAYH. Two or three months? Could you contrast the different effects of speed and the barbs?

Mr. SHARP. Well, like basically, speed is more or less like a stimulant, where, you know, where it picks your body up and it speeds up the process and stuff like that. The barbs is more or less something that gives you, you know, a drunk feeling, if that makes any sense. It is really hard to explain what it's like. You really have to experience it to find out.

Senator BAYH. Have you ever been in a position where you were taking 15 barbs a day, and then you could not get any?

Mr. SHARP. Yeah. That is basically how I am off them, because this doctor I was getting them from cut me off from my prescriptions.

Senator BAYH. You were getting both the speed and the barbs from the doctor?

Mr. SHARP. No, I never got a prescription for speed from the doctor, just barbituates.

Senator BAYH. How did you get them? Did you go to the doctor and say that you were sick?

Mr. SHARP. Well, the thing is I would go into him for heroin. For the heroin, I was getting methadone, and after the methadone was cut out, I started getting the barbituates, and he finally cut me off of them.

Senator BAYH. How long were you on heroin?

Mr. SHARP. Off and on for about 2 years.

Senator BAYH. Was that before or after——

Mr. SHARP. This was after I got into the speed.

Senator BAYH. You got into speed, and then heroin, and then barbituates, is that the way it went?

Mr. SHARP. Uh-huh.

Senator BAYH. Did you ever shoot either the speed or the barb?

Mr. SHARP. I shot speed and barbs both. I have eaten them both too.

Senator BAYH. Are you using any drugs now or have you got it licked?

Mr. SHARP. No, I still use them every now and then.

Mr. HARTIG. I might say that Steve is in a lot better shape, however, than when we first met him a few months ago. I think he has cut down a great amount. One thing we do not allow in the center is the use of drugs or the distribution of them. We try to get at the problems of these young people. I think Gary can explain a little more on that. But I can clarify that statement, that he is a lot better shape than we had known him a few months ago.

Senator BAYH. Is it possible to get barbs now without prescription?

Mr. SHARP. You can get barbs in the street almost any time.

Senator BAYH. What do they cost?

Mr. SHARP. Usually about 50 cents now because they are a little

harder to acquire now that the doctors have stopped giving out the prescriptions.

Senator BAYH. Is it the same for amphetamines and speed?

Mr. SHARP. Basically the same, but I can acquire them on the streets with no problem.

Senator BAYH. On the street?

Mr. SHARP. But you can acquire them on the streets.

Senator BAYH. Do you know who's pushing them?

Mr. SHARP. Well, I know where to get it if I want it.

Senator BAYH. What kind of barbs are generally available?

Mr. SHARP. Desbutols—a large variety of them.

Senator BAYH. Gary, what has been your experience with drugs?

Mr. DOBY. Well, my first introduction to speed was through a physician. I was a little overweight and had high blood pressure. I went to a physician and he prescribed some diet tablets for me, and after taking them for a short time, I started doubling my dosage, and felt much better, felt quite energetic, so I started taking them, abusing them, rather, by taking the larger amount than was prescribed for me. That is how I first was introduced to speed.

And then after that I met a nurse that had prescription pads, and she used to write out prescriptions and sign physician's names, and then I would take those to the drug store and get them fillled for amphetamines. And I probably—we would get maybe a prescription for 60 pills, and then in 1 weekend, between about three and four people, they would all be gone. Se we used them quite often for a period of about 6 months, and after that time, it got to where coming down from the speed was a real hassle. You were real dragged out and just dull, and achy all over. So I started doing some downs to start aleviating that and help to sleep and so on, and ended up getting strung out on heroin.

Senator BAYH. You started with the amphetamines, with speeed?

Mr. DOBY. Right.

Senator BAYH. And then you tried to get down off the speed and got involved with downs?

Mr. DOBY. Opiates and heroin and stuff like that.

Senator BAYH. Could you get up a little bit closer to the mike, please?

Mr. DOBY. After coming down off the speed to get away from the speed, I started getting into heroin and delota.

Senator BAYH. And de—what?

Mr. DOBY. Delota. It is a derivative of morphine, I think. I was also doing morphine, just downs in general. But I was addicted to delota and heroin for a period of time.

Senator BAYH. Where did the barbs fit into the picture then?

Mr. DOBY. Barbs—I really have not gotten into barbs too much, only on occasion I have had a few barbs, and not particularly liked the high that comes from barbs. I never really got into it enough that I was addicted or had a need for it.

Senator BAYH. Do you feel you were addicted on the speed?

Mr. DOBY. I think I was because it was, you know, like I said, I needed something to help me get away from it, and the heroin and the delota and things like that will take away the pain of anything,

you know. So, that is how I got into those, by trying to quit the speed, because I had a particularly bad experience with speed because a friend of mine had been doing crystal methadrine, shooting it, and we were at the pop festival in Atlanta a couple of years ago, and he really flipped out. He was really completely paranoid to everyone around him except a couple of particular friends of his, and the last I heard of him he was in the hospital. I rapped with him about 6 or 8 hours trying to help him straighten his head out, and that's when I really realized that I needed to get away from speed because I might end up just like him. So, I started getting in the heroin and the downs.

Senator BAYH. You got the speed through prescriptions.

Mr. DOBY. Yes, that is how I was first introduced to it, and then I used prescriptions for about 6 to 8 months, and after that, I started getting speed, you know, through other people. They would come down there through a channel where they would be diverted at a warehouse, and shipments would be diverted or stolen, and then they would come through other people that I would know, large quantities, and so I would acquire them there.

Senator BAYH. Were the pills stolen?

Mr. DOBY. Some were stolen, some were. Well, in a sense they were all stolen, but some of them—they were actually stolen where somebody would go up to a truck and take them, steal them off of a dock or something, or they might be, you know, rerouted in the shipment to another particular place.

Senator BAYH. What is your situation now relative to heroin?

Mr. DOBY. Right now I am not addicted to anything, I am not doing any hard drugs at all. I have not for several months now.

Senator BAYH. What does one experience when you are addicted to amphetamines like you suggest you were, and then you cannot get them?

Mr. DOBY. It is quite frustrating.

Senator BAYH. What happens, how do you feel?

Mr. DOBY. You become quite irritable, and upset, and violent, when you cannot acquire them.

Senator BAYH. Have you or any of your friends committed any type of violent act while high on speed?

Mr. DOBY. I have not actually done any physical violence, but I have become quite hostile and fearful, you know, hollering and arguing and so forth, but because I was among friends it did not actually come down to anything.

Senator BAYH. Have you seen this type of thing happen with others though?

Mr. DOBY. Yes I have.

Senator BAYH. Having had experience with both speed and heroin, which is worse as far as the withdrawal effect, on the way you think and your physical action?

Mr. DOBY. I think probably the amphetamines because they are—they drain your body, the fluid, when you are coming down, you are mentally dull. I mean, you are really dull and like you cannot understand some of the most simple things that might be said to you. You know, you are just completely tired mentally and physically. It

is almost like a complete breakdown of your whole system, especially if you have been up on the amphetamines for several days, a week or something like that. It is really a hard thing to crack, and usually to avoid the crashing, you go out and get some more.

Senator BAYH. If you wanted to get some amphetamines this afternoon, would you have any trouble getting them?

Mr. DOBY. It might take me a couple of hours.

Senator BAYH. A couple of hours? Barbituates the same thing?

Mr. DOBY. Barbituates would not take that long. All you have to do is see a particular doctor or something like that.

Senator BAYH. See a what?

Mr. DOBY. Just go and see certain doctors. I understand now that there are certain doctors that give out speed that way too.

Mr. HARTIG. I wonder, Senator Bayh, if I just might give a little brief comment on Gary. As you have readily seen and heard, he has sort of gone the gambit in the drug usage and abusage, from the hard narcotics all the way down to soft drugs. I think it was about 2 months ago Gary first came into the Topic House. He was in bad shape, flipped out right there, and crashed, and he was in the house, and we just have an old home, furnished like a living room and so forth, sort of like a home away from home, and we waited for him to wake up. And then we talked with him and counseled him. I wonder, Gary, if you could take it up from there, how you came in, and then since then, what you have done and so forth?

Mr. DOBY. Like I said, when I first went to the Topic House, I was taken there by some friends because I was really messed up on barbiturates. I was really high, or I was down on barbiturates when I first went to the Topic House and friends of mine took me there, and immediately on arriving, and sitting down, I passed out. And several hours later when I came to, one of the roving leaders there talked with me, and he told me that if I needed help or wanted help, that I could come back there and talk to one of the roving leaders, or Mr. Hartig. So, a few days later I came back and talked with them, and I decided that I, you know, would like to have some help from them and immediately they showed that they were interested, so that I was very enthused with coming there and talking with them.

And at the time, I was out of a job, and they helped me to acquire a job. And also, I am going to be able to go to college very shortly, this fall, and also to help straighten my head out, to help me get away from the drugs. I associate with people who are straight now, and who do not use drugs, and through the therapy sessions with the guide program, they are helping quite a bit. And as of now, I have no desires to do any of the hard drugs at all. Well, I have not been in a situation where it was done around me and offered to me, and I have no desire to do it, and it has completely left me with the desire to not accept these drugs or to get high on them.

There are periods that do come occasionally when there is a desire. It is a mental thing, and that is the thing I am trying to get away from now, completely get away from the mental desire to do drugs. And I think I am accomplishing that because it is more seldom, and comes less often, the desire to do them, and I also have the will power now to put them aside and not to accept them.

Senator Bayh. Well, I congratulate you for that.

I appreciate, Mr. Hartig, your coming and what you are doing in the Topic House, and Mary and Steve and Gary. I appreciate your candor. Some of us who have not been there cannot understand, I suppose, fully, but you can help by sharing your personal experiences, and I do appreciate that. I hope we can continue to keep the door open and you can communicate with us.

Thank you very much for what you are all doing.

Mr. Hartig. Thank you.

Senator Bayh. Mr. Arthur Goldstein is our next witness. He is chairman of the Huntington Narcotics Guidance Council, Huntington, Long Island, N.Y.

STATEMENT OF MR. ARTHUR GOLDSTEIN, CHAIRMAN, HUNTINGTON NARCOTICS GUIDANCE COUNCIL, HUNTINGTON, LONG ISLAND, N.Y.

Mr. Goldstein. Senator Bayh, I appear on behalf of the Huntington Narcotics Guidance Council, and I am chairman of that council. As you may know, Huntington is a town of approximately 200,000 residents, and the narcotics guidance council is a volunteer group of people that makes recommendations to the town with respect to narcotics and drug problems that exist in the town and the Nation.

As you also know, this very subcommittee held hearings on the Comprehensive Drug Abuse Prevention Control Act 2½ years ago, and we at the community level, of course, have had the opportunity to observe what had transpired and is transpiring in our community.

It is our observation, and we relay this to you, that the Bureau of Narcotics and Dangerous Drugs has made tremendous impact in their activity in general with respect to the diversion of all drugs, including amphetamines. We must tell you that we are not as enthusiastic over the activities of the Food and Drug Administration. We just feel that there has been a complete lack of any, to us, the bad word, speed, in this area. In terms of any activity of quota regulation and production, we are not enthused, and I will demonstrate that for you in a minute.

But, while the FDA was studying and conferring, the physicians of Huntington and of Suffolk County voluntarily agreed, to cease the prescription of amphetamines except for cases of narcolepsy and hyperkinesis. These physicians have said that what our overweight patients need are not the amphetamines or the speed, but what they need are 5 minutes more of our time, and we will agree that rather than prescribe amphetamines for cases of obesity, what we are going to do is that we are going to take more time with the patient. The physicians in the town agreed that the only cases in which they would prescribe amphetamines are in cases of hyperkinesis and in the case of narcolepsy, and all of the other cases, the physicians said what they will do, is we will not use, and we do not have to use the amphetamine.

Senator Bayh. They are not prescribing amphetamines for overweight problems?

Mr. Goldstein. That is correct. Now, I must say that there are also exceptions in every community, and we have some of the physicians that only use this as their main source of revenue in their practices, and they are prescribing amphetamines. But, other than those doctors, the majority of the doctors in our community will not prescribe amphetamines for short-weight or for long-term obesity problems, and we are not the only community. Other areas in the State have done this as well.

Amphetamines are among the most dangerous of the psychoactive drugs, and among the most easily obtained. Continued use of amphetamine drugs can cause physical and psychological dependence, behavioral toxicity, and in extreme cases a condition of mental unbalance resembling paranoid schizophrenia. It is instructive to note that in a study of some 50 "speed freaks" or amphetamine dependents taking the drug by injection, Dr. David Lewis of the Harvard Medical School indicated that 90 percent had begun using amphetamines by taking the drug in commercial tablet form. This indicates the great need for strict control over the production and distribution of amphetamine drugs.

Realistic quotas will avert this kind of initiation into drug use and will diminish the use of pep pills by the adult community.

An indirect but important result will ensue from the reduction of the production of amphetamines. A correlation exists between parental use and the misuse and abuse of drugs by the children of drug users.

Data from studies in New Jersey, California, Ontario, Canada, support the thesis that drug abuse is substantially greater by those students and teenagers whose parents regularly use drugs. The Canadian study indicated that the teenager who shoots speed is five times as likely to do so if the parent is a drug user. (New York Times, July 23, 1971.)

Now, we find that frequently in speaking to groups of people, and we have had physicians on panels, and we have participated in speaking to the youngsters, that it is very, very difficult to talk to the youths, and to address yourself to a youth problem when the adult community is using the drugs themselves, legally or illegally. It really matters very little whether they are getting it for short term weight loss or anything else. If they see their parents using that drug every morning it is unlikely that the children will do anything but turn a deaf ear to our pleas and warnings about misusing drugs.

You asked the question before as to the social significance of this adult drug usage, and I submit that the use of pep pills has become so acceptable that when the BNDD regulated these drugs, it is my understanding that people wrote to Federal agencies objecting the requirement for renewal prescriptions, with letters stating:

> We have been using this prescription for five or ten years, I have been using amphetamines for this time, and now you fellows have the audacity to pass regulations requiring me to go back to the doctor to get some further prescription for it.

Now, I say that it is not a question of the FDA studies of efficacy for short term weight loss, and that that has nothing at all to do with it. It may work, it may take off 6 pounds in a 4-week period of

time, but so what? If the doctor sat down for 5 more minutes with a patient and tried to get to the cause of the problem, that is what is needed. The short term efficacy study is irrelevant.

Now, if I may allude to the chart, you can see the effect of these so-called quotas. You asked the question about what did they request, and the industry requested exactly double the amount that they produced in 1971. Now, I say, something is wrong someplace, when a responsible pharmaceutical house can, dealing with the Federal Government, cavalierly submit a need for 18,000 kilos of drugs where they know they only produced 9,000 the year before. Now, to me, it seems sort of funny, and maybe I do not understand Federal Government, but I hardly see a point of departure as to what was produced in past years. If I were analyzing a problem, that would not seem to me the place to begin. The Commissioner of the FDA has said, that is where they started.

The Commissioner of the FDA further testified that the FDA cut down the quotas requested. Well, if they requested double what they produced, by industry then that also is an irrelevant figure.

Senator Bayh. You were here, I believe, were you not, when Dr. Edwards talked about BNDD suggesting the drug companies should include in the request, a 50 percent increase for reserve supplies? Inasmuch as you have pretty much given BNDD a clean bill of health, what is your judgment about that?

Mr. Goldstein. To use the youngster's phrase, they are bad rapping another Federal agency and that does not really help the problem at all. I do not know whether or not, and I would find it hard to believe that BNDD told the manufacturers to add this in, and I just find it very hard to believe, because what has happened is the FDA recommended the quota, and the quota that FDA recommended was exactly the quota that BNDD accepted. And that, I would submit, Senator, may be some area where legislation is necessary, that BNDD should not be mandated to accept that FDA suggested quota. I think that there ought to be some further action on the part of the BNDD.

The proposed aggregate a production quota of 8,000 kilos, or a billion and three quarters 5 miligram unit pills, is a step in the right direction but are in the opinion of the Council substantially higher than necessary or required. We have determined after analysis, study and consultation with medical and pharmacology experts that the quotas proposed by the Bureau of Narcotics and Dangerous Drugs, based upon FDA recommendation, are predicated too heavily upon the quantity of pills produced in past years and upon the production quotas which the drug companies requested. It is respectfully submitted that neither of these factors are entitled to the weight which they were accorded by the Director of the Bureau of Narcotics and Dangerous Drugs. The industry requests were patently inflated and arrived at by requesting a 1972 production quota double that of the 1971 production:

	1970 production (kilos)	1971 production (kilos)	Industry request (kilos)
Amphetamine	27,000	9,356	19,956
Methamphetamine	7,000	4,926	8,941

The production in past years is as unreliable an index of future production as is the industry request. Past misuse should not determine 1972 quotas.

Medically, amphetamines have been used most heavily for weight control, and the BNDD quotas include provisions for production of quantities of the drugs for this purpose. The time has come to lay to rest once and for all the myth that amphetamine compounds are specifics for weight reduction and control. Despite the fact that these drugs do cause a temporary anorexia or loss of appetite, they have repeatedly been shown to be of little or no value in the establishment of a program of continued or long-term weight loss. A report issued by the American Medical Association expressed grave doubts about the value of amphetamines in weight control after the first 2 weeks of administration of therapeutic doses. It has further been noted that the average weight loss on a diet controlled by the use of amphetamines only (that is without any other regulation of intake, exercise, et cetera) was in the neighborhood of 6 pounds total, an amount not cosmetically significant. The U.S. Food and Drug Administration has reported that the anorectic effect of amphetamine drugs often plateaus or diminishes after a few weeks of administration, thus allowing the patient to regain even the small amount of weight he has managed to lose.

When it is noted that, in 1970, close to 90 percent of the amphetamine prescriptions in this country were for purposes of weight control, the magnitude of the problem becomes clear. For example, a study by the New York State Narcotic Addiction Control Commission in that year indicated that 11.8 percent of the people of New York State had used diet pills at least once and that 222,000 were regular users, taking six doses a month or more. Only 76 percent of these regular users, most of them housewives, had obtained the drugs by prescription, the rest through illicit sources. Thus, controls at the distribution level are important, but they are not enough; stringent controls must be exerted on production.

Production allowances should not allow for the use of amphetamines for weight control at all, since this is a medically valueless use of the drugs, and is, therefore, an abuse.

There are, of course, areas where the amphetamine drugs have proven to be therapeutic agents of some value, chiefly in the treatment of two types of disorder: Narcolepsy and the hyperkinetic child syndrome. I am astonished to read statements made by representatives of the FDA, that one can only guess at the requirements for the treatment of these disorders.

For example, the National Center for Health Statistic has estimated that the average American makes about 4.3 visits per year to a physician (1969 data). A recent survey of outpatient pharmacy prescriptions at eight New York City teaching hospitals revealed that in 1970 amphetamine prescriptions at their outpatient departments averaged only 0.106 5 mg. tablets per patient visit. (Survey by Mr. Norman Baker, chief pharmacist of New York Hospital, June 1971.) (These hospital departments had about 1.3 million patient visits in 1970.) Taking medical practice at these outpatient departments as representative of good medical practice, the esti-

mated annual medical need for amphetamines in the United States (with a population of about 204 million) would be about 100 million 5 mg. tablets. This amount is little more than 5 percent of 1971 production.

Narcolepsy is a disorder characterized by frequent periods of decreased wakefulness in spite of adequate nocturnal sleep. It is an organic dysfunction of the central nervous system, and, like some other even less common sleeping sicknesses, it seems amenable to amphetamine therapy. In the town of Huntington, with a population of 200,000 persons, none of the physicians we canvassed reported seeing even a single case of narcolepsy in the past year. Suffolk County, with an urban/suburban/rural populace of over 1 million is reasonably representative of the country as a whole; here two of the hundreds of physicians surveyed reported seeing only one case of narcolepsy each in the past 2 years.

It has been reliably estimated that there are presently perhaps 20,000 cases of this disorder in the entire country. The maximum amount of drug required to treat these cases would be 730 kilograms annually, assuming an average daily dosage of 100 milligrams. Please note that this amount assumes that amphetamine drugs would be the sole treatment modaility in all 20,000 cases. However, most physicians in this area agree that amphetamines are not the preferred drugs in this disorder because of undesirable side effects, and that the drug of choice is a nonamphetamine, methylphenidate, better known by its trade name, Ritalin. The use of Ritalin in treatment of most of the cases would make 100 kilos of amphetamine a reasonable amount of production for the treatment of this disorder.

The other major area of usefulness for amphetamine drugs is in the treatment of the hyperkinetic child. Hyperkinesis is one manifestation of the so-called minimal brain dysfunctions occurring in children roughly between the ages of six and 10. Children exhibiting this disorder show an extreme degree of excess activity, as well as inability to concentrate, difficulty in paying attention, and disorders of memory. Reliable estimates indicate that the incidence of hyperkinesis is approximately 3 percent of the total population of children between the ages of five and 12. A panel under the auspices of the Department of Health, Education, and Welfare and chaired by Dr. Daniel X. Freedman of the University of Chicago Medical School found that approximately 60 percent of the children showing this disorder would respond favorably to stimulant therapy. Using 1970 census figures we can thus estimate that about 585,000 children would be appropriate for this treatment. Assuming again that every case were treated with amphetamine drugs, this disorder would require a production of 4,270 kilos of amphetamines based on a maximum daily dosage of 20 milligrams. However, the drug of choice in treating this disorder is again Ritalin which is used in approximately 75 percent of hyperkinesis cases. Taking this and other factors into account, indicates that a reasonable production figure for the treatment of hyperkinesis would be in the neighborhood of 1,000 kilos of amphetamines.

Allowing for treatment of certain other disorders which have an even lower incidence of occurrence than narcolepsy and hyperkinesis

and assuming the use of amphetamines exclusively in the treatment of all these disorders, we find that an absolute maximum would be an annual production of 5,100 kilos of amphetamine drugs, including Ritalin and Preludin. This is 3552 kilos less than the proposed BNDD quotas. If we then take into account the use of other forms of chemotherapy, we come to a more realistic figure of 1,200 kilos as a reasonable production. The proposed BNDD quotas are in excess of this figure by 700 percent.

The quotas for Ritalin and Preludin have still not been proposed by the Bureau of Narcotics nor has the FDA suggested these quotas to the Bureau of Narcotics.

Senator Bayh. Supposedly these quotas will be published by March 1st.

Mr. Goldstein. Well they may—to them, time makes no difference, but if you have a gap of 6 months and another 6 months, why time rolls on.

Senator Bayh. You know, I am not apologizing for that. I just wondered if you were aware that that is happening?

Mr. Goldstein. That hopefully, now that it is in schedule II, hopefully I understand that regulations will be forthcoming within the next few weeks.

It was difficult for our community to really assess the effect of the amphetamine or metamphetamine without knowing what was going on with respect to Preludin, because they are producing 10,000 kilos of preludin at the present time. Now, that is 2 billion pills of Preludin, and Preludin, I understand, is used only for obesity.

Now, it is not hard, therefore, to project the actual medical need. This figure for Ritalin is the figure that is used, I suggest, to treat 75 percent of the cases of narcolepsy and hyperkinesis, and if one consults any pediatric neurologist or any knowledgeable GP they will tell you that the drug of choice unquestionably is Ritalin, and if one had to get to the figures, this Ritalin figure is probably reasonably reliable, and that a percentage of that should go for hyperkinesis and narcolepsy, reducing all to the bottom line where the very, very maximum conceivable use, medical use, is this one and a quarter billion pills. And we in this country, if the quota were enacted as it is, would be producing 4¼ billion of these pills. Now, I think there are two problems, and the statistics and the quotas are somewhat important, but I think that we can learn something from this with respect to the other drugs, and what I think we do need, and I respectfully suggest this for your committee to study, I think that it is obvious that we need something more than the doctor alone being the intermediary between the pharmaceutical manufacturer and the consumer.

I think that just as in the case of truth in lending, where we found the lawyer telling the client as to what an interest rate was, that was not sufficient. I think we need a direct notice at this point to the consumer on buying a prescription, that when the person buys a prescription, she will be told.

What was under this original act—

Madam, what you are buying—
is a dangerous drug. You are buying a drug which can cause mental and physical damage to yourself, or the person that is using it, and you are buying

a drug that with its continued use, you may develop paranoia, schizophrenia, and it may also, through your continued use of this drug, mean that your children are five times more likely to use drugs if you are on these drugs.

Now, I think it is in these areas where one has to begin to look toward further legislation to consider this problem. To consider the amphetamines alone, as important as they are, I think will not be sufficient. I respectfully suggest this, and I think we have to go beyond. The youngsters told us today, that they wound up getting into the entire drug scene, and the amphetamines frequently are probably the initiator sometimes into this whole drug atmosphere. This may result from the youngster using pep pills but the parent's use of drugs is another contributing factor.

We would like to thank you for the opportunity of giving you some of the community reactions to this Federal legislation.

Senator Bayh. I appreciate your taking the time and I want to compliment you and the Huntington Narcotic Guidance Council and the Suffolk County Medical Society for taking the initiative in this area. Apparently you have been successful in your joint efforts to educate the professionals involved about the dangers of abusing amphetamines and the whole area of obesity control.

Mr. Goldstein. We feel that we have been somewhat successful in that area. We are, I might say, continuing with an education program sponsored by the Suffolk County Medical Society, educating the doctor with respect to barbituates. But, every time there is Federal legislation or publicity, we find that it has a direct reaction of a dimunition in the use of these drugs.

Senator Bayh. Somebody is listening?

Mr. Goldstein. I think so.

Senator Bayh. Sometimes we wonder.

Well, thank you very much, Mr. Goldstein. You have been very helpful, and if medical society has any additional information we certainly would appreciate it.

Mr. Goldstein. Thank you very much.

(Mr. Goldstein's prepared statement is as follows:)

Prepared Testimony of Arthur Goldstein, Chairman, Huntington Narcotics Guidance Council

I appear on behalf of the Town of Huntington, as Chairman of the Huntington Narcotics Guidance Council. The Town of Huntington, consisting of 200,000 residents, is in Suffolk County, New York. The Narcotics Guidance Council is the appointed body responsible to the Town for the recommendation and implementation of programs to combat drug abuse.

This committee held hearings on the Comprehensive Drug Abuse Prevention Control Act two and one-half years ago and from the observations of our council the activities and effort of the Bureau of Narcotics and Dangerous Drugs, under this act, have made substantial impact. We believe that the Food and Drug Administration has not acted with the same responsiveness or responsibility.

While the F.D.A. has been studying and conferring the 250 physicians in the Town of Huntington and the 1100 physicians in Suffolk County found that it was not necessary to prescribe amphetamines for cases of obesity. The physicians pledged to confine their prescription of amphetamines to cases of Narcolepsy and Hyperkinesis. Thus we have been in a unique position to assess the medical necessity for these drugs, and to see the effects of a marked reduction in their prescription and use.

Amphetamines are among the most dangerous of the psychoactive drugs, and among the most easily obtained. Continued use of amphetamine drugs can

cause physical and psychological dependence, behavioral toxicity, and in extreme cases a condition of mental unbalance resembling paranoid schizophrenia. It is instructive to note that in a study of some 50 "speed freaks" or amphetamine dependents taking the drug by injection, Dr. David Lewis of the Harvard Medical School indicated that 90% had begun using amphetamines by taking the drug in commercial tablet form. This indicates the great need for strict control over the production and distribution of amphetamine drugs.

Realistic quotas will avert this kind of initiation into drug use and will diminish the use of pep pills by the adult community.

An indirect but more important result will ensue from the reduction of the production of amphetamines. A correlation exists between parental use and the misuse and abuse of drugs by the children of drug users.

Data from studies in New Jersey, California, Ontario, Canada, support the thesis that drug abuse is substantially greater by those students and teenagers whose parents regularly use drugs. The Canadian study indicated that the teenager who shoots speed is five times as likely to do so if the parent is a drug user. (New York Times, July 23, 1971.)

The proposed aggregate production quotas for 1972, are a step in the right direction, but are in the opinion of the Council substantially higher than necessary or required. We have determined after analysis, study and consultation with medical and pharmacology experts that the quotas proposed by the Bureau of Narcotics and Dangerous Drugs, based upon F.D.A. recommendation, are predicated too heavily upon the quantity of pills produced in past years and upon the production quotas which the drug companies requested. It is respectfully submitted that neither of these factors are entitled to the weight which they were accorded by the Director of the Bureau of Narcotics and Dangerous Drugs. The industry requests were patently inflated and arrived at by requesting a 1972 production quota double that of the 1971 production:

	1970 production (kilos)	1971 production (kilos)	Industry request (kilos)
Amphetamine	27,000	9,356	19,956
Methamphetamine	7,000	4,926	8,941

The production in past years is as unreliable an index of future production as is the industry request. Past misuse should not determine 1972 quotas.

Medically, amphetamines have been used most heavily for weight control, and the BNDD quotas include provisions for production of quantities of the drugs for this purpose. The time has come to lay to rest once and for all the myth that amphetamine compounds are specifics for weight reduction and control. Despite the fact that these drugs do cause a temporary anorexia or loss of appetite; they have repeatedly been shown to be of little or no value in the establishment of a program of continued or long-term weight loss. A report issued by the American Medical Association expressed grave doubts about the value of amphetamines in weight control after the first two weeks of administration of therapeutic doses. It has further been noted that the average weight loss on a diet controlled by the use of amphetamines only (that is without any other regulation of intake, exercise, etc.) was in the neighborhood of six pounds total, an amount not cosmetically significant. The U.S. Food and Drug Administration has reported that the anorectic effect of amphetamine drugs often plateaus or diminishes after a few weeks of administration, thus allowing the patient to regain even the small amount of weight he has managed to lose.

When it is noted that, in 1970, close to 90% of the amphetamine prescriptions in this country were for purposes of weight control, the magnitude of the problem becomes clear. For example, a study by the New York State Narcotic Addiction Control Commission in that year indicated that 11.8% of the people of New York State had used diet pills at least once and that 222,000 were regular users, taking six doses a month or more. Only 76% of these regular users, most of them housewives, had obtained the drugs by prescription, the rest through illicit sources. Thus, controls at the distribution level are important, but they are not enough; stringent controls must be exerted on production.

Production allowances should not allow for the use of amphetamines for weight control at all, since this is a medically valueless use of the drugs, and is, therefore, an abuse.

There are, of course, areas where the amphetamine drugs have proven to be therapeutic agents of some value, chiefly in the treatment of two types of disorder: narcolepsy and the hyperkinetic child syndrome. I am astonished to read statements made by representatives of the F.D.A. that one can only guess at the requirements for the treatment of these disorders.

For example, the National Center for Health Statistic has estimated that the "average" American makes about 4.3 visits per year to a physician (1969 data). A recent survey of out-patient pharmacy prescriptions at eight New York City teaching hospitals revealed that in 1970 amphetamine prescriptions at their out-patient departments averaged only 0.106 5 mg. tablets per patient visit. (Survey by Mr. Norman Baker, Chief Pharmacist of New York Hospital, June, 1971.) (These hospital departments had about 1.3 million patient visits in 1970.) Taking medical practice at these out-patient departments as representative of good medical practice, the estimated annual medical need for amphetamines in the United States (with a population of about 204 million) would be about 100 million 5 mg. tablets. This amount is *little more than five per cent* of 1971 production.

Narcolepsy is a disorder characterized by frequent periods of decreased wakefulness in spite of adequate nocturnal sleep. It is an organic dysfunction of the central nervous system, and, like some other even less common "sleeping sicknesses", it seems amenable to amphetamine therapy. In the Town of Huntington, with a population of 200,000 persons, none of the physicians we canvassed reported seeing even a single case of narcolepsy in the past year. Suffolk County, with an urban/suburban/rural populace of over one million is reasonably representative of the country as a whole; here two of the hundreds of physicians surveyed reported seeing only one case of narcolepsy each in the past two years.

It has been reliably estimated that there are presently perhaps 20,000 cases of this disorder in the entire country. The maximum amount of drug required to treat these cases would be 730 kilograms annually, assuming an average daily dosage of 100 milligrams. Please note that this amount assumes that amphetamine drugs would be the sole treatment modaility in all 20,000 cases. However, most physicians in this area agree that amphetamines are not the preferred drugs in this disorder because of undesirable side effects, and that the drug of choice is a non-amphetamine, methylphenidate, better known by its trade name, Ritalin. The use of Ritalin in treatment of most of the cases would make 100 kilos of amphetamine a reasonable amount of production for the treatment of this disorder.

The other major area of usefulness for amphetamine drugs is in the treatment of the hyperkinetic child. Hyperkinesis is one manifestation of the so-called minimal brain dysfunctions occurring in children roughly between the ages of six and ten. Children exhibiting this disorder show an extreme degree of excess activity, as well as inability to concentrate, difficulty in paying attention, and disorders of memory. Reliable estimates indicate that the incidence of hyperkinesis is approximately three per cent of the total population of children between the ages of five and twelve. A panel under the auspices of the Department of Health, Education and Welfare and chaired by Dr. Daniel X. Freedman of the University of Chicago Medical School found that approximately sixty per cent of the children showing this disorder would respond favorably to stimulant therapy. Using 1970 census figures we can thus estimate that about 585,000 children would be appropriate for this treatment. Assuming again that every case were treated with amphetamine drugs, this disorder would require a production of 4270 kilos of amphetamines based on a maximum daily dosage of 20 milligrams. However, the drug of choice in treating this disorder is again Ritalin which is used in approximately 75% of hyperkinesis cases. Taking this and other factors into account, indicates that a reasonable production figure for the treatment of hyperkinesis would be in the neighborhood of 1000 kilos of amphetamines.

Allowing for treatment of certain other disorders which have an even lower incidence of occurrence than narcolepsy and hyperkinesis and assuming the use of amphetamines exclusively in the treatment of all these disorders, we find that an absolute maximum would be an annual production of 5100 kilos of amphetamine drugs, including Ritalin and Preludin. This is 3552 kilos *less* than the proposed BNDD quotas. If we then take into account the use of other forms of chemotherapy, we come to a more realistic figure of 1200 kilos as a

reasonable production. The proposed BNDD quotas are in excess of this figure by 700%.

The title of the law which is the subject of these hearings was originally "The Controlled Dangerous Substances Act." The titles of law can be euphemisticly changed but the act of the housewife, student, businessman, truck-driver who pops a pill is not changed and whether by prescription or not, a dangerous substance has been consumed.

We appeal to you to eliminate from allowable production quotas those pills produced for the treatment of obesity. The current proposed quotas exceed medical need by one and one-half billion pills.

The Narcotics Council further respectfully submits that this committee should consider legislation which would require that the customer be warned at the retail level, by label on the prescription or otherwise, that he or the person using the prescription of any drug under Schedule II is using a dangerous drug, a drug which can cause dependence, mental or physical damage.

Medical societies and communities over the nation have joined the Town of Huntington in taking voluntary action in this battle of the legal and illegal misuse of pills. Thank you for affording our Narcotics Guidance Council the opportunity of appearing before you to request further legislative action we believe is necessary.

CHART SUBMITTED BY ARTHUR GOLDSTEIN—FEB. 7, 1972

	Kilos	10 milligram units	5 milligram unit
Amphetamines, 1971 production—industry request (double 1971)	9,356	1,000,000,000 (335,600,000)	2,000,000,000 (1,871,200,000)
Proposed quota	5,870	500,000,000 (586,000,000)	1,000,000,000 (1,172,000,000)
Methamphetamines, 1971 production—industry request (double 1971)	4,926	500,000,000 (492,600,000)	1,000,000,000 (985,200,000)
Proposed quota	2,782	250,000,000 (278,200,000)	500,000,000 (556,400,000)
Total quota (amphetamines and methamphetamines)	8,652	750,000,000 (865,200,000)	1,750,000,000 (1,730,400,000)
Required medical need	1,200	125,000,000 (120,000,000)	250,000,000 (240,000,000)
Ritalin, 1971 production	2,781	250,000,000 (278,100,000)	500,000,000 (556,200,000)
Preludin, 1971 production	10,387	1,000,000,000 (2,182,000,000)	2,000,000,000 (4,364,000,000)
Total—Ritalin production, Preludin production, Amphetamines quota, Methamphetamines quota	21,820	2,000,000,000 (2,182,000,000)	4,250,000,000 (4,364,000,000)
Maximum conceivable medical need	5,100	500,000,000 (510,000,000)	1,250,000,000 (1,200,000,000)

Senator Bayh. We will ask unanimous consent to include at this point in the record a statement of Senator Eagleton from Missouri.

(The statement was marked "Exhibit No. 13" and is as follows:)

Exhibit No. 13

Prepared Statement of Senator Thomas F. Eagleton

February 7, 1972.

Mr. Chairman: Since my appearance before the Juvenile Delinquency Subcommittee last July, we have come a long way toward curbing abuse of stimulant drugs.

We met at that time to consider S. 674, my proposal to move amphetamines, methamphetamines, methylphenidate, and phenmetrazine into Schedule II of the Controlled Substances Act. That change in scheduling has been accomplished, I am pleased to say. These drugs are now subject to more stringent

record keeping and prescription requirements designed to cut down on diversion of drugs into illicit channels.

Most important, however, is the fact that these dangerous drugs may now be produced only within quota limits set by the federal government. Testimony on S. 674 amply demonstrated that the key to curbing amphetamine abuse is cutting down on the blatant and irresponsible overproduction of these drugs by legitimate manufacturers. Based on the currently proposed quotas issued by the Attorney General, it is likely that production in 1972 will be decreased at least 40% from last year's level.

The proposed quotas for amphetamine and methamphetamine, although markedly below previous production levels, still represent nearly one billion 10-milligram capsules. Nearly all of these pills, it must be assumed, are intended for diet control; only a small fraction will be required for the treatment of narcolepsy and hyperkinesis. Surely if we are serious about cutting production of stimulant drugs to a level reasonably related to legitimate needs, we must face the issue of whether it is appropriate to prescribe them for diet control.

This inquiry takes on special urgency in view of the skepticism that has developed within the medical profession with regard to the efficacy of these dangerous drugs in the treatment of obesity. Several medical societies in this country and abroad have asked their members to refrain from prescribing amphetamines for diet control. The American Medical Association, although falling short of outright opposition to amphetamine prescription for obesity, has cautioned its membership to prescribe them only with discretion.

The Food and Drug Administration has shown some sensitivity to the problem of amphetamine abuse and the possibility that their legitimate medical use may be limited. Having restricted labeling to *short-term* use for diet control, the FDA announced that efficacy studies for all amphetamine products would be required by August 1971. These reports have been in for six months; yet, in spite of action by the Justice Department, Congress, and members of the medical profession, no action has been taken on them.

I am pleased that the Subcommittee on Juvenile Delinquency will undertake to find out why no action has been taken by the FDA on this question of efficacy and I want to add my voice to those urging the FDA to act. If it is determined that the potential for abuse far outweighs any beneficial effect of amphetamine therapy in cases of obesity, the production levels can be drastically reduced and, with that reduction, the likelihood of diversion and abuse further lessened.

Senator Bayh. I wish to include in the record at this point an invitation letter to Bruce J. Brennan, vice president and general counsel, Pharmaceutical Manufacturers Association, dated January 28, 1972 anad his reply dated February 2, 1972.

(The letters were marked "Exhibit Nos. 14 and 15" and are as follows:)

Exhibit No. 14

January 28, 1972.

Bruce J. Brennan,
Vice President and General Counsel,
Pharmaceutical Manufacturers Association,
Washington, D.C.

Dear Mr. Brennan: The Juvenile Delinquency Subcommittee is planning to hold public hearings on the efficacy of amphetamines for the short-term treatment of obesity and the related issue of lower production quotas for amphetamines.

The Subcommittee would be pleased to have you testify on February 7th, at 10:00 a.m., in Room 2228, New Senate Office Bldg., Washington, D.C.

I would appreciate your forwarding 5 copies of your prepared statement at least 72 hours prior to your scheduled appearance. For purposes of introduction, please include a biographical sketch.

I am sure you are aware that the Department of Justice has established production quotas for amphetamines and methamphetamines. In view of the high potential for abuse, the actual extent of abuse, and the questionable

efficacy of these dangerous substances for the short-term treatment of obesity, I think it appropriate that this matter be aired publicly.

I am certain that your testimony will be a valuable contribution to our inquiry and I look forward to your appearance before the Subcommittee. If you have any questions, please refer them to K. Mathea Falco, Staff Director and Chief Counsel of John M. Rector, Deputy Chief Counsel at 225-2951.

Sincerely,

BIRCH BAYH.
Chairman.

Exhibit No. 15

PHARMACEUTICAL MANUFACTURERS ASSOCIATION,
Washington, D.C., February 2, 1972.

Hon. BIRCH BAYH,
Chairman, Committee on the Judiciary, Subcommittee to Investigate Juvenile Delinquency, U.S. Senate, Washington, D.C.

DEAR SENATOR BAYH: Thank you for your letter of January 28 inviting the Pharmaceutical Manufacturers Association to present its views before the Senate Juvenile Delinquency Subcommittee concerning certain questions relating to drugs containing amphetamines and methamphetamines. We note that the Subcommittee is particularly interested in obtaining information concerning the effectiveness of these substances in the short-term treatment of obesity and production quotas for these substances.

The specific areas of inquiry outlined in your invitation are not subjects about which the Pharmaceutical Manufacturers Association could present a detailed statement. We have not accumulated any direct experience or information on these subjects as an Association. We feel that individual drug manufacturers would be a much better source of information relating to these areas of inquiry. In addition, we might suggest that you inquire of the medical profession for some assistance on a more thorough presentation of the facts relating to these questions.

Once again, let me express the appreciation of this Association for being invited to participate in these hearings. If we felt that we possessed some information which could be useful to the Subcommittee's inquiry, we would have been pleased to have submitted it.

Sincerely,

BRUCE J. BRENNAN,
Vice President and General Counsel.

Senator BAYH. I wish to include in the record at this point statements prepared by several physicians relating to the use of amphetamines in their practices.

(The following prepared statements by Dr. S. K. Fineberg is marked "Exhibit No. 16"; Joseph W. Still, M.D., M.P.H., is marked "Exhibit No. 17"; and, William S. Asher, M.D., President, American Society of Bariatrics is marked "Exhibit No. 18" and are as follows:)

Exhibit No. 16

A RATIONAL APPRAISAL OF ANOREXIANTS IN OBESITY

By: S. K. Fineberg, M.D., FACP[1]

The use of anorexiants as adjunctive agents in the treatment of obesity is being strongly challenged. The reason for the renewed criticism of such medical use is the wide-spread abuse of these medications for non-medical purposes. The major thrust of the attack is the belief that there is a direct cause and effect relationship between the prescription of appetite suppressing medication in the treatment of patients with obesity and the frequency with which these drugs are taken in serious overdosage for their stimulatory effect on the central nervous system.

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[1] Clinical Assistant Professor of Medicine, N.Y. Medical College, N.Y.C. Chief, Diabetes and Obesity-Diabetes Clinics, Metropolitan Hospital, New York City.

Whether this sequence commonly occurs and the medical use of these drugs really plays an important role in causing their abuse is an important question. This should be carefully and dispassionately considered with the objectivily and logic of the scientific mind and attitude.

It is generally acknowledge that a significant but unknown number of individuals are seriously abusing various types of stimulating drugs, including the amphetamines and related compounds. The vast majority of the offenders appear to be under the age of 30. What percentage of these young drug abusers began their unauthorized and hazardous misuse of these medications as patients undergoing a medically supervised regimen for weight problems?

Consideration of this question based on case histories or clinical experience leads to the conclusion that the percentage is very small—probably even less than the small number of narcotics users who became addicted as a result of the use of drugs in the treatment of a painful illness.

The obvious truth is that the vast majority of drug abusers of this type and degree are emotionally unstable, confused or psychologically disturbed young people who are seeking escape from the tensions, pressures and mental created by the numerous social problems existing today. Society appears to be the major etiology—not the legitimate attempts to correct a serious public health menace, obesity. Possibly there exists somewhere in this land a 35 to 55 year old obese matron who, for various reasons has turned from a laudable and proper concern about her obesity to the frequent intravenous injection of metamphetamine—but this is seriously doubted. (If this situation does exist, the woman will not remain obese very long because of the severe anorexia and other serious effects of such action.)

This type of patient—the 35 to 55 year old obese matron—is the one most often treated by physicians for their obesity. Despite the obvious logical conclusion as to their addiction to amphetamines as a result of the treatment for obesity, some members of the medical profession have actually, if indirectly, expressed their acceptance of the guilt for amphetamine abuse by vowing publicly never to prescribe such medications again. Unfortunately, many of these physicians had seldom, if ever, prescribed appetite suppressing medication to begin with and, as most physicians, had avoided actively involving themselves at all in the treatment of obesity!

The many recent descriptions of the hazards and serious effects of amphetamines are based on the effects of large—sometimes massive—*overdoses* of these drugs, taken either orally or parenterally. While these effects are well documented and do not appear to be exaggerated, *they do not occur when doses in the therapeutic range are used*!

Very few, if *any* drugs do not have serious toxic, even lethal, effects in massive overdosage. It is an extremely prejudicial and fear-inspiring technique to emphasize the hazards of such dosages in any discussion of whether amphetamines should or should not be used in the treatment of obesity. What is really pertinent to such a discussion is whether the progression to self-inflicted overdosage occurs with any real frequency in the setting of a physician's management of his obese patient.

That it does has erroneously been assumed without statistical data or even clinical experience for corroboration. On the contrary, the experience indicates that the physician can easily prevent even the infrequent occurrence of habituation if it begins to appear in a psychologically predisposed individual. Habituation, even addiction, to most drugs—and particularly to anorexiants—is psychological, not physical. Patients do not easily or frequently become unwitting and unwilling victims of appetite suppressant drugs. The potential for harm becomes almost minimal when their purpose and place in the treatment is properly described initially, *and if they are withdrawn when the patient loses motivation and is no longer cooperating with the dietary regimen.*

It must be concluded, therefore, that the use of amphetamine and amphetamine-like drugs in a medically supervised treatment for obesity does not promote abuse and that the dangers of such drugs when used properly are actually very small. Obviously they should not be used in the treatment of obese patients who have a history of psychosis, serious emotional instability, alcoholism or abuse of other drugs. Nor should they be used, as a rule, for treating obesity which is the outward manifestation of a psychoneurosis.

If there is little or no advantage to be gained from the chemical suppression of appetite in the treatment of obesity, as some contend, then the fact that

there is really little danger when they are properly used in this condition becomes purely academic. Doubts about the efficacy and mode of action of these drugs have been disinterred recently by individuals who appear to have experience with their *abuse*—but little or no experience with their *use* in the actual treatment of obese patients. They practically ignore the considerable body of laboratory and clinical evidence which indicates a strong decrease in physiological hunger in most individuals taking anorexiants, pointing only to the poor end results of most efforts to control obesity. This means only that controlling hunger is not a simple solution to the complex problems of obesity.

Repeated investigations have been performed in the laboratory on the hypothalamus. These have demonstrated involuntary appetite suppression in animals. Several carefully controlled objective, triple-blind clinical investigations of appetite suppression in humans indicate almost conclusively that amphetamines have a direct suppressant effect on the appetite center in the ventrolateral nuclei of the hypothalamus. This effect appears to be entirely separate and distinct from the stimulating effects on the CNS (sympathomimetic activity) for which these drugs are notorious. Appetite suppression with these drugs usually continues *after the CNS stimulation of therapeutic doses wears off, and in its complete absence.* On the other hand, the recently revived and quoted opinions of 10 years or more ago that anorexigenic drugs work as "central-stimulating appetite distractors" by producing euphoria or by "significantly modifying the patient's drive toward overeating" (!) are *unsubstantiated conclusions not based on any properly controlled investigations or proof.* They are truly unworthy of the scientific approach, although usually stemming from its fountain-head, the halls of *academe*!

The appropriate and proper use of anorexigenic drugs in an overall program for weight reduction *is to relieve the acute symptoms* which are invariably produced by a sharply lowered caloric intake. They should *never* be used as the sole means of treatment. When used alone it has been conclusively demonstrated that they *will* cause a short term reduction in weight by inducing a moderate, practically involuntary, reduction of caloric intake. This will occur even in individuals who are totally unaware of the purpose or effects of these drugs.

As repeatedly stated, their use should be only as part of an intensive program which includes patient motivation, and instructions in diet, good nutrition and caloric content of foods. *The evanescent effectiveness of the treatment of obesity based solely or mainly on anorexiants is quite well-known and is due to the glaring deficiencies of such an approach, not to ineffective or evanescent appetite suppression. THIS DISTINCTION IS AN IMPORTANT ONE!* It is the weaknesses of even the most enlightened approach to the treatment of obesity in which the medical profession needs to be more thoroughly strengthened and indoctrinated. If there is guilt to be assumed, it is for the avoidance of real responsibility and involvement with the victims of obesity and not for the exaggerated dangers of their being prescribed amphetamines.

Today's treatment of obesity which is based on diet restrictions, nutritional education and strongly motivating the patient to a permanent change in his eating habits has a high rate of failure because it demands so much, not only of the patient, but also of his physician. Yet at this time it is all that medical science has to offer. It fails so often, particularly in severe degrees of obesity, because the patient concludes that the treatment which consists of permanent, if only partial, starvation is more unendurable than the disease or fear of its consequences.

In the actual practice of medicine, anorexigenic drugs are often of distinct help in furnishing relief of symptoms produced, particularly with the initiation of the total treatment program. In view of the weakness of the total treatment, every weapon at our disposal should be utilized. Effective appetite suppression *is* available. It is not indicated, and should not be used, in the continuous, long-term management of obesity. But in skilled, knowledgeable and experienced hands it has a potential for good which outweighs its potential for harm *as a medical prescription.*

Appetite suppression often means the difference between a significant degree of initial—then continued—success or control, and total failure. For this reason, it seems more beneficial and logical to educate and regulate the medical profession and the public in the wise and proper use of anorexiant medications rather than to condemn and prohibit their use entirely.

Exhibit No. 17

PREPARED STATEMENT OF JOSEPH W. STILL, M.D., M.P.H., PRESIDENT AND DIRECTOR, PERSONAL PREVENTIVE MEDICAL GROUP, INC.

I will begin by saying that I have no quarrel whatsoever with the careful control, distribution and prescription of amphetamines or with the concept of establishing quotas. What I want is to insure that in future, practicing physicians like myself, who understand the proper *use* of these drugs for the treatment of obesity, have an opportunity to present our evidence and views to the FDA or other administrative or legislative agencies.

I have four basic goals in making this statement:

1. To bring to your attention a letter which I sent on September 4, 1971 to Dr. Henry E. Simmons, Director, Bureau of Drugs, Food and Drug Administration. This letter was a response to a form letter Dr. Simmons sent to physicians to explain the Drug Efficacy Study. He ended his letter by saying, ". . . we welcome your comments and suggestions." But to date I have not even had an acknowledgement of my letter. This experience adds to my belief that the FDA communicates mostly with ivory-tower disease- and research-oriented physicians and has little interest in the observations or opinions of practicing physicians like myself whose main interest is in *preventing* disease.

2. My second goal is to show you gentlemen enough evidence of the potentialities of personal preventive medicine to convince you that a large part of the Medical Establishment—including the FDA—is standing in the way of a most important medical advance, just as medical establishments have repeatedly done throughout history. I say this because it is a generally acknowledge fact that the most important epidemic in our society is overweight and yet the FDA banned cyclamates for what I believe most physicians agree were insufficient reasons, and now it is considering the banning of amphetamine appetite depressants and saccharine. I only wish I had the writing skill of Lewis Carroll. I'd write another chapter or two for Alice in Wonderland.

3. Third, I hope to convince you that it is only necessary to make a thorough study of the evidence that can be obtained from my records and by interviewing an appropriate sample of my patients to convince the members of this committee that: (a) The widespread practice of Personal Preventive Medicine could substantially extend the life expectancy of millions of Americans; and (b) The importance of the proper uses of amphetamines to treat narcolepsy, hyperkinetic children and obesity, is such as to make it absurd to place unnecessary barriers in the way of the millions of patients who can benefit from their use.

4. Finally, I hope that if I succeed in these first three objectives, this committee will insist that NIH make a thorough and *fair* study of my practice and report back to this committee before any drastic decisions with resepect to legitimately used amphetamines are made.

My letter to Dr. Simmons, to which I have had no response, follows:

These claims can also be documented with pictures, records and live patients.

SEPTEMBER 4, 1971.

HENRY E. SIMMONS, M.D., M.P.H.,
Director, Bureau of Drugs,
Food and Drug Administration, HEW,
Rockville, Md.

DEAR DR. SIMMONS: This is to comment on your explanation of *The Drug Efficacy Study*, which I have studied carefully.

It confirms what has concerned me ever since I first read about the way the Efficacy Study was to be carried out. Let me tell you why I am concerned:

1. The panel with some 200 medical and scientific specialists is described as ". . . predominantly physicians with academic affiliations for the obvious reason that these best met the legal qualification of 'experts qualified by scientific training and experience to evaluate the effectiveness of the drug(s) involved'."

I'm sorry but it is not "obvious" to me that the individuals on the panel that considered combination drugs in the amphetamine-barbital group "best met the legal qualifications etc."

First of all, there has been no release of the names of the few men who made up the panel that considered the efficacy question as it related to the

amphetamine-based drugs. I'm sorry to tell you that neither the FDA nor the NAS/NRC has established their credentials with me to the point that I will accept from them decisions—decisions that so critically affect my ability to treat patients—without my knowing (a) who made the decisions, (b) what reasons they offered for making their decisions, and (c) the specific literature references they offered as the foundations for their decisions. Without this you are asking American physicians to bow to Big Brother in the form of the NAS/NRC panels.

I'm afraid there are too many physicians who have been trained to do their own thinking and who have witnessed more than one such Establishment boo-boo—such as the latest one by the U.G.D.P. group—for the Food and Drug Administration's screening plan to be accepted by the medical profession. The reason I went into medicine was because I thought it offered a way of life in which I could be independent of everything except the best interests of my patients. I consider this procedure a fundamental violation of my professional rights and my responsibility to my patients.

2. The combination drugs with which I am most experienced are several combinations of dextro- and levo-amphetamine sulfate with barbiturates. The specific combinations which I use most extensively are generic drugs which have been in clinical use for many years. When they were first placed in use, it was not customary to subject drugs to the kind of extensive study now required for new drugs. Therefore, it is not reasonable to expect that an extensive justification literature exists in support of these new generic drugs. But there is a vast amount of clinical experience which demonstrates that these drugs are both safe and effective.

Unfortunately very little of this clinical experience has been quantified, summarized and reported, for at least one very good reason. The funds available for medical research over the past 25 years have gone almost exlusively to those working in medical schools or long-established medical institutions. When I am now told that academically based physicians are best qualified to evaluate combination drugs, I'm reminded of a wise comment I once heard—"They cut off your legs and then call you Shorty."

As you no doubt are aware, there is no more difficult or expensive kind of research than the kind of clinical research that the Food and Drug Administration now suddenly asks the manufacturers of and physician users of these combination drugs to supply.

I have good records on hundreds of overweight and hypertensive patients who have lost weight and reduced their blood-pressure with the help of combination amphetamine-barbiturate drugs. And I have several hundred overweight and hypertensive patients continuously under treatment with these combinations. As a physician-scientist with considerable experience in both epidemiology and research, I feel certain it would take no more than a thorough study of this one source of data to convince even the National Academy of Science panel that these combinations are both safe and effective and also that they are not a useful drug on which to get high. But an adequate study might well cost as much as $100,000.

Now, you may say it is not the job of the Food and Drug Administration to fund clinical research studies or to set the granting rules and policies of the National Institutes of Health.

If you do respond in that way and the Food and Drug Administration proceeds to ban these combinations, I ask you what drugs do you recommend I use to help overweight people to stay on diets which average 500 calories per day less than their bodies are using? Unless a drug or technique that is as effective as these combinations have shown themselves to be can be offered as a substitute, I believe that the Food and Drug Administration will have to bear responsibility for condemning millions of overweight Americans to as short, unhappy life.

I am satisfied that if we knew the "training and experience" of the "physicians with academic affiliations", we would find that a very high percentage of their time (I'll hazard the guess that it will be 90 to 95%) is spent in questioning, studying and analyzing patients who are sick enough to be in "academic" hospital beds. They are experts, I presume, in the diagnosis and treatment of diseases. I and other physicians like me are experts in *preventing* disease, and that's what amphetamines are mainly for.

Those of us who are at any given moment treating *with success* a few million overweight and obese patients *in our offices* are the real specialists in the legitimate and justifiable *medical uses* of amphetamine-based drugs to suppress appetite. I've had no experience with the use of amphetamines to treat hyperkinetic children but since this also is largely an out-patient procedures, I wonder if this group of physicians and their patients were adequately represented on the amphetamine panel.

By now you may be wondering about the nature of my practice. I treat such *pre-disease conditions* as obesity, hypertension, hypothyroidism, hypoglycemia, diabetes, psoriasis, osteoporosis, arteriosclerosis and gonadal hypofunction. I do this in such a way that I achieve long-term control of these conditions for a substantial percentage of my patients. I'll not go into the details of how I do this, but I invite a *thorough study* of my practices and results by a competent and properly constituted study group.

Now, as I'm sure you are aware, the most serious treatable and correctable threat to the lives of the American people is overweight and obesity. And so it is only natural that about 75 percent of my practice is devoted to that problem. It turns out that many of these unfortunate people really are mildly hypothyroid and respond favorably to thyroid. Many of them are also hypoglycemic. Some are both hypoglycemic and diabetic. Most of these can be helped a great deal by teaching them what to eat and how often to eat. Many overweight people, as you know, are also hypertensive. When the fundamental cause of their overweight is removed, their blood pressure usually returns to and stays normal.

But Dr. Simmons, losing twenty, fifty, one hundred or more pounds is not an easy job either for patients or for their physicians. Aside from accurate diagnosis of the fundamental cause, appropriate nutritional and health education and the permanent administration of thyroid to those who are hypothyroid, there were two important therapeutic tools available to overweight people when I entered this field about eight years ago. One of these was cyclamate, which enabled many patients to use readily low calory drinks to appease their hunger between meals. The other was appetite depressants.

Cyclamates were abruptly taken away two years ago and now my principal supplier of appetite depressants (Darby Drug Company) has abruptly stopped supplying me with the DAS 15 mgm/Amobarb 60 mgm R.D. spansule that has proven effective, safe and nonaddictive to obese patients. The supply has been cut off because the manufacturer who formerly supplied Darby has simply stopped making it. Since I can get plain DAS T.O. spansules—which I admit do have a potential for getting high if used in large doses—I can only assume that the manufacturer decided it wasn't worth it to go to the trouble and expenses of trying to defend this combination under the conditions outlined in your section marked "The F.D.A. response."

You see, Dr. Simmons, one of the ways by which those of us who treat the overweight and obesity of large numbers of people with moderate and even low incomes is that we keep the total cost down by dispensing, without charge, the largely generic drugs which we use. If we sent our patients out with prescriptions or if we provided them with proprietary drugs, the total cost would of necessity be significantly higher.

Inasmuch as many of my patients drop out from time to time because of what you and I would consider minor financial crises, it is apparent that everything should be done to keep down the cost of treating this, the largest, most endangered and most neglected group of disabled Americans. But the effect of the efficacy study and of transferring the control of these drugs to the I.R.S. will be both to increase the cost of the drugs and the cost of handling and administering them.

To deny 50 million hard-working, disabled Americans an opportunity to be reduced in a safe and relatively painless way in order theoretically to cut down on the illegal use of Speed, an amphetamine which I understand is very little used as an appetite depressant, will show once more that the medical establishment only talks about prevention but does everything it can to handicap those of us who try to practice it.

In order to make clear that I am writing in a constructive spirit, I offer to support every claim I make here with the proviso that any actual study of my practices and results be carried out in a way acceptable to me.

Finally, I urge that before the Food and Drug Administration makes final decisions with respect to the efficacy of the amphetamine combinations, it solicit the advice and hear the experience that many reputable physicians have had in the legitimate use of these drugs to combat the most serious epidemic in our society—overweight and obesity, which are so often the precursors of early diabetes, arteriosclerois, heart attacks and strokes.

Yours sincerely,

JOSEPH W. STILL, M.D., M.P.H.

The contents of this letter can also be taken as a response to the testimony to this committee made by Dr. Charles Edwards. While I believe Dr. Edwards is an honest, energetic and capable official, I know he has had very little experience as a practicing physician. And I know that he must make most of his decisions on the basis of advice he receives from so-called experts. He *cannot* personally study all of these matters. That is the main hazard of all high-level administrators. I know because I've had several such jobs myself. The trouble in this case is that Dr. Edwards failed to talk to the real experts in this matter—physicians like myself who have had enough interest in this important medical condition to make a specialty out of treating it.

To support the major claims and opinions in my letter, I offer the following statements of fact or of opinions which I am certain can be factually verified by the research study of my practice that I hope this committee will request NIH to make:

1. It is not necessary to use highly stimulating amphetamine drugs, such as Speed, to depress appetites. I have never prescribed Speed for any purpose. Nor is it necessary to use large doses of the less stimulating amphetamines in order to give most patients on restricted diets, substantial relief from hunger.

2. Through the use of these drugs, the vast majority of patients experience immediate and substantial weight loss. And those who stay on the program for sufficient time lose large amounts of excess fat. I can present many pictures as well as live patients who, with the aid of appetite depressants, other drugs such as thyroid and diuretics, and appropriate education, have lost large amounts of weight.

3. Many of this group have histories of years of being overweight. Some of them have even been fat since childhood. Many such patients have now been reduced to normal weights and *maintained at those weights for many months and years.*

4. The principal reasons that all my patients do not lose down to normal weights are these:

(a) They move too far away from my office to be able to continue with me. I know many continue with other physicians because they ask me to refer them to others who specialize in weight reduction.

(b) Financial crises arise which cause quite a few patients to drop out of the program—often only temporarily.

(c) The steady din of scare stories about the alleged dangers of appetite depressants frightens a few of my patients into dropping out of the program. No doubt they also frighten many into never starting who could be greatly helped by the kind of care that I and others with similar knowledge and skills can give.

5. Through the combined use of appetite depressants and thyroid, we have reduced the blood pressure and excessive weight of many individuals with dangerously high blood pressure. Our success ratio in doing this is so high that I feel safe in saying that if all the hypertensives and seriously overweight people in the U.S. could be treated in similar fashion, the reduced numbers of premature deaths would be sufficient to make a substantial increase in the average life expectancy of Americans. In other words, I am claiming that I practice the kind of preventive medicine that everyone wants to see practiced but which no one has yet told Congress how to do it.

I will now present a few statements made to this committee by Dr. Arthur Goldstein, and comment on them. I will first present a quotation from him which will be underlined, and then follow with my comments. *While the FDA has been studying and conferring, the 250 physicians in the town of Huntington and the 1100 physicians in Suffolk County found that it was not necessary to prescribe amphetamines for cases of obesity. The physicians pledged to confine their prescription of amphetamines to cases of narcolepsy and hyperkinesis.*

Comment: This statement leaves the impression that all of these physicians have previously been using amphetamines to treat obesity and have now stopped. What kind of sense would that make? As Dr. Wolfson and Dr. Edwards and thousands can testify, these drugs are useful in the treatment of obesity.

The fact is that the vast majority of physicians in Huntington and Suffolk County like the vast majority of physicians in the U.S., don't understand obesity, don't know how to treat it, and aren't even interested in treating it. I say this because practically all of my patients have tried to get help at some time or other from their family physician. Most of these patients were dismissed, without any study, with the simple remark, "Oh, there's nothing wrong with you except you eat too much." This is another basic fact that my patients will readily verify. Incidentally, my practice is made up mostly of hard-working middle-class men and women—housewives, teachers, lawyers, nurses, police officers, engineers, businessmen. They are hard-headed intelligent people and most of them have come for my help because they were referred to me by other hard-headed intelligent patients whom I had helped to lose weight and regain their health. *Amphetamines are among the most dangerous of the psychoactive drugs, and among the most easily obtained. Continued use of amphetamine drugs can cause physical and psychological dependence, behavioral toxicity, and in extreme cases a condition of mental unbalance resembling paranoid schizophrenia.*

Comment: The first sentence is an essentially correct statement. But the second sentence is flatly untrue with respect to the proper use of these drugs to help obese patients undereat. Never once have I had a patient who stopped taking appetite depressants show the slightest evidence of "dependence". And well over 4,000 of the 5,000 patients I've treated stopped taking them not only once but several times.

The second sentence refers to Speed addicts and not to the normal use of amphetamines. My study of addiction has convinced me that the *principal cause of addiction is not drugs but the underlying psychosocial pathology of the individual.* The drugs they take—heroin, LSD, amphetamines, barbiturates or alcohol—are secondary factors and are taken to relieve their psychic pain Thus addiction is basically a symptom and not a cause.

Two of the outstanding students of addiction in this country are Dr. Daniel Casareal and Dr. Lewis Yablonsky. They have been full-time students of this problem for more than ten years. I suggest this committee invite them to testify on this point. *The time has come to lay to rest once and for all the myth that amphetamine compounds are specifics for weight reduction and control. Despite the fact that these drugs do cause a temporary anorexia or loss of appetite, they have repeatedly been shown to be of little or no value in the establishment of a program of continued or long-term weight loss.*

Comment: This myth has not been created by physicians who use these drugs extensively, as I do. Of course these, *like most drugs, have only temporary affects.* But through their temporary use it is possible to remove the discomfort that brings the patient to a doctor. In some cases it is a temporary infection. The penicillin cures the patient but doesn't prevent a recurrence. The same is true of amphetamines. They help the patient to lose his or her excess fat. The fact that it may recur after a time is no more a reason to stop the use of these drugs than it would be to stop the production of penicillin for similar reasons *Production allowances should not allow for the use of amphetamines for weight control at all, since this is a medically valueless use of the drugs, and is, therefore, an abuse.*

Comment: This extreme statement proves that Dr. Goldstein is *not* a thoughtful and wise man, and therefore causes me to distrust every word of his statement.

Now I will comment on statements made to this committee by Dr. Edward A. Wolfson. Again I will present his quotes and underline them, and then my comment. *There are many authorities who believe that this is the most dangerous of the currently abused psychoactive drugs, yes, more dangerous than the opiates, and that for the most part, its presumed effectiveness, even under medical aegis, is most likely a result of euphoria—a chemical nirvana.*

Comment: I spent more than a year's time during 1962–1963 doing fulltime research on the entire subject of drug abuse and have continued to be a student of the problem ever since that time. In all my studies and conversations I

have never before heard any similar statement. I suggest this committee ask Dr. Wolfson for the names and relevant statements of the "many authorities".

A very important point that this committee must consider is this:

Those who want to get "high" on Speed usually don't take it by mouth, as most doctors prescribe it. Speed freaks use it intravenously. And they use it in doses that are often 10 to 20 times as large as are ordinarily used to reduce appetite with *the less stimulating members of the amphetamine family of drugs*. Besides these facts about Speed, it seems clear from all the information I can gather that most of the amphetamines found on the "street" were *not* produced by legitimate drug companies but by "bootleg" factories which can make these drugs easily and cheaply. With the added expenses that legitimate drug manufacturers now have, in order to safeguard these drugs the economic scales are tipped even further to the advantage of the bootleg factory. *The scientific literature now abounds with the well documented detrimental effects of long-term, high-dosage use of these chemicals and recently a chemical model of acute psychosis has been induced within 1 to 5 days by the hourly administration of average amphetamine dosages to presumably psychologically normal volunteers with a previous history of stimulant abuse.*

Comment: I'll not dispute this statement but what has this kind of massive dosage misuse of amphetamines got to do with its use in the usual dose range of about 10 to 30 mgm per day? *There is finally appropriate recognition that chronic use of these substances, whether prescribed or not, often results in evident antisocial behavior, severe psychological and probably physical damage, and a strong dependence.*

Comment: Having treated at least 5000 patients with these drugs over substantial periods of time and *never once* seeing any evidence of such affects, I say this statement is flatly untrue and again suggest that Dr. Wolfson be asked to prove it. I am not saying that all people can tolerate amphetamines. I estimate that somewhat less than 1% of my patients are unable to tolerate these drugs. But I assure this committee that these people do not become addicts. They are made so uncomfortable that they usually discontinue the drug themselves or I do so when I see them after a few days trial of the drug. *The economic value of sales is substantial. Recall that the patent rights on the basic drug have long expired and that the drug is easily manufactured from inexpensive chemicals.*

Comment: The first sentence would seem to be in conflict with the second. It is well known that the most expensive drugs are those protected by patents and that when patients run out, drugs then are sold on the generic market and their prices drop substantially. *Perhaps the "expert" is a practicing physician who historically demands the right of medical decisions without interference, regulation, or control and who jealously guards his right to prescribe what he deems best for the individual patient. Or we might hear from the representatives of public health who have the primary concern of the health of populations or, finally, the authority in the drug scene who sees and treats the dropouts from a drug-oriented society*

Comment: Having had professional experience in all of these three capacities, I am amazed by the statement that "representatives of public health have the primary concern of the health of populations." That might have been true a century ago before modern medicine and surgery acquired the knowledge and skills now possessed.

Public health—that is, environmental medicine—was born several centuries ago when men first began to notice that diseases such as smallpox were spread from village to village by disease carriers, by infected water and food and the like. Modern public health developed to equip public health personnel with the tools of chemistry, bacteriology, statistics and epidemiology. But it did not make the field of public health the overarching umbrella of medicine that Dr. Wolfson claims.

Indeed, the successes of modern medicine, surgery *and* public health have so reduced deaths in the early years of life that now the principal job of medicine lies in the fields of rehabilitation and of prevention of premature disability and death from the degenerative conditions that most Americans now live long enough to acquire. *The dangers (in the selective and controlled use of amphetamines) are minimal while the potential gains are substantial. Indeed almost every study using amphetamines in controlled or uncontrolled tests, has demonstrated that over a four-week period, patients taking amphetamines lose weight more readily than patients on placebo or on no medication.*

Comment: This is the basic truth about the proper use of amphetamines as I and I'm sure most knowledgeable and conscientious physicians use them. The only thing wrong with the statement is the implication that these drugs are only useful for four weeks. Apparently Dr. Wolfson had in mind studies that only lasted for four weeks. Many studies of longer duration also show that these drugs are of continued effectiveness both in humans and animals. *Certainly the amphetamines and like substances are not a cure for a complex, frequently lifetime, problem with predominantly social and psychological determinants.*

Comment: I agree that most overweight patients have a lifelong problem to contend with, but I vigorously deny that this problem is "predominantly social and psychological" in its causation. I made a study of the PBI values of 600 overweight patients and found that approximately 400 of them were suffering from some degree of hypothyroidism (underactive thyroid production with resulting symptoms, the most apparent of which is overweight). Additionally, a good many of the 400 also suffered from hypoglycemia—a condition that is only recently beginning to receive the attention it deserves. A large percentage of those who have been labelled neurotic compulsive overeaters suffer from this condition.

Now while neither of these conditions can be cured, the fact is that with proper treatment, which means the use of thyroid and amphetamines in most patients and individual *education* of *all* patients, I am sure it is possible to reduce most patients *and to maintain them for the rest of their lives at those reduced weights.*

The important point to bear in mind is that according to Dr. Edwards' testimony there are at least 31 to 34 million Americans who are potential beneficiaries of the proper use of amphetamines. That is, their health and their actual length of their lives requires them to lose weight. Doing this is extremely painful on a pure "cold turkey" basis. *How do we best regulate the obvious and flagrant overuse and sometimes indiscriminate over-prescribing?*

Comment: I believe this is the key question before this committee, and I will close my statements by offering my answer to it.

According to Dr. Edwards' testimony before this committee, the following numbers of patients can theoretically benefit from the use of one or other amphetamine-type drug:

	Thousands
Persons suffering from narcolepsy	25–1, 000
Hyperkinetic children	900–3, 000
Adults [1] 21 to 65 who are 20 percent or more overweight	30, 000
Total, about	31, 000–34, 000

[1] Of course, there are many millions of seriously overweight people who are less than 21 years old. Not many over 65 are overweight because most seriously overweight people die before age 65.

I estimate that the average dose of amphetamines given to my patients *while they are reducing* is about 15 mgms per day. Since I have found that at least 99 out of 100 patients have no serious side effects from their use.

It is firmly established that being 20 percent or more overweight is a serious health hazard. If it is a proper goal of medicine to help fat people to reduce and stay reduced, then it would seem that the amount of amphetamines required for legitimate medical uses to treat overweight people is potentially at least 30 million times about 15 mgm times 365 days. That works out to about 33 billion 5 mgm. doses which I understand is about four to five times the present legitimate production in this country

So I would say that there is no reason to cut production. And in fact this committee could do a great deal for the health of these unfortunate 30 million-plus fat people if it would reassure them to the effect that the carefully supervised use of these drugs is a safe and legitimate and desirable practice.

As for the abuse of these drugs which I am as anxious as anyone to see stopped, I offer the following suggestions:

1. Placing the production and distribution of drugs under strict controls as has been done is a useful first step which I applaud.

2. The establishment of production quotas is also reasonable, provided that the quotas are made on the basis of needs established by physicians acquainted with the legitimate uses of these drugs rather than by those whose

main concern is with the illegitimate uses of them (as is the case with Dr. Wolfson) or by those whose primary interests center in the Ivory Towers where there isn't even enough interest in the subject of obesity to see more than a handful of research studies of it being made.

3. The final thing that might be done, which I believe has not yet been recommended to this committee, is this. Have the BNDD establish a standard prescription form for prescribing all dangerous drugs. Each physician would be provided with blanks which contained an identifying number similar to bank code numbers. Whenever a dangerous drug prescription was written, it would contain the Social Security number of the patient. With such a basic report system in operation, it then would be easy to feed this data into a central computer and quickly identify those patients who might be going to several doctors at once in order to get excessive amounts of a given drug. And of course, the system would readily identify those doctors who prescribe large amounts of these drugs—as I do.

I have no objection to exercising reasonable controls over the handling of these drugs. What I do object to is the fact that the abuse of these drugs has been so overemphasized by the media that their legitimate uses—which is their only legitimate reason for being manufactured—has been almost completely ignored. I hope this committee will give concern to this point as well as to the steps needed to prevent abuse. Finally I hope the committee will also give serious consideration to my proposal that a sort of pilot research study be made of my practice to *prove or disprove the statements I have made to this committee*. If they are true, they have great significance for the health of many millions of Americans. If they are true these facts should be made known to the medical profession in general. I have had a long and, I believe, reasonably successful career in medicine and am now approaching retirement. I think there is nothing I have done or will ever do that is more important for the health of the American people than to make and publicize the research I have proposed. I'm willing to stake my professional integrity on the result.

Thank you.

Exhibit No. 18

PREPARED STATEMENT OF WILLIAM S. ASHER, M.D. PRESIDENT, AMERICAN SOCIETY OF BARIATRICS, CONCERNING THE AMPHETAMINES

I make this statement concerning the amphetamines as President of the American Society of Bariatrics (ASB). The Society speaks for approximately 2500 physicians from all parts of the United States who have a special interest in the problems of obesity. It is the only viable national organization whose members have a special interest in obesity. Our members are practicing physicians who deal with this difficult problem on a daily basis. Our opinions come from being on the firing line. It is probable that a number of our members see more patients individually than do most of the ivory tower experts combined.

I have personally had experience with the use of the amphetamines in approximately 1500 patients and have also had the opportunity to study a number of other practices where amphetamines have been used. Yet it is with a certain feeling of reluctance that I express the views, which I believe reflect the feelings of the majority of these physicians concerning the amphetamines.

In this atmosphere of mass hysteria concerning the ill effects of the amphetamines even an attempt at objectivity is apt to earn one the label of supporter of drug abuse. Yet nothing could be further from the truth. Long before there were governmental controls on the amphetamines most of our members required their patients to return to the office to be checked before they received further medication, including the amphetamines. Most of our members retain tight control over the amphetamines in their practices by dispensing their own drugs. The refillable amphetamine prescription, made illegal in 1971 by placing the amphetamines in Schedule II, had rarely been used by our member physicians for two decades prior to this.

I suppose we are also more concerned by amphetamine abuse than the average physician since we are painfully aware that abuse by a few may ultimately make this useful drug unavailable to the millions of patients with an obesity problem.

I will address myself briefly to three questions. They are:

(1) What is the extent of the abuse problem?

(2) Will removing these drugs from the market place solve the problem?

(3) Does the benefit/risk ratio justify the use of the amphetamines in the treatment of obesity?

The third question I feel quite qualified to discuss. The others I have only limited information on; however, I expect I am as qualified to discuss drug abuse as are the drug abuse "experts" who discuss (and denounce) the use of amphetamines in the treatment of obesity with which they have had little or no experience

It goes without saying that there is a drug abuse problem by a segment of our society. A portion of these abusers are "speed freaks" or they are lesser abusers of the amphetamines. Yet I would venture the abusers of amphetamines are a small segment of our society compared with the abusers of another commonly used drug—alcohol. And many of our legislators, who censure the amphetamines, continue to support the alcohol industry by the use of their products.

It is easy in this era of mass hysteria to conclude that "we have become a society of habitual drug seekers." But does hard data support that conclusion? Apparently not. One can only get hard data by well done cross-sectional surveys. Dr. Mitchell B. Balter, of the Psychopharmacology Research Branch, National Institute of Mental Health, and Dr. Glen D. Mellinger and Dean I. Manheimer, of the Institute for Research in Social Behavior, Berkeley, California, have published a paper "Patterns of Psychotherapeutic Drug Use Among Adults in San Francisco," Archives of General Psychiatry, *25*, p. 385, 1971. In this study they obtained data on the use of psychotherapeutic drugs in personal interviews with a cross-sectional sample of adults in San Francisco. Their data covered drugs gotten by medical means, over the counter, and nonmedical means They concluded: ". . . there is little evidence from this study that large numbers of adults are becoming long-term users of psychotherapeutic drugs. In fact, most persons appear to be relatively conservative in their use of these drugs. Our findings indicate that ambivalence about the use of drugs such as minor tranquilizers is very common, even among persons who use them. While it may well be true that attitudes and values are changing with respect to drugs, it is much too early to claim that we have become a society of habitual drug-seekers."

Now again I wish to stress that the American Society of Bariatrics in no way supports the nonmedical use of the amphetamines. I only wish to point out that we may be moving into an era of drug "overkill." There is real danger that the net effect of our regulatory agencies attempting to remove drugs from the street will be the removal of useful drugs from the physician's armamentarium.

Question 2. Will removing the amphetamines from the market place solve the problem of their abuse? I think no one knows. I would expect it might have some impact on misuse and minor abuse. Another unanswered question is whether the abuser or potential abuser of amphetamines will, if the amphetamines are not available, turn to harder drugs. I doubt that restricting the medical use of amphetamines will significantly affect the "speed freak" who obtains the bulk of his amphetamines for intravenous use from illicit manufacturers. This was true in California even in 1967 when the diversion of medical amphetamines was relatively easy ("Amphetamine Abuse," by John C. Kramer, M.D., et al, in the Journal of the American Medical Association, *201*, p. 89, 1967.) Methods for amphetamine production are readily available in our libraries. However C. L. Hider, whose paper "Preparation of Evidence in Illicit Amphetamine Manufacturing Prosecutions," in the Journal of The Forensic Science Society, *9*, p. 75, 1969, publishes eight methods for the production of the amphetamines points out this is of little consequence since the methodology is now passed from one to the other "cookbook" fashion. Control of precursors to make the amphetamines is difficult since they, in turn, may be made from other precursors as common as molasses (see "Amphetamine Synthesis" attached). In short, the impact on the drug abuse segment of our society must be weighed against impact on another much larger segment—the obese segment, if the medical use of the amphetamines is restricted. It should be pointed out that use of the amphetamines by the "speed freak" is really not

analogous to the medical use of the drug. First the "speed freak" usually takes the drug intravenously rather than orally and second the "speed freak" may take up to 1000 times (15,000 mg) the usual prescribed daily dose (Kramer, et al, see above). That they survive at all is some testimony to the drug's relative safety.

Question 3. Does the benefit/risk ratio justify the use of the amphetamines in the treatment of obesity? First, is there an obesity problem in America? Yes. Although there is no real hard data on the prevalence of obesity, estimates of those overweight or obese have ranged from 20 to 60 million Now, what segment of the obese population is at significant risk? Again hard data is lacking. Although the morbidity-mortality risk for those 20 to 25 lbs over ideal weight is increased a little we have at times I suspect been inclined to overemphasize the risk of mild obesity. However, as we move on to those who are 50 to 100 lbs, and more, overweight the mortality curve sweeps up rapidly. So I think we can safely say there are multimillions of people in the United States who are at significant risk because of obesity. And of course other medical conditions such as adult-onset diabetes are not infrequently associated with obesity.

Why do people get fat? I submit the body of evidence indicates people are born with a predisposition to leanness or fatness just as they are born with the predisposition to be short or tall. However, there is some recent evidence that nutrition during the first few years of life may influence this predisposition. Now does being born with this predisposition or having it thrust on us early in life mean that one who is so unfortunate must be obese? No. Certainly availability of food, desire to be thin, exercise patterns, emotional stresses, etc., play a part but they play against a backdrop of preprogrammed fatness levels. And there appears to be a tendency during early and midlife for these levels to be set higher as time progresses in many individuals with tendency to obesity.

What are the results of treatment? They are poor on a short term basis and even bleaker on a long term basis. A review of the studies reported in the literature between 1928 and 1958 where the emphasis was primarily on diet showed that 24% of the 1269 patients lost 20 lbs or more, and 5% lost 40 lbs or more. A review we did of bariatricians using medications in addition to diet indicated 38% of the patients lost 20 lbs or more and 10% lost 40 lbs or more. So the medicated group was, on the average, considerably more successful than the other group. Now I wish to emphasize the relative "poorness" of the results in both the medicated group and the nonmedicated group must be considered in the following context. First, these figures are based on all starting patients whether or not they were cooperative and whether or not they dropped out of treatment; second, it should also be emphasized that it is the "hard core" obese who tend to see the physicians, since a fair segment of the obese population are able to control their tendency to obesity without medical help.

A reduction in food intake is paramount in controlling obesity. An increase in energy expenditure by exercise is of course also desirable. It is a painful and tedious task for most obese patients to change a lifetime of eating habits. It is here that the amphetamines, as appetite suppressants, have their prime usefulness. The stimulating effect of the amphetamines is also generally beneficial since studies have shown the obese tend to be more lethargic than their normal weight counterparts.

All of the presently marketed appetite suppressants are amphetamines, or chemical cousins (modified amphetamines). All produce some degree of stimulation. When we speak of amphetamines the whole broad class must be considered.

As a group, bariatricians have favored the generically obtainable amphetamines over the modified amphetamines (name brand appetite suppressants, all of which are patented). There is no evidence that any of the modified amphetamines are more effective appetite suppressants than the common amphetamines. The former group are a minimum of 10 times more expensive than the common amphetamines. The members of the American Society of Bariatrics are most interested in holding the line on rising medical costs. Thus we believe it is absolutely essential that the generic amphetamines remain freely available to the practicing bariatrician and other physicians who desire to use them *in* the treatment of obesity.

It is unfortunate that some physicians have used the amphetamines *as the treatment for obesity* and not *in the treatment of obesity.* The amphetamines are of little value when combined with a 3 minute office call, a 1000 calorie diet sheet and the admonition to return when the excess weight has been lost.

I will discuss briefly how the amphetamines work. There is, of course, the stimulating effect on the brain we are all familiar with. In addition the amphetamines also apparently cause the release of norepinephrine from tiny nerve endings near the fat cells. This in turn causes mobilization of fat from the fat cells. Pinter and Patee have demonstrated a rise in circulating free fatty acids when patients receive the amphetamines ("Fat-Mobilizing Action of Amphetamine," in Journal of Clinical Investigation, 47, p. 394, 1968). As practicing physicians we are more interested in what happens when the patients receive these drugs. than theory. The majority of our members feel the amphetamines are of value in the treatment of obesity. We also believe the general acceptance of the amphetamines by practicing physicians at large is indicative of their feeling on the usefulness of the appetite suppressants.

The Geriatric Marketer, published by the Market Research Department of Geriatrics Magazine (October 1970. Vol. 10, No. 1) reported a survey of geriatric physicians. Of those responding 64% usually or occasionally use amphetamines in the treatment of obesity and 74% usually or occasionally use the anorectic agents. These are physicians who treat obesity in the course of their practice in the older age patients.

What about those physicians who have a significant interest in the treatment of obesity—the bariatricians? In the fall of 1970 we made a survey of our members and other practicing physicians who were particularly interested in the treatment of obesity. We asked these physicians if they felt the benefits outweighed the risks of the amphetamines when used in conjunction with diet, etc., in the treatment of obesity, and for what period of time. Only 4.2% found the amphetamines of little value. Eleven and six-tenths percent found the amphetamines of value and benefit outweighed the risk for up to 3 months. The vast majority, 84.2% found them of value and the benefit outweighed the risk for 3 months or more.

It is time that the views of these physicians be considered.

We also asked these bariatricians about the evidence of drug dependence seen in their practices. The percentage reporting no drug dependence seen was 45.7. An additional 48.9% saw little evidence of dependence. Frequent evidence of dependence was indicated by 5.4% (some of these were physicians who treated psychiatric patients). My personal experience parallels the results of this survey. In approximately 1500 of my patients who have received amphetamines I have seen evidence of dependence in 3 or 4. In fact, approximately 30% of my patients change their appointment, or fail to show for their appointment, on a given day. If dependence were a problem they should be camped on my doorstep. I think most bariatricians using the amphetamines have to find out about amphetamine dependence by reading about it. Perhaps those who are prone to abuse these drugs are of different personality type, or perhaps potential drug abusers aren't obese.

Patients generally, but not always, feel better when receiving the amphetamines and the amphetamines do usually help to make the necessary change in eating habits less painful. To deny these patients this help is akin to denying all pain killing drugs to our suffering patients. Certainly in most cases the patient will survive without pain medication but is there any virtue in enduring a headache when it can be relieved by two aspirin? And I point out the asprins are used to treat a symptom and do not cure the underlying cause. Is there any less rationale for using the amphetamines in a symptomatic manner?

I believe there is general agreement that the amphetamines on a short term basis significantly enhance weight loss. What about their long term use? The National Academy of Sciences, National Review Committee recommendation was that these drugs were either possibly or probably effective for short term use in the treatment of obesity. I am told the committee reviewing amphetamines was composed primarily of nonpracticing psychiatrists, or psychiatrists from the nonrepresentative teaching hospital environment. No practicing bariatricians sat on that committee. Their short term recommendation must be viewed in that context.

One of the few fairly well done studies on the appetite suppressants is attached ("Comparison of Continuous and Intermittent Anorectic Therapy in

Obesity," by J. F. Munro, et al. British Medical Journal, *1*, p. 352, 1968). The authors reported the results of using phentermine, a chemically modified amphetamine, over a 9 month period. They found an average weight loss of 10.5 lbs in 25 patients taking a placebo, who remained in treatment. An average weight loss of 27 lbs was found in 17 patients on the phentermine who remained in treatment. Using the phentermine every other month, the 22 patients who remained in treatment lost an average of 28.7 lbs.

We believe well designed long term studies of the amphetamines are needed. We had in fact proposed such studies to the officials at the FDA who share in our belief that more objective long term data on the amphetamines is needed. However, the present rush to judgment on the amphetamine labeling may make such studies academic. We hope not, and we hope such studies can be done.

One of the problems with past studies is that they have been so designed that all patients received a standard dose of 15 mg of amphetamines over a period of time is a problem. A study should allow, we feel, some flexibility in dosage schedules. A study allowing, in addition to diet, a daily dose up to 30 mg of amphetamine for those who need it, we believe will show a meaningful weight loss in the majority of the obese study patients. Ande we believe the risk will prove to be exceedingly low.

The views of the practicing physician concerning drug effectiveness continue to receive little consideration from the FDA. In the report on the second conference on the Philosophy and Technology of Drug Assessment, conducted by the Interdisciplinary Communications Program of the Smithsonian Institution, the following conclusions are stated relative to the Drug Efficacy Study of NAS/NRC: "The Drug Efficacy Study by the FDA panels was an exercise in utilizing the talents of academic advisors. A principal criticism in retrospect is that it brought to bear the judgments of experts whose medical experience was obtained primarily in the non-representative environments of teaching hospitals. Inputs from office practitioners were not obtained."

In closing we ask:

(1) That governmental agencies not be allowed to come between the physician and his patient.

(2) That rash decisions not be made until we see the impact of the change of amphetamines to Schedule II on their diversion. This rescheduling became effective in August 1971. We believe the enforcement of these new regulations will take care of most of the previous diversion problem.

We urge:

(3) That amphetamine quotas not be unreasonably restricted. We believe the present 1972 quotas which are 18% to 20% of 1971 quotas are totally unrealistic. We believe that 60% quotas originally suggested by the Bureau of Narcotics and Dangerous Drugs were realistic. We were assured when the amphetamines were rescheduled that enough would be available for legitimate medical use. This will not be the case with the 18% to 20% quotas. Upward revision is necessary.

(4) Legislative interest: (a) in funding research to better define the extent of and risk of the obesity problem; (b) in funding a crash program to develop better tools than the amphetamines to work with in treating obesity. Until these are available I plead with you to do everything in your power to see that the amphetamines and other anorexic agents are not denied to our needy millions of overweight patients.

Comparison of Continuous and Intermittent Anorectic Therapy in Obesity

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Obese outpatients treated initially with diet and an anorexigenic drug usually lose more weight than those treated by diet alone. It is generally

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stated, however, that in most patients the anorectic loses its effect after two to four months of administration, and for this reason repeated short courses of drug treatment have been advocated (Silverstone, 1967). We report the results of a double-blind 36-week study undertaken to determine the efficacy of continuous and intermittent therapy with the anorexiant phentermine (Duromine).

MATERIAL AND METHODS

One hundred and eight women aged from 21 to 60 were included in the trial at the time of their first referral to the department. All were clinically obese and overweight by at least 20% of their standard (U.S.A. Medico-Actuarial Investigation, 1912). None had evidence of endocrine or cardiovascular disease, and patients who had previously experienced troublesome side-effects to amphetamine or its derivatives or who were throught to be psychologically unsuitable were excluded. No patient had knowingly taken an anorectic agent at any time during the previous two years, and though many stated that they were "dieting" none was on a prescribed dietary regimen.

Each patient was initially weighed, examined, had a dietary history taken, and was allocated to one of three comparable groups, each comprising 36 patients. Those in the first group were given four weeks' supply of dummy capsules, those in the second group were given capsules of identical appearance containing 30 mg. of phentermine, and patients in the third group were given alternate four-week supplies of the active and dummy capsules. They were told to take one capsule daily before breakfast, as phentermine is a drug-resinate complex which need be taken only once daily. Phentermine is also available as capsules containing 15 mg. of active drug. All patients were instructed in a diet based on the principles of simple carbohydrate restriction and designed to provide approximately 1,000 calories daily. No dietary advice was thereafter given.

Patients were asked to attend a special clinic every four weeks, wearing as nearly as possible the same clothing. Those who failed to report within a week of their appointment were withdrawn from the trial (Table I). At each visit the patient was weighed and was asked if any symptoms had occurred that she attributed to the capsules. She was then given a further four weeks' supply of capsules, the nature of which was not known to either the doctor or the patient. When the last patient had completed the 36-week period of study the pharmaceutical company supplying the capsules revealed which had been the active and which the inert ones.

RESULTS

For various reasons 44 patients failed to complete the trial (Table I).

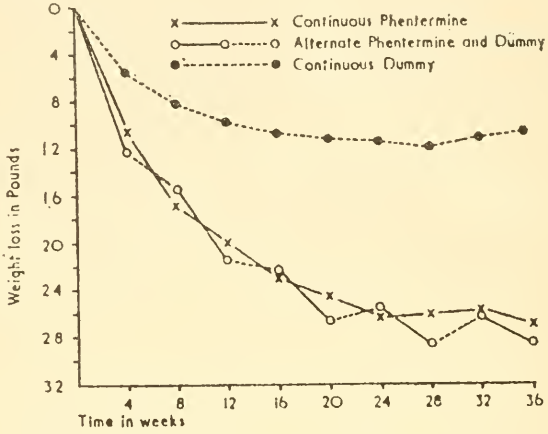
The relevant details of the 64 patients who completed the study are set out in Table II. The mean loss of weight in the 25 patients taking the dummy was 10.5 lb (4.8 kg.), whereas in the 17 patients treated with phentermine and in the 22 with the alternate regimen the mean loss was 27.0 and 28.7 lb. (12.2 and 13.0 kg.) respectively (see Chart).

TABLE I.—REASONS FOR PATIENTS FAILING TO COMPLETE THE TRIAL. EACH GROUP INITIALLY COMPRISED 36 PATIENTS

	Dummy	Phentermine	Alternate phentermine and dummy
Treatment:			
Defaulted	7	7	6
Stopped capsules for more than 1 week	3	5	3
C.N.S. stimulation		3	[1] 4
Left district		2	
Intercurrent illness	1		1
Pregnancy		2	

[1] 1 patient experienced symptoms while on dummy capsules.

Five (20%) of the patients continuously taking the dummy and 12 (71%) of those taking phentermine felt less hungry, but only one in the latter group said that this persisted throughout the study. Of the 18 (82%) who felt less hungry with alternate therapy 10 did so only when taking phentermine, and of the other eight seven thought phentermine more effective, one noticing no difference between phentermine and the dummy. Nine of the patients in this group continued to report an anorectic effect with phentermine at the end of the study. Symptoms attributable to C.N.S. stimulation—insomnia, irritability, agitation, tension, and anxiety—were severe enough for discontinuance of treatment in seven patients, one of whom was receiving the dummy (Table I). Similar but transient symptoms were admitted by 12 patients who completed the study (Table III).



Mean weight loss in each group during the study.

DISCUSSION

Though only 64 (59%) of the patients completed the 36-week study, this is rather more than might have been expected in view of the duration of the trial (Silverstone and Solomon, 1965), and because obese patients are notorious defaulters (Seaton and Rose, 1965).

TABLE II.—CLINICAL DATA AND WEIGHT CHANGE IN 3 GROUPS OF PATIENTS

[Last line in each group gives means]

Age	Diet (calories)	Standard weight (pounds)	Pounds over standard weight	Percent over standard weight	Weight change per 4 weekly followup visit (pounds)									Total weight change (pounds)
					1	2	3	4	5	6	7	8	9	
CONTINUOUS TREATMENT WITH DUMMY PREPARATION														
55	1,780	153	47	31	−2.0	−2.0	−3.0	−10.0	−3.0	−3.0	−6.0	+3.0	+3.0	−23.0
31	2,150	141	43	31	−2.0	−4.0	−3.0	−6.0	−12.0	+8.0	−8.0	−4.0	−4.0	−35.0
55	1,310	145	36	25	−3.0	−2.0	+1.0	−4.0	−2.0	+1.0	−1.0	+2.0	0	−8.0
40	1,290	131	73	56	+2.0	+2.0	−5.0	+4.0	−9.0	−2.0	+1.0	+1.0	0	−6.0
24	2,310	124	82	66	−6.0	+2.0	+3.0	+2.0	+3.0	0	+2.0	+3.0	0	+9.0
54	1,950	147	46	31	+1.0	+4.0	0	−3.0	−2.0	+4.0	+1.0	−2.0	−1.0	+2.0
28	2,850	132	138	105	−13.0	−6.0	+1.0	+4.0	+8.0	−3.0	+4.0	−1.0	+4.0	−2.0
47	2,180	149	60	40	−10.0	−9.0	−5.0	−1.0	+1.0	+1.0	−5.0	0	+2.0	−20.0
28	1,440	130	81	62	−4.0	−2.0	+4.0	−6.0	+1.0	−1.0	−1.0	0	+1.0	−8.0
56	1,640	131	71	54	−10.0	+2.0	−5.0	0	+4.0	−4.0	+6.0	+2.0	+2.0	−3.0
41	2,930	148	62	42	−3.0	−3.0	−3.0	−4.0	+1.0	−2.0	+1.0	+2.0	+8.0	−3.0
52	1,060	131	59	45	−9.0	−5.0	−3.0	+2.0	0	+1.0	+1.0	0	+1.0	−12.0
57	1,560	138	54	39	−4.0	+1.0	−5.0	+3.0	0	−1.0	0	+2.0	0	−4.0
54	1,700	137	105	77	−1.0	−3.0	−1.0	+3.0	−5.0	−2.0	−1.0	+5.0	−2.0	−2.0
47	1,700	143	82	57	−12.0	−11.0	−3.0	0	−2.0	+1.0	−6.0	+2.0	+9.0	−22.0
54	2,460	153	46	30	−7.0	−2.0	−3.0	−2.0	+3.0	−3.0	+2.0	+2.0	−1.0	−11.0
25	2,000	142	87	61	−10.0	−6.0	+2.0	+2.0	+5.0	−1.0	+1.0	+4.0	−3.0	−6.0
48	890	137	75	55	+2.0	−2.0	−3.0	0	+4.0	+1.0	+2.0	+3.0	+2.0	+9.0
35	3,250	131	61	47	−7.0	−7.0	−2.0	−2.0	−4.0	+7.0	0	−1.0	−2.0	−18.0
26	1,350	120	99	83	−10.0	−2.0	0	−4.0	−5.0	+3.0	+3.0	−2.0	−3.0	−20.0
32	2,060	131	39	30	−3.0	−1.0	−1.0	−1.0	+2.0	+2.0	−2.0	−2.0	0	−6.0
36	1,950	155	57	37	−8.0	−6.0	−3.0	−2.0	+5.0	−9.0	−2.0	−3.0	0	−28.0
40	1,910	125	37	30	−1.0	0	−2.0	+1.0	−1.0	+2.0	−3.0	+2.0	+2.0	0
39	2,320	141	48	34	−9.0	−6.0	+3.0	0	−1.0	−4.0	0	0	−1.0	−18.0
55	1,530	131	34	26	−8.0	−3.0	−2.0	−3.0	−1.0	−2.0	+2.0	+1.0	−1.0	−17.0
42	1,880	138	65	48	−5.5	−2.8	−1.5	−1.1	−.1	−.2	−.4	+.8	+.6	−10.5

TABLE II.—CLINICAL DATA AND WEIGHT CHANGE IN 3 GROUPS OF PATIENTS—Continued

[Last line in each group gives means]

Age	Diet (calories)	Standard weight (pounds)	Pounds over standard weight	Percent over standard weight	Weight change per 4 weekly followup visit (pounds)									Total weight change (pounds)
					1	2	3	4	5	6	7	8	9	
CONTINUOUS TREATMENT WITH PHENTERMINE														
50	3,190	138	150	109	−20.0	−9.0	−1.0	−4.0	−4.0	+5.0	+6.0	−1.0	−1.0	−29.0
28	2,100	149	57	38	−13.0	−8.0	−4.0	−5.0	0	−5.0	−3.0	+2.0	−3.0	−39.0
58	1,760	135	60	44	0	−14.0	+3.0	−4.0	+1.0	+3.0	−3.0	−4.0	+2.0	−16.0
35	1,870	126	121	96	−12.0	−11.0	−11.0	−6.0	−6.0	−4.0	−1.0	−2.0	−1.0	−54.0
46	1,310	142	65	46	−7.0	−10.0	−4.0	−2.0	−8.0	−1.0	−6.0	−6.0	−4.0	−48.0
22	1,710	130	68	52	−18.0	−9.0	−8.0	−3.0	−5.0	−5.0	−4.0	+3.0	−2.0	−51.0
27	1,440	120	90	75	−7.0	+1.0	−3.0	−4.0	−1.0	−4.0	−2.0	−1.0	−6.0	−27.0
38	1,710	152	83	55	−8.0	−4.0	−7.0	−1.0	+1.0	−1.0	+3.0	+9.0	−7.0	−15.0
21	1,560	130	154	119	−14.0	−12.0	0	−6.0	+2.0	−8.0	+9.0	+7.0	+4.0	−18.0
28	2,200	130	68	52	−11.0	−4.0	−3.0	−1.0	−1.0	0	+3.0	+2.0	+2.0	−13.0
24	1,110	121	43	36	−6.0	−5.0	−5.0	+2.0	−3.0	−3.0	+1.0	−3.0	−1.0	−23.0
50	3,730	142	87	61	−15.0	−4.0	−5.0	−8.0	+2.0	0	−5.0	+7.0	−6.0	−34.0
33	1,370	126	50	40	−12.0	−7.0	0	−3.0	0	−1.0	0	−3.0	+3.0	−23.0
35	1,750	121	32	26	−14.0	−4.0	−4.0	−2.0	+1.0	−3.0	+2.0	−1.0	0	−25.0
21	3,000	117	93	80	−16.0	−6.0	−4.0	−5.0	−3.0	−2.0	+1.0	−2.0	−5.0	−42.0
58	1,710	126	29	23	−1.0	+1.0	+1.0	+2.0	+1.0	+1.0	−2.0	+4.0	−1.0	+6.0
23	1,600	129	40	31	−4.0	−5.0	+1.0	+4.0	−7.0	−1.0	+4.0	−4.0	+3.0	−9.0
35	1,950	131	76	58	−10.5	−6.5	−3.2	−2.7	−1.8	−1.7	+0.2	+.4	−1.4	−27.0

36	1,300	134	107	80	−1.0	−13.0	−3.0	0	−7.0	−4.0	+1.0	+2.0	−2.0	−24.0
36	2,260	136	67	50	−14.0	−1.0	−6.0	−3.0	−7.0	+5.0	−4.0	+1.0	−2.0	−31.0
54	1,310	149	52	35	−6.0	+6.0	−9.0	0	−2.0	−2.0	+2.0	+6.0	−4.0	−9.0
47	1,920	140	49	35	−14.0	−2.0	−9.0	+2.0	−5.0	+4.0	−1.0	+2.0	−2.0	−25.0
44	950	142	58	41	−15.0	−3.0	−3.0	+5.0	−8.0	+8.0	−13.0	+3.0	+2.0	−24.0
21	1,700	129	76	59	−14.0	−1.0	−5.0	−1.0	−5.0	+7.0	−6.0	+2.0	−5.0	−28.0
28	3,470	154	142	92	−19.0	−12.0	−15.0	−5.0	−12.0	−3.0	−4.0	+13.0	−3.0	−60.0
48	2,100	129	41	31	−5.0	−1.0	0	0	−2.0	+1.0	−5.0	+6.0	0	−6.0
21	1,760	120	40	33	−6.0	0	−7.0	−6.0	−1.0	+4.0	+2.0	+1.0	−4.0	−17.0
37	1,750	126	79	60	−9.0	−2.0	−8.0	−6.0	−4.0	0	−5.0	−3.0	−1.0	−38.0
39	2,320	138	56	41	−12.0	−6.0	−9.0	−3.0	−4.0	−1.0	−3.0	−4.0	0	−42.0
50	2,570	158	86	54	−18.0	−1.0	−5.0	−1.9	−10.0	+2.0	−8.0	+6.0	−6.0	−41.0
27	1,640	123	82	67	−9.0	+3.0	−4.9	−1.9	−2.0	+2.0	−4.0	+2.0	−4.0	−17.0
35	2,000	158	94	60	−21.0	−9.0	−16.9	−9.9	−7.0	−6.0	−4.0	+2.0	−1.0	−71.0
42	3,000	152	125	82	−14.0	−5.0	0	+11.0	−5.0	+9.0	−11.0	+3.0	−10.0	−22.0
29	1,850	138	83	69	−13.0	−2.0	−7.0	−2.0	−5.0	−1.0	−5.0	−2.0	0	−37.0
54	1,790	134	40	30	−8.0	0	−2.0	+2.0	−2.0	+2.0	−1.0	+5.0	−1.0	−5.0
39	2,500	138	51	67	−16.0	+1.0	−5.0	+4.9	−3.0	0	+2.0	−1.0	+5.0	−13.0
36	2,000	142	71	50	−15.0	−3.0	−5.9	−1.0	−7.0	0	−6.0	+2.0	−1.0	−36.0
30	2,290	131	71	54	−17.0	−1.0	−6.0	0	+2.0	+1.0	+1.0	+4.0	−11.0	−27.0
48	1,120	143	101	71	−1.1	−3.0	−1.0	−2.0	+1.0	−1.0	0	+2.0	−1.0	−16.0
42	1,830	142	84	59	−16.9	−10.0	−8.0	−5.9	−2.0	−2.0	−2.0	+2.0	0	−43.0
38	1,930	139	75	55	−12.4	−3.0	−6.0	−1.0	−4.4	+1.1	−3.2	+2.5	−2.3	−28.9

The present study confirms previous reports that phentermine reduces appetite (Freed and Hays, 1959; Le Riche, 1960; Seaton *et al.*, 1964a 1964b; Lorber, 1966). Like all anorectics its effectiveness varied considerably from patient to patient and was unrelated to the individual's degree of obesity, age, or previous dietary habits.

In earlier studies of patients who had "refractory obesity," administration of any one of several anorectics caused a maximum mean weight loss of from 2.6 to 9.3 lb. (1.2 to 4.2 kg.), this being achieved at the 8th to 12th week of treatment (Duncan *et al.*, 1960; Seaton *et al.*, 1961, 1964a, 1964b; Munro *et al.*, 1966). The present study shows that weight is lost more rapidly and over a longer period of time by newly referred obese patients treated with an anorectic. However, this is not entirely due to the latter patients being more sensitive to the appetite-reducing properties of the drug, since they were also given proper dietary advice for the first time, the effect of which is reflected by the response of those given the dummy (See Chart). The Chart also shows that alternating therapy with phentermine and placebo, each given for four weeks at a time, was just as effective as continued daily treatment with the anorectic.

It is difficult to determine for how long the appetite-reducing effect of the drug persisted. During the last four months there was no statistically significant difference between the mean weight change in all three groups of patients. Nevertheless, the Chart shows that the overall anorectic effect of phentermine when given intermittently persisted throughout the study but became less with each course of treatment, and that latterly weight was regained during the month the dummy was being taken. Also, 56% of patients treated intermittently or continuously with phentermine lost weight during the last 16 weeks of treatment, whereas only 28% of those given dummy capsules did so. However, this may merely reflect the greater mean weight loss of the phentermine-treated groups during the first 20 weeks, since, irrespective of treatment, those who lost most weight initially were those who continued to do so in the latter half of the study. Thus those gaining weight during the last 16 weeks had during the previous 20 weeks lost a mean of 9.5 lb. (4.3 kg.) if treated with the dummy and 15.4 lb. (7.0 kg.) if treated with phentermine, whereas those who continued to lose weight had lost 15.2 lb. and 29.7 lb. (6.9 and 12.6 kg.) respectively.

TABLE III.—SUBJECTIVE EFFECTS REPORTED DURING TREATMENT AND ATTRIBUTED BY PATIENTS TO THE CAPSULES

Treatment	Dummy	Phentermine	Alternate phentermine and dummy
Total patients in group	25	17	22
Reduced appetite	5	12	18
G.N.S. stimulation	2	4	6
Depression	1		1
Constipation	2	1	
Headaches		1	
Dry mouth			4

It may be that the weight loss achieved in this study can be improved (1) by extending the interval between courses of anorectic treatment from four to, say, eight weeks in an attempt to postpone the development of drug tolerance, (2) by altering the patient's dietary habits during the periods when an anorexiant is not being taken, or (3) by changing the anorectic agent from one course to another. These possibilities require further evaluation.

SUMMARY

The appetite-reducing effect of phentermine administered continuously and intermittently was evaluated against an inert capsule during a 36-week double-blind trial in 108 women newly referred to hospital for dietary advice. Seven were withdrawn because of troublesome symptoms suggesting C.N.S. stimulation, though one was receiving the inert capsule.

Sixty-four patients completed the trial. The mean weight loss was 27.0 lb. and 28.7 lb. (12.2 and 13.0 kg.) for those who received phentermine continuously and intermittently, compared with 10.5 lb. (4.8 kg.) in the group treated with the dummy. The individual response to therapy was very variable, but irrespective of the method employed weight loss diminished with duration of treatment. There seems to be no advantage in taking an anorectic continuously, since intermittent treatment is as effective, is cheaper, and is possibly safer. Further clinical studies are still required to find out how anorectic drugs can best be used.

We wish to thank Riker Laboratories Ltd. for the supplies of phentermine (Duromine) and dummy capsules. We are grateful to the dietetic and nursing staff of the Diabetic and Dietetic Department.

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Senator Bayh. We will recess our hearings now pending the call of the Chair.

(Whereupon at 12:35 p.m. the hearing was recessed subject to the call of the Chair.)

APPENDIX

(Additional Materials Submitted for the Record)

(A) Federal Register, Rules and Regulations: Amphetamines-Diet Pills

1. [Federal Register, vol. 35, No. 154, Saturday, August 8, 1970]

TITLE 21—FOOD AND DRUGS

Chapter I—Food and Drug Administration, Department of Health, Education, and Welfare

Part 130—New Drugs

SUBPART A—PROCEDURAL AND INTERPRETATIVE REGULATIONS

Amphetamines (Amphetamine, Dextroamphetamine, and Their Salts, and Levamfetamine and Its Salts) For Human Use; Statement of Policy

Pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502(f), (j), 505, 701(a), 52 Stat. 1051–53, as amended, 1055; 21 U.S.C. 352(f), (j), 355, 371(a)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120), Part 130 is amended by adding to Subpart A the following new section:

§ 130.46 Amphetamines (Amphetamine,xtroamphetamine, and their salts and levamfetamine and its salts) for humane; statement of policy

(a) *Amphetamine and dextroamphetamine and their salts.* (1) Pursuant to the drug efficacy requirements of the Federal Food, Drug, and Cosmetic Act, the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, has evaluated certain dosage forms of amphetamines and other sympathomimetic stimulant drugs intended for use in the treatment of obesity and for other uses. The Academy found that such drugs as a class have been shown to have a generally short-term anorectic action. They further commented that clinical opinion on the contribution of the sympathomimetic stimulants in a weight reduction program varies widely, the anorectic effect of these drugs often plateaus or diminishes after a few weeks, most studies of them are for short periods, no available evidence shows that use of anorectics alters the natural history of obesity, some evidence indicates that anorectic effects may be strongly influenced by the suggestibility of the patient, and reservations exist about the adequacy of the controls in some of the clinical studies. Their significant potential for drug abuse was also cited.

(2) In addition to those dosage forms that were reviewed for efficacy by the Academy, other dosage forms of amphetamine drugs are on the market that were not cleared through the new-drug procedures. While certain amphetamines were marketed prior to enactment of the Federal Food, Drug, and Cosmetic Act in 1938, some of the conditions of use now prescribed, recommended, or suggested in their labeling (for example, for the treatment of obesity) differ from uses claimed for the amphetamines before said enactment. Such uses have not been cleared through the effectiveness provisions of the Drug Amendments of 1962 (Public Law 87–781 which amended the Federal Food, Drug, and Cosmetic Act). These drugs are very extensively used in the treatment of obesity. The extent of use for such purposes as narcolepsy and minimal brain dysfunction in children is believed to be insignificant as compared with the total usage of these drugs. Because of their stimulant effect on the central nervous system, they have a potential for misuse by those to whom they are available through a physician's prescription, and their abuse by those who obtain them through illicit channels is well documented. Production data indicate that amphetamines are produced and prescribed in quantities greatly in excess of demonstrated medical needs.

(3) On the basis of the foregoing, the Food and Drug Administration finds that the current labeling of amphetamine or dextroamphetamine or their salts neither adequately reflects the present state of knowledge concerning their limited medical usefulness nor emphasizes the necessary warning information regarding their potential for misuse and abuse. Such drugs must be relabeled in accord with the information shown below. Amphetamines labeled as required by this section are regarded as new drugs and must be subjects of new-drug applications.

(4) Pending conclusions reached pursuant to information that may become available through new-drug applications or other sources, the labeling of orally administered amphetamine and dextroamphetamine and their salts should be substantially as follows:

Amphetamine and Dextroamphetamine

Amphetamines have a significant potential for abuse in view of their limited short-term anorectic effect and rapid development of tolerance, they should be used with extreme caution and only for limited periods of time in weight reduction programs.

Description

(To be confined to a statement of the physical and chemical properties of the drug.)

Actions

Amphetamines are sympathomimetic amines with CNS stimulant activity. Peripheral actions include elevation of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action. The anorectic effect diminishes after a few weeks.

Indications

Narcolepsy.

Minimal brain dysfunction in children (hyperkinetic behavior disorders), as an aid to general management.

Exogenous obesity, as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction.

Contraindications

Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines.

Agitated states.

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors, hypertensive crises may result.

Warnings

Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: Amphetamines have a significant potential for abuse. Tolerance and extreme psychological dependence have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonges high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with amphetamines include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

Usage in Pregnancy: Safe use in pregnancy has not been established. Reproduction studies in mammals at high multiples of the human dose have suggested both an embryotoxic and a teratogenic potential. Use of amphetamines by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

USAGE IN CHILDREN: Amphetamines are not recommended for use as anorectic agents in children under 12 years of age.

Precautions

Caution is to be exercised in prescribing amphetamines for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of amphetamines and the concomitant dietary regimen.

Amphetamines may decrease the hypotensive effect of guanethidine.

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

Adverse Reactions

Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.

Central nervous system: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely, psychotic episodes at recommended doses

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, other gastrointestinal disturbances. Anorexia and weight loss may occur as undesirable effects when amphetamines are used for other than the anorectic effect.

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

Dosage and Administration

Regardless of indication, amphetamines should be administered at the lowest effective dosage and dosage should be individually adjusted. Late evening medication should be avoided because of the resulting insomnia.

1. Narcolepsy: Usual dose 5 to 60 milligrams per day in divided doses.

2. Minimal brain dysfunction:

a. Not recommended for children under 3 years of age.

b. Children from 3 to 5 years of age: 2.5 milligrams daily, raised in increments of 2.5 milligrams at weekly intervals until optimal response is obtained.

c. Children 6 years of age and older: 5 milligrams once or twice daily, increased in increments of 5 milligrams at weekly intervals. Only in rare cases will it be necessary to exceed a total of 40 milligrams per day.

3. Obesity: Usual adult dose 5 to 30 milligrams per day in divided doses.

Overdosage

Manifestations of acute overdosage with amphethamines include restlessness, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute amphetamine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

(5) Distribution of any such preparation currently on the market without an approved new-drug application may be continued provided that all the following conditions are met:

(i) Within 60 days following the date of publication of this section in the FEDERAL REGISTER, the labeling of any such preparation shipped within the jurisdiction of the act is in accord with the labeling conditions described in this section. After said 60 days any such preparation labeled or advertised contrary to this section will be regarded as misbranded within the meaning of section 502(f) (1) and (2) and (j) of the act and will be subject to regulatory proceedings. New drug charges will be included in appropriate cases.

(ii) The manufacturer, packer, or distributor of such drug submits to the Food and Drug Administration, within 1 year after the date of publication of this section in the FEDERAL REGISTER, a new-drug application providing substantial evidence derived from adequate and well-controlled clinical investigations that the drug is effective for each of its labeled indications. Since the treatment of obesity necessarily requires a prolonged period of time, data in support of the drug's long-range effectiveness in this condition must be based on studies conducted over periods exceeding a few weeks: intermittent administration of the drug may be required. Such studies should also include data

on long-term toxicity; for example, cardiovascular and central nervous system. Such information is essential for an evaluation of the benefit-to-risk ratio.

(iii) The applicant submits within a reasonable time additional information required for the approval of the application as specified in a written communication from the Food and Drug Administration or in a notice published in the Federal Register.

(iv) The application has not been ruled incomplete or unapprovable.

(v) The Food and Drug Administration has not, by publication in the FEDERAL REGISTER, announced further conclusions concerning amphetamines based upon information submitted in new-drug applications or other information available.

(6) The labeling of any combination drug containing amphetamine or dextroamphetamine or their salts which includes any of the same indications for use as are listed in the labeling in this section should be revised to reflect the substance of those parts of the labeling set forth in this section that are applicable to the amphetamine component. Combination products labeled as required by this section are regarded as new drugs and must be subjects of approved new-drug applications.

(b) *Levamfetamine and its salts.* (1) Levamfetamine preparations currently on the market are represented to be useful in the treatment of obesity. The Food and Drug Administration finds there is neither substantial evidence of effectiveness nor a general recognition among qualified experts that these drugs are safe and effective for such use. Accordingly, these preparations are regarded as new drugs requiring approved new-drug applications.

(2) Regulatory proceedings based on section 505 of the act may be initiated with regard to any such drug shipped within the jurisdiction of the act for which an approved new-drug application is not in effect. Those products claiming exemption from the efficacy provisions of the Drug Amendments of 1962 (Public Law 87–781; 76 Stat. 780 et seq.) under the "grandfather" provisions (sec. 107(c)(4) of that act; 76 Stat. 789) will be considered on an individual basis.

(Secs. 502 (f), (j), 505, 701(a), 52 Stat. 1051–53, as amended, 1055; 21 U.S.C. 352 (f), (j), 355, 371(a))

Dated: July 30, 1970.

CHARLES C. EDWARDS,
Commissioner of Food and Drugs.

[F.R. Doc. 70–10353; Filed, Aug. 7, 1970; 8:47 a.m.]

[From the HEW News, Wednesday, August 5, 1970]

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
Washington, D.C.

Dr. Charles C. Edwards, Commissioner of the Food and Drug Administration, said today he has moved to limit sharply the use of amphetamine drugs, now being widely sold as stimulants and appetite suppressants in this country, and he appealed to manufacturers to reduce the production and sale of the drug.

He said an FDA order, to be issued this week, will seek to confine the use of amphetamines to three specific medical uses: uncontrollable sleepiness (narcolepsy), Hyperkinetic behavior disorders in children, and short-term treatment of obesity

Citing the widely documented abuse and misuse of amphetamines, the FDA Commissioner said he believed that along with this new order the amphetamines problem must be attacked by a nationwide effort involving close cooperation between government, the drug manufacturers, and practicing physicians.

"Industry has not faced its responsibility with these drugs," he said. "It is time for the manufacturers to accept the challenge of working closely with the FDA and the Department of Justice to stop the unnecessary production of amphetamines."

He said last year three and a half billion amphetamine dosage units were made in this country, many more than medical need required.

Such tremendous production makes easy the diversion of large supplies into

improper channels of trade, Dr. Edwards said, and noted that last year the Justice Department's Bureau of Narcotics and Dangerous Drugs was unable to account for the sale of 38 percent of the supply produced in this country.

Dr. Edwards emphasized that use of amphetamines against obesity, mentioned in this week's order, should be short-term because a report by the National Academy of Sciences-National Research Council has stated that in obesity the effectiveness of amphetamines often begins to diminish within a short period of time.

The FDA order will also require revised labeling on all amphetamines. Some present labeling, Dr. Edwards said, lacks the specific direction to the physician which reflect the limited medical uses of amphetamines or sufficient warning about their potential for misuses and abuses.

By terms of the FDA order, manufacturers of amphetamines and methamphetamines will have 60 days to revise labeling on these drugs to match the FDA's model labeling. Within one year all manufacturers will be required to submit proof of effectiveness for all the claims made for amphetamines.

Manufacturers of combination drugs containing amphetamines must also relabel their products concerning their amphetamine components.

A related class of drugs, levoamfetamine preparations, was found not to have substantial evidence of safety and effectiveness, the order says, and FDA will now require proof of safety and effectiveness from manufacturers who want to retain these drugs on the market.

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2. [From the Federal Register, vol. 35, No. 154—Saturday, August 8, 1970]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[DESI 5378]

CERTAIN ANORECTIC DRUGS

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following anorectic drugs:

1. Biphetamine '7½' Capsules, Biphetamine '12½' Capsules, and Biphetamine '20' Capsules, respectively, containing 3.75 milligrams, 6.25 milligrams, and 10 milligrams each of dextroamphetamine and amphetamine per capsule, all as cation exchange resin complexes of sulfonated polystyrene; Strasenburgh Laboratories Division of Wallace and Tiernan Inc., Post Office Box 1710, Rochester, N.Y. 14603 (NDA 10-093).

2. Biphetamine-T '12½' Capsules and Biphetamine-T '20' Capsules, respectively, containing 6.25 milligrams each of dextroamphetamine and amphetamine, and 40 milligrams methaqualone per capsule, and 10 milligrams each of dextroamphetamine and amphetamine and 40 milligrams methaqualone per capsule all as cation exchange resin complexes of sulfonated polystyrene; Strasenburgh Laboratories Division of Wallace and Tiernan Inc. (NDA 11-538).

3. Ionamin '15' Capsules and Ionamin '30' Capsules, respectively, containing 15 milligrams phentermine and 30 milligrams phentermine per capsule, both as cation exchange resin complexes of sulfonated polystyrene: Strasenburgh Laboratories Division of Wallace and Tiernan Inc. (NDA 11-613).

4. Du-Oria Tablets containing 10 milligrams methamphetamine hydrochloride, and 0.25 milligram reserpine per sustained release tablet; B. F. Ascher and Co., Inc., 5100 East 59th Street, Kansas City, Mo. 64130. (NDA 9-946).

5. Obetrol-10 and Obetrol-20 Tablets, respectively, containing 2.5 milligrams each or 5 milligrams each of methamphetamine saccharate, methamphetamine hydrochloride, amphetamine sulfate, dextroamphetamine sulfate per tablet; Obetrol Pharmaceuticals, Division of Rexar Pharmacal Corp., 382 Schenck Avenue, Brooklyn, N.Y. 11207. (NDA 11-522).

6. Prelu-Vite Capsules containing 25 milligrams phenmetrazine hydrochloride 2,000 USP units vitamin A, 200 USP units vitamin D, 2 milligrams thiamine mononitrate, 2 milligrams of riboflavin, 20 milligrams niacinamide, 3 milligrams calcium pantothenate, 1 milligram pyridoxine hydrochloride, 0.5 micro-

gram cobalamin concentrate, 37.5 milligrams ascorbic acid 5 milligrams from, 140 milligrams calcium, 108 milligrams phosphorus, 0.1 milligram iodine and 1 milligram copper per capsule; Geigy Chemical Corp., Ardsley, N.Y. 10502 (NDA 12–371).

7. Methedrine Tablets containing 5 milligrams methamphetamine hydrochloride per tablet; Burroughs Wellcome & Co. (U.S.A.), Inc., 1 Scarsdale Road, Tuckahoe, N.Y. 10707 (NDA 5504).

8. Amphedroxyn Hydrochloride Tablets containing 5 milligrams methamphetamine hydrochloride per tablet; Eli Lilly and Co., Post Office Box 618, Indianapolis, Ind. 46206 (NDA 6390).

9. Delfeta-sed Stedytabs containing 30 milligrams de-methamphetamine hydrochloride and 120 milligrams amorbarbital per sustained-release tablet; Eastern Research Laboratories Inc., 302 South Central Avenue, Baltimore, Md. 21202 (NDA 12–415).

10. Delfetamine Stedytabs containing 30 milligrams de-methamphetamine hydrochloride per sustained-release tablet; Eastern Research Laboratories Inc. (NDA 12–416).

11. Desoxyn Tablets containing 2.5 milligrams or 5 milligrams methamphetamine hydrochloride per tablet, Desoxyn Gradumet Tablets containing 5, 10, or 15 milligrams methamphetamine hydrochloride per tablet, and Desoxyn Elixir containing 20 milligrams methamphetamine hydrochloride per 30 milliliters; Abbott Laboratories, 14th and Sheridan Road, North Chicago, Ill. 60064 (NDA 5378).

12. Drinalfa Tablets containing 5 milligrams methamphetamine hydrochloride per tablet; E. R. Squibb and Sons, Inc., Georges Road, New Brunswick, N.J. 08903 (NDA 5756).

13. Bamadex Tablets containing 5 milligrams dextroamphetamine sulfate and 400 milligrams meprobamate per tablet; Lederle Laboratories Division, American Cyanamid Co., Post Office Box 500, Pearl River, N.Y. 10965 (NDA 11–280).

14. Bamadex Sequels containing 15 milligrams meprobanate per sustained release capsule; Lederle Laboratories Division, American Cyanamid Co. (NDA 12–570).

15. Tenuate Dospan Tablets containing 75 milligrams diethylpropion hydrochloride per continuous release tablet; The William S. Merrell Co., Division of Richardson-Merrell Inc., 110 East Amity Road, Cincinnati, Ohio 45215 (NDA 12–546).

16. Appetrol Tablets containing 5 milligrams dextroamphetamine sulfate and 400 milligrams meprobamate per tablet; Wallace Pharmaceuticals, Division of Carter-Wallace, Inc., Half Acre Road, Cranbury, N.J. 08512 (NDA 12–127).

17. Appetrol-S.R. Capsules containing 15 milligrams meprobamate per sustained release capsules; Wallace Pharmaceuticals (NDA 12–624).

18. Eskatrol Spansule containing 15 milligrams dextroamphetamine sulfate and 7.5 milligrams prochlorperazine (as the maleate) per sustained release capsule; Smith Kline and French Laboratories, 1500 Spring Garden Street, Philadelphia, Pa. 19101 (NDA 12–042).

19. Racemic Desoxyephedrine Hydrochloride Tablets containing 5 milligrams dl-methamphetamine hydrochloride per tablet; Hligh Chemical Co., 1760 North Howard Street, Philadelphia, Pa. 19122 (NDA 5–969).

20. Miller-Drine Tablets containing 10 milligrams dl-methamphetamine hydrochloride per tablet; Smith, Miller and Patch, Inc., 401 Joyce Kilmer Avenue, New Brunswick, N.J. 08902 (NDA 6–003).

21. Dexserpine "5" Tablets containing 5 milligrams dextroamphetamine sulfate and 0.1 milligram reserpine per tablet; Nysco Laboratories, Inc., 34–24 Vernon Boulevard, Long Island City, N.Y. 11106 (NDA 10–207).

22. Norodin Tablets containing 5 milligrams methamphetamine hydrochloride per tablet; Endo Laboratories, 1000 Steward Avenue, Garden City, Long Island, N.Y. 11533 (NDA 5X632).

23. D-O-E Tablets containing 5 milligrams methamphetamine hydrochloride per tablet; Tilden-Yates Laboratories, Inc., 295 Lafayette Street, New York, N.Y. 10012 (NDA 5–603).

A. *Effectiveness classification.* 1. The Food and Drug Administration has considered the reports of the Academy, as well as other evidence, and concludes that there is a lack of substantial evidence of effectiveness of the methamphetamine-containing preparations for: use as an adjunct in some cases in which nervousness, tension, and irritability are combined with feelings of de-

pression, anxiety, and lassitude; use in the management of alcoholism (acute and chronic); enuresis; nausea and vomiting of pregnancy; use as a mild analeptic in barbiturate overdosage; restoration of optimism and mental alertness in the case of depressive state of mind; and temporary or emergency use as a cerebral stimulant to decrease fatigue and increase the urge to work.

2. All the above-listed drugs are regarded as possibly effective for their claimed anorectic effects; for their claims for prolonged, continuous, or sustained release; and for all other labeled indications not listed in paragraph A1.

B. *Marketing status.* 1.a. Within 60 days from the date of publication of this announcement in the FEDERAL REGISTER, the labeling of methamphetamine-containing drugs should be revised as needed to delete those indications described in paragraph A1 for which substantial evidence of effectiveness is lacking.

b. The holder of any previously approved new-drug application for such drug is requested to submit a supplement within 60 days after publication hereof to provide for such revised labeling. The supplement should be submitted under the provisions of § 130.9 (d) and (e) of the new-drug regulations (21 CFR 130.9 (d) and (e)), which permit certain changes to be put into effect at the earliest possible time. Failure to put such labeling into use may result in a proposal to withdraw approval of the new-drug application.

2. a. Holders of previously approved new-drug applications for the drugs listed above and persons marketing any of these drugs without approval will be allowed 6 months from the date of publication of this announcement in the FEDERAL REGISTER to obtain and to submit in a supplemental or original new-drug application data to provide substantial evidence of effectiveness for those indications for which these drugs have been classified as possibly effective.

b. For preparations claiming sustained-action, time-release, or other delayed or prolonged effect, such data should be adequate to assure the biological availability of the drug in the formulation which is marketed and should show that the drug is available at a rate of release which will be safe and effective and that it has the prolonged effect claimed.

3. At the end of the 6-month period, any such data will be evaluated to determine whether there is substantial evidence of the effectiveness for such uses. After the evaluation, the conclusions concerning the drug will be published in the FEDERAL REGISTER. If no studies have been undertaken or if the studies do not provide substantial evidence of effectiveness, procedures will be initiated to withdraw approval of the new-drug applications for these drugs, pursuant to the provisions of section 505(e) of the Federal Food, Drug, and Cosmetic Act. Withdrawal of approval of the applications will cause any such drugs on the market to be new drugs for which an approval is not in effect.

The above-named holders of the new-drug applications for these drugs have been mailed a copy of the NAS-NRC reports. Any interested person may obtain a copy of a report by writing to the office named below.

Communications forwarded in response to this announcement should refer to DESI 5378 which identifies this announcement and should be directed to the attention of the following appropriate office and addressed, unless otherwise specified, to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20852:

Supplements (identify with new-drug application number): Office of Marketed Drugs (BD–200), Bureau of Drugs.
Original new-drug applications: Office of New Drugs (BD–100), Bureau of Drugs.
Comments on this announcement: Special Assistant for Drug Efficacy Study Implementation (BD–201), Bureau of Drugs.
Requests for NAS–NRC reports: Press Relations Staff (CE–200), Food and Drug Administration, 200 C Street SW., Washington, D.C. 20204.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050–53, as amended; 21 U.S.C. 352, 355) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: July 30, 1970.

CHARLES C. EDWARDS,
Commissioner of Food and Drugs.

[F.R. Doc. 70–10354; Filed, Aug. 7, 1970; 8:47 a.m.]

3. [From the Federal Register, vol. 36, No. 102—Wednesday,May 26, 1971]

DEPARTMENT OF JUSTICE

Bureau of Narcotics and Dangerous Drugs

[21 CFR Part 308]

SCHEDULES OF CONTROLLED SUBSTANCES

Proposed Transfer of Amphetamine and Methamphetamine and Their Salts, Optical Isomers, and Salts of Their Optical Isomers From Schedule III to Schedule II, With Certain Exceptions

Based upon the investigations of the Bureau of Narcotics and Dangerous Drugs and upon the scientific and medical evaluation and recommendation of the Secretary of Health, Education, and Welfare, received pursuant to section 201(b) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(b)), the Director of the Bureau of Narcotics and Dangerous Drugs finds that amphetamines and methamphetamine and their salts, optical isomers and salts of their optical isomers:

(1) Have a high potential for abuse;

(2) Have a currently accepted medical use in treatment in the United States with severe restrictions; and

(3) That abuse of these substances may lead to severe psychological dependence.

Therefore, under the authority vested in the Attorney General by section 201 (a) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(a)), and redelegated to the Director, Bureau of Narcotics and Dangerous Drugs by § 0.100 of Title 28 of the Code of Federal Regulations, the Director proposes a ruling that:

1. Section 308.12(d) of Title 21 of the Code of Federal Regulations be deleted and replaced with a new subparagraph to read:

§ 308.12 Schedule II

* * * * * *

(d) *Stimulants.* Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following sustances having a stimulant effect on the central nervous system:

(1) Amphetamine, its salts, optical isomers, and salts of its optical isomers, 1,100.

(2) Methamphetamine, its salts, optical isomers, and salts of its optical isomers, 1,105.

2. That § 308.13(b) of Title 21 of the Code of Federal Regulations be amended to read:

§ 308.13 Schedule III

(b) *Stimulants.* Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system:

(1) Phenmetrazine and its salts, 1,630.

(2) Methylphenidate, 1,726.

(3) Those compounds, mixtures or preparation in dosage unit form containing any stimulant substance which are currently listed as excepted compounds under 21 CFR 308.32, and any other drug of the quantitative composition shown in that list for those drugs or which is the same except that it contains a lesser quantity of controlled substances.

* * * * * * *

All interested persons are invited to submit their comments or objections in writing regarding this proposal. These comments or objections should state with particularity the issues concerning which the person desires to be heard. Comments and objections should be submitted in quintuplicate to the Office of Chief Counsel, Bureau of Narcotics and Dangerous Drugs, Department of Justice, Room 611, 1405 Eye Street NW., Washington, DC 20537, and must be received no later than 30 days after publication of this proposal in the Federal Register.

In the event that an interested party submits objections to this proposal which present reasonable grounds for this rule not to be finalized and requests

a hearing in accordance with 21 CFR 308.45, the party will be notified by registered mail that a hearing on these objections will be held at 10 a.m. on June 30, 1971, in Room 1210, 1405 Eye Street NW., Washington, DC 20537. If objections submitted do not present such reasonable grounds, the party will so be advised by registered mail.

If no objections presenting reasonable grounds for a hearing on the proposal are received within the time limitations, and all interested parties waive or are deemed to waive their opportunity for the hearing or to participate in the hearing, the Director may cancel the hearing and, after giving consideration to written comments, issue his final order pursuant to 21 CFR 308.48 without a hearing.

A petition dated May 14, 1971, was submitted to the Director by counsel for the American Public Health Association and the D.C. Public Health Association under the provisions of section 201(a) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(a)) requesting that the Director initiate the above proceedings. This petition was received after the Director had requested from the Secretary of the Department of Health, Education, and Welfare the scientific and medical evaluations required under the statute (21 U.S.C 811(b)). Accordingly, since the Director had already determined to initiate proceedings of the type requested by the petition, the petition will be considered as a request for appearance in the proceedings.

Dated: May 21, 1971.

JOHN E. INGERSOLL,
Director, Bureau of
Narcotics & Dangerous Drugs.

[FR Doc. 71-7351 Filed 5-25-71; 8:53 am]

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4. [From the Federal Register, vol. 36, No. 130—Wednesday, July 7, 1971]

TITLE 21—FOOD AND DRUGS

Chapter II—Bureau of Narcotics and Dangerous Drugs, Department of Justice

PART 301—REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

PART 308—SCHEDULES OF CONTROLLED SUBSTANCES

AMPHETAMINE, METHAMPHETAMINE, AND OPTICAL ISOMERS

A notice was published in the Federal Register of May 26, 1971 (36 F.R. 9563) proposing the transfer of amphetamine and methamphetamine and their salts, optical isomers, and salts of the optical isomers from Schedule III to Schedule II of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (Public Law 91-513), with certain exceptions. All interested persons were given 30 days after publication to submit their objections, commends, or requests for hearing.

No objections nor requests presenting reasonable grounds for a hearing regarding the proposed order in its entirety were received. However, the following objections and requests for hearing were received as to specific combination products:

(1) Smith Kline & French Laboratories requested a hearing on the transfer of Eskatrol Spansule Capsules, a combination product containing 15 mg. of dextroamphetamine sulfate and 7.5 mg. of prochlorperazine, from Schedule III to Schedule II.

(2) Mission Pharmacal Co. requested a hearing on the transfer of Fetamin, a combination product containing 5 mg. of d-methamphetamine hydrochloride and 20 mg. of sodium pentobarbital with vitamins and minerals, from Schedule III to Schedule II.

(3) Pennwalt Corp. requested a hearing on the transfer of Biphetamine, a resin complex of d-and d,l-amphetamine, and Biphetamine-T, a resin complex of d-and d,l-amphetamine and methaqualone, from Schedule III to Schedule II.

The following comments were also submitted regarding the proposed order:

(1) The National Wholesale Druggists Association expressed concern over the Schedule II security requirements at the wholesale level for amphetamine and methamphetamine.

(2) The Minnesota State Board of Pharmacy also expressed concern over the Schedule II security requirements at the pharmacy level for amphetamine and methamphetamine. The Board further suggested that a major educational effort be instituted to inform prescribing practitioners of the Schedule II prescription refill limitations and the emergency prescription procedures. Finally, the Board suggested that the Schedule III recordkeeping requirements be deemed adequate for amphetamine and methamphetamine after their placement in Schedule II.

(3) The U.S. Pharmacopeial Convention, Inc., expressed concern as to, and requested exemption from, the increased Schedule II requirements for distribution of amphetamine and methamphetamine as U.S.P Reference Standards.

(4) The National Association of Chain Drug Stores, Inc. (NACDS), requested sufficient time for compliance with the Schedule II security, prescription refill and order form requirements. NACDS also raised questions as to whether an additional inventory must be taken for amphetamine and methamphetamine products and whether State or Federal laws and regulations apply where a conflict exists as to the maintenance of prescription records. Lastly, NACDS requested that a list of the specific combination products excluded or exempted from the order be published.

(5) The Christian Life Commission expressed its support of the proposed order in its entirety as a means of diminishing amphetamine and methamphetamine abuse.

(6) The city of New York submitted a memorandum in support of the proposed order in its entirety, together with a "Report of the New York City Special Committee on Amphetamine Abuse."

(7) Abbott Laboratories expressed its support of the proposed order in its entirety; but did request that sufficient time for compliance with the various Schedule II requirements be granted and that the separate recordkeeping requirements of Schedule II not be applied to amphetamine and methamphetamine substances. Abbott also raised a question as to whether an additional inventory must be taken for amphetamine and methamphetamine upon transfer to Schedule II.

(8) The American Medical Association expressed its support of the proposed order in its entirety by the following resolutions passed by its House of Delegates:

Resolved, that the American Medical Association urge all physicians to limit their use of amphetamines and other stimulant drugs to specific, well-recognized medical indications, and be it further

Resolved, that the American Medical Association support the proposal of the Bureau of Narcotics and Dangerous Drugs to transfer Amphetamine and Methamphetamine and their Salts, Optical Isomers, and Salts of their Optical Isomers from Schedule III to Schedule II published in the May 26, 1971 Federal Register.

The Manufacturers Educational Drug Information Association (MEDIA) objected to, and requested a hearing as to, the proposed order in its entirety on the grounds that the increased security requirements and manufacturing controls and production and procurement quotas of Schedule II would force small independent manufacturers to cease manufacturing amphetamine and methamphetamine. After consultation with members of the Bureau, MEDIA withdrew its objections and request for a hearing in this proceeding, reserving its right, however, to intervene in the forthcoming quota proceedings and security regulations proceedings.

After careful consideration of the comments submitted and in view of the fact no objections nor requests for a hearing were received as to the proposed transfer order in its entirety and based upon the investigation of the Bureau of Narcotics and Dangerous Drugs and upon the scientific and medical evaluation and recommendation of the Secretary of Health, Education, and Welfare, received pursuant to section 201(b) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(b)), the Director of the Bureau of Narcotics and Dangerous Drugs finds that amphetamines and methamphetamines and their salts, optical isomers, and salts of their optical isomers:

(1) Have a high potential for abuse;

(2) Have a currently accepted medical use in treatment in the United States with severe restrictions; and

(3) That abuse of these substances may lead to severe psychological dependence.

Therefore, it is ordered, That:

1. Section 301.02 of Title 21 of the Code of Federal Regulations be amended by revising paragraph (b)(6) and adding a new paragraph (b)(7) to read:

§ 301.02 Definitions

* * * * * * *

(b) (6) Methamphetamine, its salts, isomers, and salts of its isomers.

(7) Amphetamine, its salts, optical isomers, and salts of its optical isomers.

* * * * * * *

2. Section 308.12(d) of Title 21 of the Code of Federal Regulations be deleted and replaced with a new paragraph to read:

§ 308.12 Schedule II

* * * * * * *

(d) *Stimulants.* Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system:

(1) Amphetamine, its salts, optical isomers, and salts of its optical isomers, 1.100.

(2) Methamphetamine, its salts, and salts of its isomers, 1.105.

3. Section 308.13(b) of Title 21 of the Code of Federal Regulations be amended to read:

§ 308.13 Schedule III

* * * * * * *

(b) *Stimulants.* Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system:

(1) Phenmetrazine and its salts, 1.630.

(2) Methylphenidate, 1.726.

(3) Those compounds, mixtures or preparations in dosage unit form containing any stimulant substances which are currently listed as excepted compounds under 21 CFR 308.32, and any other drug of the quantitative composition shown in that list for those drugs or which is the same except that it contains a lesser quantity of controlled substances.

* * * * * * *

4. The additional requirements imposed upon amphetamines and methamphetamine, their salts, optical isomers and salts of their optical isomers by virtue of their reclassification into Schedule II shall become effective as follows:

(a) *Labeling and packaging.* All labels and seals on commercial containers of, and all labeling of, the above controlled substances, which are packaged more than 180 days following the effective date of this order shall comply with the requirements of 21 CFR Part 302.

(b) *Order forms.* All distributions of the above controlled substances shall comply with the order form requirements of 21 CFR Part 305 within 30 days from the effective date of this order.

(c) *Records and inventories.* All separate and other recordkeeping requirements of 21 CFR 304 for the above controlled substances shall be complied within 30 days of the effective date of this order. Records maintained and inventories taken prior to the above compliance date, which are in compliance with the recordkeeping requirements for Schedule III controlled substances, shall not be affected by this order. No new inventories of the above controlled substances, in addition to that of May 1, 1971, is required as a result of this order. Where a positive conflict exists between the recordkeeping requirements of State and Federal laws and regulations, so that the two cannot stand together, Federal law governs in accordance with section 708 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 903).

(d) *Prescriptions.* All prescriptions for the above controlled substances shall comply with 21 CFR 306.01–306.15 within 30 days from the effective date of this order. Any prescriptions for the above controlled substances, which are entitled to be refilled under § 306.22, shall not be entitled to such refill in accordance with § 306.12 on and after the above compliance date.

(e) *Importation and exportation.* All importation and exportation of the above controlled substances shall be in compliance with 21 CFR Part 312, specifically as to import and export permits, within 30 days of the effective date of this order.

(f) *Security.* Since the regulations regarding security for Schedule II controlled substances are undergoing revision, compliance with the present security requirements shall be deemed adequate pending publication of the final order on security regulations.

(g) *Registration.* Any registrant presently not authorized to handle amphetamines or methamphetamines or both and/or Schedule II controlled substances should apply to modify his registration to authorize the handling of such controlled substances by submitting within 30 days of the effective date of this order a letter of request to the Registration Branch. Bureau of Narcotics and Dangerous Drugs. Post Office Box 28083, Central Station, Washington, DC 20005. The letter shall contain the registrant's name, address, registration number, and the substances and/or schedules to be added to his registration, and shall be signed by the same person who signed the most recent application for registration or re-registration. No fee shall be required to be paid for the modification. The request for modification shall be handled in the same manner as an application for registration.

5. The hearing scheduled for June 30, 1971 is hereby canceled since no objections nor requests for a hearing on the proposed order in its entirety were received within the designated time period.

It is further ordered, That application of this order to Eskatrol, Fetamin, Biphetamine, and Biphetamine-T, the combination products for which hearings were requested, is reserved pending review of these products by the Bureau. Hearings regarding their transfer to Schedule II will be held after such review.

This order does not amend 21 CFR 308.32. Those combination products containing amphetamine or methamphetamine currently excepted under § 308.32 will remain excepted. The Bureau recognizes that certain combination drugs containing amphetamine or methamphetamine excepted under the Drug Abuse Control Amendments of 1965 have not been excepted under § 308.32. As a matter of policy, those substances shall be deemed excepted under § 308.32 pending further action by the Bureau.

This order is effective on the date of its publication in the Federal Register (7–7–71).

Dated: June 30, 1971.

JOHN E. INGERSOLL,
Director, Bureau of
Narcotics and Dangerous Drugs.

[FR Doc. 71–9470 Filed 8–16–71; 8:45 am]

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5. [From the Federal Register, vol. 36, No. 160—Wednesday, August 18, 1971]

TITLE 21—FOOD AND DRUGS

Chapter II—Bureau of Narcotics and Dangerous Drugs, Department of Justice

PART 301—REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

PART 308—SCHEDULES OF CONTROLLED SUBSTANCES

TRANSFER OF ESKATROL TO SCHEDULE II

A final order was published in the Federal Register on July 7, 1971 (36 F.R. 12734) transferring amphetamines and methamphetamine and their salts, optical isomers, and salts of their optical isomers from Schedule III to Schedule II of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (Public Law 91–513), with certain exceptions.

Application of the order to Eskatrol, a combination product for which a hearing was requested, was reserved pending review by the Bureau. Eskatrol, which contains 15 mg. of dextroamphetamine sulfate and 7.5 mg. of prochlorperazine, is manufactured by Smith Kline & French Laboratories.

A notice was published in the Federal Register on July 23, 1971 (36 F.R.

13689) scheduling a hearing regarding the transfer of Eskatrol to Schedule II for 10 a.m., on August 16, 1971, in Room 1210, 1405 Eye Street NW., Washington, D.C.

Smith Kline & French Laoratories withdrew its request for a hearing on Eskatrol on August 9, 1971 after a consultation with members of the Bureau.

Therefore, it is ordered, That:

1. Reservation of the application of the Bureau's order published in the Federal Register on July 7, 1971, be rescinded as to Eskatrol;

2. Eskatrol be transferred to Schedule II; and

3. The additional requirements imposed upon Eskatrol by virtue of its reclassification into Schedule II become effective as follows:

(a) *Labeling and packaging.* All labels and seals on commercial containers of, and all labeling of, the above controlled substance, which is packaged more than 180 days following the effective date of this order, shall comply with requirements of 21 CFR Part 302.

(b) *Order forms.* All distributions of the above controlled substance shall comply with the order form requirements of 21 CFR Part 305 by October 1, 1971.

(c) *Records and inventories.* All separate and other recordkeeping requirements of 21 CFR Part 304 for the above controlled substance shall be complied with by October 1, 1971. Records maintained and inventories taken prior to the above compliance date, which are in compliance with the recordkeeping requirements for Schedule III, shall not be affected by this order. No new inventories of the above controlled substance, in addition to that of May 1, 1971, is required as a result of this order. Where a positive conflict exists between the recordkeeping requirements of State and Federal laws and regulations, so that the two cannot stand together, Federal law governs in accordance with Section 708 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 903).

(d) *Prescriptions.* All prescriptions for the above controlled substance shall comply with 21 CFR § 306.01–306.15 within 30 days of the effective date of this order. Any prescription for the above controlled substance, which is entitled to be refilled under § 306.22 shall not be entitled to such refill in accordance with § 306.12 on and after the above compliance date.

(e) *Importation and exportation.* All importation and exportation of the above controlled substance shall be in compliance with 21 CFR Part 312, specifically as to import and export permits, within 30 days of the effective date of this order.

(f) *Security.* Since only the proposed order on security regulations for Schedule II controlled substances has been published, compliance with the present security requirements shall be deemed adequate pending publication of the final order on security regulations.

It is further ordered, That the hearing regarding the transfer of Eskatrol to Schedule II is hereby canceled.

This order is effective on the date of its publication in the Federal Register (8–18–71).

Dated: August 10, 1971.

JOHN FINLATOR,
Acting Director, Bureau of Narcotics and Dangerous Drugs.

[FR. Doc 77–11981 Filed 8–17–71; 8:46 am]

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6. [From the Federal Register, vol. 36, No. 181—Friday, September 17, 1971]

DEPARTMENT OF JUSTICE

BUREAU OF NARCOTICS AND DANGEROUS DRUGS

[21 CFR Parts 301, 308]

SCHEDULES OF CONTROLLED SUBSTANCES

Phenmetrazine and Its Salts and Methylphenidate

Based upon the investigations of the Bureau of Narcotics and Dangerous Drugs and upon the scientific and medical evaluation and recommendation of

the Secretary of Health, Education, and Welfare, received pursuant to section 201(b) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(b)), the Director of the Bureau of Narcotics and Dangerous Drugs, in view of the order transferring amphetamines and methamphetamine to Schedule II published in the Federal Register of July 7, 1971 (36 F.R. 12734), and the resulting strict production and distribution controls imposed upon amphetamines and methamphetamine by this transfer, finds that persons disposed to abuse amphetamines and methamphetamine now may direct their attention to methylphenidate and phenmetrazine, drugs which presently are not known to be the subject of substantial abuse in the United States. Further, there is no evidence to indicate that there is any abuse of methylphenidate and phenmetrazine when administered with proper medical supervision.

Therefore, under the authority vested in the Attorney General by section 201(a) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C 811(a)), and redelegated to the Director, Bureau of Narcotics and Dangerous Drugs by § 0.100 of Title 28 of the Code of Federal Regulations, the Director proposes a ruling that:

1. Section 301.02 of Title 21 of the Code of Federal Regulations be amended by adding new paragraphs (b) (8) and (9) to read:

§ 301.02 Definitions

* * * * * * *

(b) * * *

(8) Phenmetrazine and its salts.

(9) Methylphenidate.

* * * * * * *

2. Section 308.12(d) of Title 21 of the Code of Federal Regulations be deleted and replaced with a new paragraph to read:

§ 308.12 Schedule II

* * * * * * *

(d) *Stimulants.* Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system:

(1) Amphetamine, its salts, optical isomers, and salts of its optical isomers, 1,100.

(2) Methamphetamine, its salts, isomers, and salts of its isomers, 1,105.

(3) Phenmetrazine and its salts, 1,630.

(4) Methylphenidate, 1,726.

3. Section 308.13(b) of Title 21 of the Code of Federal Regulations be amended to read:

§ 308.13 Schedule III

* * * * * * *

(b) *Stimulants.* Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system:

(1) Those compounds, mixtures, or preparations in dosage unit form containing any stimulant substances which are currently listed as excepted compounds under 21 CFR 308.32, and any other drug of the quantitative composition shown in that list for those drugs or which is the same except that it contains a lesser quantity of controlled substances.

* * * * * * *

Conferences have been held with CIBA-CEIGY Corp., the manufacturer of methylphenidate and phenmetrazine, and with Boehringer Ingelheim, G.m..h., the owner of the U.S. patent on phenmetrazine hydrochloride. These firms have fully cooperated with the Bureau and have consented to the transfer of methylphenidate and phenmetrazine without a hearing to insure that these drugs do not become subject to abuse.

All other interested persons are invited to submit their comments or objections, in writing regarding this proposal. These comments or objections should state with particularity the issues concerning which the person desires to be heard. Comments and objections should be submitted in quintuplicate to the Office of Chief Counsel, Bureau of Narcotics and Dangerous Drugs, Department

of Justice, Room 611, 1405 I Street NW., Washington, DC 20537, and must be received no later than 30 days after publication of this proposal in the Federal Register.

In the event that an interested party submits objections to this proposal which present reasonable grounds for this rule not to be finalized and requests a hearing in accordance with 21 CFR 308.45, the party will be notified by registered mail of the date and place of the hearing on the objections submitted. If objections submitted do not present such reasonable ground, the party will be so advised by registered mail.

If no objections presenting reasonable grounds for a hearing on the proposal are received within the time limitations, and all interested parties waive or are deemed to waive their opportunity for the hearing or to participate in the hearing, the Director may cancel the hearings and, after giving consideration to written comments, issue his final order pursuant to 21 CFR 308.48 without a hearing.

Dated: September 14, 1971.

JOHN E. INGERSOLL,
Director, Bureau of Narcotics and Dangerous Drugs.

[FR Doc. 71-13729 Filed 9-16-71; 8:50 am]

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7. [From the Federal Register, vol. 36, No. 234—Saturday, December 4, 1971]

DEPARTMENT OF JUSTICE

BUREAU OF NARCOTICS AND DANGEROUS DRUGS

AMPHETAMINES AND METHAMPHETAMINE

Notice of Proposed Aggregate Production Quotas

On April 24, 1971, § 303.42 of the regulations implementing the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 801 et seq.) was published in the Federal Register (36 F.R. 7789). This section required that all persons requesting a 1972 procurement quota, according to § 308.12 of the regulations, or a 1972 individual manufacturing quota, according to § 303.22 of the regulations, for basic classes of controlled substances listed in §§ 308.11 (schedule I) and 308.12 (schedule II) of the regulations, file an appropriate application with the Bureau by September 1, 1971.

On July 7, 1971, a final order was published in the Federal Register (36 F.R. 12734) transferring all amphetamines and methamphetamine into schedule II of the Act. Thus, all persons manufacturing or procuring, for compounding and formulating, amphetamines and methamphetamine prior to the rescheduling, who desires to continue to do so in 1972, were required to submit their quota requests to the Bureau by September 1, 1971.

On August 12, 1971, the Distribution Audit Branch of the Bureau mailed to all manufacturers of schedule I and II controlled substances, including those manufacturing or procuring, for compounding or formulating, amphetamines and methamphetamine, a letter of explanation of the quota procedure. Also enclosed were the appropriate Bureau forms (BND-250 or BND-189) and a comprehensive list of all the controlled substances included within schedules I and II. The date for submission to the Bureau of the quota applications was extended until September 10, 1971.

In view of the failure of a majority of those who in 1971 manufactured or procured, for compounding or formulating, amphetamines and methamphetamine to file the necessary applications to obtain their 1972 quotas, on October 15, 1971 the Bureau published a notice in the Federal Register (36 F.R. 20038) extending the time within which to submit the appropriate quota applications to October 29, 1971.

In determining amphetamine and methamphetamine aggregate production quotas for 1972, which are adequate to provide for the

(1) Estimated medical, scientific, research and industrial needs of the United States;

(2) Lawful export requirements; and

(3) Establishment and maintenance of reserve stocks, the Bureau has con-

sidered the following as required by section 306 of the CSA (21 U.S.C. 826) and § 303.11 of Title 21 of the Code of Federal Regulations:

(1) Total net disposal by manufacturers during the current and preceding 2 years and trends in the national rate of net disposal, which indicate a substantial decrease over the past 3-year period and a significant downward trend;

(2) Total actual (or estimated) inventory of amphetamine and methamphetamine and of all substances manufactured from them and trends in inventory accumulation, which also indicate a substantial decrease in inventory accumulation over the past 3-year period and a significant downward trend;

(3) Projected demand as indicated by procurement quotas requested pursuant to § 303.12 of Title 21 of the Code of Federal Regulations; and

(4) Other relevant factors affecting the medical, scientific, research and industrial needs in the United States and lawful export requirements, including:

(a) Changes in currently accepted medical use in treatment with amphetamines and methamphetamine or substances which are manufactured from them, as follows:

(i) Voluntary restrictions upon prescribing, administering, and dispensing of amphetamines and methamphetamine, except for highly limited and selective indications such as narcolepsy and hyperkinesis, adopted by an ever increasing number of medical and pharmacy associations and societies throughout the United States;

(ii) The American Medical Association's support for stronger controls over amphetamine and methamphetamine as indicated by its House of Delegates' adoption of a resolution supporting the Bureau's transfer of these substances to Schedule II resulting in increased restrictions, including production quotas, and urging all physicians to limit their use of these substances to specific well-recognized medical indications; and

(iii) The Food and Drug Administration's order published in the Federal Register of August 8, 1970 by which it severely curtailed the prescribing, administering or dispensing of amphetamine and methamphetamine for exogenous obesity;

(b) Economic and physical availability of raw materials for use in manufacturing and for inventory purposes;

(c) Yield and stability problems;

(d) Potential disruptions to production; and

(e) Unforseen emergencies.

The final factor considered by the Bureau was the estimate by Health, Education, and Welfare of legitimate needs in the United States for 1972. HEW recommended that 1972 legitimate needs in the United States could be met by a 40 percent reduction in the 1971 consumption level of amphetamines and methamphetamine in the United States.

Based upon consideration of the above factors, the Director, Bureau of Narcotics and Dangerous Drugs, under the authority vested in the Attorney General by section 306 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 826) and redelegated to the Director, Bureau of Narcotics and Dangerous Drugs y § 0.100 of Title 28 of the Code of Federal Regulations, proposes that the aggregate production quotas for 1972 for amphetamines and methamphetamine, expressed in kilograms as the anhydrous alkaloid, be established as follows:

Basic class	Produced—1971	Requested	Granted
Amphetamine	9,356	19,956	5,870
Methamphetamine	4,926	8,941	2,782

All interested persons are invited to submit their comments and objections in writing regarding this proposal. Comments and objections should be submitted in quintuplicate to the Office of Chief Counsel, Bureau of Narcotics and Dangerous Drugs, Department of Justice, Room 611, 1405 Eye Street NW., Washington, DC 20537, and must be received by January 3, 1972.

Dated: December 2, 1971.

JOHN FINLATOR,
Acting Director, Bureau of Narcotics and Dangerous Drugs.

[FR Doc. 71-17854 Filed 12-3-71; 8:52 am]

8. [From the Federal Register, vol. 37, No. 30—Saturday, February 12, 1972]

DEPARTMENT OF JUSTICE

Bureau of Narcotics and Dangerous Drugs

Amphetamines and Methamphetamines

Aggregate Production Quotas

On April 24, 1971, § 303.42 of the regulations implementing the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 801 et seq.) was published in the Federal Register (36 F.R. 7789). This section required that all persons requesting a 1972 procurement quota, according to § 303.12 of the regulations, or a 1972 individual manufacturing quota, according to § 303.22 of the regulations, for basic classes of controlled substances listed in §§ 308.11 (schedule I) and 308.12 (schedule II) of the regulations, file an appropriate application with the Bureau.

On July 7, 1971, a final order was published in the Federal Register (36 F.R. 12734) transferring all amphetamines and methamphetamine into schedule II of the Act. Thus, all persons manufacturing or procuring, for compounding and formulating, amphetamines and methamphetamine prior to the rescheduling, who desired to continue to do so in 1972, were required to submit their quota requests to the Bureau.

On December 4, 1971, the proposed aggregate production quotas for amphetamines and methamphetamine expressed in kilograms as the anhydrous alkaloid, were published in the Federal Register (36 F.R. 23165) as follows:

Basic class	Produced—1971	Requested—1972	Proposed—1972
Amphetamine	9,356	19,956	5,870
Methamphetamine	4,926	8,941	2,782

In determining the final amphetamine and methamphetamine aggregate production quotas for 1972, which are adequate to provide for the

(1) Estimated medical, scientific, research and industrial needs of the United States:

(2) Lawful export requirements; and

(3) Establishment and maintenance of reserve stocks, the Bureau considered the following as required by section 306 of the CSA (21 U.S.C. 826) and § 303.11 of Title 21 of the Code of Federal Regulations:

(1) Total net disposal by manufacturers during the current and preceding 2 years and trends in the national rate of net disposal, which indicate a substantial decrease over the past 3-year period and a significant downward trend;

(2) Total actual (or estimated) inventory of amphetamines and methamphetamine and of all substances manufactured from them and trends in inventory accumulation, which also indicate a substantial decrease in inventory accumulation over the past 3-year period and a significant downward trend;

(3) Projected demand as indicated by procurement quotas requested pursuant to § 393.12 of Title 21 of the Code of Federal Regulations; and

(4) Other relevant factors affecting the medical, scientific, research, and industrial needs in the United States and lawful export requirements, including:

(a) Changes in currently accepted medical use in treatment with amphetamines and methamphetamine or substances which are manufactured from them as follows:

(i) Voluntary restrictions upon prescribing, administering, and dispensing of amphetamines and methamphetamine, except for highly limited and selective indications such as narcolepsy and hyperkinesis, adopted by an ever increasing number of medical and pharmacy associations and societies throughout the United States;

(ii) The American Medical Association's support for stronger controls over amphetamine and methamphetamine as indicated by its House of Delegates' adoption of a resolution supporting the Bureau's transfer of these substances to schedule II resulting in increased restrictions, including production quotas, and urging all physicians to limit their use of these substances to specific well-recognized medical indications; and

(iii) The Food and Drug Administration's order published in the Federal Register of August 8, 1970, by which it severely curtailed the prescribing, administering or dispensing of amphetamine and methamphetamine for exogenous obesity;

(b) Economics and physical availability of raw materials for use in manufacturing and for inventory purposes;

(c) Yield and stability problems;

(d) Potential disruptions to production; and

(e) Unforeseen emergencies.

Another factor considered by the Bureau was the estimate by Health, Education and Welfare of legitimate needs in the United States for 1972. Prior to the publication of the Bureau's proposed aggregate production quotas, HEW recommended that 1972 legitimate needs in the United States could be met by a 40 percent reduction in the 1971 consumption level of amphetamines and methamphetamine in the United States. However, HEW indicated that this recommendation would be subjected to upward or downward revision if clear-cut evidence of greater or lesser medical need should be presented. Thus, prior to publication of this order, HEW recommended that 1972 legitimate needs in the United States could be met by an additional 30 percent reduction in the 1972 consumption level of amphetamines and methamphetamine in the United States.

The final factor considered by the Bureau was the effect of the Bureau's recently completed "Operation Blackjack," which resulted in the issuance of an order to show cause on January 18, 1972 to Strasenburgh Prescription Products, Division of Pennwalt Corp., as to why the Bureau should not deny its application for a certificate of registration to export amphetamines and as to why the proposed 1972 aggregate production quota for amphetamines should not be reduced by the amount allocated for export purposes. By letter dated January 25, 1972, Pennwalt Corp. amended its application for certificate of registration to export by deleting from the application the exportation of amphetamines and requested that the proposed 1972 aggregate production quota be reduced correspondingly. The proposed quota for amphetamine was, thus, subject to further downward revision.

Based upon consideration of the above factors, the Director, Bureau of Narcotics and Dangerous Drugs, under the authority vested in the Attorney General by section 306 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 826) and redelegated to the Director, Bureau of Narcotics and Dangerous Drugs by § 0.100 of Title 28 of the Code of Federal Regulations, orders that the aggregate production quotas for 1972 for amphetamines and methomphetamine, expressed in kilograms as the anhydrous alkaloid, be established as follows:

Basic class	Produced—1971	Requested—1972	Granted—1972
Amphetamine	9,356	19,956	1,564
Methamphetamine	4,926	8,941	969

At the present time, the Food and Drug Administration is conducting a review of the question of the use of amphetamines and methamphetamine in short-term treatment of obesity. A final determination on the efficacy question will be announced by FDA on July 1, 1972. Since this announcement could result in significant alterations in the medical need for these substances, with a corresponding revision of the above quotas, the Bureau reserves its authority under this order to revise the above quotas after the July 1, 1972 report.

The Huntington Narcotics Guidance Council objected to the 1972 quotas originally proposed by the Bureau and requested a hearing on the issue of consideration and inclusion by the Bureau of short term obesity in determining the legitimate medical needs in the United States. In view of the additional reduction by the Bureau and the further quota revision, which will occur after the July 1, 1972, obesity report by FDA, the Huntington Narcotics Guidance Council has consented to deferment of the hearing as requested until its review of the revised 1972 quota following the FDA obesity report.

All persons who submitted an application for either an individual manufac-

turing quota or procurement quota for 1972 will be notified by mail as to their respective 1972 quota established by the Bureau.

This order is effective upon the date of its publication in the Federal Register (2–12–72).

Dated: February 10, 1972.

JOHN E. INGERSOL,
Director, Bureau of
Narcotics and Dangerous Drugs.

[FR Doc. 72–2235 File 2–11–72; 8:53 am]

(B) SUPPLEMENTAL ARTICLES, CORRESPONDENCE, EXCERPTS, PAMPHLETS, REPORTS, AND STATEMENT PERTAINING TO THE USE AND ABUSE OF AMPHETAMINE DIET PILLS

[From the S 16928, Congressional Record—Senate, October 27, 1971]

1. TRANSFER OF RITALIN AND PRELUDIN TO SCHEDULE II

Mr. BAYH. Mr. President, I am pleased to announce that the Nixon administration, has finally, though belatedly, endorsed the view of a majority of the Members of this body, including this Senator and other members of the Subcommittee To Investigate Juvenile Delinquency, that unrestricted production and distribution of all amphetamine-like stimulants presents a threat to public safety and to the welfare of the citizens of this country, particularly its youth.

Recently, John E. Ingersoll, Director of the Bureau of Narcotics and Dangerous Drugs, moved administratively to impose production and distribution controls on methylphenidate—Ritalin—and phenmetrazine—Preludin. The Director's order subjects these stimulants to schedule II controls, only recently imposed on all amphetamines and methamphetamines—"speed." Attorney General Mitchell characterized this move as "part of the Nixon administration's continuing program to strengthen controls on drugs with a high potential for abuse." Such a statement brings to mind Mr. Mitchell's enjoinder to watch what this administration does, not what its representatives say. In the light of that admonition, the administration's past year performance regarding these drugs is in order.

Last October, this body passed, as an amendment to the Comprehensive Drug Abuse Prevention and Control Act, a provision which would have imposed tighter controls over the manufacture and distribution of amphetamines and amphetamine-like substances. Following intensive lobbying by representatives of the drug industry and bolstered by White House opposition to this measure, it was deleted by our colleagues in conference. In February of this year, Senator Eagleton and I with 36 cosponsors introduced S. 674, an identical bill.

Then on May 26, under immense pressure from a public alerted to the destructive nature of "speed" drugs, the administration shifted some of these stimulants from schedule III to the more stringent schedule II imposing production, marketing and export quotas as well as stricter prescription controls. The Attorney General's order provided for the rescheduling of amphetamines and methomphetamines but not methylphenidate and phenmetrazine, popularly known respectively at Ritalin and Preludin.

RITALIN AND PRELUDIN

As chairman of the Senate Juvenile Delinquency Subcommittee, I, like others who are concerned about the overproduction, diversion, and abuse of this class of drugs, was amazed at the insensitivity of naiveté of the Department of Justice in this matter. If Ritalin and Preludin remained in schedule III, while similar drugs were shifted to schedule II, it was clear to us that these two stimulants would become the subject of increasing abuse and might in fact become abusers' drugs of choice.

The track record and abuse potential of these two drugs is no mystery to students of stimulant abuse. While not abused in every region of this country, they have the same abuse potential as amphetamines and methamphetamines. Dr. Jerome Jaffe, now Director of President Nixon's Special Action Office for

Drug Abuse Prevention, recognized the similarity of these amphetamine equivalents and their potential for abuse when he commented in 1969:

A number of other CNS (central nervous stimulants) can produce subjective effects that are almost indistinguishable from those of amphetamines. These include dextroamphetamine, methomphetamine, and phenmetrazine (Preludin). Drugs such as . . . methylphenidates (Ritalin) are sufficiently similar in their subjective effects, toxicity, and patterns of abuse to justify inclusion in this class.

While Preludin and Ritalin, are less familiar to the American public than others in this class, such as the plain amphetamines, their serious abuse abroad has brought them to the forefront.

Sweden, a highly industrial country not unlike our own, experienced a pandemic of Preludin abuse. Youths were the ones most often victimized by the availability of this stimulant and Ritalin as well. Abuse of both drugs began on the average at age 16—somewhat earlier in girls than in boys. Initially the amphetamines were the starting drugs, but as these were more strictly controlled and their distribution restricted, the drugs of choice in the stimulant class became almost exclusively Preludin. A 1967 study of abuse patterns among Swedish juvenile abusers of stimulants revealed that 81 percent abused Preludin, 36 percent abused Ritalin, and 6 percent abused amphetamines. Today all central nervous stimulants are banned in Sweden.

The Swedes were well advised to prohibit the distribution of these dangerous stimulants. According to Dr. John D. Griffith, assistant professor of psychiatry and instructor in pharmacology at Vanderbilt University School of Medicine, observations of amphetamine addicts now make it clear that amphetamine addiction is more widespread, more incapacitating, more dangerous and socially disruptive than narcotic addiction.

An equally important consideration is the relationship of amphetamine-type central nervous system stimulant abuse to the commission of criminal acts by the abuser. The Select Committee on Crime's report "Amphetamines" notes that relationship and cites a study by Swedish psychiatrist Prof. Goasta Rylander, in which he commented as follows:

The crime-causing influence of central stimulants . . . can be studied in the light of three different types of mental states.

First, the increased self-assurance which can give a feeling of omnipotence, the stimulation of energy and heightened activity, the ignoring of difficulties and consequences, involve disposition to crime. This was expressed in the same words by two girls who did not know each other: 'I always turn "criminal" after Preluding (phenmetrazine) shots,' they said. An addict with long experience of the drug declared that crime was a natural outlet for the drug-induced overactivity, without any thought being given to the nature of the act committed. When caught red-handed, the addict may be astonished at the action of the (arresting) policeman. Of course, the addicts need money to buy tablets illegally, but even if that need is not acute, they may still commit crimes. 'I would never have committed such a clumsy and stupid crime, if I hadn't been high,' the addicts often say.

Two of my patients with no crimes of violence in their records committed robberies when high on Preludin. One of them, a man, knocked down a jeweler in his shop, the other, a girl, inspired two foreigners, whom she met by chance, to a robbery and a holdup. She helped them in both cases. The crimes mentioned were quite ruthless, and from the criminals' point of view, very stupid. They committed the crimes without bothering about the obvious risks of being caught; in fact, they were caught.

Two of my addicts who had not been sentenced for crimes of violence before, committed murder under the influence of Preludin and a small amount of alcohol. This seems to be a very dangerous combination . . .

In states of acute paranoid psychosis, panic-filled addicts can commit dangerous acts of different types. One of my addicts killed another addict because he felt sure this man was sent out by a gang to kill him. In a similar state, another of my patients drove through the central part of Stockholm at high speed against red lights and through a one-way street in the wrong direction until he ran into another car at a street corner, badly injuring both the passengers of this car and himself. Another one tried to force his way into the police headquarters in Stockholm with a knife in his hand, crying for help from the Swedish Secret Service against his prosecutors.

Finally, addicts who intravenously inject large doses of central stimulants decline socially more quickly than alcoholics. They become parasites, living on relatives, friends, or sometimes on sickness benefits, peddling alcohol or narcotics. They are inclined to all sorts of petty crimes and anti-social acts by which they can get some money with which to buy drugs.

Furthermore, several laboratory experiments have verified the ease with which Ritalin and Preludin can substitute for the more traditionally abused amphetamines. For example, Dr. Maurice H. Seevers, Ph.D., M.D., professor and chairman of the University of Michigan Department of Pharmacology, has demonstrated that monkeys, under selfadministration, readily substitute doses of amphetamine, methomphetamine, Ritalin, and Preludin.

Thus, to permit these two drugs to remain in schedule II with lesser controls, with no production quotas, lower accountability, and relaxed controls seemed folly—a patent invitation to further stimulant abuse and more ruined lives.

In light of our knowledge of the actual abuse of these two drugs and their high potential for abuse, as well as the rescheduling of the plain amphetamines, I announced hearings on June 17, 1972, on S. 674 which would place all central nervous stimulants including Ritalin and Preludin in schedule II where they belong.

During 2 full days of hearings July 15 and 16, we heard testimony from 29 witnesses, including testimony from Senator Eagleton, medical authorities, major drug producers, Government officials, and young people who were formerly a part of the "speed scene."

The Task Force on Drug Abuse, a privately funded nonprofit "Nader-like" group, reported that Ritalin abuse had reached "epidemic proportions" in Seattle, Wash., area, and its abuse was noticeably increasing in at least a half dozen other areas in the country. Robert Brandon, project director of the task force, told the subcommittee that the intravenous administration of Ritalin had been identified as the cause of 12 Seattle deaths in the first 6 months of 1971. He also testified that there had been at least 22 Ritalin deaths during the combined years of 1968 and 1971. Brandon revealed that four 1970 deaths in Portland, Oreg., were attributed to Ritalin abuses and that there are as many as 2,500 "regular Ritalin abusers" in Seattle alone.

Brandon concluded his statement as follows:

There is every reason to believe that if amphetamines themselves are effectively controlled, then the drug abuser will turn to similar, less carefully controlled drugs. Tighter controls should be placed on Ritalin and Preludin immediately. By moving them to Schedule II this can be accomplished. The problem is here with us, and it is growing. We urge you not to await further studies and statistics. One need only speak to people on the street—police officers, doctors, abusers, and victims—to see the urgency of the problem. We cannot afford to wait until today's potential victim becomes tomorrow's statistic.

Further documentation of the Seattle epidemic is found in a letter from Mr. Al Weese, coordinator of drug and alcohol program for the city of Seattle. He states:

For reasons as yet unknown, Seattle has for some time had the dubious distinction of being known as the "Ritalin Capital." Historically, its use has been largely confined to the older, hard drug-using black community. More recently (within about the past year) its use has moved into the younger, white, "hip" drug-using community. Its reputation as a drug of choice in conjunction with Methadone is increasing. (Perhaps, an updated version of the old "speed ball"—heroin used with amphetamine and/or cocaine.)

The feeling is common locally that Ritalin is largely obtained through loose pharmaceutical dispensing, although some may be bled off through hospitals.

Dr. Richard Jaffe, a radiologist in the Clinics Division of the National Institute of Health, reported the findings of his study of 20 chronic Ritalin abusers in the Seattle area. He prefaced his remarks with the comment that heroin and Ritalin were, far and away, the most commonly abused drugs in the Seattle area. He reviewed for the subcommittee's benefit the serious medical complications related to intravenous Ritalin abuse. Referring to a series of slides indicating the destructive effects of Ritalin abuse, he commneted:

This is not a very pretty picture, but this is a young Ritalin addict who had lost almost all his veins and was forced to use the vein near his ankle. You can see this is a festering abscess related to the site of injection of Ritalin. You

can see also several other abscesses adjacent to it, one here on top, a blister on the bottom and one in the center.

Now, what is the importance of this? The infection spreads to the underlying vein and causes thrombophlebitis or to the heart valve, resulting in severe complications. Infected blood clots from these veins can break off and travel to the lung where they cause multiple lung abscesses, as in these three patients.

I call your attention to these two large infected abscesses in his right lung. This left lung is normal and clear as it should be. This is a 41-year old addict with a 13-year history of intravenous Ritalin and heroin abuse. I call your attention to the large abscess in the lung here, and a larger one in this lung here. This gentleman is now dead.

In summary, Ritalin has a high propensity for serious medical complication when used intravenously by addicts. This is due to its frequent association with infection about the injection site and the passage of the Ritalin talc particles to the lung and the blockage of pulmonary vessels.

In addition to the vivid documentation of lives wrecked by Ritalin abuse, Dr. Jaffe offered his opinion that Ritalin currently constitutes a significant drug abuse problem, and that as amphetamine production declines and distribution is more stringently controlled, Ritalin abuse would be on the rise.

In view of this evidence of actual and potential abuse of these stimulant drugs the Nixon administration's position was startling.

The spokesman for the Attorney General, Mr. John Finlator, Deputy Director of the Bureau of Narcotics and Dangerous Drugs, agreed that Ritalin and Preludin are drugs with a potential for abuse but stated:

We do not feel that we have seen sufficient evidence of abuse to justify the serious step of placing these drugs into a higher schedule.

He continued:

For example, if we find that drug abusers switch from amphetamine or methamphetamine to these other stimulant compounds, we are prepared to take rapid action to place the more stringent controls into effect. However, we do not feel that such action is indicated at present. These drugs are currently controlled in Schedule III, and the controls of III appear to be adequate to safeguard the public health and safety.

Mr. Finlator acknowledged, however, that much of the evidence of Ritalin abuse assembled by the Brandon task force was unknown to his office. It is incredible that the BNDD and other Federal agencies responsible for enforcing drug abuse laws enacted by Congress could be so grossly underinformed. I strongly recommend that the monitoring procedures of BNDD be reviewed immediately and altered drastically. Our citizens deserve far better performance from those responsible for responding to the drug abuse crisis engulfing this country.

Nor was the Food and Drug Administration persuaded that these drugs should be subject to more stringent controls. Dr. Henry Simmons, testifying on behalf of FDA Commissioner Dr. Charles Edwards, indicated that as of May 31, 1971, the Department of Health, Education, and Welfare was not prepared to recommend the rescheduling of Ritalin and Preludin. Dr. Simmons expressed the "hope" that these drugs would be rescheduled soon.

However, in the light of the evidence adduced by the subcommittee, it is my belief that it is better to err on the side of safety. This administration by its opposition to a comparable measure in 1970 chose to overlook the lesson learned abroad, the studies indicating a probably shift of abuse to these stimulants, as well as the evidence of the growing incidence of actual abuse in this country. I take strong exception to this "wait and see" approach—a body count.

ESKATROL

In addition to the demonstrated need for the rescheduling of Ritalin and Preludin, our attention had also been directed to several amphetamine combination drugs whose manufacturers had formally objected to being moved to schedule II. These drug firms sought exemption from the stricter controls for some of their products:

Smith Kline & French for its amphetamine combination, Eskatrol;

Pennwalt Corp. for its amphetamine combinations, Biphetamine and Biphetamine-T; and

Mission Pharmacal Co. for its methamphetamine combination, Fetamin.

Representatives from each of these firms were invited to testify before our subcommittee. Two days before our first day of hearing: both Pennwalt and Mission firms withdrew their requests for special exceptions for their products. This resulted in an automatic transfer of these products to schedule II. Smith Kline & French, however, insisted that its drug, Eskatrol, did not have a significant potential for abuse.

Our hearings revealed substantial evidence of the abuse potential of Eskatrol. Several witnesses, one, formerly a heavy abuser of amphetamines—a so-called speed freak—spoke of frequent abuse of Eskatrol. Testimony revealed that Eskatrol was water soluble, and that with little difficulty the liquid amphetamine can be separated and administered intravenously. This characteristic, coupled with the fact that the amphetamine particles in Eskatrol were color-coded, made clear the abuse potential of this drug, which constitutes at least 20 percent of the diet pill market. If Eskatrol were excepted from schedule II controls, it was apparent that it would capture a sizable portion of the market, licit and illicit, resulting from the rescheduling of plain amphetamines.

ADMINISTRATIVE ACTIONS SINCE THE HEARINGS

Since the adjournment of our hearings July 16, 1971, two significant events have occurred. On August 9, 1971, Smith Kline & French withdrew its request for special classification of its amphetamine combination, Eskatrol. Contrary to claims made by Smith Kline & French before our subcommittee, a Justice Department spokesman indicated that substantial amounts of Eskatrol had been diverted by thefts for illicit purposes. This, coupled with the evidence presented during our hearings regarding the ease with which the water soluble amphetamine could be extracted from the amphetamine combination, clearly supported the BNDD August 18, 1971, order transferring Eskatrol to schedule II.

A more dramatic turn of events was the recent announcement, on September 17, 1971, in the Federal Register that BNDD had moved Ritalin and Preludin to schedule II status. Since the appearance of the administration spokesman before our subcommittee barely 2 months ago, the administration has taken an about face and accepted my long held belief that the public health and safety demand that these two drugs be subject to the strict production and distribution controls of schedule II. The MNDD relied almost exclusively on our contention that persons disposed to abuse amphetamines were likely to switch to abuse of Ritalin and Preludin as the basis for its order.

Ciba-Geigy Corp., the manufacturer of methylphenidate—Ritalin—and phenmetrazine—Preludin—and the Boehringer Ingeljeim, G.m.b.h., the owner of the U.S. patent on Preludin, both consented to the transfer without a hearing. Thus, clearing the way for the expeditious rescheduling of these two stimulants.

I am gratified that the administration relented and finally recognized the clear abuse potential of Ritalin and Preludin and decided to shift any risk involved to the manufacturers of these products rather than to the youth of this country.

The next step in the rescheduling process is the establishment of production quotas to meet the legitimate medical, scientific, research, and industrial needs for all of the amphetamine and amphetamine-like substances. It is essential that the quotas set by the Attorney General reflect actual need. The medical community should play an important role in this regard.

In addition to the overproduction of all amphetamines and similar substances, a significant factor in the availability of these drugs, is the rather casual manner in which far too many of our physicians prescribe amphetamines. If production quotas reflecting true medical needs are to be established the medical community must check these practices. Voluntary efforts by several medical associations have met with striking success.

During the series of hearings held by the Juvenile Delinquency Subcommittee in July, Dr. James M. Blake, testifying on behalf of the Suffolk County, N.Y. Medical Society, explained the measures taken which made his county the first community in the Nation to organize a voluntary ban on prescribng and dispensing of amphetamines. A substantial majority of their physicians have pledged to restrict the prescription of amphetamines. It was Dr. Blake's view that such voluntary programs would cut down the base that the Justice Department would use in determining production quotas for stimulant drugs and would therefore further limit the supply available.

In my own State of Indiana 96 percent of the La Porte County Medical Society, took similar action after learning that stimulants taken from home medicine cabinets were being sold in the corridors of local schools. This program has drawn favorable responses from the general public, pharmacists and law enforcement authorities. Law enforcement officials believe that the embargo makes it easier for them to concentrate on prime illegal distributors, instead of "kids who were selling their mothers' amphetamines at school."

Similar programs have been initiated by medical societies in Utah, South Carolina, and Texas. This type of voluntary action is a credit to the medical profession and a service to the public.

As chairman of the Juvenile Delinquency Subcommittee, I intend to continue a vigilant review of the procedures followed by BNDD in establishing these quotas and other regulatory controls provided in schedule II. In this manner we will be able to assure that this administration truly acts in accord with its current policy regarding these dangerous stimulant drugs.

2. Statement of Senator Thomas F. Eagleton

Mr. Chairman: I am grateful to you and to the members of your Subcommittee for scheduling these hearings on S. 674, my proposal to move the central nervous system stimulants from Schedule III to Schedule II of the Controlled Substances Act.

At the outset of my statement, I want to put to rest the notion that in talking about the need of tightening controls over stimulant drugs we are "beating a dead horse." I am, of course, aware that the Justice Department has published an order moving amphetamine and methamphetamine drugs into Schedule II. On the face of it, it would appear that the increased control over the production and distribution of these drugs which Congressman Pepper and I have sought to achieve has been realized. Unfortunately, that is not so.

While I commend the Justice Department on their action—particularly in view of the Administration's previous opposition to my proposal—we must not be misled into believing the issue is closed. I believe it is essential that the people know what has in fact been accomplished by this order . . . and what in fact has been left undone. Congress has a responsibility for closing the gaps left by the Justice Department order.

Let me briefly review the ground covered rather thoroughly in the hearings and report of the House Select Committee on Crime and in the Senate debate of last October 7. I assume that a general acceptance of this data formed the basis of the Justice Department action.

The heart of the problem of amphetamine and methamphetamine abuse is overproduction by legitimate drug manufacturers. I say that knowing that "bathtub" amphetamine is easily manufactured.

Somewhere in the neighborhood of 8 billion dosage units of these drugs are produced by legitimate manufacturers in this country each year. Estimates range from the 2 billion figure preferred by the drug companies to the 3½ billion figure used by Commissioner Edwards last August, to the 10 billion figure I recently noticed in a government pamphlet on drug abuse. The 8 billion figure comes from testimony before the House Select Committee on Crime. I personally see little to be gained from a continuing debate over these numbers. The inescapable point is that even the most conservative estimates far exceed any legitimate medical requirement.

According to an FDA order of August 8, 1971, labeling of amphetamines and methamphetamines must reflect that their medical usefulness is limited to three uses. These are (1) narcolepsy (a rare sleeping illness), (2) hyperkinesis (minimal brain dysfunction in children manifesting itself in hyperactivity) and (3) obesity. Prescription of amphetamines and methamphetamines for appetite control is to be limited to short term treatment.

The FDA order states that "These drugs are very extensively used in the treatment of obesity. The extent of use for such purposes as narcolepsy and minimal brain dysfunction in children is believed to be insignificant as compared with the total usage of these drugs." Within the medical profession, however, a spirited controversy is in progress as to whether these drugs should be prescribed for appetite control at all.

I regret that Dr. William Asher, Director of the Society for Bariatrics, has declined the Subcommittee's invitation to testify. Dr. Asher strongly advocates

the use of amphetamines for appetite control and has expressed to me his opposition to S. 674. So that the record may reflect his views, I ask that a copy of our correspondence be inserted in the record as an appropriate point. Other medical people disagree with the position of the Bariatrics Society. The Utah State Medical Society, for example, has passed a resolution asking its members to refrain from prescribing amphetamines in the treatment of obesity, and in Huntington, Long Island, a group of physicians and pharmacists voluntarily have agreed to stop perscribing and dispensing these drugs for appetite control. Just a few weeks ago, the American Medical Association urged its members to limit prescriptions for amphetamines.

In urging the adoption of stricter controls over amphetamines, I have purposely avoided comment on the nature and extent of medical requirements.

I have insisted only that production levels be tied to the actual medical needs, as determined by those expertise in the medical field. It is clear, however, that the limited uses currently considered appropriate by the FDA, the AMA, and individual members of the medical profession do not justify the outrageous rate of production that has continued through the years.

If further evidence is necessary that production far exceeds medical requirements, it lies in the fact that half of the legitimately produced amphetamines and methamphetamines are diverted into *illicit* channels. Even with this massive rate of diversion, there are enough pills left to fill all the prescriptions written for them.

I will not describe in detail the serious abuse to which this high rate of production and diversion obviously contributes. I do want to remind the Subcommittee, however, that the "shooting" of high dosage "speed" into the veins is only the most severe kind of stimulant abuse; it is not the whole problem. In addition to the dilution of pills for intravenous use by the so-called "freaks," we must also recognize as dangerous abuse the unsupervised use of these drugs by housewvies who need a life, truckdrivers who try to make another fifty miles without a rest stop, and students who stay up all night at exam time.

Because of the very serious effects of totally unsupervised, high dosage "shooting" of speed, I ask that the Subcommittee accept for the record a fine statement by David E. Smith, Director of the Haight-Ashbury Clinic in San Francisco, on the nature of the "speed" scene and the very dire effects of this kind of amphetamine abuse.

A change of these drugs to Schedule II deals with the problems of overproduction, diversion and abuse in several ways. Under Schedule II:

The Attorney General is directed to set manufacturing quotas which reflect the legitimate medical, scientific, research, and reserve needs of the country.

It is illegal for any person to distribute drugs without a written order issued by the Attorney General. These written orders are already required for all narcotic drugs distributed in this country. And this procedure has reduced the diversion of legally produced narcotics into illegal channels to an irreducible minimum.

Drugs can only be dispensed by a physician with a written prescription—and a doctor's permission is required for a refill of the prescription.

It is illegal to import drugs unless the Attorney General finds it necessary to provide for the medical, scientific, or other legitimate needs of the country.

Exporting drugs is permitted only when a permit has been issued by the Attorney General. This would prevent, for example, the continuation of the current practice whereby vast quantities of "speed" pills are being shipped to Mexican border towns—and smuggled back across the border to be sold on the streets of our western cities.

Let me now turn to what I consider to be the deficiencies in the Justice Department order of July 7.

The Controlled Substances Act vests authority to effect changes in scheduling in the Attorney General. Parties who object to a proposed change may file their objections along with requests for hearing of their complaint. Not surprisingly, several drug companies did file for hearings on certain of their products following the proposed rescheduling of amphetamines and methamphetamines. One of these companies, Pennwalt Corporation, has withdrawn its petition for hearing on Biphetamine and Biphetamine-T products that account for about 15% of the amphetamine sales market. Hearings are still to be held on Eskatrol, a dextroamphetamine sulfate product of Smith, Kline and French and the largest selling diet pill in the country. Eskatrol accounts for about 20% of the amphetamine

sales market, or $11–$12 million in annual sales. Mission Pharmacal Company has also filed for a hearing on a relatively small seller, Fetamin, which brings in about $100,000 in annual sales.

Leaving Eskatrol out of the rescheduling of amphetamine drugs is a loophole that threatens to swallow the order. It automatically *excludes* from the Justice Department order one-fifth of the amphetamine market. But even more disturbing is the likelihood that prescribing doctors will prefer to prescribe this lesser controlled drug to its more strictly regulated competitors. Conceivably, Eskatrol could grow to half the amphetamine market or more, displacing other diet pills almost entirely. Nor can we afford to overlook the high potential for abuse of this drug—a capsule whose amphetamine ingredient can be easily separated from the other components of the combination. The profit motive is a strong one and where a product earns about one dollion dollars every month even a delay of a few months can be worth the trouble. At some point, however, the public interest has to be thrown on the scale, too. If Smith, Kline and French chooses not to recognize it, we must help them along. Under a legislative rescheduling, Eskatrol would be moved with the other dextro-amphetamine combination diet pills.

Justice Department personnel have assured me that hearings of these products will be scheduled soon and that these drugs will be moved immediately into Schedule II should the drug companies fail to carry their burden of proof. I am concerned, however, that Justice Department regulations issued pursuant to the Controlled Substances Act fail to state explicitly that no administrative stays will be granted. I hasten to add that even if administrative stays are denied, the drug companies may appeal to the courts for stays pending judicial review of their cases . . . possibly as long as two years.

While I am on the subject of Justice Department regulations and policy, I want to mention another issue of some concern to me. It has come to my attention that over the years between 500 and 1000 amphetamine products have been excepted on a one-by-one basis from some requirements of Schedule III. These products are in Schedule III, but they need not comply with the recordkeeping, labeling and prescription requirements that apply to other Schedule III drugs. Under the July 7 order, these drugs will remain right where they are. I am hopeful that the Subcommittee can elicit from the Justice Department a commitment to review each of these exceptions with an eye to moving them into Schedule II. At the least, those drugs should be subject to all the requirements of Schedule III.

The second major deficiency of the Justice Department rescheduling order is that it fails to include two amphetamine-like central nervous system stimulants, methylphenidate and phenmetrazine. These drugs, more commonly called Ritalin and Preludin, would be moved to Schedule II under S. 674. Ciba-Geigy Corporation is the sole producer of these drugs, Retalin being produced by Ciba Pharmaceutical and Preludin by Geigy Pharmaceuticals.

Mr. Chairman, you may recall that Ritalin attracted considerable attention a few months ago when the news media reported that this drug was being administered to children in the public schools to "control" disruptive behavior. Following these reports, President Nixon appointed a panel of medical experts to look into the practice of prescribing Ritalin for children. The Conference on the Use of Stimulant Drugs in the Treatment of Behaviorally Disturbed Young School Children issued its report last March. They concluded that the use of Ritalin for treatment of hyperkinesis—a form of hyperactivity related to minimal brain dysfunction in children—is appropriate where certain precautions in the prescribing and dispensing of these drugs are observed.

In view of this Subcommittee's special interest in the welfare of juveniles, you may want to look into the reported use of Ritalin in the schools to determine whether it has been dispensed under proper medical supervision, with parental consent, and only in cases of hyperkinesis . . . not as a general tool for improving discipline in the classroom. I want to stress that S. 674 makes no assumptions as to the validity of this form of treatment. It would simply make available as much Ritalin as necessary for "legitimate medical needs," as determined by medical experts.

Preludin is probably less familiar to the American public, although its serious abuse abroad has brought it to the forefront of attention in other countries. It is a diet pill similar in its medical effects to the amphetamine-based prescriptions.

In Sweden today amphetamines and methamphetamines are subject to the strictest controls, available only through specially licensed practitioners. These unusual precautions came about as a result of a serious epidemic of central nervous system stimulant abuse in the 1940's and 1950's. As the abuse of amphetamines increased, the Swedish government responded with increasingly strong controls, including the treatment of these drugs as "narcotics under Swedish law. The result was a switch by abusers to Ritalin and Preludin, subject in the 1950s to controls less strict than those imposed on amphetamines. So great was the abuse of these substances that in 1965 Preludin was taken off the Swedish drug register and Ritalin was voluntarily withdrawn by the manufacturers 3 years later.

At a Symposium on Abuse of Central Stimulants held in 1968, a Swedish health official made a statement that seems to speak directly to us today. He said:

"Developments in Sweden can well serve as a warning to those countries which have not yet understood the nature of what has been looming and still disregard trends already evident within their open borders. Unless they act quickly and with determination they will soon find themselves in the same situation as Sweden."

To move amphetamines to Schedule II without imposing similar controls over Ritalin and Preludin is to invite abuse of drugs, in my opinion. Those of us with the responsibility for protecting the public against the hazards of drug abuse cannot afford to overlook the lessons learned by governments abroad. The Swedish experience indicates beyond a doubt that Ritalin and Preludin, like amphetamines, have a high potential for abuse. Moreover, that potential grows when amphetamines become harder for a drug abuser to get. The effects of these drugs are sufficiently similar to encourage a switch over to these lesser known but equally dangerous substances.

Mr. John Ingersoll, Director of the Bureau of Narcotics and Dangerous Drugs, stated in a letter to me on May 12 that, "As of this writing, this Bureau does not have sufficiently documented information as required by P.L. 91–513 to recommend additional controls for either methylphenidate or phenmetrazine. . . . Although the actual abuse of these two drugs in this country has been limited, we are continuing to monitor these substances and when sufficient evidence is compiled, we will take the appropriate steps at that time.'

If Mr. Ingersoll's letter says what I think it does, it says we must wait until we can document abuse of these drugs in this country on a substantial scale. But the Controlled Substances Act does not require that we wait for tragic addictions to occur. The criterion for Schedule II drugs is not "widespread abuse," but rather a "high potential for abuse," and that potential has been amply demonstrated abroad.

I confess to being somewhat confused about the Administration's position on the transfer of these stimulant drugs to Schedule II. Mr. Ingersoll has indicated that they will not support a transfer until further documentation of abuse is available. However, that position seems to be contrary to the policy espoused by President Nixon in his recent drug abuse message to Congress.

President Nixon stated, "I am submitting to the Senate for its advice and consent the Convention on Psychotrophic Substances which was recently signed by the United States and 22 other nations. In addition, I will submit to the Congress any legislation made necessary by the Convention including the complete licensing, inspection and control of the manufacture, distribution and trade in dangerous synthetic drugs." Under that Convention, now pending before the Senate Foreign Relations Committee, Ritalin and Preludin are classified with amphetamines in Schedule II. Based on the President's stated commitment to the terms of this treaty, I hope we can look forward to Administration support for a domestic rescheduling of Ritalin and Preludin.

In closing, Mr. Chairman, let me say that I feel as strongly now as I did when I first brought this issue to the Senate last October that these stimulant drugs should be brought under stricter controls. Let's not be lulled into thinking that this has already been accomplished.

American Society of Barbiatrics,
Englewood, Colo., November 11,1970.

Hon. Thomas F. Eagleton,
U.S. Senator From Missouri, New Senate Office Building,
Washington, D.C.

Dear Senator Eagleton: We wish to compliment you on the zeal with which you are endeavoring to do something tangible regarding the growing drug abuse problem in this country. We of the American Society of Bariatrics have always been violently opposed to both the unsupervised and illicit use of drugs—particularly the amphetamines. In fact, most Bariatricians, when amphetamines are used as an aid in developing new eating habits, dispense them each 28 days and the patients receive no more amphetamines unless they are personally seen and examined by the physician involved. I think you can see this makes for rather tight controls at our level.

Yesterday, I read in detail, a copy of your letter of October 15 to Kern Smith and a copy of your talk to the Senate on October 7, 1970. I would like to point out a few items which indicate you may have been misinformed on certain items. There are over 25 million Americans more than 15% about their standard weight, over 100,000 of whom will die prematurely this year secondary to obesity and associated conditions.

Amphetamines, in spite of all of their shortcomings, are the only classes of pharmacologic agents which may be of value for use in retraining the eating habits of these obese millions. (All of our present appetite suppressants are amphetamines or chemical cousins.

Therefore, your statement, "The legitimate medical need in this country for amphetamines is only in the thousands of dosage units," would be open to question, whatever the source of your information.

The next point I wish to question is whether placing the amphetamines in Schedule 2 would significantly affect the supply of amphetamines on the streets of our western cities. You state, "This would prevent, for example, the continuation of the current practice whereby vast quantities of 'speed pills' are being shipped to Tijuana, Mexicali, and other Mexican border towns—and then smuggled back across the border to be sold on the streets of our western cities."

My question is, if the present source of amphetamines for this despicable practice were dried up, would there not be Mexican sources to replace them?

Finally, the most important point of all—would placing the amphetamines in Schedule 2 really solve the problem? I want to call your attention to a statement in the Wall Street Journal of Wednesday, October 28, 1970—a statement with which we totally agree. "Along with the drug companies HEW might oppose tougher limits on all amphetamines. The medical experts argue that drying up the supply of a drug isn't the answer to abuse, noting the continued problem of heroin addiction, a totally banned drug for years. These experts worry that stricter limits would only encourage the illicit production of amphetamines or forces abusers to switch to more readily available drugs."

If we haven't been able to control heroin, a drug which must be imported from the Orient, what chance do we have of controlling amphetamines by this method when a good high school chemist can manufacture amphetamines in his basement after getting the methodology at the library?

Your logical answer to this would be that government agencies could follow up shipments of potential precursor materials and control illicit production in this way. If production started at the phenylacetone or ephedrine state, it is possible, but not probable, that they could do this.

However, since these precursors can be made handily from a number of common sources, such as molasses or benzene, illicit production could never be effectively controlled in this manner. In fact, irreparable damage could be done to some of the young kids who might use impure preparations of amphetamines which contained contaminants of some of the chemicals used in their illegitimate production.

I am enclosing copies of a number of readily available sources on the preparation of amphetamines together with a chemical "road map" showing several methods of making the amphetamines which was derived from this source information. In particular, I wish to point out the reprint from the Journal of the Forensic Science Society, "Preparation of Evidence in Illicit Amphetamine Manufacturing Prosecutions," which nicely laws out eight methods of making the amphetamines. Actually, discussion of where library information on amphe-

tamine production may be obtained may be academic, since this article also points out" that the cookbook-like procedures have been passed from hand to hand, thereby providing many persons with an ability to manufacture these drugs without actually possessing a detailed knowledge of chemical principles."

In conclusion, we feel that placing non-liquid amphetamines in Schedule 2 would have little effect on illicit use of the drugs, but would actually limit their legitimate use 1) by requiring useless paper work by the physician when they are used, and 2) by creating an apprehension on the part of the physician that, what he and the medical community consider legitimate use, might be construed by the Attorney General as abuse.

Let me suggest a course of action which, rather than incurring the ire of thousands of physicians and hundreds of thousands of patients, would win for you, from these physicians and their patients, eternal gratitude—that is, a Federally sponsored "crash program" to develop a medicinal agent for the treatment of this insidious killer, obesity, which would make the amphetamines obsolete.

Sincerely,

W. D. Asher, M.D.,
Executive Dirccter.

November 24, 1970.

Dr. W. A. Asher,
Executive Director, American Society of Bariatrics,
Englewood, Colo.

Dear Dr. Asher: Thank you for your letter concerning my proposal to tighten restrictions on the manufacture and distribution of amphetamines and amphetamine-like substances. I am most interested in the views of the American Society of Bariatrics on this issue, and I welcome this opportunity to respond to your comments.

Let me say, first of all, that I am pleased that the American Society of Bariatrics opposes the "unsupervised and illicit use of drugs—particularly the amphetamines." Testimony in the House of Representatives indicated that over 99% of the prescriptions written for amphetamines in this country are for weight control or mood elevation. Clearly, we cannot hope to curb the abuse of amphetamines without the help of those treating patients for weight control.

Although we apparently agree that amphetamine abuse is a problem, you express doubt as to whether my amendment would "solve the problem." I can only say that I believe changing the scheduling of these substances would make very significant inroads into amphetamine abuse in this country.

Present controls over the manufacture and distribution of these drugs are appallingly lax. For the past five years, *half* of the amphetamines *legally* produced in this country have been diverted into *illegal* channels. This massive diversion of amphetamines is directly related to the fact that drug manufacturers are producing them in quantities far in excess of the legitimate medical needs. It is clear to me that the first priority in bringing amphetamine abuse under control must be the curtailing of this vast overproduction.

You question the value of my amendment because "illicit production could never be effectively controlled in this manner." Certainly it is true that curbing production of the licit drug manufacturers will not solve the problem of clandestine laboratories and manufacturing. But surely we cannot sanction diversion of legally produced drugs as a means of discouraging legal production. We have to meet this problem on both fronts—diversion of legally produced drugs *and* illegal production. I have never claimed that my amendment is a panacea, but I firmly believe it is a significant step.

I want to stress that my amendment is not intended to "dry up the supply" of amphetamines. The Attorney General is directed under the law to set manufacturing quotas sufficient "to provide for the estimated medical, scientific, research, and industrial needs of the United States, for lawful export requirements, and for the establishment and maintenance of reserve stocks." It is the production of dosage units above and beyond these legitimate needs that my amendment seeks to eliminate.

Your suggestion that alternatives to treatment with amphetamines be developed has considerable appeal, and I would hope that research in this area

will be fruitful. My immediate concern, however, is bringing under control the very serious, widespread abuse of these admittedly dangerous drugs.

Best wishes.

Yours very truly,

THOMAS F. EAGLETON,
U.S. Senator.

AMERICAN SOCIETY OF BARIATRICS.
Englewood, Colo., December 1, 1970.

HON. THOMAS F. EAGLETON,
U.S. Senator, Committee on Labor and Public Welfare,
Washington, D.C.

DEAR SENATOR EAGLETON: Thank you for your reply of November 24th.

Although our ideas on how to deal with the drug abuse problem differ, I appreciate your interest in the problem.

Sincerely,

W. L. ASHER, M.D.,
Executive Director.

AMERICAN SOCIETY OF BARIATRICS,
Englewood, Colo., February 26, 1971.

HON. THOMAS F. EAGLETON,
U.S. Senate,
Washington, D.C.

DEAR SIR: We believe the lawmaking prerogatives of Congress are being usurped by various Government agencies, specially BNDD. On February 16, 1971, Mike Sonnenreich, Deputy Chief Counsel of the BNDD, told me that he will shortly move oral methamphetamine to Schedule II and probably dextroamphetamines, Preludin and Ritalin. The A.M.A. position is that physicians should not be subject to the requirements under Schedule II (registration, prescriptions, order forms, and penalties).

Dr. Grant Gwinup, Director, Metabolic Research Laboratory, University of Californit, Irvine, states that if all deaths from cancer were eliminated, man's life span would increase 2 years, but if all deaths related to obesity were removed, the life span would jump 7 years. We conservatively estimate 50,000 U.S. citizens die prematurely each year secondary to obesity. Former A.M.A. President Dwight L. Wilbur, B.D., labeled obesity "the most serious epidemic in our society." In a recent survey we conducted among physicians with a special interest in obesity, 96% felt the amphetamines were of value and 95% saw no, or little, evidence of drug dependence. Placing amphetamines in Schedule II would interfere with the doctor-patient relationship thus discouraging the use of these most valuable medical agents.

The comprehensive 1970 drug abuse law, which requires registration of pharmacists and physicians ordering amphetamines, will effectively curb the flow into illegitimate channels. Mr. Sonnenreich told me he feels physicians are not doing their job properly and he "intends to practice some preventive medicine." We doubt BNDD is capable or, or should be practicing medicine. A few days ago, one of our members, a Board Obstetrician-Gynecologist and medical school teacher, was personally chastised by a clerk-type inspector from BNDD because he did not use the amphetamines "properly." With amphetamines in Schedule II chastisement could well become prosecution. Bureaucratic interference in the doctor-patient relationship is a most serious matter.

However, all this pales into insignificance when considered in the light of the more significant issue—who is to make the laws of our land?

With the exception of seldom used injectable methomphetamine the amphetamines were twice moved from Schedule II to Schedule III before passage of the 1970 drug abuse bill. Even though a mechanism is provided for schedule changes, it was apparently not the intent of Congress that scheduling be immediately changed and certainly not before the law is effective in May 1971. We want to be sure all of our Legislators are aware of this dangerous situation. We hope there is a remedy.

Sincerely,

W. L. ASHER, M.D.,
Executive Director.

MARCH 12, 1971.

Dr. W. A. ASHER,
Executive Director, American Society of Bariatrics,
Englewood, Colo.

DEAR DR. ASHER: Thank you for writing to let me know about your conversation with Mr. Sonnenreich of the Bureau of Narcotics and Dangerous Drugs.

Mr. Kern Smith had called this meeting to the attention of my staff and has expressed your view that Congressional action would be preferred to an administrative ruling on the scheduling of amphetamines.

Under the new drug law, the Justice Department has full authority to reschedule drugs through the rule-making process. Such an action would not, in my view, be a usurpation of Congressional authority. However, the rule-making approach is a time-consuming process. I therefore fully intend to pursue the tightening of controls over these drugs through legislative channels.

Best wishes.

Sincerely yours,

THOMAS F. EAGLETON,
U.S. Senator.

[From the Congressional Record—House, H513, February 1, 1972]

3. AMPHETAMINE POLITICS ON CAPITOL HILL

Mr. Pepper asked and was given permission to extend his remarks at this point in the Record and to include extraneous matter.)

Mr. PEPPER: Mr. Speaker, The January issue of Trans-Action magazine contains an article which records the early history of the Select Committee on Crime's efforts to establish reasonable quotas on the outrageous overproduction of amphetamines.

Early in the existence of the Crime Committee we discovered that the production was 6 to 8 billion capsules a year, enough to provide a month's supply for every man, woman, and child in the United States.

As a result of the Crime Committee's investigation, it was shown that many of these amphetamines were being illegally diverted and resold on the black market. The worst of these—methamphetamines or "speed"—was claiming the lives of many young people. In the last several years we have urged that a strict drug quota be imposed by the Bureau of Narcotics and Dangerous Drugs on the production of amphetamines. The proposed quota announced in December calls for 8,652 kilograms or 1.5 billion dosage units in 1972, down from 24,991 kilograms or 4.5 billion dosage units in 1969. This is still not good enough.

We recently read of the Justice Department's crackdown on Pennwalt Corporation, the Nation's largest exporter of amphetamines, when it was discovered that most of its capsules were showing up in large quantities in the U.S. black market. As a result, Director John Ingersoll of the Bureau of Narcotics and Dangerous Drugs announced that the 1972 quota would be further reduced to 4,680 kilograms—a 50-percent reduction from the 1971 production. Evidence before our committee has led us to the conclusion that amphetamine production should and must be further curtailed. While necessary in the treatment of narcolepsy and hyperkinetic behavior in children, the total medical need has been estimated to be no more than several hundred thousand dosage units.

More than 80 percent of all prescriptions written for amphetamines are for weight control. Witness after witness before the Crime Committee testified to their dubious value in short-term obesity control and their dangerous effects over extended periods. Indeed, when contrasted with their potential for abuse, amphetamines should not be prescribed at all in a bona fide weight reduction program.

While there have been some significant developments—including quotas—since the attached article was written for Trans-Action magazine, it is important to recall the activities in Congress that began the drive to limit the production of amphetamines.

The article by Mr. James M. Graham follows:

AMPHETAMINE POLITICS ON CAPITAL HILL

(By James M. Graham)

The American pharmaceutical industry annually manufactures enough amphetamines to provide a month's supply to every man, woman and child in the

country. Eight, perhaps ten, billion pills are lawfully produced, packaged, retailed and consumed each year. Precise figures are unavailable. We must be content with estimates because until 1970, no law required an exact accounting of total amphetamine production.

Amphetamines are the drug of the white American with money to spend. Street use, contrary to the popular myths, accounts for a small percentage of the total consumption. Most of the pills are eaten by housewives, businessmen, students, physicians, truck drivers and athletes. Those who inject large doses of "speed" intravenously are but a tiny fragment of the total. Aside from the needle and the dose, the "speed freak" is distinguishable because his use has been branded as illegal. A doctor's signature supplies the ordinary user with lawful pills.

All regular amphetamine users expose themselves to varying degrees of potential harm. Speed doesn't kill, but high sustained dosages can and do result in serious mental and physical injury, depending on how the drug is taken. The weight-conscious housewife, misled by the opinion-makers into believing that amphetamines can control weight, eventually may rely on the drug to alter her mood in order to face her monotonous tasks. Too frequently an amphetamine prescription amounts to a synthetic substitute for attention to emotional and institutional problems.

Despite their differences, all amphetamine users, whether on the street or in the kitchen, share one important thing in common—the initial source of supply. For both, it is largely the American pharmaceutical industry. That industry has skillfully managed to convert a chemical, with meager medical justication and considerable potential for harm, into multihundred-million-dollar profits in less than 40 years. High profits, reaped from such vulernable products, require extensive sustained political efforts for their continued existence. The lawmakers who have declared that possession of marijuana is a serious crime have simultaneously defended and protected the profits of the amphetamine pillmakers. The Comprehensive Drug Abuse Prevention and Control Act of 1970 in its final form constitutes a victory for that alliance over compelling, contrary evidence on the issue of amphetamines. The victory could not have been secured without the firm support of the Nixon Administration. The end result is a national policy which declares an all-out war on drugs which are *not* a source of corporate income. Meanwhile, under the protection of the law, billions of amphetamines are overproduced without medical justification.

HEARINGS IN THE SENATE

The Senate was the first house to hold hearings on the administration's bill to curb drug abuse, The Controlled Dangerous Substances Act (S–3246). Beginning on September 15, 1969 and consuming most of that month, the hearings before Senator Thomas Dodd's Subcommittee to Investigate Juvenile Delinquency of the Committee on the Judiciary would finally conclude on October 20, 1969.

The first witness was John Mitchell, attorney general of the United States, who recalled President Nixon's ten-point program to combat drug abuse announced on July 14, 1969. Although that program advocated tighter controls on imports and exports of dangerous drugs and promised new efforts to encourage foreign governments to crack down on production of illicit drugs, there was not a single reference to the control of domestic manufacture of dangerous drugs. The president's bill when it first reached the Senate placed the entire "amphetamine family" in Schedule III, where they were exempt from any quotas and had the benefit of lesser penalties and controls. Hoffman-LaRoche, Inc. had already been at work; their depressants, Librium and Valium, were completely exempt from any control whatsoever.

In his opening statement, Attorney General Mitchell set the tone of administrative policy related to amphetamines. Certainly, these drugs were "subject to increasing abuse"; however, they have widespread medical uses" and therefore are appropriately classed under the administration guidelines in Schedule III. Tight-mouthed John Ingersoll, director of the Bureau of Narcotics and Dangerous Drugs (BNDD), reaffirmed the policy, even though a Bureau study over the last year (which showed that 92 percent of the amphetamines and barbiturates in the illicit market were legitimately manufactured) led him to conclude that drug companies have "lax security and recordkeeping."

Senator Dodd was no novice at dealing with the pharmaceutical interests. In 1965 he had steered a drug abuse bill through the Senate with the drug industry fighting every step of the way. Early in the hearings he recalled that the industry "vigorously opposed the passage of (the 1965) act. I know very well because I lived with it, and they gave me fits and they gave all of us fits in trying to get it through."

The medical position on amphetamine use was first presented by the National Institute of Mental Health's Dr. Sidney Cohen, a widely recognized authority on drug use and abuse. He advised the subcommittee that 50 percent of the lawfully manufactured pep pills were diverted at some point to illicit channels. Some of the pills, though, were the result of unlawful manufacture as evidenced by the fact that 33 clandestine laboratories had been seized in the last 18 months.

* * * * * * *

The amphentamine wholesalers were not questioned in any detail about diversion. Brief statements by the National Wholesale Druggists Association and McKesson Robbins Drug Co. opposed separate inventories for dangerous drugs because they were currently comingled with other drugs. Finally, the massive volume of the drugs involved—primarily in Schedule III—was just too great for records to be filed with the attorney general.

DODGING THE DIVERSION ISSUE

The representative of the prescription drug developers was also not pressed on the question of illicit diversion. Instead, the Pharmaceutical Manufacturers' Association requested clarifications on the definitional sections, argued for formal administrative hearings on control decisions and on any action revoking or suspending registration, and endorsed a complete exemption for over-the-counter nonnarcotic drugs.

With some misgivings, Carter-Wallace Inc. endorsed the administration bill providing, of course, the Senate would accept the president's recommendation that meprobamate not be subjected to any control pending a decision of the Fourth Circuit as to whether the drug had a dangerously depressant effect on the central nervous system. On a similar special mission, Hoffman-LaRoche Inc. sent two of its vice-presidents to urge the committee to agree with the president's recommendation that their "minor tranquilizers" (Librium and Valium) remain uncontrolled. Senator Dodd was convinced that both required inclusion in one of the schedules. The Senator referred to a BNDD investigation which had shown that from January 1968 to February 1969, three drug stores were on the average over 30,000 dosage units short. In addition, five inspected New York City pharmacies had unexplained shortages ranging from 12 to 50 percent of their total stock in Librium and Valium. Not only were the drugs being diverted, but Bureau of Narcotics information revealed that Librium and Valium, alone or in combination with other drugs, were involved in 36 suicides and 750 attempted suicides.

The drug company representatives persisted in dodging or contradicting Dodd's inquiries. Angry and impatient, Senator Dodd squarely asked the vice-presidents, "Why do you worry about putting this drug under control?" The response was as evasive as the question was direct: There are hearings pending in HEW, and Congress should await the outcome when the two drugs might be placed in Schedule III. (The hearings had begun in 1966; no final administrative decision had been reached and Hoffman-LaRoche had yet to exercise its right to judicial review.)

In the middle of the hearings, BNDD Director Ingersol returned to the subcommittee to discuss issues raised chiefly by drug industry spokesmen. He provided the industry with several comforting administrative interpretations. The fact that he did not even mention amphetamines is indicative of the low level of controversy that the hearings had aroused on the issue. Ingersoll did frankly admit that his staff had met informally with industry representatives in the interim. Of course, this had been true from the very beginning.

The president of the American Pharmaceutical Association, the professional society for pharmacists, confirmed this fact: His staff participated in "several" Justice Department conferences when the bill was being drafted. (Subsequent testimony in the House would reveal that industry participation was extensive and widespread.) All the same, the inventory, registration and inspection (pri-

marily "no-knock") provisions were still "unreasonable, unnecessary and costly administrative burden(s)" which would result in an even greater "paper work explosion."

For the most part, however, the administration bill had industry support. It was acceptable for the simple reason that, to an unknown degree, the "administration bill" was a "drug company bill" and was doubtless the final product of considerable compromise. Illustrative of that give-and-take process is the comparative absence of industry opposition to the transfer of drug-classification decision and research for HEW to Justice. The industry had already swallowed this and other provisions in exchange for the many things the bill could have but did not cover. Moreover, the subsequent windy opposition of the pill-makers allowed the administration to boast of a bill the companies objected to.

When the bill was reported out of the Committee on the Judiciary, the amphetamine family, some 6,000 strong, remained in Schedule III. Senator Dodd apparently had done some strong convincing because Librium, Valium and meprobamate were now controlled in Schedule III. A commission on marijuana and a declining penalty structure (based on what schedule the drug is in and whether or not the offense concerned trafficking or possession) were added.

DEBATE IN THE SENATE—ROUND 1

The Senate began consideration of the bill on January 23, 1970. This time around, the amphetamine issue would inspire neither debate nor amendment. The energies of the Senate liberals were consumed instead by unsuccessful attempts to alter the declared law enforcement nature of the administration bill.

Senator Dodd's opening remarks, however, were squarely directed at the prescription pill industry. Dodd declared that the present federal laws had failed to control the illicit diversion of lawfully manufactured dangerous drugs. The senator also recognized the ways in which all Americans had become increasingly involved in drug use and that the people's fascination with pills was by no means an "accidental development": "Multihundred million dollar advertising budgets, frequently the most costly ingredient in the price of a bill have, pill by pill, led, coaxed and seduced post-World War II generations into the 'freaked-out' drug culture. . . . Detail men employed by drug companies propagandize harried and harassed doctors into pushing their special brand of palliative. Free samples in the doctor's office are as common nowadays as inflated fees." In the version adopted by the Senate, Valium, Librium and meprobamate joined the amphetamines in Schedule III.

HEARINGS IN THE HOUSE

On February 3, 1970, within a week of the Senate's passage of S. 13246, the House began its hearings. The testimony would continue for a month. Although the Senate would prove in the end to be less vulnerable to the drug lobby, the issue of amphetamines—their danger and medical justification—would be aired primarily in the hearings of the Subcommittee on Public Health of the Committee on Interstate and Foreign Commerce. The administration bill (HR 13743), introduced by the chairman of the parent committee, made no mention of Librium or Valium and classified amphetamines in Schedule III.

As in the Senate, the attorney general was scheduled to be the first witness, but instead John Ingersoll of the BNDD was the administration's representative. On the question of amphetamine diversion, Ingersoll gave the administration's response: "Registration is . . . the most effective and least cumbersome way" to prevent the unlawful traffic. This coupled with biennial inventories of all stocks of controlled dangerous drugs and the attorney general's authority to suspend, revoke or deny registration would go a long way in solving the problem. In addition, the administration was proposing stronger controls on imports and exports. For Schedules I and II, but not III or IV, a permit from the attorney general would be required for exportation. Quotas for Schedules I and II, but not for III or IV, would "maximize" government control. For Schedules III and IV, no approval is required, but a supplier must send an advance notice on triple invoice to the attorney general in order to export drugs such as amphetamines. A prescription could be filled only five times in a six-month period and thereafter a new prescription would be required, whereas

previously such prescriptions could be refilled as long as a pharmacist would honor them.

The deputy chief counsel for the BNDD, Michael R. Sonnenreich, was asked on what basis the attorney general would decide to control a particular drug. Sonnenreich replied that the bill provides one of two ways: Either the attorney general "finds *actual street abuse* or an interested party (such as HEW) feels that a drug should be controlled" (Speed-freaks out on the street are the trigger according to Sonnenreich; lawful abuse is not an apparent criterion.)

The registration fee schedule would be reasonable ($10.00—physician or pharmacist; $25.00—wholesalers; $50.00—manufacturers). However, the administration did not want a formal administrative hearing on questions of registration and classification, and a less formal rule-making procedure was provided for in the bill.

Returning to the matter of diversion, Sonnenreich disclosed that from July 1, 1968 to June 30, 1969 the BNDD had conducted full-scale compliance investigations of 908 "establishments." Of this total, 329 (or about 36 percent) required further action, which included surrender of order forms (162), admonition letters (31), seizures (36) and hearings (31). In addition to these full-scale investigations, the Bureau made 930 "visits." (It later came to light that when the BNDD had information that a large supply of drugs was unlawfully being sold, the Bureau's policy was to warn those involved and "90 percent of them do take care of this matter." Furthermore, 574 robberies involving dangerous drugs had been reported to the Bureau.

Eight billion amphetamine tablets are produced annually, according to Dr. Stanley Yolles, director of the National Institute of Mental Health, and although the worst abuse is by intravenous injection, an NIMH study found that 21 percent of all college students had taken amphetamines with the family medicine cabinet acting as the primary source—not surprising in light of the estimate that 1.1 billion prescriptions were issued in 1967 at a consumer cost of $3.9 billion. Of this total, 178 million prescriptions for amphetamines were filled at a retail cost of $962 million. No one knew the statistics better than the drug industry.

Representing the prescription-writers, the American Medical Association also recognized that amphetamines were among those drugs "used daily in practically every physician's armamentarium." This casual admission of massive lawful distribution was immediately followed by a flat denial that physicians were the source of "any significant diversion."

The next witness was Donald Fletcher, manager of distribution protection, Smith Kline & French Laboratories, one of the leading producers of amphetamines. Fletcher, who was formerly with the Texas state police, said his company favored "comprehensive controls" to fight diversion and stressed the company's "educational effort." Smith Kline & French favored federal registration and tighter controls over exports (by licensing the exporter, not the shipment). However, no change in present record-keeping requirements on distribution, production or inventory should be made, and full hearings on the decisions by the attorney general should be guaranteed.

The committee did not ask the leading producer of amphetamines a single question about illicit diversion. Upon conclusion of the testimony, Subcommittee Chairman John Jarman of Oklahoma commented, "Certainly, Smith Kline & French is to be commended for the constructive and vigorous and hard-hitting role that you have played in the fight against drug abuse."

Dr. William Apple, executive director of the American Pharmaceutical Association (APhA), was the subject of lengthy questioning and his responses were largely typical. Like the entire industry, the APhA was engaged in a massive public education program. Apple opposed the inventory provisions, warning that the cost would be ultimately passed to the consumer. He was worried about the attorney general's power to revoke registrations ("without advance notice") because it could result in cutting off necessary drugs to patients.

Apple admitted organizational involvement "in the draft stage of the bill" but all the same, the APhA had a very good and constructive working relationship" with HEW. Apple argued that if the functions are transferred to Justice, "We have a whole new ball game in terms of people. While some of the experienced people were transferred from HEW to Justice, there are many new people, and they are law-enforcement oriented. We are health-care oriented." Surely the entire industry shared this sentiment, but few opposed the transfer as strongly as did the APhA.

Apple reasoned that since the pharmacists were not the source of diversion, why should they be "penalized by costly overburdensome administrative requirements." The source of the drugs, Apple said, were either clandestine laboratories or burglaries. The 1965 Act, which required only those "records maintained in the ordinary course of business" be kept, was sufficient. Anyway, diversion at pharmacy level was the responsibility of the pharmacists—a respinsibility which the APhA takes "seriously and (is) going to do a better job (with) in the future."

Congress should instead ban the 60 mailorder houses which are not presently included in the bill. (One subcommittee member said this was a "loophole big enough to drive a truck through.") The corner druggist simply was not involved in "large-scale diversionary efforts."

The Pharmaceutical Manufacturers' Association (PMA) was questioned a bit more carefully in the House than in the Senate. PMA talked at length about its "long and honorable history" in fighting drug abuse. Its representative echoed the concern of the membership over the lack of formal hearings and requested that a representative of the manufacturing interests be appointed to the Scientific Advisory Committee. Significantly, the PMA declined to take a position on the issue of transfer from HEW to Justice. The PMA endorsed the administration bill. PMA Vice-President Brennan was asked whether the federal government should initiate a campaign, similar to the one against cigarettes, "to warn people that perhaps they should be careful not to use drugs excessively." Brennan's response to this cautious suggestion is worth quoting in full:

"I think this is probably not warranted because it would have the additional effect of giving concern to people over very useful commodities. . . . There is a very useful side to any medicant and to give people pause as to whether or not they should take that medication, particularly those we are talking about which are only given by prescription, I think the negative effect would outweigh any sociological benefit on keeping people from using drugs."

LIMITED MEDICAL USE

There was universal agreement that amphetamines are medically justified for the treatment of two very rare diseases, hyperkinesis and narcolepsy. Dr. John D. Griffith of the Vanderbilt University School of Medicine testified that amphetamine production should be limited to the needs created by those conditions: "A few thousand tablets (of amphetamines) would supply the whole medical needs of the country. In fact, it would be possible for the government to make and distribute the tablets at very little cost. This way there would be no outside commercial interests involved." Like a previous suggestion that Congress impose a one cent per tablet tax on drugs subject to abuse, no action was taken on the proposal.

The very next day, Dr. John Jennings, acting director of the Food and Drug Administration (FDA) testified that amphetamines had a "limited medical use" and their usefulness in control of obesity was of "doubtful value." Dr. Dorothy Dobbs, director of the Market Drug Division of the FDA further stated that there was now no warning on the prescriptions to patients, but that the FDA was proposing that amphetamines be labeled indicating among other things that a user subjects himself to "extreme psychological dependence" and the possibility of "extreme personality changes . . . (and) the most severe manifestation of amphetamine intoxication is a psychosis." Dr. Dobbs thought that psychological dependence even under a physician's prescription was "quite possible."

Congressman Claude Pepper of Florida, who from this point on would be the recognized leader of the antiamphetamine forces, testified concerning a series of hearings which his Select Committee on Crime had held in the fall of 1969 on the question of stimulant use.

Pepper's committee had surveyed medical deans and health organizations on the medical use of amphetamines. Of 53 responses, only one suggested that the drug was useful "for *early* stages of a diet program." (Dr. Sidney Cohen of NIMH estimated that 99 percent of the total legal prescriptions for amphetamines were ostensibly for dietary control.) Pepper's investigation also confirmed a high degree of laxness by the drug companies. A special agent for the BNDD testified that by impersonating a physician, he was able to get large

quantities of amphetamines from two mail-order houses in New York. One company, upon receiving an order for 25,000 units asked for further verification of medical practice. Two days after the agent declined to reply, the units arrived. Before Pepper's committee, Dr. Cohen of NIMH testified that amphetamines were a factor in trucking accidents due to their hallucinatory effects.

Dr. John D. Griffin from Vanderbilt Medical School, in his carefully documented statement on the toxicity of amphetamines, concluded "amphetamine addiction is more widespread, more incapacitating, more dangerous and socially disrupting than narcotic addiction." Considering that 8 percent of all prescriptions are for amphetamines and that the drug companies make only one-tenth of one cent a tablet, Dr. Griffith was not surprised that there was so little scrutiny by manufacturers. Only a large output would produce a large profit.

Treatment for stimulant abuse was no easier than for heroin addiction and was limited to mild tranquilization, total abstinence and psychiatric therapy. But, heroin has not been the subject of years of positive public "education" programs nor has it been widely prescribed by physicians or lawfully produced. A health specialist from the University of Utah pointed out that the industry's propaganda had made amphetamines: "One of the major ironies of the whole field of drug abuse. We continue to insist that they are good drugs when used under medical supervision, but their greatest use turns out to be frivolous, illegal and highly destructive to the user. People who are working in the field of drug abuse are finding it most difficult to control the problem, partly because they have the reputation of being legal and good drugs."

The thrust of Pepper's presentation was not obvious from the questioning that followed, because the subcommittee discussions skirted the issue. Pepper's impact could be felt in the subsequent testimony of the executive director of the National Association of Boards of Pharmacy. The NABP objected to the use of the word "dangerous" in the bill's title because it "does little to enhance the legal acts of the physician and pharmacist in diagnosing and dispensing this type of medication." (The Controlled Dangerous Substances Act would later become the Comprehensive Drug Abuse Prevention and Control Act of 1970.)

As in the Senate hearings, Ingersoll of the BNDD returned for a second appearance and this time, he was the last witness. Ingersoll stated that he wished "to place . . . in their proper perspective" some "of the apparent controversies" which arose in the course of testimony. A substantial controversy had arisen over amphetamines, but there was not a single word on that subject in Ingersoll's prepared statement. Later, he did admit that there was an "overproduction" of amphetamines and estimated than 75 percent to 90 percent of the amphetamines found in illicit traffic came from the American drug companies.

Several drug companies chose to append written statements rather than testifying.

Abbott Laboratories stated that it "basically" supported the administration bills and argued that because fat people had higher mortality rates than others, amphetamines were important to the public welfare, ignoring the charge that amphetamines were not useful in controlling weight. Abbott then argued that because their products were in a little sustained-release tablet, they were "of little interest to abusers," suggesting that "meth" tablets per se cannot be abused and ignoring the fact that they can be easily diluted.

Eli Lilly & Co. also endorsed "many of the concepts" in the president's proposals. They as well had "participated in a number of conferences sponsored by the (BNDD) and . . . joined in both formal and informal discussions with the Bureau personnel regarding" the bill. Hoffman-Laoche had surely watched, with alarm, the Senate's inclusion of Librium and Valium in Schedule III. They were now willing to accept all the controls applying to Schedule III drugs, including the requirements of record-keeping, inventory, prescription limits and registration as long as their "minor tranquilizers" were not grouped with amphetamines. Perhaps, the company suggested, a separate schedule between III and IV was the answer. The crucial point was that they did not want the negative association with speed and they quoted a physician to clarify this: "If in the minds of my patients a drug which I prescribe for them has been listed or branded by the government in the same category as 'goofballs' and 'pep pills' it would interfere with my ability to prescribe . . . and could create a mental obstacle to their . . . taking the drug at all."

When the bill was reported out of committee to the House, the amphetamine family was in Schedule III, and Hodman-LaRoche's "minor tranquilizers" remained free from control.

DEBATE IN THE HOUSE—ROUND I

On September 23, 1970, the House moved into Committee of the Whole for opening speeches on the administration bill now known as HR 18583. The following day, the anti-amphetamine forces led by Congressman Pepper carried their arguments onto the floor of the House by way of an amendment transferring the amphetamine family from Schedule III into Schedule II. If successful, amphetamines would be subject to stricter import and export controls, higher penalties for illegal sale and possession and the possibility that the attorney general could impose quotas on production and distribution. (In Schedule III, amphetamines were exempt from quotas entirely.) Also, if placed in Schedule II, the prescriptions could be filled only once. Pepper was convinced from previous experience that until quotas were established by law the drug industry would not voluntarily restrict production.

Now the lines were clearly drawn. The House hearings had provided considerable testimony to the effect that massive amphetamine production coupled with illegal diversion posed a major threat to the public health. No congressman would argue that this was not the case. The House would instead divide between those who faithfully served the administration and the drug industry and those who argued that Congress must act or no action could be expected. The industry representatives dodged the merits of the opposition's arguments, contending that a floor amendment was inappropriate for such "far reaching" decisions.

"Legislating on the floor . . . concerning very technical and scientific matters," said subcommittee member Tim Lee Carter of Kentucky, "can cause a great deal of trouble. It can open a Pandora's Box" and the amendment which affected 6,100 drugs "would be disastrous to many companies throughout the land."

Paul G. Rogers of Florida (another subcommittee member) stated that the bill's provisions were based on expert scientific and law enforcement advice, and that the "whole process of manufacture and distribution had been tightened up." Robert McClory of Illinois, though not a member of the subcommittee, revealed the source of his opposition to the amendment:

"Frankly . . . there are large pharmaceutical manufacturing interests centered in my congressional district. . . . I am proud to say that the well-known firms of Abbott Laboratories and Baxter Laboratories have large plants in my (district). It is my expectation that C. D. Searl & Co. may soon establish a large part of its organization (there). Last Saturday, the American Hospital Supply Co. dedicated its new building complex in Lake County . . . where its principle research and related operations will be conducted."

Control of drug abuse, continued McClory, should not be accomplished at the cost of imposing "undue burdens or (by taking) punitive or economically unfair steps adversely affecting the highly successful and extremely valuable pharmaceutical industries which contribute so much to the health and welfare of mankind."

Not everyone was as honest as McClory. A parent committee member, William L. Springer of Illinois, thought the dispute was basically between Pepper's special committee on crime and the subcommittee on health and medicine chaired by John Jarman of Oklahoma. Thus phrased, the later was simply more credible than the former. "There is no problem here of economics having to do with any drug industry."

But economics had everything to do with the issue according to Representativ Jerome R. Waldie of California: "(T)he only opposition to this amendment that has come across my desk has come from the manufacturers of amphetamines." He reasoned that since the House was always ready to combat crime in the streets, "crime that involved a corporation and its profits" logically merits equal attention. Waldie concluded that the administration's decision "to favor the profits (or the industry) over the children is a cruel decision, the consequences of which will be suffered by thousands of young people." Pepper and his supporters had compiled and introduced considerable evidence on scientific and medical opinions on the use and abuse of amphetamines. It was

now fully apparent that the evidence would be ignored because of purely economic and political considerations. In the closing minutes of debate, Congressman Robert Giaimo of Connecticut, who sat on neither committee, recognized the real issue: "Why should we allow the legitimate drug manufacturers to indirectly supply the (sic) organized crime and pushers by producing more drugs than are necessary? When profits are made while people suffer, what difference does it make where the profits go?"

Pepper's amendment was then defeated by a voice vote. The bill passed by a vote of 341 to 6. The amphetamine industry had won in the House. In two days of debate, Librium and Calium went unmentioned and remained uncontrolled.

DEBATE IN THE SENATE—ROUND II

Two weeks after the House passed H.R. 18583, the Senate began consideration of the House bill. (The Senate bill, passed eight months before, continued to languish in a House committee.) On October 7, 1970, Senator Thomas Eagleton of Missouri moved to amend H.R. 18583 to place amphetamines in Schedule II. Although he reiterated the arguments used by Pepper in the House, Eagleton stated that his interest in the amendment was not solely motivated by the abuse by speak freaks. If the amendment carried, it would "also cut back on abuse by the weight-conscious housewife, the weary long-haul truck driver and the young student trying to study all night for his exams."

The industry strategy from the beginning was to center congressional outrage on the small minority of persons who injected large doses of diluted amphetamines into their veins. By encouraging this emphasis, the drug companies had to face questioning about illicit diversion to the "speed community," but they were able to successfully avoid any rigorous scrutiny of the much larger problem of lawful abuse. The effort had its success. Senator Thomas J. McIntyre of New Hampshire, while noting the general abuse of the drugs stated that the real abuse resulted from large doses either being swallowed, snorted or injected.

Senator Roman Hruska of Nebraska was not surprisingly the administration and industry spokesman. He echoed the arguments that had been used successfully in the House: The amendment seeks to transfer between 4,000 and 6,000 products of the amphetamine family; "some of them are very dangerous" but the bill provides a mechanism for administrative reclassification; administration and "HEW experts" support the present classification and oppose the amendment; and, finally, the Senate should defer to the executive where a complete study is promised.

It would take three to five years to move a drug into Schedule II by administrative action, responded Eagleton. Meanwhile amphetamines would continue to be "sold with reckless abandon to the public detriment." Rather than placing the burden on the government, Eagleton argued that amphetamines should be classed in Schedule II and those who "are making money out of the misery of many individuals" should carry the burden to downgrade the classification.

Following Eagleton's statement, an unexpected endorsement came from the man who had steered two drug control bills through the Senate in five years. Senator Dodd stated that Eagleton had made "a good case for the amendment." Senator John Pastore was sufficiently astonished to ask Dodd pointedly whether he favored the amendment. Dodd unequivocably affirmed his support. Dodd's endorsement was clearly a turning point in the Senate debate. Hruska's plea that the Senate should defer to the "superior knowledge" of the attorney general, HEW and BNDD was met with Dodd's response that, if amphetamines were found not to be harmful, the attorney general could easily move them back into Schedule II. In Schedule II, Dodd continued, "only the big powerful manufacturers of these pills may find a reduction in their profits. The people will not be harmed." With that, the debate was over and the amendment carried by a vote of 40 in favor, 16 against and 44 not voting.

Dodd may have been roused by the House's failure without debate to subject Librium and Valium to controls which he had supported from the beginning. Prior to Eagleton's amendment, Dodd had moved these depressants in Schedule IV. In that dispute, Dodd knew that economics was the source of the opposition: "It is clearly evident . . . that (the industry) objections to the inclusion of Librium and Valium are not so much based on sound medical practice as they are on the slippery surface of unethical profits." Hoffman-LaRoche annually

reaped 40 million dollars in profits—"a tidy sum which (they have) done a great deal to protect." Senator Dodd went on to say that Hoffman-LaRoche reportedly paid a Washington law firm three times the annual budget of the Senate subcommittee staff to assure that their drugs would remain uncontrolled. "No wonder," exclaimed Dodd, "that the Senate first, and then the House, was overrun by Hoffman-LaRoche lobbyists," despite convincing evidence that they were connected with suicides and were diverted in large amounts into illicit channels.

By voice vote Hoffman-LaRoche's "minor tranquilizers" were brought within the control provisions of Schedule IV. Even Senator Hruska stated that he did not oppose this amendment, and that it was "very appropriate" that it be adopted so that a "discussion of it and decision upon it (be) made in the conference."

The fate of the minor tranquilizers and the amphetamine family would now be decided by the conferees of the two houses.

IN CONFERENCE

The conferees from the Senate were fairly equally divided on the issue of amphetamine classification. Of the eleven Senate managers, at least six were in favor of the transfer to Schedule II. The remaining five supported the administration position. Although Eagleton was not appointed, Dodd and Harold Hughes would represent his position. Hruska and Strom Thurmond, both of whom had spoken against the amendment, would act as administration spokesmen.

On October 8, 1970, before the House appointed its conferees, Pepper rose to remind his colleagues that the Senate had reclassified amphetamines. Although he stated that he favored an instruction to the conferees to support the amendment, he inexplicably declined so to move. Instead, Pepper asked the conferees "to view this matter as sympathetically as they think the facts and the evidence they have before them will permit." Congressman Rogers an outspoken opponent of the Pepper amendment, promised "sympathetic understanding" for the position of the minority.

Indeed, the minority would have to be content with that and little else. All seven House managers were members of the parent committee, and four were members of the originating subcommittee. Of the seven, only one would match support with "sympathetic understanding." The other six were not only against Schedule II classification, but they had led the opposition to it in floor debate: Jarman, Rogers, Carter, Staggers and Nelsen. Congressman Springer, who had declared in debate that economics had nothing to do with this issue, completed the House representation. Not a single member of Pepper's Select Committee on Crime was appointed as a conferee. On the question of reclassification, the pharmaceutical industry would be well represented.

Hoffman-LaRoche, as well, was undoubtedly comforted by the presence of the four House subcommittee conferees: The subcommittee had never made any attempt to include Valium and Librium in the bill. On that question, it is fair to say that the Senate managers were divided. The administration continued to support no controls for these depressants.

At dispute were six substantive Senate amendments to the House bill: Three concerned amphetamines, Librium and Valium; one required an annual report to Congress on advisory councils; the fifth lessened the penalty for persons who gratuitously distributed a small amount of marijuana; and the sixth, introduced by Senator Hughes, altered the thrust of the bill and placed greater emphasis on drug education, research, rehabilitation and training. To support these new programs, the Senate had appropriated $26 million more than the House.

The House, officially, opposed all of the Senate amendments.

From the final compromises, it is apparent that the Senate liberals expended much of their energy on behalf of the Hughes amendment. Although the Senate's proposed educational effort was largely gutted in favor of the original House version, an additional 25 million dollars was appropriated. The bill would also now require the inclusion in state public health plans of "comprehensive programs" to combat drug abuse and the scope of grants for addicts and drug-dependent persons was increased. The House then accepted the amendments on annual reports and the possession charge for gratuitous marijuana distributors.

The administration and industry representative gave but an inch on the amphetamine amendment: Only the liquid injectible methamphetamines, speed, would be transferred to Schedule II. All the pills would remain in Schedule III. In the end, amphetamine abuse was restricted to the mainlining speed freak. The conference report reiterated the notion that further administrative action on amphetamines by the attorney general would be initiated. Finally, Librium and Valium would not be included in the bill. The report noted that "final administrative action" (begun in 1966) was expected in a matter of weeks." Congress was contented to await the outcome of those proceedings.

ADOPTION OF THE CONFERENCE REPORT

Pepper and his supporters were on their feet when the agreement on amphetamines was reported to the House on October 14, 1970. Conferee Springer, faithful to the industry's tactical line, declared that the compromise is a good one because it "singles out the worst of these substances, which are the liquid, injectible methomphetamines and puts them in Schedule II." If amphetamine injection warranted such attention, why, asked Congressman Charles Wiggins, were the easily diluted amphetamine and methomphetamine pills left in Schedule III? Springer responded that there had been "much discussion," yes and "some argument" over that issue, but the conferees felt it was best to leave the rest of the amphetamine family to administrative action.

Few could have been fooled by the conference agreement. The managers claimed to have taken the most dangerous and abused member of the family and subjected it to more rigorous controls. In fact, as the minority pointed out, the compromise affected the least abused amphetamine: Lawfully manufactured "liquid meth" was solid strictly to hospitals, not in the streets, and there was no evidence of any illicit diversion. More importantly, from the perspective of the drug manufacturers, only five of the 6,000 member amphetamine family fell into this category. Indeed, liquid meth was but an insignificant part of the total methomphetamine, not to mention amphetamine, production. Pepper characterized the new provision as "virtually meaningless." It was an easy pill for the industry to swallow. The Senate accepted the report on the same day as the House.

Only Eagleton, the sponsor of the successful Senate reclassfiication amendment, would address the amphetamine issue. To him, the new amendment "accomplish(ed) next to nothing." The reason for the timid, limpid compromise was also obvious to Eagleton: "When the chips were down, the power of the drug companies was simply more compelling" than any appear to the public welfare.

A week before, when Dodd had successfully classified Librium and Valium in the bill, he had remarked (in reference to the House's reaction): "Hoffman-LaRoche, at least for the moment, have reason to celebrate a singular triumph, the triumph of money over conscience. It is a triumph . . . which I hope will be shortlived."

Richard Nixon appropriately chose the Bureau of Narcotics and Dangerous Drugs offices for the signing of the bill on November 2, 1970. Flanked by Mitchell and Ingersoll, the president had before him substantially the same measure that had been introduced 15 months earlier. Nixon declared that America faced a major crisis of drug abuse, reaching even into the junior high schools, which constituted a "major cause of street crime." To combat this alarming rise, the president now had 300 new agents. Also, the federal government's jurisdiction was expanded: "The jurisdiction of the attorney general will go far beyond, for example, heroin. It will cover the new types of drugs, the barbiturates and amphetamines that have become so common *and are even more dangerous because of their use*" (author emphasis).

The president recognized amphetamines were "even more dangerous" than hroin, although he carefully attached the qualifier that this was a result "of their use." The implication is clear: The president viewed only the large dosage user of amphetamines as an abuser. The fact that his full statement refers only to abuse by "young people" (and not physicians, truck drivers, housewives or businessmen) affirms the implication. The president's remarks contained no mention of the pharmaceutical industry, nor did they refer to any future review of amphetamine classification. After a final reference to the destruction that drug abuse was causing, the president signed the bill into law.

4. Highlights of Testimony at the Hearings on Amphetamines
(April 14 and 15, 1971—New York City)

(Numbers in parentheses designate the location of the particular testimony for convenience in finding it: that is, 3–350 means tape cassette #3, 350 feet from the beginning)

April 14, 1971

DR. MORTON B. GLENN, CHIEF OF NUTRITION CLINIC AT MORRISIANA HOSPITAL, ALSO CHIEF OF OBESITY AT KNICKERBOCKER HOSPITAL

The amphetamines and the amphetamine-like substances are primarily prescribed and dispensed as appetite suppressants. Acknowledging the importance of controlling overweight is not tantamount to acknowledging the importance of using drugs to take away one's appetite.

Every advertising section in medical journals is replete with ads delineating the enormous effectiveness of appetite suppressants. Every subject section of these same journals contain articles that conclude that long-term weight control is only achieved in 5 to 20 percent of most weight control programs.

If one accepts the fact that permanent weight control depends upon appropriate eating habits together with long-term appetite conrol, then might not appetite elimination by the drugs actually deter and delay the development of this control? It is somewhat like trying to teach the use of a tool, in this case the appetite, without the tool. Can one teach a child to write without a pencil anymore than one can teach an individual to control his appetite without his appetite? I think not.

In my personal experience, I consider appetite suppressants as deterrents to permanent weight control. I feel that they are truly rarely indicated in obesity let alone in minor weight problems. The problem of weight control is much too complicated and its solutions require sophisticated understanding of the many social, psychological and metabolic factors involved.

Side-effects are common and often quite severe. They vary from moderate nervousness to abnormal cardiac rhythms, fainting and even frank psychoses.

Tolerance to amphetamines may develop rapidly and frequently results in a tendency to increase the dosage for enhanced therapeutic effect.

More often the toxic effect is more apparent than is the therapeutic effect. The potential and frequent development of dependency, habituation and true addiction, particularly in unstable individuals even though this instability is at first not readily apparent. (1–59)

The latter point is most significant. How many physicians can truly recognize the potentially unstable individual on the first visit: the visit when amphetamines are most often prescribed or dispensed, especially if the patient is well mannered and articulate?

Amphetamines do have some values—they are useful in mild depressions, in the hyperkinetic behavior disorders in children as well as in a few even less common conditions such as narcolepsy.

In order to control and prevent the diversion of these medications into illicit channels, I would suggest the following three-pronged attack. First, an educational campaign describing the ineffectiveness of amphetamines in long-term weight control. Secondly, the prohibition of the dispensing of amphetamines by physicians and restricting its use except by prescription in small quantities to be filled at licensed pharmacies. A physician's time is better spent treating than dispensing. Dispensing should be the province of the pharmacist upon proper prescription.

Thirdly, acknowledge that the patient who travels from physician to physician collecting prescriptions by subterfuge also has a responsibility. He should be required to sign a statement on the prescription that he has not had a similar prescription filled within two weeks.

Dr. Glenn said that he specializes in weight control, that practically all of his patients have overweight problems, that he prescribes amphetamines for less than one-tenth of one percent of his patients. In retrospect he finds that they were unnecessary even in some of those cases. (1–117)

Many physicians who do weight control will purchase amphetamines in any shape, color, form that they choose so that they are not identifiable. They can

be tablets, capsules, big ones, small ones, varied colors, with no identification on the capsule.

Chairman Hardt asked Dr. Glenn about the American Bariatric Association, a group of doctors specializing in treatment of obesity. The Chairman also indicated that the Commission had received a number of communications from doctors who stated that amphetamines have an important role in weight control, that they had never known any adverse effects to result from prescription of amphetamines, and urging that no further regulatory controls be imposed.

Dr. Glenn said that there are 60 different amphetamines or amphetamine-like substances and that the average dose is a 5 milligram tablet taken 3 times a day. The medication might be given in a longer acting form as one 15 milligram tablet per day. In the case of a hyperkinetic child under careful medical supervision, he thought that 30 milligrams per day might sometimes be appropriate.

Chairman Hardt mentioned the report of the British Advisory Commission on Drug Dependence, and quoted their statement: "amphetamines and amphetamine-like compounds should only be prescribed for those conditions for which no reasonable alternative exists or as a part of the therapy in those patients already dependent on these drugs. These drugs should be avoided as far as possible in the treatment of obesity, but if in individual cases the doctor feels that they must be employed, they should be prescribed for a limited period only." Dr. Glenn indicated his complete agreement with that position. (1-245)

The British report went on to state that the use of amphetamines in the treatment of depression should be "generally avoided." Dr. Glenn indicated that he felt they might occasionally have some value in treatment of mild depression, as well as hyperkinesis and narcolepsy, but he did indicate his belief that other drugs have been developed in the last few years that might do the job just as well. He also thinks that these other drugs are now being used more than amphetamines for these purposes.

Dr. Glenn pointed out that there are important social and phychological aspects to each individual's food intake and that these cannot possibly be dealt with by a drug. (1-295)

The emphasis in weight control must be on diet control. In his office, he takes at least 45 minutes and usually one hour with new patients to explain details of the prescribed diet. He contrasted this with the practice of some "fat doctors" who talk with the patient for a minute or two and then prescribe amphetamines. He suspects that there are thousands of doctors who do exactly this.

Dr. Glenn believes that obesity is our number one health problem. (1-322)

Dr. Glenn believes that among internists, the great majority feel as he does that amphetamines are almost completely useless in proper medical practice. He believes that the great majority of physicians associated with medical schools would also agree on this. (1-346)

In answer to Assemblyman Wager's question, Dr. Glenn said that he would guess that about half of all amphetamines which doctors direct their patients to take are actually dispensed by those doctors (as opposed to the writing of a prescription which is filled at a pharmacy). He recognizes that prescription as opposed to dispensing increase the cost to the patient, but he thinks that this increased cost is insignificant in relation to the advantages in minimizing drug abuse that would accrue from the elimination of direct dispensing by physicians. (1-426) He thinks we should recognize that controlling drug abuse will cost money. Almost every amphetamine addict got started by a dispensing physician.

If people are going to misuse things there will be a cost to it—"I would rather that there be a cost in money than a cost in lives."

Asked by Dr. Freedman whether the complete banning of amphetamines would have any material effect upon medical practice Dr. Glenn said no. (1-397)

Dr. Glenn considers amphetamines to be truly addictive, but his experience is that this addiction can be completely cured in a very short time—i.e., a week or ten days.

He feels that an educational campaign is necessary to inform both physicians and patients that amphetamines are basically completely ineffective in weight control. Physicians tend to shy away from diseases or problems to which they do not have effective solutions; weight control is such a problem. There are

no really effective solutions and this leads some physicians to simply prescribe the pills in order to save time and turn their attention to other areas of medicine in which they feel their efforts may be more successful. (1–590)

He does not believe there is any appropriate use whatever for injectable amphetamines. They have been used for treatment of barbiturate poisoning, but the common view is that such patients who respond to amphetamines would have also responded without any medication. (1–660)

He thinks that amphetamines are definitely addictive, in the sense that some people literally cannot get up in the morning without taking them or experiencing withdrawal symptoms. He has encountered a number of patients with histories of amphetamine addiction. (2–20)

There has been a serious problem in Sweden of abuse of Preludin, which is an amphetamine-like drug manufactured by Geigy.

In answer to a question from Chairman Betros, Dr. Glenn said that he was not aware of any decisive action taken by either the AMA or the New York County Medical Society to counteract excessive prescribing of amphetamines by physicians or to police the medical profession in this area. (2–180)

In treatment of hyperkinesis we usually use Ritalin in preference to amphetamines.

He favors total prohibition of the manufacture of amphetamines and pointed out that Burroughs-Welcome voluntarily discontinued making methamphetamine.

He believes that more people use amphetamines than use marihuana. (2–260)

He considers amphetamines extremely dangerous for everybody, but he does not think that there is any special additional danger in their use by young people.

He agreed with Assemblyman Wager that the use of amphetamines by "fat doctors" is "good business." He is concerned with a family pattern set when a parent takes amphetamines. Often the whole family begins using them.

DR. BARRETT SCOVILLE, DIVISION OF NEUROPHARMACOLOGY, FOOD AND DRUG ADMINISTRATION, WASHINGTON, D.C.

The Comprehensive Drug Abuse Prevention and Control Act of 1970 set up five schedules of dangerous drugs. Schedule I includes drugs with abuse potential and no medical use whatever such as heroin and marihuana. Schedule II includes drugs with some medical use but very high abuse potential such as morphine and liquid methamphetamine. Schedule III includes drugs with somewhat less abuse potential.

With the exception of liquid methamphetamine, all amphetamines have been placed in Schedule III. There has been strong and vocal support in Congress and elsewhere for a proposal to move amphetamines to Schedule II. This would have a number of effects, some of the principal ones being that quotas could then be imposed upon the amount of the drug manufactured and that prescriptions for Schedule II drugs may not be refilled.

Dr. Scoville said that the proposed move of the amphetamines to Schedule II was under intensive study by the FDA and the Secretary of HEW but that they had not yet reached their decision.

In August 1970 the FDA published in the Federal Register its conclusion that amphetamines were "possibly effective in appetite control" and invited manufacturers to submit evidence of such efficacy by August 1971. In the case of some oral amphetamines, the evidence had to be submitted by March 1971 and is now under review.

The FDA's intent in publishing this regulation was not to extend but to limit the use of amphetamines.

The indications for narcolepsy and the hyperkinetic syndrome or minimal brain dysfunction in children would require only minimum manufactured amounts of these drugs in contrast to their use in appetite control—a far more frequent prescription use and major cause of misuse. It may be judicious to wait until manufacturers have had time to submit any evidence for efficacy of these drugs in appetite control before making any decision regarding the rescheduling of amphetamines.

The basic questions in this decision are essentially these: do these drugs have a high potential for abuse; can these drugs lead to serious psychological or physical dependence?

The amphetamines are stimulant-type drugs with a tendency to cause tolerance to develop with continued use. England, Japan, Sweden and the United States have all experienced widespread street abuse of thse drugs following extensive prescription use.

The misuse of amphetamines, the improper unethical prescription by physicians, also accounts for large amount of dependence on amphetamines. This usually stems from the prescription of these drugs to reduce appetite in weight control programs.

There are more than 70 preparations containing amphetamine-type drugs available in the American market for prescription use. The principal drugs in use are Dextrometh-amphetamine, Desoxiaphedrine, and compounds with amphetamine-like activity, Phenmetrazine, Preludin, Dietanpopion, Tenuate and Phentermine.

These drugs have been noted for many years for their use as central nervous system stimulants to relieve depression and fatigue, or to reverse severe drug induced respiratory and/or cardiavascular depression.

On chronic administration of increasingly higher dosage the amphetamines will generally produce a paranoid psychosis. This may be related to the deprivation of sleep produced by long amphetamine intake, but there is considerable doubt about this and the real cause if not known. Dependence and chronic usage ultimately produce constant tension, irritability, sleeplessness, feelings of hostility and suspiciousness and often frank paranoid psychosis. There is usually a decrease in appetite, at times weight loss and a lessening of self care. Acute intake of large amounts produces the same behavioral effects at times with marked aggressiveness and even assaultiveness. Withdrawal from amphetamines after prolonged use produces feelings of depression, fatigue and often a craving for the stimulant effects of the drug. In essence these drugs produce both psychological and physical dependence.

In summary, all amphetamines, not simply injectable methamphetamine or speed, have a large potential for abuse, produce both psychological and physical dependence, are in fact being abused both in illicit street use and by loose prescription practices, are consumed in this country in far greater amounts than can possibly be accounted for by reasonable medical need and certainly can be controlled more effectively even if not completely.

Thus far voluntary medical control has not been effective. This may still be a solution but if so it would have to be forthcoming soon to avoid public control.

In answer to a question submitted to him in advance, Dr. Scoville said that Ritalin and Preludin will probably be treated differently from the amphetamines. Although he indicated that he believes these drugs are abused somewhat less than amphetamines, the principal reason for the different treatment seems to be administrative convenience. The FDA has not yet made a recommendation to the Attorney General regarding them.

In answer to a question, he indicated that the FDA would favor a requirement that every pill, capsule and tablet carry a mark identifying its manufacturer. A colloquy ensued on the question of whether this should be done at a federal or state level, with Dr. Scoville indicating, perhaps as a personal opinion, that it should be done federally. (2–555)

Dr. Scoville estimated that the number of children with minimal brain dysfunction is in the millions. (2–632)

Assemblyman Wager asked whether the FDA was contemplating any restrictive action to regulate the dispensing (as opposed to prescription) by physicians specializing in weight control of very large quantities of amphetamines. Dr. Scoville indicated a belief that the new labeling and evidence requirements announced in August 1970 would have some effect upon over prescription and that a more powerful restraint will be imposed if and when amphetamines are moved to Schedule II. He said that he personally does not believe the evidence is yet sufficient to suport completely banning amphetamines from the market.

Assemblyman Wager asked why, in view of the virtually unanimous agreement about the dangers of amphetamines, the FDA had not moved faster against them, and inquired whether pressure from the drug companies might not be a factor (3–99) Dr. Scoville indicated that pressure came from physicians and others as well as drug companies, and said that an abrupt withdrawal of amphetamines would be a sudden reversal of 40 years of American medical

practice and could not be done until the scientific evidence and support were overwhelming.

One of the difficulties in moving amphetamines to Schedule II is that an administrative agency cannot properly counteract the demonstrated intent of Congress, and Congress considered this question at some length—there was extensive testimony in committee hearings—and it then decided to put them into Schedule III. (3–197)

The government has no hard data on the number of amphetamines produced. He uses an estimate in the area of four to five billion per year but would not be able to say that a higher figure would be inaccurate—he simply doesn't know. (3–208) Twenty percent of the estimated doses manufactured are unaccounted for by prescription.

They have examined the triplicate prescription proposal and the others in our Second Interim Report and endorse them heartily. (3–232) Indeed, they favor anything that increases accountability of amphetamines.

The FDA believes that most amphetamines used illegally are diverted from legal channels, but this does not apply as to injectable methamphetamine, most of which they believe is produced illegally. (3–284)

The FDA believes that its new regulations, promulgated in August 1970, which effectively restrict use of amphetamines to three uses (weight control, narcolepsy, and hyperkinesis) and which require new labeling and new evidence of efficacy to be submitted, will have a significant deterrent effect upon physicians and after its full effect is felt they believe it will bring about a significant reduction in the prescribing of amphetamines.

Dr. Scoville said he would support the Commission's triplicate prescription suggestion. Mr. Polsky pointed out that the new federal regulations require that records be filed of prescriptions but not of drugs dispensed in a doctor's office.

Dr. Scoville agreed that that was true and that this was a loophole. "We need to tighten the regulations of Schedule II drugs rather than to reschedule amphetamines to correct this loophole."

It was also pointed out to Dr. Scoville that since oral amphetamines can be made injectable very easily it accomplished very little to move the injectable amphetamines into Schedule II while leaving the oral ones in Schedule III.

Chairman Hardt asked Dr. Scoville to convey to HEW the Commission's suggestion that every pill carry stamped on it numbers or marks identifying the manufacturer.

DR. ARNOLD J. FRIEDHOFF, PROFESSOR OF PSYCHIATRY AT NEW YORK UNIVERSITY SOHOOL OF MEDICINE, ALSO DIRECTOR OF CENTER FOR STUDY OF PSYCHOTIC DISORDERS AT BELLEVUE HOSPITAL

Dr. Friedhoff and his associates have had extensive experience with amphetamine psychosis.

Over-prescribing of amphetamines takes a number of forms, including prescribing for long-term when only short-term use is appropriate, prescribing higher doses than appropriate, prescribing escalating doses, and prescribing when there is no appropriate medical indication.

There has not been sufficient research to date to demonstrate whether amphetamines are beneficial only to hyperactive children with brain damage (this is the common belief) or also to other categories of hyperactive children.

When used for weight control, amphetamines should properly be prescribed only in level doses. If and after several weeks the appetite depressing effect is reduced (and this is the expectation) the physician should not respond by escalating the dosage—if he does, the patient may develop dependence and possibly psychosis. However, Dr. Friedhoff said that in his experience, very few of the patients who develop psychosis have done so as a result of escalating prescriptions.

He sees a small but appropriate medical use for amphetamines in control of bed-wetting and in treatment of patients who are taking heavy doses of transquilizers and as a result are extremely drowsy. (4–66)

Studies conducted by his associates show that as many as 50% of all college students may have used amphetamines at one time or another to help in staying awake to study.

Use for this purpose is usually sporadic and therefore does not tend generally to lead to dependence and toxicity. Very rarely toxicity can occur from

ingestion of even very small doses, and there are instances where this happened, however there are certain dangers involved in even sporadic use since amphetamines tend not only to increase alertness but also to produce jitteriness, irritability, and increased fatigue and tiredness when their effect wears off.

Professional drivers, for instance, could have serious consequences since drowsiness and fatigue can occur unexpectedly when the medication stops acting. Also, use of this medication for non-medical purposes tends to foster pill taking as a normal way of life with long range consequences of a potentially more serious nature.

Bellevue has something like 15,000 to 18,000 psychiatric admissions per year of which around 50 usually are cases of amphetamine psychosis. (4–91) These are usually hard core drug abusers who have used the drug in large quantities and have almost always progressed to intravenous use. They sometimes develop a psychosis which is very similar to paranoid schizophrenia. When amphetamines are used in large doses, the toxic consequences are serious and characterized by psychotic reactions, personality changes, perhaps brain damage in some cases, aggressive behavior and sometimes death. (4–113)

He believes that if additional controls are imposed upon amphetamines they should also be extended to include all amphetamine-type stimulants, since in his experience they are virtually interchangeable and the stimulant of preference at any given moment will be the one most readily available.

He favors production controls and believes they would effectively reduce diversion, but he thinks they will be useless unless they are extended to the precursors. If the precursors are not controlled; the clandestine and bathtub manufacture will increase enormously. Unfortunately, there is a very large number of precursors.

Physicians should be further alerted to the potentially dangerous nature of these compounds and the limited medical indications for their use. This education should be carried out through medical channels and through public statements by drug regulatory agencies.

Consumer resistance to unwarranted medical prescriptions of these compounds should be developed. One means which I would like to suggest would be to require labeling on all stimulants with a warning as to their dangerous nature on the package that goes to the medical consumer from the pharmacist.

He also recommends elimination of distorted drug advertising to physicians and he recommends the elimination of all prescription drug advertising to the lay public.

These control measures will have no significant effect upon the use of amphetamines by the hard core drug users—he estimates that up to 50% of this group have psychiatric disturbances before they begin drug use. (4–152)

He feels that amphetamines may be appropriately used for a short time in a small number of exertmely difficult obesity cases. He does not quite go all the way toward recommending banning amphetamines. Furthermore, he believes that all stimulants should be treated together and there definitely are appropriate medical indications for stimulants. (4–160)

He has known people to use as much as 500 milligrams per day, as compared to a normal and appropriate dose of 5 to 15 mg. per day.

In answer to Dr. Freedman's question, he said that he had not encountered any toxic effect in children resulting from amphetamines. (4–249)

In answer to Chairman Hardt's question, he said that severe psychiatric disturbances are rarely produced by barbituates or opiates. At one time, they saw large numbers of psychotic patients who had used LSD, but recently this has dropped sharply and they are now seeing far fewer LSD-induced psychosis than amphetamine-induced psychosis (4–295)

In connection with the serious problem of physicians irresponsibility overprescribing amphetamines, the following exchange took place between Assemblyman Wager and the witness (4–365) :

"How about the medical profession itself, doesn't it do anything to police that kind of practice at all?"

"Not really, I mean once you get a license to practice short of doing something totally unethical there's very little regulation of what you do."

Asked by Chairman Betros whether there is any specific dosage level that could be definitely described as dangerous, he answered that any escalation of dosage brought about because the lower dosage was no longer producing the

desired result was dangerous because such escalation indicated that tolerance had begun to develop. (4–428)

MR. STANLEY GELLER, ATTORNEY, CHAIRMAN OF MAYOR LINDSAY'S SPECIAL COMMITTEE ON AMPHETAMINES

Mr. Geller indicated that the committee had been appointed quite recently and had held its organizational meeting only two weeks ago. He indicated a desire to work with and remain in contact with our commission, and Chairmen Hardt and Betros responded that we would be happy to do this.

Mr. Geller also stated that the City of New York through his committee intended to intervene in the proceedings in Washington looking toward the possible transfer of amphetamines from Schedule III to Schedule II, and that they expected to take a position in favor of such transfer.

DR. HENRY BRILL, DIRECTOR OF PILGRIM STATE HOSPITAL, FORMER VICE CHAIRMAN, NEW YORK STATE NARCOTIC ADDICTION CONTROL COMMISSION

Dr. Brill traced the history of previous epidemics of amphetamine abuse in other countries, particularly the epidemic of abuse in Preludin in Sweden and that of methamphetamine in Japan. The Japanese epidemic took place right after the end of World War II. The drug had been imported to Japan by Germany for use by combat troops and after the war was dumped on the market.

Dr. Brill stated "we would not lose anything medically by limiting access to amphetamines to prescriptions given for the treatment of hyperkinesis and narcolepsy, but we would start a debate not likely to be settled soon."

Dr. Brill was asked whether it would be more acceptable to the medical profession as an alternative to prescribing the appropriate medical usage of amphetamines to limit production to the amount needed for the treatment of narcolepsy and hkperkinesis and a very small amount for the treatment of mild depressions. Dr. Brill responded yes, this is a good approach.

Dr. Brill was asked whether increasing restrictions on stimulants might lead to other problems. He replied that in order for such restrictions to be effective they would have to apply to all six classes of stimulants, amphetamine, dextroamphetamine, methamphetamine, Preludin, Ritalin and Meratrin. Even if this were done, some former amphetamine users would turn to cocaine which is even more dangerous. The more likely switch, however, would be from one medically available stimulant to another.

Dr. Brill explained that the resistance of the medical profession to any limitation being placed on their judgment in prescribing or dispensing amphetamines stemmed from the fact that the drug has been in wide use for a number of years and that therefore doctors are comfortable in using it and have come to rely upon it. This was not true of Thalidomide which had been on the market only a very short time.

Regarding the use of amphetamine in weight control programs, Dr. Brill stated that in his opinion amphetamines are not indicated for long-term use. They have some short-term value for some people; after a short time, however, tolerance develops to both their appetite control effect and their "high."

Even with controlled, medically supervised use, the normal effect of the drug on most people is extreme tension and nervousness, heart palpitation, and teeth grinding. With the generally healthy person these effects are uncomfortable rather than damaging. However contraindications for the use of amphetamines are cardiac disease and hypertension. Where these conditions exist use of amphetamines can do damage.

Damage which is possible from the abuse of amphetamines include the infections produced by dirty needles and unsterile dosages, high blood pressure, rupturing of the blood vessels, and cardiac attacks. Also a disease of the blood vessels called enditeritis has been described. The disease is unusual but it is possible that it would develop.

There is much controversy about whether amphetamine abuse produces brain damage. Dr. Brill considers that the damage is more to the mental state of the abuser including psychotic "drop outs."

April 15, 1971

DR. STANLEY H. TITLE, A PRACTICING NEW YORK PHYSICIAN SPECIALIZING IN TREATMENT OF OBESITY

In his six years of general practice, Dr. Title has become vividly aware of the enormous need for specialized practice in weight control so that obese patients can receive better counsel than the ordinary general practitioner is able to give them. He treats some patients by diet alone and others by diet combined with various medication. He finds amphetamines extremely important in his practice. (5–37) He feels that his views on amphetamines are shared by virtually all of the members of the American Bariatric Society, an association of doctors specalizing in weight control.

Dr. Title quoted Goodman and Gillman, the recognized authority on pharmaceuticals, to the effect that "amphetamines under carefully controlled conditions can produce a loss of body weight in obese persons." Dr. Title believes that it is appropriate to use amphetamines for periods ranging from "a few weeks up to a year or more" in order to reduce or eliminate the discomfort which accompanies a sharp reduction in food intake.

Dr. Title cited a recent survey made by the American Bariatric Society of "hundreds of doctors." Ninety-five percent of them expressed the view that amphetamines were of considerable value in weight control and stated that they had seen "little or no evidence" of resulting drug dependence. (It was not clear whether this survey extended beyond the membership of the Society.) (5–52)

Dr. Title expressed the view that there is no danger in taking amphetamines under proper medical supervision and there are "no major side effects" when used in the proper medical dosage. Since, when used properly, these drugs can safely be prescribed for children, there is no reason to consider them dangerous for adults in appropriate dosages under medical supervision.

Dr. Title points out that present regulations require every physician to keep careful records of purchases, inventory and prescription of amphetamines subject to government inspection. Also, he believes that the new federal law, requiring registration of all physicians and pharmacists, will effectively prevent the sale by mail order drug wholesalers of dangerous drugs to unauthorized persons. He therefore believes that no additional controls are needed. (5–71) Additional reporting requirements, if imposed upon the physician, will greatly increase his paper work and thus add substantially to what he must charge his patients.

Furthermore, the greatest abuse of amphetamines, in his opinion, is the intravenous use of liquid methamphetamine—and practically all of this comes from clandestine manufacturers; therefore, additional controls upon legitimate drug firms and practitioners would have no effect upon this abuse. He recommends that any additional legislative or regulatory steps be taken against illicit manufacturers and distributors.

In answer to a question from Chairman Betros, Dr. Title confirmed that amphetamines do not actually cause a loss of body weight; what they do is to depress appetite, enabling the patient to eat less and lose weight in that way. He reiterated that amphetamines alone cannot produce a permanent weight reduction; they are useful only when used as an adjunct to a complete program of counseling, planned scheduling of activity, encouragement of motivation and dietary control.

The amphetamine most commonly used by bariatricians is dextroamphetamine sulfate. (5–133)

Dr. Title generally dispenses the medication rather than prescribing it. The envelope or box he gives the patient carries no warning of the dangers of excessive use, nor does it carry any precise identification of the drug. He buys drugs directly from manufacturers.

Asked whether there is any difference of opinion in the medical profession on the value of amphetamines, Dr. Title did not answer directly but said that there was virtual unanimity in the Bariatric Society. (5–187) Chairman Hardt said that he understood most internists opposed the use of amphetamines, and the witness responded that internists probably see very few overweight patients while he and his co-practitioners spend all of their time with overweight patients. "A tailor should not express opinions about plumbing."

He volunteers some of his time in a City nutrition clinic—amphetamines are not used there because the necessary medical supervision is not present. The results obtained in the clinic without using amphetamines are far inferior to those obtained in his own practice where amphetamines are used.

He controls his patients carefully, usually prescribes amphetamines "on and off for two or three months," on rare occasions continues the medication for "a year or so" and has never encountered a single case in which a patient of his developed into an amphetamine abuser.

He said that while there are indications that "a slight tolerance" might develop with extended use, "there is no proof of any tolerance to the appetite depressing effect." (5–238) Asked by Chairman Hardt whether it was not true, as extensively reported in medical journals, that the appetite depressing effect largely disappears after a few weks, Dr. Title said that this could be attributed to the intense motivation of the patient at the beginning of the treatment and a weakening of motivation as the novelty wore off.

He would vigorously oppose banning the amphetamines, he considers them useful in his practice and "a very necessary supplement" to other weight control measures. (5–305)

Dr. Burton Angrist, representing Dr. Alfred Freedman, asked what typical dosages were used. Dr. Title answered that it might range from 2.5 or 5 milligrams three times a day before each meal to as much as 15 milligrams three times a day depending on which particular drug was used and that patient's particular need.

He sees his patients every two weeks and supervises them closely. He almost never encounters a case of a patient escalating the dosage by obtaining additional amphetamines elsewhere. He does not use and has never used injectable amphetamines in his practice. He does not consider them necessary and does not know any other physician who has used them. (5–352)

Asked how many amphetamine capsules he might dispense in a year, he said "it would be almost impossible to estimate." (5–397) Chairman Hardt said that we had heard of a doctor who ordered five hundred thousand amphetamine tablets or capsules in three months and asked Dr. Title whether he considered such a quantity excessive. Dr. Title would not say that the amount seemed too large—he pointed out that a physician must order in large quantities to get the particular colors and sizes he wanted at the best prices, and he suggested that this doctor might have been ordering several years' supply. (5–417 to 442)

He said that the average patient might use three or four capsules a day, "or twelve hundred to fifteen hundred a year." He considers obesity America's number one health problem. He thinks there may be as many as 20 million overweight people in this country. (5–485)

He said that in his practice, and also in the practice of most bariatricians, the patients are mostly between 35 and 50 years of age, "with a few on either side of that" and that 90% are women.

Asked why he dispenses amphetamines rather than writing prescriptions, he said in order to reduce the cost to the patient. He estimates that his patients pay him about $20 a month ($9 or $10 per visit for two visits) and that it would cost them about $35 per month if he wrote prescriptions.

If he were required to fill out a form each time he dispensed amphetamines, it would be "extremely time-consuming and troublesome" and he also considers it needless. (5–552)

MR. MICHAEL COSTELLO, DEPUTY DIRECTOR, NEW YORK REGIONAL OFFICE, U.S. BUREAU OF NARCOTICS AND DANGEROUS DRUGS

The BNDD is an arm of the Department of Justice. Its principal functions are (1) to attempt to control the importation and distribution throughout the country of illicit drugs such as heroin, LSD, and marihuana, and (2) to exercise surveillance over the manufacture and distribution of *legal* dangerous drugs in ordinary commercial and medical channels to attempt to prevent diversion from such legal channels into the illicit market.

Based on his experience and that of his associates, Mr. Costello believes that there is indeed substantial diversion of amphetamines into illegal channels. The principal sources of this diversion are:

(1) pilferage, often in small amounts each day, from legitimate pharmaceutical manufacturers by their employees and others;

(2) pilferage and petty thefts from wholesalers;

(3) hijacking, burglary and theft of large quantities from manufacturers and wholesalers;

(4) direct sale by wholesalers, pharmacies and physicians to persons not authorized to purchase the drugs;

(5) fictious exportation of large quantities to nonexistent persons or addresses in Mexico and elsewhere—these drugs are then smuggled back into the United States.

It is his opinion that something like 80% of the amphetamines which ultimately appear in illegal channels were originally produced legitimately and were then diverted at some stage. He bases this opinion upon "pillistic" analysis made by the Bureau's laboratory in Washington, which can ascertain the source of drugs seized by chemical analysis. (6–74)

It is his opinion that most clandestine manufacturers concentrate on hallucinogenics rather than amphetamines.

They have found, through undercover activities, that it is very easy for unauthorized persons to purchase drugs from wholesalers and physicians by mail. In answer to Chairman Hardt's question, he said he was not aware of this kind of diversion (i.e., purchase by unauthorized persons) at the manufacturer level, but there is diversion at that level through thefts and in other ways.

Chairman Hardt asked whether a manufacturer's trademark on every pill and capsule would assist in law enforcement. He replied that it would be of very great assistance. (6–116) At the present time the Bureau does not receive sufficient reports with respect to amphetamines to *readily* determine where the diversion is taking place. (They do receive good reports on narcotics.) Only by time-consuming examination of records can they detect suspicious shipments. In answer to a question, he said that he feels our triplicate prescription proposals and our proposal for manufacturer and wholesaler reporting would be "excellent investigative tools" (6–181). However, he considers it essential that they be extended to physicians as well, because he believes they constitute an important source of diversion. However, this would undoubtedly incur vigorous opposition from the AMA on the grounds, among others, that this provision would tend to violate the confidential doctor-patient relationship.

The Bureau has found evidence of doctors ordering quantities that seem far out of line—such as a million dosage units of amphetamines within a few months. (6–215)

Mailing of large quantities of samples by manufacturers is less of a problem in dangerous drugs than it used to be. He understands that in some product groups as much as 10% of total production goes to samples. The Bureau has for many years discouraged the mailing of samples of narcotics and this is now virtually eliminated. As to depressants and stimulants, most manufacturers have cut down sharply on sampling, but there is still too much of it.

Where the Bureau obtains information showing that there has been a sizable unexplained quantity of amphetamines shipped or sold by a manufacturer, wholesaler, retailer or physician, it has the power to confiscate the drugs, and if necessary the manufacturing equipment, as an "executive seizure." This may be done entirely on the basis of inadequate record keeping and may or may not be followed or accompanied by an indictment. Since July 1 of last year the Bureau has confiscated 22 million dosage units of stimulants and 13 million units of depressants. Some of these were from wholesalers or pharmacists but *most of these seizures were from medical practitioners.* (6–319) The Bureau does not take drastic action if a man's records are incomplete by 5% or even 10%. The objective is to catch the most flagrant violators and bring them into compliance.

The New York State agencies involved in this regulatory area are the Board of Medical Examiners, Board of Dental Examiners, Board of Pharmacy, State Police, and the State Health Department's Bureau of Narcotic Control. This latter bureau registers and licenses manufacturers, wholesalers and nursing homes. It has 25 investigators, but he understands that the Bureau has been ordered not to engage in investigatory work of violations that might border on criminal activity.

On frequent occasions, the Federal Bureau has furnished leads to the Health Department's Bureau of improper practices by pharmacists and physicians. Usually, nothing was done. Mr. Costello said, "if a state agency had adequate manpower and adequate tools for investigation and enforcement in this area

it would be a real boon to law enforcement in New York." (6–415) He does not feel that this type of investigative work can be done effectively by police. It requires someone trained in the examination and auditing of books and records of professionals.

If there were a state agency to whom the Federal Bureau could pass on its leads in this area, that agency could keep 70 or 80 investigators busy and the Federal Bureau could concentrate on this larger interstate trafficking cases.

California has an excellent Bureau of Narcotics with 150 investigators having peace officer status; this agency works closely with the BNDD. Similar agencies are the Florida Bureau of Investigation and units in the Illinois Department of Public Safety and the Pennsylvania Department of Health.

The State of New York has 425 firms that manufacture or wholesale drugs, 5,624 retail pharmacies and more than 45,000 practicing physicians. (7–58) In terms of drug manufacture and distribution there is far more activity in BNDD's Region II (New York State and northern New Jersey) than in any of its eleven other offices.

JOHN J. FENSTERNMAKER, VICE PRESIDENT OF DRUG MARKETING, L. W. WILLSON, VICE PRESIDENT FOR WHOLESALE DRUG OPERATIONS, MC KESSON AND ROBBINS DRUG COMPANY, A DIVISION OF FOREMOST-MC KESSON, INC.

The company is primarily in the business of distributing pharmaceuticals, proprietary drugs, cosmetics and sundries. Its customers include some 28,000 pharmacies and 5,700 hospitals. It is the only nationwide wholesaler of drug products.

The company does not ship directly to doctors as a matter of policy, except in the State of Hawaii and in isolated areas where no pharmacy is located. It has a policy against selling to other wholesalers. Substantially all of its distribution is by its own delivery men or common carrier trucks; it has no mail order business. (However, a mail order operation is about to be started in Chicago for competitive reasons.)

Amphetamines have been a "sizable part" of our business, and this business has been growing in recent years. However, they anticipate that the FDA labeling and new drug application requirements will cause a number of amphetamine products to be dropped from the market.

They described in detail the security measures taken by their company, including the following: (1) careful screening of all employees; (2) 24 hour of electrical burglar alarm systems at all warehouses; (3) narcotics stored in vaults approved by BNDD; (4) unannounced door checks and searches of employees leaving the premises at least once a week, with purses and pockets emptied; (5) periodic inspection of employee lockers; (6) all employees involved in order filling directed to report any unusual large quantities to supervisors.

The company knows its customers through investigation and salesmen calling on them. It does business regularly with its established customers. If an order is received from a new customer, a careful investigation is made before it is filled.

The mail order wholesalers came into being shortly after World War II in the New York area and then spread to other parts of the country. A number of the large ones are in New York State. The mail order firms quote lower prices and give less service. In answer to a question, Mr. Fenstermaker said that he believes a mail order wholesaler can be just as conscientious as an old-line firm such as McKesson.

They said that our proposal for reporting by manufacturers and wholesalers of every order shipped would be "a substantial burden"—this burden would apparently consist of Xeroxing, collecting the orders and mailing them in once a month. (6–470) They indicated that it would be a tremendous burden upon them if amphetamines were transferred to Schedule II.

In answer to a question, they said that they frequently catch pilfering employees in their door searches and that they usually prosecute.

MR. HARRY O'BRIEN, ASSISTANT DISTRICT ATTORNEY, SUFFOLK COUNTY

He believes that amphetamines and barbiturates are the most abused drugs in Suffolk County high schools. Dexedrines are sold in the street for 3 for $1.00. (8–142)

He is aware of a number of seizures of amphetamines intended to be sold in the streets which originally came from doctors specializing in weight control. He also cited a case in which a young Suffolk County man set himself up as ostensibly a pharmacy and succeeded in ordering and having delivered a 50 pound drum of methamphetamine crystals worth over a million dollars in the street market.

He urges that a felony count be established for possession of large quantities of amphetamines; at present, no matter how large the amount, it is only a misdemeanor unless intent to sell can be proved, and it is sometimes difficult to persuade juries of this intent. He did not feel qualified to state what amount should be the cut-off point for the possession felony. (8–180)

He believes that amphetamines are extremely dangerous and when abused can cause severe psychotic episodes and brain damage. (8–215)

He feels that there is an enormous urge among our immature young people to experiment with almost any drug that happens to be available and that therefore it is extremely necessary to take drastic action to reduce the availability of these drugs. He feels that right now nothing is being done, and indeed he considers the new federal law "hypocritical" because it failed to authorize production quotas for amphetamines and other Schedule III drugs and in reality these are the *only* drugs which are manufactured in this country.

He recommends a complete ban on amphetamines, such as has been imposed in Sweden—he would permit its prescription under severe controls for hyperkinesis and narcolepsy. (8–295)

He believes that most of the amphetamines sold illegally have been diverted from legitimate channels rather than manufactured clandestinely. (8–345)

His office occasionally but rarely investigates a pharmacy, usually on complaint from someone in the neighborhood. He feels that there is a great need for state action in supervising pharmacies more closely.

He is also very much concerned about proprietary drugs, some of which he considers dangerous. He encountered a case of paranoia resulting from taking Sleepeez. Both Sleepeez and Contac contain belladonna, which is a very dangerous drug. (8–384)

Amphetamines are now widely used in junior high schools in Suffolk County as well as high schools. (8–490)

Dr. Angrist, representing Dr. Freedman, stated that there was no evidence as yet of permanent brain damage resulting from amphetamine abuse and that amphetamine psychosis is inevitably self-limiting, usually ending after a week or so. (9–50)

MR. JOHN DE FRANCESCO, CURRICULUM CONSULTANT, HEALTH SCIENCES CENTER, STATE UNIVERSITY OF NEW YORK AT STONY BROOK, FORMERLY ASSISTANT DEAN OF STUDENTS

He has had extensive experience with young people who use drugs and wanted to present the attitudes and conceptions about amphetamines held by young people:

(1) Although not physically addictive, amphetamines can create a powerful dependence, based primarily upon the desire to avoid the "crash" when one stops taking them. As one continues to take the drug, tolerance develops, thus raising fears of an even greater crash and an even greater desire to continue taking the drug.

(2) Amphetamine users believe that the drug improves intelligence and memory, but most of them realize that it impairs judgment.

(3) Amphetamines are very freely available on campuses and no conceivable controls on prescriptions, such as triplicate prescriptions, will have any signfiicant effect upon this availability.

(4) One of the principal physical effects is dehydration and enormous thirst. In addition, the "speed freak" experiences a gnashing of teeth so violent as to jar them loose—this is known as "amphetamine mouth." (9–160)

(5) The belief is that sustained heavy amphetamine use produces psychosis because of the lack of rapid-eye-movement sleep, and that after the crash it takes a week or so to get over the psychosis.

(6) Nobody sleeps when high on amphetamines—he may close his eyes, he may be in a stupor, but he does not sleep.

(7) It is generally believed that amphetamines remove calcium from the body and thus abusers sometimes chew calcium pills or drink huge amounts of milk. They also take vitamin C. (9–200)

(8) Amphetamine sellers are interested strictly in money; one does not find friendly or "accommodation" sellers as in marihuana.

(9) Most of the speed (methamphetamine) in the New York area is illegally manufactured, much of it in the East Village.

(10) Most campus amphetamine users know that speed kills and stay away from it, but in the street drug scene speed is still extensively used.

(11) Among drug users there are the "searchers," who are seeking to expand their consciousness—these mostly use amphetamines. Then there are the "oblivion seekers"—they use barbiturates and sometimes heroin. (9–348) In the street, drug use takes an even more frightening term among early teenagers who simply use any drug that is available without purpose or sense.

He reports that a single drug store in Suffolk County was burglarized and two million barbiturate capsules were taken. (9–435)

Codeine preparations, sold without prescription, are very extensively used by high school students. (9–221)

He believes that the legitimate production of amphetamines is grossly excessive. He thinks they should be banned.

In answer to Chairman Hardt's question as to what are the most prevalent drugs of abuse on campus, he said "hashish, mescaline and LSD in that order, with a healthy influx of heroin also." (9–500)

DR. IRIS LITT, PEDIATRICIAN, MONTEFIORE HOSPITAL

Her unit has treated 4,000 youthful drug users in the last 2 years. They are encountering about 1700 juvenile heroin users a year (about double what it was 2 years ago), about 400 glue sniffing cases a year (unchanged from 2 years ago), and a very rapid increase in users of stimulants, depressants, and hypnotics. In the first year they encountered only a handful of such cases but in the last 6 months they have had 70 amphetamine cases and 227 abusers of Doriden, a sedative produced by Ciba. Many patients took up sedatives after discontinuing heroin. There is no legitimate use for Doriden, which is stored in the fatty tissue and released into the bloodstream erratically, thus causing overdoses. It should be completely banned.

Most of the patients she sees are between 12 and 19. The inner city patients have a pattern of progression from glue sniffing to heroin and now to Doriden. (10–95) It is by no means true that all youthful drug abusers start with marihuana.

Among the patients from the northeast Bronx and Westchester glue sniffing is less common. Marihuana and mescaline are very common.

MR. ROBERT PINCO, OFFICE OF THE CHIEF COUNCEL, BUREAU OF NARCOTICS AND DANGEROUS DRUGS

The purpose of the 1970 Federal law was to combine and recodify all Federal dangerous drug laws passed since 1914. The Bureau feels that this also should be done at the state level. First, it feels that the states should, as the federal government now has done, combine their control activities rather than having them divided among revenue agencies, health agencies and law enforcement agencies. Also, the Bureau feels that the states need automatic procedures to deal with the new drugs that are constantly being developed. (10–220) Almost 90% of the drugs now being used were unknown 30 years ago. (10–235)

The five schedules in the new Federal Act permit now drugs which suddenly appear on the scene to be brought rapidly into law enforcement framework without the long delays usually required for the legislative process. The Uniform Act would provide the same benefit to any state which adopts it.

If New York adopted the Uniform Act, it would not necessarily have to slavishly follow the federal pattern in every detail. It might, for example, choose to retain its present penalty structure and simply adopt the administrative features of the Act. (10–345)

The Bureau feels that it has, based upon testimony before the House Interstate and Foreign Commerce Committee, a "semi-mandate" to move adminis-

tratively to put all amphetamines into Schedule II. (10–426) In accordance with the procedures specified in the law, the Bureau has compiled scientific and other data in support of this recommendation and has forwarded it to HEW, where it is now under review. We understand informally that they have also requested an opinion from the National Academy of Sciences-National Research Council. After HEW renders its opinion, the Bureau will move rapidly to hold hearings and to move amphetamines into Schedule II by regulation.

Under the new law, the regulation will go into effect immediately, even if the drug manufacturers challenge it in courts—unless of course they are successful in obtaining a court injunction staying the effectiveness of the order.

Under the new federal law, the Bureau has the power to require that records be kept of amphetamines *dispensed* by doctors; however, it has not yet chosen to exercise that power.

In answer to Chairman Betros' question, Mr. Pinco said that the federal government has *not* preempted the drug regulation field as it sometimes does in other areas of legislation. The intention is that federal and state regulations exist in parallel and this is specified in Title 2, Section 708. There would of course be an exception if state and federal law were in direct conflict—in that case the federal law would prevail. Mr. Pinco assured the Commission that there would be no such problem if the federal government kept amphetamines in Schedule III and New York, after adopting the Uniform Act, put them in Schedule II. (11–31)

Thirteen states have now adopted the Uniform Act and 28 others have it in the legislative process.

Mr. Pinco offered the cooperation of his office to the Commission and to New York State in any study or consideration of the adoption of all or part of the Uniform Act.

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5. STATEMENTS AND MATERIALS RELATING TO THE PENNWALT CORP., ITS STRASENBURGH PRESCRIPTION PRODUCT DIVISION, ITS AFFILIATE, LABORATORIES STRASENBURGH DE MEXICO AND THEIR DIET PILLS BIPHETAMINE, BIPHETAMINE–T, AND BIFETAMINA

KLEINFELD AND KAPLAN,
Washington, D.C., June 25, 1971.

DIRECTOR, BUREAU OF NARCOTICS AND DANGEROUS DRUGS,
Department of Justice,
Washington, D.C.

DEAR SIR: Pursuant to Section 201(a) of the Controlled Substances Act [Act] and in accordance with the procedures specified in 21 CFR 308.45 and 316.47, the undersigned, on behalf of the Pharmaceutical Division of Pennwalt Corporation [Pennwalt], whose mailing address is Post Office Box 1710, Rochester, New York 14603, hereby requests a hearing in the matter entitled "Proposed Transfer of Amphetamine and Methamphetamine and Their Salts, Optical Isomers, and Sales of Their Optical Isomers From Schedule III to Schedule II, With Certain Exceptions." The proposal was published in the Federal Register of May 26, 1971 (36 F.R. 9563).

(A) On June 17, 1971, representatives of Pennwalt met with representatives of the Bureau of Narcotics and Dangerous Drugs [Bureau] to explain that two Pennwalt drug preparations containing resin complexes of amphetamine and dextroamphetamine, and marketed under the trade names Biphetamine and Biphetamine-T, were not and should not be subject to the control contemplated by the May 26 proposal. Pennwalt pointed out that these resin complexes are not classifiable as amphetamine or amphetamine salts within the reasonable and proper factual meaning of those terms and that no other term used in the May 26 proposal was applicable to either of the Biphetamine products.

On June 21, 1971, a representative of the Bureau notified Pennwalt that, contrary to the position taken by Pennwalt, it was the Bureau's conclusion that the scope of the term "amphetamine salts" did in fact encompass the resin complexes contained in the Biphetamine preparations and accordingly, that Biphetamine and Biphetamine-T were presently subject to Schedule III classification and, under the May 26 proposal, Biphetamine and Biphetamine-T would become subject to Schedule II classification if the proposed transfer were to be accomplished.

As a consequence of the nature of the controls imposed upon Schedule II controlled substances, the manufacture and distribution of Biphetamine and

Biphetamine-T would be severely and unnecessarily restricted were the proposal, as interpreted by the Bureau, to be made into a final regulation. Such restrictions would be to the substantial detriment of Pennwalt, medical practitioners, and patients who are presently being benefitted by these safe and effective aborectic drugs.

It is respectfully submitted that a hearing on the record as provided for in Section 201(a) of the Act and Sections 4 and 7 of the Administrative Procedure Act [APA] (5 U.S.C. §§553 and 556), is required in order to resolve the issues raised by the objections set forth below and to determine whether there exists reliable, probative, and substantial evidence in support of subjecting Biphetamine and Biphetamine-T to Schedule II classification. Under §7 of the APA, the Bureau, as the proponent of the rule, has the burden of establishing at a hearing on the record the validity of the factual allegations upon which the rule is required to be based and Pennwalt, as the opponent, is entitled to present its case, "to submit rebuttal evidence, and to conduct such cross-examination as may be required for a full and true disclosure of the facts."

(B) The objections as they appear below comprehend the issues for a hearing and present reasonable grounds in support of Pennwalt's opposition to the proposed rule, as it is interpreted by the Bureau:

1. THERE IS NOT SUFFICIENT RELIABLE, PROBATIVE, AND SUBSTANTIAL EVIDENCE TO SUPPORT THE FACTUAL DETERMINATION MADE BY THE BUREAU THAT AMPHETAMINE RESIN COMPLEXES ARE INCLUDED WITHIN THE PROPER MEANING OF THE TERM "AMPHETAMINE SALTS," OR WITHIN THE MEANING OF ANY OF THE OTHER TERMS USED IN PROPOSED SECTION 308.12(d)(1).

Pennwalt, in rebuttal of testimony that may be offered by the Bureau, is prepared to present scientific and factual evidence, including the testimony of highly qualified chemists and other scientists, that, due to the distinct differences in chemical structure and physical, biochemical and pharmacological characteristics between amphetamine salts and amphetamine ion exchange resin complexes, it is factually and scientifically incorrect, inappropriate, and misleading to classify amphetamine resin complexes as amphetamine salts or as any of the other substances included within the terms used in proposed Section 308.12(d)(1) of the regulations.

2. THERE IS NOT SUFFICIENT RELIABLE, PROBATIVE, AND SUBSTANTIAL EVIDENCE TO SUPPORT THE PLACEMENT OF BIPHETAMINE AND BIPHETAMINE-T IN SCHEDULE II.

The Director, in the May 26 Federal Register proposal, made a blanket assertion that amphetamines and methampetamine and their salts, optical isomers, and salts of their optical isomers, all meet the criteria for Schedule II control. Pennwalt denies the truth of this assertion as it may be sought to be applied to the preparations Biphetamine and Biphetamine-T. Pennwalt is prepared to rebut by adequate factual and scientific evidence any testimony that the Director may offer which might seek to establish that Biphetamine and Biphetamine-T are salts of amphetamine or, even if they are such salts, that they meet the Schedule II criteria (1) of having a "high potential for abuse" and (2) that their abuse may lead to severe psychological dependence. The Pennwalt rebuttal evidence includes scientific data which demonstrate that the abuse potential of amphetamine resin complexes is substantially less than that of amphetamines, amphetamine salts and any substance currently listed in Schedule II. At most, a relatively minimal risk of psychological dependence would be associated with the abusive use of amphetamine resin complexes. In addition, at the hearing Pennwalt will, if necessary, show that the history and pattern of abuse of Biphetamine and Biphetamine-T does not support a Schedule II classification.

Under Section 202(b) of the Act, in order to subject a drug or other substance to Schedule II control, the Director of the Bureau must find that the substance meets the criteria for inclusion specified in Section 202(b)(2)(A)(B) and (C). Such findings may be made only after the Director has received a scientific and medical evaluation and recommendation from the Secretary of Health, Education and Welfare. By letter dated May 7, 1971, the Director formally requested the Secretary to provide his evaluations and recommenda-

tions on methamphetamine, the amphetamines, and on Ciba's Ritalin and Geigy's Preludin. In a letter dated May 13, 1971, from the Secretary of Health, Education, and Welfare to the Attorney General, the Secretary set forth certain naked findings and recommendations which related solely to the amphetamines and methamphetamine. These findings and recommendations in no manner dealt with amphetamine resin complexes. Consequently, no proper foundation presently exists to initiate proceedings to subject such complexes to Schedule II controls.

(C) In conclusion, Pennwalt requests a hearing in order to determine the legal and factual bases, if any, of the Bureau's assertion that Biphetamine and Biphetamine-T may appropriately be subjected to Schedule II control and, if necessary, present its evidence rebutting the assertion. Included among the factual issues for determination at such a hearing are:

1. Whether amphetamine resin complexes as present in Biphetamine and Biphetamine-T are sales of amphetamine;

2. Whether Biphetamine and Biphetamine-T specifically were the subject of a scientific and medical evaluation and recommendation by the Secretary of Health, Education and Welfare as to whether they should be controlled;

3. Whether: (a) Biphetamine and Biphetamine-T have a high potential for abuse; and (b) Abuse of Biphetamine and Biphetamine-T may lead to severe psychological dependence.

All notices to be sent pursuant to the proceeding should be addressed to: Kleinfeld and Kaplan, 1320 19th Street, N.W., Washington, D.C. 20036.

Respectfully yours,

KLEINFELD AND KAPLAN,
By VINCENT A. KLEINFELD,
ALAN H. KAPLAN.

(b) UNITED STATES DEPARTMENT OF JUSTICE

BUREAU OF NARCOTICS AND DANGEROUS DRUGS
WASHINGTON, D.C. 20537

IN THE MATTER OF

Strasenburgh Prescription Products
Division of Pennwalt Corporation
755 Jefferson Road
Rochester, New York

ORDER TO SHOW CAUSE

Pursuant to Section 1008 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 958),

NOTICE is hereby given to afford you an opportunity to Show Cause as to why the Bureau of Narcotics and Dangerous Drugs should not deny your application, dated December 27, 1971, for a Certificate of Registration to export amphetamine, its salts, optical isomers and salts of its optical isomers and resin complexes of amphetamine and dextroamphetamine (hereafter "Schedule II, 1100") and as to why the 1972 production quota for Schedule II, 1100 fixed under Section 306 of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 826) should not be reduced by the amount now allocated by you for export purposes, for the reason that the Director of the Bureau of Narcotics and Dangerous Drugs (hereafter "Director") is unable

to determine that your application for registration to export Schedule II, 1100 is consistent with the public interest.

More particularly, the Director in applying the factors of Section 303(a) of the Comprehensive Drug Abuse Prevention and Control Act (21 U.S.C. 823(a)), notes that you have not maintained effective controls against diversion into other than legitimate medical, scientific, research, or industrial channels, of Schedule II, 1100 shipped by you into the Republic of Mexico under authority granted under your present BNDD registration (No. PS 0003183).

The Director further notes that information has been furnished to him indicating:

1. That Schedule II, 1100 is shipped by you to Laboratorios Strasenburgh de Mexico S.A. de C.V. (a subsidiary of Pennwalt Corporation) at Mexico City, Mexico, where it is used in making an amphetamine product under the trade name "Bifetamina";
2. That a substantial percentage of this Bifetamina is then smuggled into the United States and is then sold illegally in the United States. For example:

(a) On November 5, 1971, Special Agents of the Bureau of Narcotics and Dangerous Drugs arrested two individuals at Atlanta, Georgia, and seized 20,000 dosage units of Bifetamina in the original bottles;

(b) On November 13, 1971, Special Agents of the Bureau of Narcotics and Dangerous Drugs arrested two individuals at Glendale, Kentucky, and seized 40,000 dosage units of Bifetamina in the original bottles; on November 14, 1971, a third individual was arrested in connection with this case;

(c) On December 10, 1971, Special Agents of the Bureau of Narcotics and Dangerous Drugs arrested two individuals at Hattiesburg, Mississippi, and seized 72,000 dosage units of Bifetamina in the original bottles;

(d) On December 16, 1971, Special Agents of the Bureau of Narcotics and Dangerous Drugs arrested two individuals at San Antonio, Texas, and seized 30,000 dosage units of Bifetamina which were not in bottles used by Laboratorios Strasenburgh de Mexico S.A. de C.V.; on December 17, 1971, two additional individuals were arrested in connection with this case;

(e) On January 6, 1972, Special Agents of the Bureau of Narcotics and Dangerous Drugs arrested an individual at Birmingham, Alabama, and seized 24,000 dosage units of Bifetamina in the original bottles;

(f) On January 11, 1972, Special Agents of the Bureau of Narcotics and Dangerous Drugs concluded investigations into two entirely unrelated cases. In one case, two individuals were arrested at El Paso, Texas, and 60,000 dosage units of Bifetamina in the original bottles were seized. In the other case, also at El Paso, Texas, one individual was arrested and 62,000 dosage units of Bifetamina in the original bottles were seized;

(g) Beginning on November 8, 1971, and ending on January 15, 1972, a special BNDD project designated "Operation Blackjack" was in effect. Information developed by Special Agents assigned to Operation Blackjack indicates that Bifetamina enters the United States at six principal points along the Mexico-Texas border -- El Paso, Del Rio, Eagle Pass, Laredo, McAllen and Brownsville. Across the border from each of these Texas locations there exists in Mexico a "farmacia" from which the Bifetamina begins its journey into the

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United States; in the United States Bifetamina is illegally sold under the street names "Black Beauties", "Black Mollies", "Black Widows", and "R.J.Ss.".

(h) Beginning in April of 1971 and continuing through January 11, 1972, Special Agents of the Bureau of Narcotics and Dangerous Drugs seized and otherwise acquired over 1,210,000 dosage units of Bifetamina in New Mexico, Texas, Oklahoma, Louisiana, Alabama, Tennessee, Georgia, Kentucky, Florida, Colorado, Mississippi and Arkansas; of this amount over 896,000 dosage units of Bifetamina were seized or otherwise acquired since November 8, 1971, by Special Agents of the Bureau of Narcotics and Dangerous Drugs;

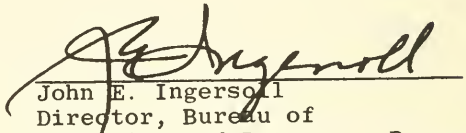
(i) Beginning on November 8, 1971, and ending on January 11, 1972, Special Agents of the Bureau of Narcotics and Dangerous Drugs arrested 39 individuals in connection with illicit sales of Bifetamina; State and local police, working in cooperation with the Bureau on Operation Blackjack, arrested 10 individuals.

3. That on May 26, 1971, a notice was published in the Federal Register proposing, in pertinent part, the transfer of amphetamines from Schedule III to

Schedule II of the Comprehensive Drug Abuse Prevention and Control Act (Public Law 91-513); that on June 25, 1971, Pennwalt Corporation requested a hearing on the transfer of Biphetamine and Biphetamine-T (amphetamine drugs manufactured by you at Rochester, New York, and similar in contents and effects to Bifetamina); that this request was later withdrawn by Pennwalt Corporation and on July 23, 1971, Biphetamine and Biphetamine-T were included in Schedule II and thus made subject to the stringent requirements of that Schedule regarding record keeping, labeling, order forms, import and export controls, security, and prescriptions; that, finally, the illicit importation of Bifetamina from Mexico and the subsequent illegal sales of Bifetamina in the United States substantially subverts the purpose of placing all amphetamines, and in particular Biphetamine and Biphetamine-T, in Schedule II.

A hearing on this Order to Show Cause will take place at the Bureau of Narcotics and Dangerous Drugs, 1405 Eye Street, N.W., Washington, D.C., on the 23rd day of February, 1972, or as soon thereafter as this matter may be heard. Correspondence should be directed

to the Bureau of Narcotics and Dangerous Drugs,
1405 Eye Street, N.W., Washington, D.C. 20537,
Attention: Robert J. Rosthal, Deputy Chief Counsel.
(Telephone: 202-382-3411)



John E. Ingersoll
Director, Bureau of
Narcotics and Dangerous Drugs

January 14, 1972

FOR IMMEDIATE RELEASE
Tuesday, January 18, 1972

A 10-month investigation by the Bureau of Narcotics and Dangerous Drugs (BNDD), covering 12 states and Mexico, has resulted in the arrest of 39 persons and the seizure of about one million amphetamine tablets with an illicit street value of about $1.5 million, Attorney General John N. Mitchell announced today.

Called "Operation Blackjack," the investigation has also resulted in a major pharmaceutical company being ordered to show cause why its license to export amphetamines should not be revoked.

Mr. Mitchell said the order was served today at Rochester, New York, on the Strasenburgh Prescription Products Division of the Pennwalt Corporation of Philadelphia.

At issue is a patented amphetamine product manufactured at Rochester by the firm and shipped in bulk to Mexico City where another Pennwalt Corporation affiliate, Laboratorios Strasenburgh de Mexico, markets under the trade name, Bifetamina.

John E. Ingersoll, BNDD Director, said that beginning in April, 1971, BNDD special agents began detecting the product in the illicit market in New Mexico, Texas, Oklahoma, Louisiana, Alabama, Tennessee, Georgia, Kentucky, Florida, Colorado, Mississippi and Arkansas.

Mr. Ingersoll said that the investigation revealed that Bifetamina was entering the United States at six principal points along the Mexico-Texas border -- El Paso, Del Rio, Eagle Pass, Laredo, McAllen and Brownsville.

He said that once over the border the pills were then carried along established truck routes through the southeastern and southwestern states.

Most of the smuggling operation across the border was usually accomplished by concealing the drugs in trucks carrying legitimate merchandise. Another method of getting the drugs into the United States has been by light aircraft which landed at remote air strips in the mountainous border area.

The solid black Bifetamina capsule is sold in the illicit market under the street names, "Black Beauties," "Black Mollies," "Black Widows," and "R.J.S.s".

A majority of the BNDD seizures were of unopened 40 capsule bottles packaged at Mexico City, bearing the Laboratorios Strasenburgh de Mexico label.

The company was also ordered to show cause why the 1972 industry-wide amphetamine production quota should not be rolled back by the amount now allocated by the company for export purposes.

Mr. Ingersoll said that the action against Strasenburgh is the first of its kind taken under the Drug Abuse Prevention and Control Act which went into effect on May 1, 1971.

U.S. law requires that bulk amphetamine powder exported be used exclusively in the particular country for legitimate medical and scientific use.

According to the show cause order, Bifetamina is "similar in contents and effects" to Biphetamine and Biphetamine-T, amphetamine drugs produced by the Strasenburgh Division for sale only by prescription within the United States.

Mr. Ingersoll noted that shortly before the May 1, 1971, effective date of the comprehensive drug law, Bifetamina was among those amphetamines appearing in the illicit drug traffic in the United States.

In July 1971, BNDD placed stringent controls on the manufacture, sale and distribution of all amphetamines.

As a result, the amount of domestic amphetamines available for diversion into illicit channels in this country fell sharply, almost immediately.

At about the same time, BNDD found that the Mexican product, Bifetamina, was being illegally sold in ever-increasing amounts and ever wider areas within the United States.

The BNDD investigation revealed that the price for a single Bifetamina capsule in the illicit market in Mexico ranges between nine cents and 13 cents.

Within the illicit market in the United States, the same capsule sells for an average of about $1.50.

Mr. Ingersoll said "Operation Blackjack" was intensified last November 8 and the 39 arrests were made between then and January 11.

State and local police, working with BNDD, arrested 10 suspects.

Mr. Ingersoll also said that the U.S. Bureau of Customs assisted BNDD special agents in some facets of the investigation and subsequent arrests.

He noted that Mexican federal officials have been fully advised and have agreed to help in resolving the problem.

A hearing on the show cause order has tentatively been set for February 23, 1972.

(d) Statement of Dr. William F. Head, Vice President, Technical Operations, Pharmaceutical Division, Pennwalt Corp., Submitted to the House Subcommittee on Public Health and Environment, Committee on Interstate and Foreign Commerce

At the request of your committee, I am appearing on behalf of the Strasenburgh Prescription Products Division of Pennwalt Corporation, in order to provide the Committee with information dealing with the export of our amphetamine-containing products to our Mexican subsidiary, Laboratorios Strasenburgh de Mexico S.A. de C.V. (Mexico City), and to discuss briefly the subject of our sales of these products in the Mexican market.

CORPORATE HISTORY

The Pharmaceutical Division of Pennwalt Corporation was formerly the R. J. Strasenburgh Company, with its main production, research and marketing organizations headquartered at its home office in Rochester, N.Y. The Strasenburgh company was privately owned, by the Strasenburgh family, until 1960, at which time it was acquired by the Wallace & Tiernan, Inc., headquartered in East Orange, N.J., with plants located in several areas of the United States. On March 31, 1969, the Wallace & Tiernan, Inc. was acquired by Pennwalt Corporation, headquartered in Philadelphia, Pa.

Shortly thereafter, the Strasenburgh Corporation became known as the Pharmaceutical Division of Pennwalt. However, it retained its operating subsidiary in Mexico under the name of Laboratorios Strasenburgh de Mexico S.A. de C.V., as a wholly-owned subsidiary of Pennwalt Corporation.

Pennwalt Corporation has annual sales of approximately $410 million and approximately 14,000 employees. The Pharmaceutical Division has annual sales of approximately $40 million (and therefore consists of slightly less than 10% of Pennwalt's total sales) and has approximately 800 employees or approximately 5.7% of Pennwalt's total employees.

CORPORATE ORGANIZATION

Pennwalt Corporation is divided into three operating groups: Chemicals, which account for about 48% of total sales; Equipment, which accounts for about 28% of total sales; and Health Products (including pharmaceutical and dental) which, combined, account for 24% of total sales. The corporate organization is composed of the senior corporate officers: a Chairman and Chief Executive Officer, a Vice President-Finance, a Vice President-Secretary, a Vice President-Technical, and three Group Vice Presidents in charge, respectively, of Chemicals, Equipment, and Health, and each of these Groups is subdivided into divisions, such as the Pharmaceutical Division, which have their own Presidents, Vice Presidents, and full organizational structures for Manufacturing, Sales, Research, Engineering and the like.

As I have just noted, the Pharmaceutical Division is organized in a manner comparable to an independent company except for its reporting relationship to the Group Vice President-Health. I am the Vice President in charge of Technical operations for the Pharmaceutical Division, and my responsibilities include both domestic manufacturing, which encompasses raw material control, process control, quality control, and export of our products as required. I am conversant with the procedural requirements for the handling of our products in the United States and am equally conversant with the requirements for export of our product from the United States.

BNDD ORDER TO SHOW CAUSE AND PENNWALT'S ACTIONS IN RESPONSE

On January 18, 1972, Pennwalt Corporation and its Pharmaceutical Division each learned *for the first time*, that the Bureau of Narcotics and Dangerous Drugs (BNDD) had been investigating the alleged illicit purchase of our product in Mexico by individuals who allegedly were bringing it into the United States for the purpose of illicit transactions. Incidently, this information first came to us from NBC reporters.

Prior to that date, no employee of Pennwalt Corporation, at its corporate headquarters nor at the Pharmaceutical Division headquarters or elsewhere, had been advised that the product we manufactured in Mexico, "Bifetamina" (our Mexican counterpart of our Biphetamine product in the United States),

was the subject of any investigation. So far as we are aware, no employee of ours, either in the United States or in Mexico, has been suspected or accused of dealing in these products for any illicit purpose, nor has any employee been accused of knowingly making them available to the illicit market.

On January 19, 1972, Pennwalt Corporation's headquarters received the BNDD's Order to Show Cause, and immediately instructed the management of our Mexican pharmaceutical operations to cease production and sale of any amphetamine-containing product until further notice.

On that same date, Pennwalt began a complete review of the marketing of amphetamine-containing products by its Mexican pharmaceutical operation, Laboratorios Strasenburgh de Mexico S.A. de C.V.

At this point, I should like to summarize what has occurred and what we have ascertained since this matter was first brought to Pennwalt's attention on January 19, 1972:

1. The sales of "Bifetamina,' our amphetamine-containing product in Mexico, were made only through channels of distribution licensed by the Mexican government.

2. No Bifetamina in any form was exported by our Mexican operations to the United States.

3. Our Mexican subsidiary has manufactured Bifetamina capsules in Mexico since 1967. Our Pharmaceutical Division, in the United States, has not exported any amphetamine-containing capsules to Mexico since 1967. I did continue to export to Mexico the raw materials from which capsules are manufactured, until June, 1971. Since that time, there have been no exports of amphetamine in any form to Mexico.

4. On January 20, 1972 (the day after the company halted the manufacture and sale of amphetamine-containing products in Mexico), Pennwalt learned that the Mexican government had notified the producers of amphetamine-containing products in Mexico that, as of January 14, 1972 (one week easlier) such products and other specified pharmaceuticals had become subject to even more stringent regulatory control. In addition, the Mexican government's notice advised us that amphetamine could no longer be contained in these products by the end of a 180-day period, commencing as of January 14, 1972.

5. On January 25, 1972, Pennwalt representatives made an appointment with the Bureau of Narcotics and Dangerous Drugs to discuss the Order to Show Cause, and met with the BNDD on January 26th. In that meeting, Pennwalt made the following statement:

(1) That we had ordered the *permanent* cessation of manufacture and marketing of our amphetamine containing products in Mexico and that we were therefore out of the business in Mexico and intended to remain out of it.

(2) That we wished to withdraw our application to export any amphetamine-containing products from the United States to any other country, including Mexico.

(3) That we had begun and were continuing our investigation of this matter in order to ascertain whether there had been any failure on the company's part, through any of its representatives at any level, to maintain effective controls against diversion of the company's products into other than legitimate channels.

(4) That it had always been Pennwalt's policy to cooperate fully with the government and that we would continue to do so.

(5) On the following day, Thursday, January 27th, we were advised by the BNDD that the hearing on the Order to Show Cause had been cancelled and the subpoena withdrawn.

It is evident from the foregoing that Pennwalt decided that by discontinuing the manufacture and sale of amphetamine-containing products in Mexico and discontinuing all export of these products from the United States it could be certain that the manufacture and sale of these products would hereafter be limited to the United States and Canada, where rigorous regulatory controls exist.

SALE OF OUR AMPHETAMINE-CONTAINING PRODUCT IN MEXICO

Although our amphetamine-containing products are an important part of our pharmaceutical operations which had total sales of $40 million in both ethical and proprietary products in 1971, our sales of amphetamine-containing products amounted to slightly less than 2% of Pennwalt's total sales.

It is not my purpose today, however, to say to this committee that the allegations with respect to the sale of these products are not meaningful to Pennwalt. I believe that the summary of actions taken by the company since January 19, 1972, including the cessation of all manufacture and sale of the product in Mexico, the decision to cease any export of the products hereafter from the United States, and the determination to continue its investigation of the allegations with respect to its operations in Mexico, demonstrate a full awareness of the seriousness of the matters in which this committee has also expressed an interest.

We feel we must be candid with you in saying that our investigation, to date, has disclosed to us a growth in the sales of our product in Mexico that seems out of proportion to what the normal expectations for that product should have foreseen. I think it important to stress, at the same time, that we are not aware of any evidence that the growth of the sales of our products in Mexico was a result of any intention by any of our employees, here or there, to realize any personal financial gain.

It appears to us, at this point, that our amphetamine-containing products were only sold in lawful channels of distribution in Mexico, but that for reasons over which we had and have no direct control the ultimate purchaser of the product in Mexico found it more readily available than it would have been in the United States.

I am confident that had the marketing patterns in Mexico been more fully analyzed and increases in distribution been noted, we would have had prompt action, within our organization, to curtail or eliminate the sale of these products, either in specific areas or entirely if the situations required.

By the same token, I am confident that had the corporate headquarters of Pennwalt in Philadelphia been advised ten months ago—when, we were told, the BNDD investigation commenced—or at any time thereafter, that the appropriate federal agencies were concerned about the apparent appearance of our product "Bifetamina" in the illicit market in the Southern United States, we would have cooperated at once with such authorities to ensure the prompt termination of any opportunity for illicit distribution of our product. In short, I think it quite safe to say that Pennwalt would have terminated manufacture and sale of amphetamine-containing products in Mexico immediately upon advice by the federal government that there was cause for concern. My confidence on this point is based on the fact that as soon as we did learn of these matters upon receipt of the Order to Show Cause on January 19, 1972, we shut down the Mexico operations.

In order that you may be aware of the market figures which were relevant to our decision to terminate operations, I would summarize our recent sales of amphetamine-containing products in Mexico as follows:

1969	$354, 000
1970	619, 000
1971	1, 218, 000

We do not yet have an analysis of the distribution of these products for these years by geographic area. Nevertheless, as we review this history in our current internal analysis, it seems evident to us that the rate of growth was sufficiently fraught with risk so that it might well have raised questions of qualitative analysis for our personnel to consider.

At the same time, however, the changes in Mexican law which I noted above had made it clear to our Mexican management that amphetamine-containing products were to have a short life in Mexico. The Mexican government's Order of January 14, 1972 confirmed this fact.

SUMMARY

I trust that this brief review has conveyed to this committee some sense of the impact of these recent events on Pennwalt Corporation, its Pharmaceutical Division in the United States, and our Mexican subsidiary. Our parent company was founded in Philadelphia in 1850, and in all of its existence has never experienced an event so disturbing.

We are deeply aware that we are fallible and that we can make mistakes in judgment, mistakes of delegation, and mistakes of focus. However, we have always valued as our most prized asset our reputation for integrity and, be-

cause of our faith in our system of government, have sought to cooperate for countless years with every government agency with whom we have had any relationship. We believe we have had sufficient empathy to understand wherein we and others might disagree, and yet together recognize higher and more important purposes.

In this instance, I assure this committee, on behalf of Pennwalt, that we regret that some way was not found, far earlier, to stem or stop the flow of any of our amphetamine-containing products into this country, assuming, as alleged by the BNDD, that our products were in fact coming into this country illicitly. We regret, further, any failure on our part which may have contributed in any way to the possibility of the alleged illicit market continuing. We hope and trust that we have learned, indeed that all of us involved in any way have learned, what this entire experience has to teach us.

(e) Statement of John E. Ingersoll, Director, Bureau of Narcotics and Dangerous Drugs, U.S. Department of Justice, Before the House Subcommittee on Public Health and Environment, Committee on Interstate and Foreign Commerce

Mr. Chairman and Distinguished Members of the Subcommittee: I am pleased to have this opportunity to address your Subcommittee on the problem of the abuse and control of amphetamines. The development of this problem is the story of a creeping malignancy of which our fellow citizens have only lately become aware. It has a complex history stretching over many years and which can be viewed from several different perspectives. At one level it is an illustration of our society's lag in grasping the impact and danger of new scientfiic and technological developments. At another it is the drama of clandestine criminal enterprise, of international traffickers, illicit laboratories, and huge criminal profits. Or, it may be viewed as the tragedy of wayward teenagers who have lost faith in their culture, become alienated from their families, and fallen into the deadly spiral of the "speed freak". There is a final dreary dimension which may be found in the injudicious prescribing of medication, the drug-dependent housewife, or the obese patient who has gained a habit while attempting to lose weight.

The problem facing us is one of individual tragedy and injury to the nation's health, but it is one of which I can now speak with some optimism. I believe I can state with conviction that we are finally breaking the back of the amphetamine abuse problem in the United States. This is the result of an effort on the part of our Bureau in which I take great pride. It involves the diligent and concerted activity of a number of Bureau components ranging from our agent force whose duty is to police both legitimate and illicit drug commerce, to our competent staff of lawyers and scientists who serve the Bureau's mission at its headquarters. It is also an outstanding justification for the maintenance of different skills and professions within the service of a law enforcement agency. This progress has further been made possible by the vigorous encouragement of Members of the Congress.

I should now like to recount the highlights of this unfolding problem and pinpoint the issues with which we must yet deal.

The amphetamines constitute a class of powerful synthetic stimulants, which includes also the methamphetamine compounds. Perhaps their closest natural equivalent in terms of both physical and sociological effects is the very powerful stimulant cocaine, derived from the leaves of the coca bush of South America. This drug, however, unlike amphetamines, has for years been relegated to medical uses of no great quantitative significance.

I shall not attempt here to describe in depth the various physical and psychological effects of these stimulants which is a subject better addressed by a competent medical authority. I think it sufficient to note that all authorities are agreed that the drugs have a high potential for abuse often resulting in considerable damage to the use and those around him. Continued abuses may result in toxic psychosis, physical exhaustion, paranoia, hallucinations, necrosis, and even violence. Though many abusers take the drug orally, a pattern of intravenous injection has developed within the decade of the sixties which results in the addition of other types of damage customarily accompanying intravenous drug abuse.

Although amphetamine compounds were first synthesized in the nineteenth century, no medical uses were found for them until the thirties. Nevertheless, by the 1960's amphetamines were one of the most common drugs to be found in the United States in the homes of millions of citizens.

In calendar year 1970, a total of 45,456 pounds of amphetamines (including methamphetamine) were manufactured and available for domestic consumption. To state this in other terms, this amounted to a total of 2,066,193,000 dosage units of 10.2 dosage units for every man, woman, and child in the United States. During the sixties we also witnessed the development of the pattern of amphetamine abuse which we refer to as the "speed freak". Though amphetamines had become increasingly subject to abuse throughout the post-World War II period, the problam was rapidly accelerated by the drug abuse revolution associated with Timothy Leary's psychedelic cult.

This pathetic development which consumed so many of our young people caused thoughtful leaders to look more closely at this drug and the problems associated with it. Looking at the startling volume of production which I have outlined, it became clear that the nation was literally being drowned in a sea of amphetamines. The first Federal response was the passage of the Drug Abuse Control Amendments of 1965, which imposed some commercial record-keeping requirements and made possible the first enforcement efforts against the illicit traffic in amphetamines by the former Bureau of Drug Abuse Control.

An analysis of the agency's statistics, spanning its approximately 2½ years of activity, shows that 44.2% of its arrests involved amphetamine drugs. The quantity of amphetamines removed from the illicit traffic has continued to increase. In FY 1969 our agency, as the successor to the responsibilities of the former Bureau of Drug Abuse Control, seized or purchased a total of 4,831,458 dosage units of amphetamine compounds. This increased in FY 1970 to 7,196,481, and again in 1971, our latest available figures, to 10,319,923 dosage units. Similar increases, though far more dramatic within the last fiscal year, are reflected in our seizures of these drugs as a result of our industrial compliance program.

The former law was found inadequate to the needs of effective drug law enforcement, and one of the first tasks which our new Bureau undertook was the design of new comprehensive legislation, now known as the Controlled Substances Act of 1971. In the course of developing this new law, the entire amphetamine problem was subjected to reexamination. A great many officials in all branches of Government were of the view that the dangers of amphetamine abuse had not been fully appreciated. This was supported by a growing body of medical opinion and clinical reports.

The new law divided controlled drugs into various Schedules designating Schedule II as the classification for the most dangerous drugs of abuse having some legitimate medical need but subjected to the most rigorous controls. The Congress placed amphetamines in Schedule III with the exception of liquid injectable methamphetamine but made it clear that administrative action reclassifying them into Schedule II would be expected if supported by the available evidence.

The Congress fully understood that inclusion of injectable methamphetamine within Schedule II could have only the most negligible effect on the problem. For example, in a sample of 3,808 speciments examined in our laboratories, none were found to be injectable methamphetamine from legitimate sources, and only 1.5% of the total were liquid methamphetamine from clandestine sources. By far, the more common practice is for the abuser to crush the pills or make solution from powder just prior to injection.

Beginning in October of 1970, our Bureau's Drug Control Division began collection of available scientific data while our staff attorneys simultaneously interviewed witnesses and began preparation of position papers. Thereafter, our findings, supported by nearly one foot of scientific papers, were forwarded to the Secretary of HEW requesting his concurrence. On May 26, 1971, we published our proposal for the transfer of amphetamines from Schedule III to Schedule II. Most of the amphetamines were rescheduled by a publication of the *Federal Register* on July 7, 1971. After vigorous negotiations between representatives of industry and our own Office of Chief Counsel, those remaining were rescheduled by publication on November 6, 1971, without contest.

The rescheduling of amphetamines has brought about the imposition of four

major regulatory controls which we believe will go far to solve the present problem. These are:

1. The subjection of all transfers of amphetamines, except to a patient, to the system of triplicate Order Forms which has traditionally been applied to narcotics,
2. The requirement of special permits for their import or export,
3. A blanket prohibition on the refilling of amphetamine prescriptions, and
4. The establishment of annual production quotas for the entire country.

Let me elaborate briefly on each of these points.

The triplicate Order Form system has been used with narcotic drugs since the passage of the Harrison Act in 1914. It requires that persons lawfully entitled to obtain narcotics from a supplier execute an Order Form in triplicate, a copy of which will be kept by the transferor and the transferee with a third copy being forwarded to our Bureau. This provides a separate record at both ends of the transaction and at our headquarters, which can be reviewed to enable precise accountability audits without excessive expenditures of manpower. It seems that the mere logical possibility of such a complete accounting has deterred diversion of narcotics for over 50 years. We have every reason to believe that the same result can now be obtained with regard to amphetamines.

The new export/import permit requirement will give us a much tighter control than the former Schedule III system which merely requires that we be notified of shipments in advance. Exports of amphetamines have been a major problem. We have found that drugs being legitimately exported from the United States often re-enter the country illegally. A classic illustration of this is the famous Bates Laboratories case in which approximately 1,200,000 amphetamine tablets were consigned to a non-existent firm in Mexico whose address turned out to be on the Tijuana Golf Course. I shall mention later an important case which we have just concluded which also illustrates this danger.

From now on companies engaging in such exports will have to justify their requests and obtain a permit. We are hopeful that the Senate will soon give its advice and consent to the new Psychotropic Convention which will place new international controls over amphetamines. It was my pleasure to have participated in the negotiation of this treaty as the official U.S. delegate. Compliance with the new international requirements would naturally be required before the granting of any export permits.

Until the rescheduling, prescriptions for amphetamines could be refilled up to five times within a six-month period. Students of the amphetamine problem are convinced that this has enabled significant diversion at the household level from medicine cabinets across the country. These prescriptions, and the ease with which they are refilled, have provided a common source enabling so many teenagers to begin their unfortunate careers of abuse. It has also helped to unwittingly create the extensive amphetamine dependence which has become so frequent among housewives and persons attempting to lose weight. The new restriction will mean that prescriptions can only be filled once. If the patient thereafter feels the need for more medication, the matter will have to be redetermined by the family physician. I might add in this regard that the American Medical Association by its resolution of June, 1971, fully supported this tightening of controls.

The imposition of quotas is also a restraint which has been traditional for narcotic drugs. Its purpose is to insure that no more of the drug than is necessary for legitimate uses, including adequate stockpiles, is manufactured. Ascertaining the extent of these uses cannot be done with absolute precision; however, the techniques traditionally applied for the purpose to narcotics can as easily be applied to amphetamines. Moreover, commercial and medical records and trend reports are becoming increasingly reliable.

It must be realized that within the nature of things it is impossible for the Government to investigate every reported transaction involving these substances. We have learned from hard experience that quantities of drugs manufactured in excess of legitimate requirements will, nevertheless, be disposed of. The temptations and pressures placed on the regulatory system in such a circumstance will inevitably result in undetected diversions. The concept of the quota system is designed to prevent this.

Our concern for tightening the regulations over amphetamines and our faith in the result which will thus be achieved is justified by all of the evidence. Although amphetamine compounds are clandestinely manufactured, it appears

that the bulk of those found in the illicit traffic are actually the product of what begins as legitimate enterprise. One of the few useful attempts which has been made to essay the extent of this diversion is the compilation by Dr. Greenwood of our scientific staff, a summary of which is attached. He concluded that perhaps 20% of our legitimate production is diverted into illicit traffic, and this would not include the socially significant diversion from the family medicine cabinets. At the present time black market amphetamines are selling at an average cost of 40¢ per dosage unit of $100 per thousand dosage units at a wholesale level. This contrasts with an estimated cost of from $2 to $10 per 1000 on the legitimate commercial market. Such inflated profits obviously constitute a great temptation and pressure on the existing regulatory system.

Beyond these efforts to quantify the probable percent of diversion, we have as further proof, a continuing series of criminal investigations showing conclusively that large amounts of amphetamines do in fact enter the illicit market from diversion. I have mentioned the famous Bates/Tijuana Golf Course case. In another typical case concluded as a part of our Operation Beacon, aimed at the upper levels of the pill traffic, we obtained 26,000 amphetamine tablets from a truck driver. His source turned out to be a physician with criminal associations whose records indicated a shortage of no less than 1,100,000 tablets within a nine-month period. In the recently concluded Operation Blackjack, of which more will be said later, 59 persons have been arrested in connection with illegal sales of approximately 1,000,000 dosage units of bifetamina, an amphetamine product of the Strasenburgh Company, referred to by drug abusers as "Black Beauties."

I have mentioned but a few of the more outstanding examples of the kinds of investigations with which our Offices of Compliance and Enforcement are constantly concerned.

In my testimony before you today, I am consciously placing emphasis on the problems of industrial regulations. This is not to mislead you into thinking that the possibility of clandestine manufacture of amphetamines is negligible. We are, in fact, anticipating a possible increase in this type of activity as a result of our new regulatory controls. Nevertheless, the evidence is clear that these illicit laboratories constitute the smaller part of the present problem. For example, we find that 64% of the stimulants which we seize and analyze are amphetamines although only 13% of the illicit laboratories seized produce amphetamines whereas 87% produce methamphetamine. Not only are commercially produced tablets and capsules found in great abundance in the traffic, but we know that amphetamine powder is often diverted from legitimate sources for use in illegal tableting operations as well.

I should now like to return to a more detailed consideration of our new responsibility for determining amphetamine production quotas. In establishing these quotas, the law requires that we take into account (1) the estimated medical, scientific, research, and industrial needs of the United States, (2) lawful export requirements, and (3) maintenance of necessary reserve stocks. With regard to the last element, we have determined by regulations that reserve stocks may be maintained at a level equivalent to 50% of the total figure appropriate for the first two elements. This formula is in accordance with the standards traditionally applied to narcotic quotas under international agreement.

In seeking to make determinations under the two remaining standards, we have considered all of the evidence which could be brought together in timely fashion. Let me recite for you some of the more significant points. First, there has been a marked downward trend in the amphetamine and methamphetamine production figures in the last several years. In 1968 this total dropped by an estimated 13% followed by a 9% drop in 1969, an 18% drop in 1970, and a 31% decline in 1971. This downward trend appears to have been accelerated by the reclassification of amphetamine compounds into Schedule II. Thus, the Gosselin prescription audit, a well-known and reliable prsecription index within the industry, showed a 17% decline in new and refilled prescriptions for the month of October, 1971, in contrast to the previous year. This decline has not recovered in succeeding months.

A sharper decline in medical requirements may further be induced by the distinct changes in medical opinion which are now in process. For example, a number of medical societies throughout the United States have asked its membership to eliminate all uses of amphetamines for treatment of obesity. By order

of August 8, 1970, the Food and Drug Administration limited the indications of amphetamines for obesity to short-term treatment only. Moreover, Government agencies which formerly purchased large quantities of these substances, such as the Department of Defense and Public Health Service, report that purchases for the coming year will be negligible.

Under Section 701(j) of the Comprehensive Drug Abuse Prevention and Control Act of 1970, the Surgeon General is required to report to the Attorney General on studies concerning the quantities of narcotics or other controlled drugs necessary to supply both normal and emergency requirements within the United States. In a letter of December 2, 1971, a copy of which is attached to my testimony, we received an estimate of legitimate need for amphetamines from the Surgeon General. He stated that the legitimate demands for amphetamine compounds have been reduced by 40% of the requirements for 1971 in view of the changes in recognized medical opinion and indications which have recently occurred. In view of the current declines in prescription refills, the issuance of new prescriptions, and in production generally, and further in light of the substantial diversion which we know to occur above the patient/consumer level, we concluded that the 40% recommendation was in accordance with our own most reasonable assessment of the evidence.

I shall not here suggest to you that a decrease of 35% or correspondingly of 45% could not have easily been justified. There is no magic in a precise figure other than the fact that one must somehow be derived. We have employed all of the traditional techniques in deriving our figure and have added to it every point of evidence available which could be brought together within a reasonable time. On December 4, 1971, we published in the *Federal Register* a proposal to reduce the production of amphetamines by approximately 40%.

We have now received a number of comments on our proposal. Several of these suggest that the reduction should have been greater, indeed much greater. But we note in examining these comments that they fail to recognize in their equations, uses for the drugs which are still accepted by the medical profession. This is particularly the case with regard to short-term obesity treatment. But for the continued recognition of this specific indication, a substantial further cut in the quota would be justified. In a moment, I shall speak further on this particular problem; but I should like first to point out that our quota proposal of December 4 will unquestionably be modified and further reduced as a result of recently concluded investigations.

Early in 1971 we became aware of the large-scale availability in the illicit traffic of the amphetamine product known as bifetamina manufactured by the Strasenburgh Company and incapsulated by its affiliate, Laboratorios Strasenburgh de Mexico. Moreover, we noted that this availability did not decrease as a result of the rescheduling of amphetamines. This led to the initiation of what we have called Operation Blackjack, in which eventually 1,000,000 tablets of bifetamina were obtained in undercover transactions. In an investigation covering twelve states, it was found that the drugs were entering the United States at six principal points along the Mexico/Texas border and thereafter being transported by truck throughout the adjacent southern and western region of the nation.

When the operation was finally concluded in mid-January, some few days ago, a total of 59 persons had been arrested. It was clear from collating all of the intelligence in this case that large quantities of the amphetamine produced by the Strasenburgh Company were being diverted after incapsulation in Mexico. We felt it unlikely, in view of the past managerial practices, that Strasenburgh could hereafter justify their retention of an export license for amphetamines. Moreover, since much of their production was based on this export business, we also felt that their request for a production quota was in part without justification.

On January 18 we served on the Company an order to show cause why their export permit should not be revoked and their requests for a production quota correspondingly reduced. On January 27 we were advised that the Company would not seek a renewal of its export registration. A further likely result will be an additional 9% decrease in the total United States amphetamine quota. In conclusion, two other facts are worthy of note: (1) this Company was the nation's largest exporter of amphetamine products, and (2) our investigation and subsequent actions have had the full support of the Mexican Government, which has agreed to investigate conditions at the Strasenburgh plant in Mexico.

At the present moment we are, therefore, anticipating that a quota for the production of amphetamines will be established at a level of nearly half that of the preceding year. We feel that this is an impressive rollback in the tide of amphetamines. This cut may well be followed by further reductions either in subsequent years or before the establishment of this year's quotas if there are further changes in medical indications. Some of the comments received do indeed suggest that enlightened segments of the medical community desire further cuts in production in view of the very limited uses of the drugs which they regard as legitimate. The Suffolk County Medical Society, for example, has requested that we hold public hearings on this question.

I mentioned earlier that in August of 1970 the Food and Drug Administration eliminated long-term obesity as an acceptable indication for amphetamines. We have called to their attention the comments received which are likewise critical of the use of amphetamines for short-term obesity treatment. It is no secret that the remaining needs for amphetamines, exclusive of obesity, could be met with a much smaller quota than that which we have proposed. I have been advised that the Food and Drug Administration is now assessing the changing patterns in medical thought and will advise us of their conclusions when time permits.

Our Bureau, of course, must take cognizance of established medical needs in determining drug quotas even if these needs do not represent the more enlightened views of medical leadership. We are confident, however, that the cooperation established by this Bureau as an enforcement agency with the other agencies of the Government concerned with medical matters will provide a sound base for the protection of the national welfare on this issue.

Mr. Chairman, I shall be pleased to respond to any questions you or your fellow committee members may have at this time.

STATISTIC TABLES

ANNUAL LICIT PRODUCTION OF AMPHETAMINE COMPOUNDS (IN KILOGRAMS)

	Calendar years		
	1969	1970	Estimated 1971
Amphetamine	16,548	14,575	9,356
Methamphetamine	8,444	6,087	4,926
Total amphetamine compounds	24,992	20,662	14,282

The average dosage unit strength for amphetamines and methamphetamines is 10 milligrams.

Using this dosage unit factor to the "Annual Licit Production of Amphetamine Compounds" produces the following number of dosage units available during the calendar years 1969 through 1971.

	Amphetamine	Methamphetamine	Total
1969	1,654,770,100	844,447,800	2,499,217,900
1970	1,457,459,800	608,733,200	2,066,193,000
1971 (estimate)	935,615,500	492,625,600	1,428,241,100
Dosage units per person in United States			
1969	8.2	4.2	12 4
1970	7.2	3.0	10.2
1971 (estimate)	4.5	2.4	6.9

BNDD stimulant activities—fiscal years 1969, 1970, and 1971

Stimulants removed from the illicit domestic market by BNDD:

Fiscal year:	
1969	[1] 4, 831, 458
1970	[1] 7, 196, 481
1971	[1] 10, 319, 923

BNDD domestic arrests of stimulant violators:

Fiscal year:	
1969	164
1970	145
1971	167

Stimulant seizures via compliance activities:

Fiscal year:	
1969	[1] 2, 090, 715
1970	[1] 4, 161, 945
1971	[1] 48, 128, 051

[1] Dosage units.

OPINION OF THE SURGEON GENERAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Washington, D.C., December 2, 1971.

MR. JOHN FINLATOR,
Acting Director, Bureau of Narcotics and Dangerous Drugs, U.S. Department of Justice, Washington, D.C.

DEAR MR. FINLATOR: In your letter of July 14, 1971, you requested a report from me regarding the medicinal and scientific requirements of the United States for amphetamines and methamphetamines for calendar year 1972.

Our scientists and physicians of the National Institute of Mental Health, the Food and Drug Administration, and other areas of the Department have studied this problem.

Included in the review was a study of past production figures as well as recent purchase figures for both amphetamines and methamphetamine. In addition, our scientists have attempted to assess the effects of recent changes in prescribing habits of the medical and scientific community as well as the impact of recent regulatory decisions and legislation on utilization of these substances.

More specifically, there is a markedly increased awareness by the medical community of the potential hazards of amphetamine therapy. Some medical societies have restricted the use of amphetamines. The Food and Drug Administration has required that these drugs be labeled for use in only three conditions and, moreover, amphetamine therapy for obesity should be for short-term periods only. Alternative therapies are available for these conditions and further review by FDA may result in additional limitations.

The passage of the Comprehensive Drug Abuse Act of 1970 has resulted in a decreased use of amphetamines. Also, the recent transfer of amphetamines to Schedule II means that prescriptions for those substances will not be refillable.

While data are incomplete on the incidence or prevalence of the conditions for which amphetamines and methamphetamines are indicated, the amounts of these drugs being produced at present appear to be substantially greater than clinical needs for 1972.

Therefore, I estimate and recommend that there be a 40% decrease in the amount of amphetamines and methamphetamine for medical and scientific use in 1972. This recommendation would be subject to upward or downward revision if clear-cut evidence of greater or lesser medical need should be presented to us.

Sincerely,

JESSE L. STEINFELD, M.D.,
Surgeon General.

6. Statement of Susanna McBee, Washington Correspondent for Life Magazine

U.S. SENATE SUBCOMMITTEE ON ANTITRUST AND MONOPOLY, JANUARY 23, 1968

Miss McBee. Mr. Chairman, my name is Susanna McBee and I work for Life magazine as a Washington correspondent. Knowing of your interest in the diet pill industry, I would like to relate my own experience with the doctors who dispense drugs for weight control.

Last fall, while working on an article about diet pills for the magazine, I wanted to learn firsthand about such doctors and what procedures they follow. So I went to various parts of the country and visited 10 doctors as a patient.

I should stress that I am not, nor was I last fall, overweight. I am 5 foot 5 inches, weigh 123 to 125 pounds and wear a size 10 dress. Before going to the doctors, I ate considerably more than I usually do and gained 5 or 6 pounds, but not enough to be considered a medical overweight problem. At each doctor's office, I gave my correct name but made up an occupation—usually secretary for a local firm—and a local address. When asked about my weight problem, I would say that I had lost some weight and wanted to lose more or that I wanted to trim off a few inches or that I just wanted to hold my weight down. All statements were true. The idea was to see what the doctor would do.

As it turned out, each doctor gave me pills, though I had not asked for any—and certainly did not take any. I collected 1,479 tablets and capsules from 10 doctors. Seven of them gave me pills to last for a month, two prescribed enough for a week, and one gave capsules for an undetermined period. Each doctor asked me to return for a checkup, but I did not. The prices I paid ranged from $10 to $40, and each doctor wanted payment immediately.

The first doctor I visited was an osteopath, Dr. Edward A. Devins, whose office is on the third floor of the Altman Building in Kansas City, Mo. When I arrived, a dark-haired girl in a white dress told me to fill out a form, which was called the Cornell Medical Index Health Questionnaire for Women (copyright 1949). It had 195 questions that are to be answered yes or no, starting with questions about eyesight, hearing, nose and throat conditions, chest, heart, breathing, and various past illnesses. One of the questions, I recall, asked, "Were you ever treated for 'bad blood' (venereal disease)?" The last 50 questions dealt with mental problems and included such queries as: "Do you feel alone and sad at a party?" "Do you usually feel unhappy and depressed?" "Do you often cry?" "Are you always miserable and blue?" "Does life look entirely hopeless?" "Do you often wish you were dead and away from it all?"

After I finished the questionnaire, the girl in the white dress read it over and asked if I were allergic to medicine, if I were nervous, and what was the most I had ever weighed. She weighed me with my clothes and shoes on, and I came to 130½ pounds—possibly because I had eaten a heavy lunch. She told me I should weigh 120 to 125 pounds and added, "We will get you down to 120." She took my blood pressure, pulse, and measurements. Then she said, "I am going out now and prepare your medication."

In a few minutes Dr. Devins came into the room, holding a box of pills and a small plastic vial. I was surprised that he had gotten the pills before he had even seen me. He did not examine me himself. He told me I may not feel good or bad after taking his medication but that I would feel different because, he said, "After all, you are on diet medicine." He asked a few questions based on my responses to the health questionnaire and showed me some printed instructions, which under the heading, "Your Eating Habits" began, "Please do not follow a diet." It did name certain foods to emphasize and others to avoid. Dr. Devins told me, "We do not advise going on a diet." He read me the instructions on my pillbox, which contained 140 tablets—56 pink ones and 28 each of browns, tans, and grays.

I later had the pills and those given to me by the other doctors analyzed by a chemist, Dr. J. William Magee, who owns the Chemistry and Industrial Security Co. at 4250 North Fairfax Drive, Arlington, Va. Dr. Magee, by the way, was formerly senior advisory chemist for the FBI, where he was employed for 27 years until he retired in December 1965. His analysis showed that Dr. Devins' pills contained amphetamine, laxative, and thyroidlike material.

Dr. Devins had said, "If you are nervous now, the pills will make you more nervous. If you are not nervous, they will not make any difference." He appar-

ently was talking about the amphetamines, which are sometimes called pep pills. He said I might not sleep too well with the pink pills—which were the amphetamines—but not to worry about it. I asked him what was in the pills and he did not tell me, but said the pinks would suppress the appetite, the browns would help keep me from being constipated, and the others would work with the pinks to reduce me. He directed me to the receptionist and I paid $10.

My next visit was to the Rubel Medical Building in Decatur, Ill. When I arrived at 8:40 a.m., just ten minutes before the clinic had opened, there were 15 women and two men already in the waiting room. A nurse called my name, in turn, over a microphone and gave me a one-page, 136-question form to fill out. It asked about my current physical condition, past illnesses, and eating habits. After I completed the form, I noticed several women go beyond the reception desk, apparently for their monthly checkup, and come out again, picking up a white sack of pills at the desk—all in less than 5 minutes.

The clinic is run by Dr. L. L. Rubel, a doctor of osteopathy, who has four other osteopaths working there for him. When I was there new patients took the following tests after being weighed and measured: Blood pressure, pulse, urinalysis, blood sample from a finger, an electrocardiogram, and an ankle-jerk test performed by a machine called an Achilleometer. The technician asked me to sit on my knees on a cushion beside the machine. She wired by left foot and told me to hold onto the bar in front of me. She then tapped my Achilles tendon with a small instrument. The meter indicator on the machine jumped into the middle range of the scale, and the technician said this would determine how heavy a dose of their medicine I could take. I asked how much the machine indicated. "An average dose," she replied. "Of which medicine?" I asked, and she said, "Of all our medicine."

Afterward I was given two printed forms. One announced, "You have just been checked by a machine designed to record an indication of your endocrine gland system balance." It said the same information could be obtained by a group of blood tests, "but these would require not only puncturing your vein to draw a blood sample but also a week or so of time until we receive the laboratory report." The other printed form told me about the electrocardiograph tracing and assured me, "The treatment that you will undergo for your weight will be beneficial to your heart."

Dr. William K. Franta, one of the osteopaths working for Dr. Rubel, summoned me and said, "You are not really overweight." He reviewed my tests, which came out normal, and my weight, 129½ in clothes. He asked if I took any medicine. "Just vitamins," I said.

"Well," he said, "we will give you our own vitamins so you will not have to take the others if you do not want to." He wrote a prescription and I asked what the pills were. He said one kind was a gland substance and the others were vitamins and minerals. The chemical analysis later showed that the gland substance was thyroid. Dr. Franta made no effort to examine me himself. He did not, for example, listen to the heart or feel the pulse. Instead, he gave a little talk saying weight control is a matter of glandular balance. He said that since I was in the normal weight range—119 to 129 for my height—I might not make too much progress. We would try the pills for a few months and see how I do. I should avoid milk and any kind of colas, and if I eat between meals, I should not take solid food but liquids like buttermilk and soft drinks. He said I might not lose weight the first month but would lose inches.

Dr. Franta spent 3 to 4 minutes with me. He handed me the prescription and told me to drop it in the wicker basket at the front desk. When I did, the office manager put it on a dumbwaiter behind her, and it was lifted upstairs. Shortly, three small envelopes inside a white paper bag slid down the pulley. I paid $15 and was told that succeeding visits would cost $10. When I opened the bag, I found 84 pills—28 each of vermilion-colored vitamins, magenta-colored vitamins, and lime-green thyroid. There was also a brochure explaining the Rubel program. It began: "Overweight or obesity is a very common disorder which can be corrected without dieting."

When I telephoned the office of Dr. C. C. Mendenhall of Gardena, Calif., the first thing the girl said was that the visit and medication would cost $15. That would be cash, no personal checks, she said. When I arrived, the girl at the desk asked me to sign a form saying I agree to pay cash only for my first appointments. I asked if that means all succeeding appointments and she answered, "Yes."

Another young woman led me to a small room with an ankle-jerk machine. While it warmed up, she quizzed me about my physical condition, including the state of my liver and spleen. She said I looked slim and asked what I wanted to weigh. I was then 132½. I said I wanted to weigh 120 to 125. She tapped my Achilles tendon, measured me, and took my pulse and blood pressure. She gave me a brochure which urged patients to follow a high-protein, low-fat diet, and she told me not to eat fried foods, salad oils, or soft drinks.

Dr. Mendenhall listened with a stethescope to my heart in two or three places, felt the front and back of my neck and checked my ankles for possible swelling. I asked how much a person of my height and build should weigh.

He said, "It would not do any good to tell you because you people are not going to get down to the weight you weigh anyhow." He was consigning me to the ranks of the impossibly obese, I assume. He said he was just trying to get people down to a weight where they would be happy. "I am not trying to reform the world," he said. "Very few fat people get down to their ideal weight and stay there."

I asked about the medication, and he told me I would be getting an appetite depressant, a laxative to take if I needed it, some protein, thyroid, and something for my hips, which I had said I wanted to reduce. I asked what the hip medication was and he replied, "My own preparation."

His literature recommended that patients get a complete physical checkup from their own physicians. He later mailed an announcement that as of January 8, 1968, his services to new patients would include a history and physical exam, electrocardiogram, urinalysis, and blood tests, including a PBI (protein-bound iodine), which checks a patient's thyroid condition. The price would be increased from $15 to $40, and each succeeding visit would be $20 rather than $15, the announcement said. The same terms applied: cash in advance, no personal checks.

I counted my month's supply of pills from Dr. Mendenhall—364. Had I followed his program, I would have taken 12 a day, 13 if I included the laxative. The chemical analysis showed that the other pills were—besides protein, thyroid derivative, and laxative—ampretamines and barbiturates and prednisone, an antiinflammation hormone.

The next day I went to the office of Dr. Raymond A. Landis, D.O., in Los Angeles. The receptionist had informed me over the phone that the fee would be $17. A technician weighed and measured me (I was then 131 pounds) and asked about my medical history in a series of questions that she read from a blue folder. She assisted a doctor who drew blood from a vein in my right arm, then directed me to the office of Dr. Myron F. Babcock. (Dr. Landis apparently was out.) Dr. Babcock gave me the ankle-jerk test, felt my right arm, and said, "You are not overweight, Honey." He gave me a 10- to 15-minute lecture on diet. He was very much opposed to milk and told me I should have stopped drinking it at age 1. He said milk has fat but not anything else I would need. He also opposed eating grains (cereals) and bread. He wrote in red a list of foods to avoid and in blue the foods I could eat.

He said I could cheat once in a while because I did not really have a weight problem. But he added that I was lucky I had caught the problem in time. He prescribed pills, and when I asked what they were, he said, "Things to make you lose weight." I persisted, and he said one would be a "thyroid-acting substance—something you could put young children on." I received a 28-day supply of 84 pills—pink, dark green, and cream colored. They were, according to the chemical analysis, an unknown, a thyroidlike material, and an amphetamine.

In San Diego, I saw Dr. Orville J. Davis, whose waiting room has an isinglass partition with a sign saying that the press and Wilbur J. Cohen, the Under Secretary of Health, Education, and Welfare, "have deceived America into socialized medicine." In the back room and in another waiting room there were some John Birch Society Publications: American Opinion and the Review of the News.

After filling out a questionnaire like the one I saw in Dr. Rubel's office, I was told to read a 10-page mimeographed notebook about Dr. Davis' program. It began, "Welcome Aboard."

"First," it went on, "if you are not overweight by average standards I do not want you to waste your money and my time with even an initial visit."

It said the average standard is computed by allowing 100 pounds for the first 5 feet and 5 pounds for each inch above that. At 5 feet 5 inches I should weigh

125. That day with my clothes on I weighed 130. Dr. Davis' instructions concluded, "I do not consider you to have any medical overweight problem at all unless you are 15 percent over your average weight." I was 4 percent over; so I expected Dr. Davis to dismiss me forthwith. Before I saw him, I went through his physical examination procedure: urinalysis, blood drawn from the vein in my left arm, weight, measurements, blood pressure, pulse and electrocardiogram—all handled by technicians. When I did see him, Dr. Davis seemed tired. He kept yawning throughout the consultation, which lasted about 2 minutes, and he did not examine me himself. He scanned my electrocardiograph and said I was in "great shape." He checked my health questionnaire and asked how many cocktails I drink each week. I said two or three at a party, and he stressed that I should limit myself to two or three a week.

He, too, said that I had no weight problem, that I should weigh 125. I said I wanted to lose inches around the hips and he replied that the extra inches were due to a need for estrogen and progesterone, which are sex hormones. He gave me some material to read on weight control. It advised eating proteins and avoiding sugar, starch, and fat. "Breakfast cereals," it said, "should be out, out, out." There was also a 1-page form for us to read when we reached our desired weight. It said, "Congratulations. You have reached your goal. You make yourself look good and that makes me look good." It added that to keep weight down, the patient should check the scales every day. If she is at or below the weight she wants, she should not take the daily medication. If she is 1 ounce over, the form advised, she should take the full dosage for the day.

Dr. Davis, who had just said I had no weight problem, nevertheless wrote a prescription. He told me to get it filled in his back office and said I should feel good taking the pills. If not, I should call him. He asked me to come back the next month. I paid the girl at the desk the $40, including $25 for the lab work, and picked up my sack of pills—234 of them in pink, purple, green, yellow-orange, white, and orange tablets. According to Dr. Magee's chemical analysis, they were vitamins, potassium-chloride diuretic, thyroid, more vitamins, desoxyephedrine (a nonamphetamine appetite depressant), and progesterone.

In Denver I tried by telephone to make appointments with two M.D.'s who are weight specialists, but their receptionists told me that business was so brisk I would have to wait a few weeks. I did get an appointment with Dr. Charles William Breitenstein, an osteopath. Signs in his waiting room and office said "Office calls cash." The elderly doctor weighed me and took measurements. He made no effort to examine me, even to check blood pressure and pulse, and asked no questions about my heart, allergies, general health, or whether I was already taking any medication. Since I weighed 132 with clothes on that day, I asked him what I should weigh. He pointed to a chart on the wall which said a woman of my height with a slight build should weigh 130 and if she has a medium build, 139. The doctor seemed to think I have a medium build, which meant I was 7 pounds underweight. But he insisted he wanted to take pounds as well as inches off me. He gave me a 28-day supply of pills—pinks, greens, and creams—but when I counted them, there were only 27 creams, making a total of 83 pills. I assume he had miscounted. The chemical analysis showed two of the pills to be desoxyephedrine and one to be thyroidlike material.

Dr. Breitenstein told me the monthly fee would be $12. He also charges $12 for each monthly visit thereafter, he said, because it "saves a lot of bookkeeping." He said that some patients who had been coming to him for a long time, pay him 6 months to a year in advance.

In Hillsboro, Oreg., which is about 17 miles west of Portland, I went to the office of Drs. Chester M. Rasmussen and Duane A. Thompson, D.O., where a sign at the reception desk said, "Cash will be appreciated for all weight reduction treatments."

A woman in a white dress, wearing glasses, check my hemoglobin—or she tried to. She jabbed the side of my third finger, right hand, but could not draw enough blood. She labored diligently, rubbing my finger and trying to push something, anything, out of the capillary, but the yield was meager. She apologized and tried the third finger, left hand, but only a drop or two came. She was very flustered at this point and began jabbing my middle finger, right hand with the same result. She kept saying, "You just do not know how sorry I am," but she did not know just how sorry I was. Finally, after more futile rubbing, she asked another technician to help. That woman noted that the tip

of the finger, not the side, should be punctured. She demonstrated on me, and it worked; there was a lot of blood.

The first women, still apologizing, resumed the testing—urinalysis, ankle-jerk, pulse, blood pressure, measurements, weight. I weighed 131¾ pounds. The everhelpful woman in white said, "Next time do not wear such heavy clothes and you will be encouraged by your showing on the scales." Then she asked about my medical history and wanted to know if I had any swollen extremities—hands, feet. I told her I had some swollen fingers.

At each point where I indicated that I had no medical problem, she said, "real good." She concluded that I was "real slim" and should have no problem losing weight.

After she left, Dr. Thompson came in, read my chart, said I was normal according to the tests, and warned that I would have trouble keeping my weight below 125. He said he did not want to make me look like Twiggy. He told me I should take progesterone every 3 days, dissolving the tablet under the tongue, to reduce my hips. Once I got down to my desired weight, which should take only 6 weeks, I would be put on a "maintenance" regime of pills, he said. He discussed my diet, saying I should have three good meals, including dessert at lunch, but a lighter dinner, sometimes with dessert.

As I was waiting to collect my pills, I heard the receptionist answer the phone and say, "No, I am sorry, we do not mail pills any more. Yes, we used to, but we do not any more and we do not know if we ever will again." She asked the caller to come to the office.

She collected $15 from me and gave me a sack with 268 pills—purples, yellows, blues, greens, whites. The analysis showed them to be a nonthiazide diuretic, progesterone, barbiturate, thyroid, amphetamine, potassium-chloride, diuretic, and digitalis.

All the doctors I had seen so far gave pills to last 28 days. I decided to visit the Manhattan office of Dr. Gordon L. Green, M.D., whose patients return each week for checkups and pills. Dr. Green has 19 offices in New York, most of them in Long Island. His operation is a shining example of machine-age medicine. The receptionist told me to listen to a tape recording while I was waiting for the doctor. The tape, which took about 15 minutes, said, I have been in medicine 30 years and have had a weight control practice for 20 years. It said the pills given do not affect any illness you might get one way or the other. What this medicine does is count calories for you. The voice said to read the booklet I was given called "Suggestions for Losing Weight," but not to pay too much attention to it. You can lose weight without pills, the tape said. But, you came to me for an easy way to reduce. My method will make it easier for you. If you are hungry, eat; if you are not, do not.

After listening to the tape, I asked the receptionist where Dr. Green was. She said he was not in any of the 19 offices. "He just runs the business." I asked if that voice on the tape was Dr. Green's. "Oh, no," she replied. "We got a disc jockey to do that."

She weighed me (129 with clothes on), took measurements, and asked about my medical history. She took a plastic box of capsules and tablets off a shelf and directed me to the doctor's office, where she put the pill box on his desk. The doctor introduced himself as Dr. Provenzano. He checked my blood pressure, listened to my heart, asked some questions about my medical history, then explained how I should take the pills which the receptionist had put on his desk. I received 46 pills for the week. They were amphetamines; barbiturates; combinations of barbiturates and amphetamines; combinations of barbiturates, amphetamines, and thyroid; combinations of amphetamines and thyroid; vitamins, and thiazide diuretics.

I was sent back to the office where the tape recorder played, and a blond woman in a white dress explained the schedule for the pills, stressing that I also should take tomato juice at each evening meal. I paid her $19, and she said the next visits, each week, would cost $7.

I took a Life magazine photographer along as a witness to my visit to Dr. Julius Seymour Siegel, an oestopath, in Falls Church, Va. Earlier I called his office, and the receptionist said, "You do not make an appointment. You just come in."

We just went in, and the women at the desk, whose sign said "secretary-nurse," did not take my name but asked me to wait my turn. Five women and two men were ahead of me. In 15 to 20 minutes they had taken their turns

and were out of the office. Each time anyone was to the doctor, the secretary-nurse would call out, "Next." When the photographer and I went in, Dr. Siegel did not ask our names. Instead, he asked me, "Well, now, what is the problem?" When I said I wanted to lose weight, he put me on the scales. They registered 128¾. "Aha," he said, "you weigh 129 and you ought to weigh 115." I asked how he could tell, and he replied, "By the size of your arm."

He told me, "You can eat and drink anything you want. All you have to do is take the pills I am going to give you." He took my blood pressure and pulse rate and listened with a stethoscope to my heart. "Ah perfect," he said. He asked no questions about my medical history, any current illnesses, any allergies to medicine, whether I had taken diet medication before. He gave directions on taking the capsules, three a day until I dropped to 115, then one a day as maintenance medicine. He picked up a wall phone that was a direct line to the pharmacy, the Falls Church Drug Center. He told the other party on the phone he wanted pills for—he then paused, turned to me and said, "Hey, what's your name?"

When he hung up, he gave me directions to the pharmacy, a few blocks from his office. I paid the secretary-nurse $3 for the office visit and asked if I could get the prescription filled at my own pharmacy. "Oh, no," she answered. "You must go to the Falls Church Drug Center."

I was in and out of Dr. Siegel's office in 3 minutes. I went to the drug center, received two bottles of 150 orange and gray capsules, and paid $7.50 for them. They contained barbiturates, amphetamines, and thyroidlike material.

If Dr. Siegel had the record for short office calls, Dr. Harry Needelman, an M.D., of Miami Beach, Fla., held the record for long ones.

I asked his receptionist if the Life photographer, who was posing as my husband, could come with me. "Sure," she said. "We will be glad to let him go through the factory, too. Ha. Ha."

While I was being weighed—130¼—measured, and tested—blood pressure, temperature, hemoglobin, urine—the photographer was directed to a small auditorium with a sign "doctor's office" on the door. The doctor's crescent-shaped desk was on a platform a step higher than where the patients sat. His desk had a camera for taking before and after pictures of patients, a tape recorder, and a rotary slide projector. Three of us patients had settled into the audience chairs when Dr. Needelman, a small, overweight man who appeared to be in his midfifties, took his place at the big desk and told us we could, if we want, eat six turkey sandwiches a day. "Does not that sound like a fairy tale?" he asked. All we had to do was follow his advice on eating the right foods and we would lose 5 to 7 pounds the first week and 3 to 5 pounds a week thereafter. Then, amazingly enough, he called each of us up to his desk, one by one, and discussed our individual case in front of all the other patients. I listened, for example, as he interviewed one woman who loses weight under his program but gains it back when she returns to New York. She had been going, off and on, to Dr. Needelman for 4 years. When she first came, her weight was 128; it was now 148. I asked her later about her downhill progress, and with the loyalty fat patients seem to feel for their weight doctors, she said, "Dr. Needelman can't help it if I am a pig."

It was then my turn to step up to the doctor's desk. "You are a young woman," he told me. "Would you like to get down to 120?" I said that would be fine. He promised to get me down to that in 2 weeks, then put me on a maintenance program of one pill a day for a month. In front of everyone, he reviewed the state of my kidneys, hemoglobin, and blood pressure. He listened briefly to my heart and asked about any swelling. But he took no medical history. I stepped down.

He proudly announced that what were about to see was "the longest running show in the world," that he had been giving the same lecture, with variations, for 14 years. "Now," he said, "we will put our little show on the road." He flicked on the tape recorder and sat silently as his voice came down at us from a loudspeaker in the ceiling.

The tape went on and on and on. This is a hydrating diet, it said. The more water you drink, the more weight you lose. At this point, the real Dr. Needelman walked out of the room. In marvelous synchonization with the type, the slide projector flashed on and, for what must have been 20 to 30 minutes, we saw before and after pictures of patients. The voice would name the patients and tell where they work. It mentioned a local lawyer, shoe salesman, grocer,

hotel employee, even a local bookie. "You see, I give all the local businesses a little plug," explained the voice. It told us, "The water faucet in your home is your fountain of youth. Drink 12 to 20 glasses of fluid a day. With my pills, you can eat 3,000 to 4,000 calories a day and lose weight. You can have snacks, but only those that convert in your bodies to just 1 teaspoon of sugar." The recorded lecture lasted more than an hour. Then the real Dr. Needelman continued it in person, allowing questions from the audience, asking himself questions, answering them, and reviewing what he had already said. "Aren't we having fun this afternoon?" he asked us. He kept calling himself the "talk-ingest doctor in the world."

Finally, it was time for our weekly shot, which he explained only by saying it was the first gear in revving up our body machinery. I was reluctant, but took it after he said, "Try it this time. If you do not like it, you will not have to take it next time." I also received 26 pills for the week and paid $15. A sign on the reception desk advised that after January 1, of this year, prices were going up: $20 for the first visit and $10 a week thereafter. Dr. Needelman told us our capsules contained thyroid, adding that he would be able to determine the following week if we were getting the correct dosage. The capsules also contained, according to the chemist, Dr. Magee, amphetamine and laxative. I also received barbiturates and thiazide diuretics.

Dr. Needelman's "show" was then over. I had lasted 3 hours and 15 minutes.

Among the doctors I visited, there was no consensus on diet. Some said to eat anything you want; others offered elaborate programs, to the point of including several recipes in their talks or literature. They did not agree on the value of exercise. Dr. Davis, for example, favors it; Dr. Needelman says it is unnecessary for weight reduction. The doctors did not agree on whether, or how much, liquor should be consumed. They would not tell in any detail, even when asked, what was in their medication. Their physical examinations ranged from several tests to virtually none—just weight and measurements. The only consensus seemed to be that, whether I was overweight or not, I needed pills.

Mr. Chairman, I have been subponaed to testify before your subcommittee, but I am doing so willingly in the hope that it may aid your investigation.

Senator HART. Miss McBee, thank you for a narrative that is understandably, I think, surprising. Just to nail it down, how many doctors did you see?

Miss MCBEE. Ten doctors.

Senator HART. And at no time did you weigh more than 135 pounds?

Miss MCBEE. No. No, I did not.

Senator HART. And on some occasions you weighed in the 120's?

Miss MCBEE. Yes, I did.

Senator HART. And no doctor advised you that you did not need pills?

Miss MCBEE. Some said that I was not overweight but they nevertheless gave pills.

Senator HART. A fuller understanding of the testimony, I think, would be served if the Senate had ever gotten around to permitting its records to be printed to include photographs of witnesses. And at my age I would not undertake to describe for the record your appearance.

Mr. CHUMBRIS. Jim Schultz. He is single.

Senator HART. But as a layman, I would say you would be one of those least likely to be suggested as a potential patient for figure reform.

In any of these visits, was the question asked you—since these fellows or their nurses were in the process of giving you pills—if you were being treated by any other physician?

Miss MCBEE. No, sir.

Senator HART. You told us that you received a total on these 10 trips of about 1,500 pills. You gave us the technical names for them as the chemist to whom you referred them for analysis reported to you.

If a patient were shopping around, and really had a weight problem, is not it possible that by going to doctor after doctor and collecting 1,479 tablets he could destroy himself?

Miss MCBEE. I found that it was—that it seems to be quite easy to get pills from these doctors. I suppose if one might be addicted to any one of them, that it would also be easy.

Senator HART. As the father of a large family, all young, I have heard something about amphetamines, and the trips they are said to send you on.

If you waltzed around to 10 doctors and picked up that much amphetamine,

in addition to losing weight, could you not also find yourself on a dangerous trip?

Miss McBee. I have heard, sir, that that does happen to certain people. I have also heard that if anyone has a tendency to be nervous, these pills are devastating.

Senator Hart. I missed that last.

Miss McBee. I said that I have heard that if someone is nervous and takes these pills, it can be devastating.

Senator Hart. Yes. I remember in your testimony one physician did suggest that if you were nervous, taking the pill might increase the nervousness.

Miss McBee. That is right.

Senator Hart. A layman might say that is an understatement.

The testimony indicated that some of the pills were thyroid pills. Did any physician suggest to you that you had a hypothyroid condition?

Miss McBee. No, sir; and the few tests that I did receive indicated that my thyroid situation was normal.

Senator Hart. After a few years of life, we have all been run through physical examinations. As a lay person, do you feel that you were given what we understand to be a thorough physical examination by any of the 10 doctors?

Miss McBee. No, I do not. I am not an expert and I cannot make that kind of judgment. I have talked, though, to experts—cardiologists, endocrinologists, and internal medicine specialists—and I have discussed the tests that I did undergo and none of these experts thought that I had received an adequate examination, particularly not a complete heart exam, which I should think would be essential given the possibility that many of these drugs can seriously affect the heart.

Senator Hart. In the cases of those doctors whose printed material or whose statements to you indicated that you were not overweight, but who nonetheless gave you pills, did you say to them, "What gives here? This document that I pick up that you gave me says I am not overweight. Why do you give me pills if that is true?"

Miss McBee. No. I did not do that, sir. I did ask what the medication was. In most cases, the visits with these doctors were so short that you are really sort of pushed in and pushed out and you do not have all that much time to ask questions.

Senator Hart. That last visit you describe, I would say, on the basis of the meter, that he undercharged for that. You had 3 hours with one of them, but you did not push this point.

Miss McBee. I asked about the shot, what it was, would I really need it, and he said, well, take it and if you do not like it, you will not have to take it next week.

Senator Hart. How did you like it? Did you feel better ?

Miss McBee. No, sir. I had a terrible time sleeping that night.

Senator Hart. Did you know what the shot contained or consisted of or comprised?

Miss McBee. No, I do not.

Senator Hart. Your statement has a whole series of points that one would think we ought to verify, and I would encourage staff to do it. I will restrain myself. Let me ask a general question first. In how many of these visits were you asked to pay your fee in cash?

Miss McBee. I would say in most of the offices there was either a sign or a strong indication that you were to pay in cash. However, in a few of the offices, maybe three offices, I saw women writing checks, so I assume that if you are a longtime patient, that possibly they do accept checks.

In the first office I went to there was a warning that you would be in trouble if your check bounced, so I assume they did accept checks.

Senator Hart. So, it would not be fair to assume that the reason for the insistence on cash was related to Internal Revenue. It could be that they had disappointing experiences in clearing checks of patients who felt that had a fat problem.

Miss McBee. It could be, sir. I do not know.

Senator Hart. It leaves the question open.

Miss McBee. I would say so.

Senator Hart. In one case the sign said "cash will be appreciated for all weight reduction treatment." Why would the insistence on cash be directed

toward the patient with a weight problem rather than the one with something else?

Miss McBee. I do not know. I assume the doctors in this case were making a distinction between weight patients and other patients. I assume that they do have patients who come to them for other problems. Although for most of these doctors, I would say the bulk of their practice is weight control.

Senator Hart. Your testimony indicates that in every case, you were given both barbiturates and amphetamines?

Miss McBee. No. I think there were some cases where I received a non-amphetamine type of appetite depressant rather than amphetamines, but certainly amphetamines were the most popular pill among the 10 doctors. Frequently when I received the amphetamines, I would get the barbiturates, I would assume, to counter any nervousness or insomnia that the amphetamine might cause.

Senator Hart. In how many of those visits where you were given both were you given explicit warning concerning the use of alcohol when you were taking the pair of them?

Miss McBee. Alcohol? In no case.

Senator Hart. Here again, the laymen just have to go on what they are told by the professionals, but I am told that the mix is a very dangerous one. Normally, caution is voiced when the combination prsecription is given.

Miss McBee. No; I do not recall any such warning.

Senator Hart. Maybe the information developed on your medical history showed that you did not drink and, therefore, they did not have to caution you.

Miss McBee. No. I answered the questions honestly.

Senator Hart. Mrs. Goodwin, I am sure, has questions and will be much more informed with respect to the professional problems than I am.

Mrs. Goodwin. Thank you, Mr. Chairman.

Miss McBee, I envy your figure. How much do you weigh now?

Miss McBee. I weighed 125 this morning.

Mrs. Goodwin. That is a good weight. Did you take any of the pills?

Miss McBee. No; I did not.

Mrs. Goodwin. You saw one doctor whose office girl told someone over the telephone that they no longer mailed out pills. In other words, you got the impression that one of these doctors had been in the practice of mailing pills to patients without actually seeing them.

Miss McBee. Well, that is what her conversation would indicate, I believe.

Mrs. Goodwin. You referred to Dr. Mendenhall and your visit with him. He referred to one of the products as his own medication. Do you know what that was?

Miss McBee. I assume that was the prednisone, the hormone.

Mrs. Goodwin. The clinical analysis showed that was prednisone. You are aware, are you not, that that is a very common drug. It can be obtained from any number of sources.

Miss McBee. I understand it has many uses. For arthritis, I think, is one.

Mrs. Goodwin. Did he tell you what this product would be used for in your case?

Miss McBee. No. He did not mention the name of this drug at all and he gave no special information about it.

Mrs. Goodwin. In another case you mentioned that the doctor told you that some of his patients not only paid cash but they paid 6 months in advance. Do you know what that is for? What did they pay for in advance?

Miss McBee. Well, I do not know. I guess he just assumes that these people are going to keep coming back and coming back to him. He did say that he just charges a straight $12 for everything because it aids his bookkeeping.

Mrs. Goodwin. You know that most of these doctors gave you amphetamines, which is an appetite-depressant drug. Did any of them tell you that you can build up a tolerance to this drug in from 6 to 8 weeks?

Miss McBee. No. No one said anything about that.

Senator Hart. Mr. Chumbris?

Mr. Chumbris. Thank you, Mr. Chairman.

Miss McBee, may I read just one sentence from the Life magazine that came on the stands yesterday, not from your article but from the front page of Life magazine, and I quote:

"Of course, some 'fat' doctors check patients carefully and do not prescribe pills excessively."

And in fairness to them, I would like to ask you a few questions for clarification of the record.

First, how did you arrive at the 10 doctors that you selected? Any particular schedule?

Miss McBee. Well, in various ways. Sometimes I would just look in the yellow pages of the phonebook and some of these doctors advertised themselves as such specialists. Sometimes in talking to local doctors in the community, local medical societies, I would say, "Who are the biggest in this field? Whom have you heard of?" And I would get a list of names that way.

Mr. Chumbris. Thank you. In your statement, you note: "It did name certain foods to emphasize and others to avoid. Dr. Devins told me 'We do not advise going on a diet.'"

I have been advised by those who are in the category of the sentence that I just read to you that they give to the patients a list of foods that they should eat and which foods they should avoid. Have you seen that list?

Miss McBee. Some of these doctors that I went to had material on diet and as I mentioned in my account of Dr. Green, for example, he gave a little brochure, but then the tape recording said do not pay much attention to it, it is not a bible. But others, you know, to be fair to them, did talk at great length about diet. Dr. Babcock, I believe, in Los Angeles, for example. So, I think what you can conclude here is that some of them prescribe a diet along with the pills. Others just seem to put their faith in the pills.

Mr. Chumbris. You noted that one doctor stated: "He gave me a little talk saying weight control is a matter of glandular balance."

You mentioned you only saw 10, is that right, and you have listed all of the 10 that you have seen. Are there any others that you have seen that you have not mentioned in your magazine?

Miss McBee. I have talked to the spokesmen for the American Society of Bariatrics who, in our discussion, I think, agreed pretty much with my conclusions, who said that there is an awful lot of unethical practicing going on in this field but that he believes that their society, which I think consists of 250 or 300 doctors, is trying to raise standards and is trying to give careful physical examinations. That is why I put that in the front page of the Life article. And I asked him if he ever had patients, for example, that he did not give pills to, but just offered diet, and he said, yes. So I assume that there are some who did this.

Mr. Chumbris. Yes. Thank you.

Mr. Chairman, as you know, in some of these hearings it has been my custom to try to see one or two people in the field to get a grasp of the overall background of these particular hearings, and the gentleman that I saw was Frank W. Barr, M.D., in Charlotte, N.C. I went to him because he was the closest to Washington of the several doctors that were mentioned as experts in this field. And first, Mr. Chairman, if you have no objections, I would like to submit for the record a book that he gives each of his patients, "Instructions for Acquiring and Maintaining Healthy Nutritional Habits," with an explanation, and then he lists the various foods that you should eat, the various foods that you should not eat, and, if there is no objection, I would like to have that printed in the record.

Senator Hart. I would have no objection.

I understand the doctor to whom you spoke is going to visit the staff here. It may well be that he would be able to review this, but there is no objection to introducing it.

Mr. Chumbris. Yes. I particularly avoided the three doctors who were going to be witnesses at these hearings. We will let them speak for themselves. I understand that Dr. Barr, if the subcommittee so desires, might be willing to testify.

Senator Hart. It might be that his reaction to the full record will be very helpful.

Mr. Chumbris. In talking to Dr. Barr about the cause of obesity and how to treat it, he felt that he had to treat obesity for the disease and not necessarily the symptom. In other words, he says there is no use giving a man an aspirin for his headache if he has a brain tumor. You have got to treat the brain tumor. And his main point was that those who are obese have an imbalance in their glandular metabolic composition. The doctor's job was to correct that imbalance.

We have to get medical testimony on that because I am sure none of us up here could determine whether he was telling the facts as they are or whether there is a dispute in the medical profession whether he is right or some of the others who may testify are correct.

Miss McBee. I think, sir, there may be a dispute. The endocrinology experts and some of the nutrition experts whom I talked to dispute the claim that obesity is caused in most cases by an endocrine imbalance. The experts whom I talked to contend that that is not the case in the vast majority of cases.

Mr. Chumbris. I do not want to quote too much from Dr. Barr because he may be here. But Dr. Barr was a general practitioner in Charlotte, N.C., for many years, and during the course of his practice he had people who were obese, whom he treated with the accepted formula that most general practitioners use. He felt he was not gaining the success that he should. He learned about this program. He stated to me that he studied it for at least 6 months before he decided to enter into it. He feels that what he is doing has been successful to the good health of the patient.

As I say, we can bring him here and let him state his story because it will refute some of the things that you said and some of the things that the next two witnesses are going to state. We have their statements ahead of time and we have had the opportunity to read them.

My point is that the chairman stated we have an obligation to let the general public know if there is something going wrong in the treatment in the medical profession, but at the same time we have an equal obligation not to throw fear into the hearts of the obese who are now going to certain doctors and are being properly treated with good health and cause them to desert their doctors or to cause them to dissuade others who may be in a similar position. As the opening statement states, there are 40 million people who are involved and that is a lot of people.

Now back to your statement, you said the doctor stated he was "just trying to get people down to the weight where they would be happy." If he got the people down to the weight where they would be happy, would you think that he had done a good service for his patient?

Miss McBee. I think that he would do a good service to his patients if he could get their weight down without endangering their health.

Mr. Chumbris. Right. Thank you.

I only have a few more questions—this is quoting you: "I said I wanted to lose inches around the hips and he replied that the extra inches were due to a need for estrogen or progesterone, which are sex hormones." Then he gave you some material to read on weight control. It advised eating proteins and avoiding sugar, starch, and fat. He noted breakfast cereals are out. I think the list that Dr. Barr gave us coincided with the type of suggestion that Dr. Davis gave you on that day as to what to eat. So in essense, dieting, in the true sense of the word of low-calorie count, is not important to them. They are talking about dieting, eating certain foods and not eating certain foods. You can eat all you want of certain foods and it will not make you fat. That is the way it was explained to me by Dr. Barr and, of course, that is subject to rebuttal.

Miss McBee. I think that the emphasis of many doctors is eating the right foods rather than stressing calories. But I think that ultimately most nutrition experts will agree that calories are the important thing. I mean, you eat fewer calories than the energy that you expend and you lose weight.

Mr. Chumbris. On that particular point he gave an illustration that one of his patients was eating only 1,300 calories a day under a previous prescription and he said, "Well, you are not eating enough because the World Council on Health states if you do not eat 2,200 calories a day you are starving yourself." So, he got her up to a calorie count that was above the 1,300 level but it was in the particular areas of food noted in his booklet.

Miss McBee. I assume that the emphasis should be on the kind of foods.

Mr. Chumbris. All of these statements are subject to rebuttal but I thought I would get his viewpoint into the record.

I believe you noted that only Dr. Siegel's office sent you out to get your drugs. The rest of them handed them to you in their office, is that correct?

Miss McBee. Yes, sir.

Mr. Chumbris. Now, Dr. Needelman stated that you could eat six turkey sandwiches a day and it would not hurt you. Of course, his views would be a

little bit inconsistent with some of the other views you received from the doctors that you visited; is that correct?

Miss McBee. Yes. I think it is interesting that they do not seem to agree among themselves what really is a good diet or what foods should be eaten. One doctor said, for example, Dr. Franta, I believe, said I could take soft drinks. Dr. Needelman thinks that any kind of carbonation is terrible and I think each of them has his own reasons for feeling this way.

Mr. Chumbris. You mentioned this one medical society that you visited. Did you visit any others to determine if the methods used by these doctors and the pills that they prescribe are not appropriate?

Miss McBee. Any other medical societies, sir?

Mr. Chumbris. Yes. For instance, some of the doctors are doctors of osteopathy, some of them are medical doctors.

Miss McBee. Oh, I talked quite extensively to several officials of the AMA, including Dr. Rouse, the president of the AMA, and he reminded me, by the way, of a 1967 resolution that the AMA passed saying that it does not believe that weight control is a separate specialty, that you should treat a patient for weight and any other problem that he might have all together. The AMA, I think, has written editorials in its own journals deploring the abuses in this practice. So has the American Osteopathic Association, which I also talked to, aand which sent me several editorials denouncing the practice of some of the doctors who seem to be in this business merely to make money.

Mr. Chumbris. In your study of this matter, did anyone of authority in the medical profession or among the medical or doctors' associations mention to you that they would have a top-level symposium of all range of thought in this area to determine what method is right and what method is wrong?

Miss McBee. I am not aware of that.

Mr. Chumbris. It could be that, so we have found it in medical history so many times, that the one or two doctors, who earlier were in the minority, 10 or 15 years later proved to have the prevailing thought. We up here as legislators and staff are discussing a matter that really has to be determined by the best minds in medicine, as to medical practice, as to what drugs are good and what drugs are not good, and that is the reason why I ask if any such top-level study has been made. For instance, the National Institutes of Health has made a study on tobacco. Maybe some agency such as that or a group of physicians or organizations should make a top-level study of this. Forty-million people are involved.

Miss McBee. I think that might be helpful. And I think it might turn up a lot of different points of view. I do know that I, of course, have talked to doctors at Harvard, Yale, Washington Hospital Center, University of Chicago, UCLA, USC, and the Rockefeller Institute in New York, which by the way, does specialized work in obesity. I have talked to various doctors in the different disciplines that we have discussed here. All I know is that the overwhelming weight of medical opinion, I think, would back up what I have said, and that does not mean that there is not a minority view.

Mr. Chumbris. I think almost every one of us in this room has personal experiences with friends whose lives were wasted because they were obese; that nothing medically was done to correct them of that disease that they had.

Miss McBee. I think one thing, too, is that most of the experts that I have talked to say that the field of medicine really has no easy answer to obesity.

Mr. Chumbris. Thank you very much. And, I believe that the first reading of your article may shock a lot of people in this area. But I think that in a second or third reading of your article, the professional men will use it as a guideline to correct some of the things that they have been doing, especially among the 10 that you mentioned. But three of them are going to be here and I do not want to prejudge their statements. Thank you.

Senator Hart. Miss McBee, whatever the disagreements and whatever the conflict of opinion which is to be expected in any professional discipline, one solid fact we have established is that whatever these doctors told you with respect to diet, whatever handbooks or pep talks they gave, every one of them made sure that before you left the office you had a packet of pills, right?

Miss McBee. Yes, sir.

Senator Hart. Whether you weighed 125 that day or 131, you marched off with a packet of pills, the total packet of which came to about 1,500 pills in 10 visits, right?

Miss McBee. Yes, sir.

Senator Hart. Well, I would like professional opinion to express its judgment on the prudence of that treatment.

Mr. Chumbris. I think that is going to be one of the issues.

Senator Hart. And that is exactly what we lack.

Mr. Chumbris. I think that is going to be one of the issues. If they cannot substantiate why they gave this supply of pills for that 28 days, if they cannot substantiate that, then you made your point well, Mr. Chairman, no doubt about it. That is one of the issues that this subcommittee hearing is going to have to determine.

Senator Hart. The distribution system so far as antitrust is concerned involves moving that packet and its cumulative total into consumers' hands. There is a second point on which there can be no refutation either: Our witness would meet the definition all of us had of somebody who does not need any diet treatment. We are very grateful for a stimulating start for what I hope will be a constructive set of hearings.

Miss McBee. Thank you.

Senator Hart. Are those the pills that were given?

Miss McBee. No, sir. I have the pills. I have the pills back there if you would like to see them.

Senator Hart. Well, leave them on the table and then we can ask the experts what they think about them.

I am advised that our next witness is one of the outstanding physicians in the field in the country. He is Dr. Frederick Wolff, who is the director of research at our Washington Hospital Center and professor of medicine and director of the division of clinical pharmacology at George Washington University. Dr. Wolff.

[From Life, Jan. 26, 1968]

7. The End of the Rainbow May Be Tragic—Scandal of the Diet Pills

Cheryl Oliver, the attractive college coed at left, worried constantly about her weight—so much that she went to a doctor who prescribed a galaxy of drugs in brightly colored pills. A year later, as Cheryl—now thinner—studied in her dorm at Oregon State University, she suddenly died. After painstaking research, Oregon State Medical Investigator Dr. Russell Henry announced that Cheryl's death was "probably" due to the "rainbow" pills. He said he knew of five, possibly seven, other women in Oregon who had died the same way. This week the Senate Antitrust Subcommittee, headed by Senator Philip Hart of Michigan, begins hearings on a major scandal in American medicine: *the obesity business.*

The Food and Drug Administration estimates there are 5,000 to 7,000 "fat doctors," about 1,000 of them treating "fatties" exclusively. For every M.D., three are osteopaths. They see 5 to 10 million patients, sell more than two billion diet pills, and gross a quarter to a half billion dollars a year. The drugs they dispense are not lethal in themselves and are helpful when used properly. But dispensed excessively and in dangerous combination, they can become toxic, even fatal. Those commonly prescribed for obesity are *amphetamines*, which suppress appetite; *barbiturates*, which counter the nervousness amphetamines may cause; thyroid, which increases the rate the body burns food; digitalis, a heart drug (which experts say has no place in weight control); diuretics, which flush water from the body; and laxatives. Thyroid and amphetamines each can tax the heart. Certain diuretics, called thiazides, tend to cause great potassium loss, which in turn may make the heart so sensitive to digitalis that even a small dose can cause violent spasms—and death. Of course some "fat doctors" check patients carefully and do not prescribe pills excessively. Yet many do just the opposite: run filling-station, cash-and-carry operations, see 100 or so patients a day, give only cursory physical exams or none at all, and carelessly send off their "customers" with sacks of potent—and possibly deadly—pills.

A Slender LIFE Reporter Visits 10 "Fat Doctors"

(By Susanna McBee)

No one has ever called me fat. A little on the hippy side perhaps. But never fat. I am a reliable size 10, and my weight, without clothes, is 123 to 125, respectable enough for my 5'5" frame.

By ordinary standards I would flunk out as a candidate for obesity treatments. But in a recent six-week period, traveling to nearly every section of the country, I went to 10 doctors who treat weight problems, and instead of bouncing me out of their offices, as I had expected, they welcomed me. Although three of them said I had no weight problem and another even congratulated me for catching the problem early (that is, before it developed), they all, every last one of them, gave me diet pills. My "haul" was 1,479 pills.

The pills, analyzed later by a chemist, included amphetamines, barbiturates, sex hormones, diuretics, thyroid and digitalis. They came in various sizes and colors, some of them very pretty and all of them—for me, at least—completely unnecessary. Even though I had undergone an arduous eating program—several buttered rolls with every meal, gobs of sour cream on my baked potatoes and enough cheesecake to supply a White House banquet—I had gained only five or six pounds and was definitely not a "medical overweight problem."

The first doctor I visited was an osteopath, *Dr. Edward A. Devins*, whose drab suite on the third floor of the Altman Building in *Kansas City, Missouri* had been raided less than a month earlier. Agents of the Food and Drug Administration's Food and Drug Abuse Control and a deputy U.S. marshal had confiscated 2.5 million pills, most of them amphetamines and some barbiturates. The pills were seized on the basis of a civil complaint alleging that Dr. Devins had failed to keep accurate records of the pills he received and dispensed.

At Dr. Devins' office, as at the others, I gave my correct name, made up a local address and occupation, and said only that I wanted to lose weight, never asking for pills. The day I appeared, a girl handed me a form with 195 questions, starting out conventionally enough with eyesight, hearing, nose and throat conditions, and progressing to my mental condition, which was hardly improved by the queries: "Do you feel alone and sad at a party?" "Do you often cry?" "Does life look entirely hopeless?" "Do you often wish you were dead and away from it all?"

The girl read over my questionnaire, asked if I were allergic to medicine and if I were nervous. "What is the highest your weight has ever been?" she asked; then she weighed me with my clothes and shoes on. I came to 130½ pounds. Not bad, considering I had just gorged myself at a late lunch.

"You should weigh 120 to 125," she said reprovingly, "and we'll get you down to 120." She took my blood pressure, pulse and measurements. When she got to my waist, which normally is about 25 inches, it measured 28 because I stuck out my stomach. She seemed not to notice but recorded the statistic. Then she asked who had referred me. I said I'd heard about Dr. Devins at a party from a woman whose name I couldn't remember.

"I've never heard that one before," the girl said cheerfully, "but one lady said she heard about us at a bus stop." Obviously, this girl *wanted* to believe me. She then announced, "I'm going out now and prepare your medication."

Several minutes later Dr. Devins entered, carrying a box of pills which he had picked up before even seeing me. He did not examine me but said I would feel different after taking his pills "because, after all, you're on diet medicine."

Talking rapidly, Dr. Devins said, "We don't advise going on a diet." He then read me the instructions on my pillbox, which contained 140 tablets—pinks, browns, tans and grays. "If you're not nervous (my questionnaire indicated I was not), they won't make any difference." He said I might not sleep too well with the pink pills but not to worry about it.

I asked what was in the pills. He did not tell me but said only that the pinks would suppress the appetite, the browns would keep me from being constipated ("People tend to get constipated when they lose weight") and the others would work with the pinks to reduce me. They contained, it turned out, amphetamines, laxatives and thyroid.

Dr. Devins said he would see me in a month and directed me to the receptionist, who looked at my chart and said, "Ten dollars."

That was easy, I thought, but the Rubel clinic in Decatur, Illinois, which attracts the heavy set from all over the state, might be difficult. Perhaps, if I

were rejected as a patient there, a fat man posing as my husband could go through the clinic and tell me about it. A friend in Decatur said he'd locate one, and while waiting I realized I would need a gold ring, too.

At the local Woolworth's a clerk showed me a large tray of rings. She pointed to some with stones.

"No, I just want a gold ring."

She pointed to gold rings with stones.

"No, no. Just a plain gold ring," I said, trying to smile.

Her eyebrow arched toward her scalp. Her eyes narrowed. She knew exactly what kind of woman she was dealing with. Coldly, she displayed a section of gold bands. I grabbed one, paid $1.05 and started to put it in my purse. "Don't you even want to try it on?" the clerk asked as I hurried out.

I did not find a fat husband and went alone. In the Rubel waiting room a nurse called my name over a microphone and gave me a one-page, 136-question form to fill out. It asked about my current physical condition, past illnesses and eating habits. I saw several women go beyond the reception desk, presumably for their monthly checkup, and come out again, carrying a little white sack of pills—all in less than five minutes.

The clinic, which is one of three in the Midwest run by Dr. Louis L. Rubel, has an array of tests for new patients: weight, measurements, blood pressure, pulse, urinalysis, blood sample from a finger, an electrocardiogram. There is also the ankle-jerk test, which most internists and endocrinologists regard only as a measure of hypothyroidism, and an inconclusive one at that. I took it sitting on my knees on a cushion beside a machine called an "Achilleometer," and after a technician tapped my Achilles tendon and saw the indicator on the machine jump into the middle range, she told me this meant I could take an average dose of their medicine. Of which medicine? "Of all our medicine."

Dr. William K. Franta, who saw me after my tests, is one of four osteopaths at the clinic working for Dr. Rubel, also an osteopath. "You're not really overweight," said Dr. Franta, who has a weight problem of his own. He reviewed my tests, which came out normal, and my weight, 129½. He asked if I took any medication. Just vitamins, I said.

"Well, we'll give you our own vitamins so you won't have to take the others if you don't want to." He wrote a prescription, and I asked what the pills were. He said one kind was a "gland substance" and the others were vitamins and minerals. He made no effort to examine me, not even to listen to the heart or feel the impulse over the chest—both considered part of a complete heart examination.

Instead he gave me a little talk. Weight control, he said, is a matter of glandular balance. Since I was in the normal weight range, which for me he said is 119 to 129, I might not make too much progress. We would try the pills for a few months and see how I did.

Dr. Franta spent three to four minutes with me discussing my diet, handed me the prescription and told me to drop it in the wicker basket at the front desk. When I did, the office manager put it on a dumb-waiter pulley behind her and it was lifted upstairs. Shortly, a white paper bag with three small envelopes inside slid down the pulley, and after I paid $15 and was told that each succeeding visit would cost $10, I was given the bag. It housed 84 pills, 28 each of vermilion vitamins, magenta vitamins and lime-green thyroid. There was also a brochure explaining the Rubel program and beginning with the words that fatties love to hear: "Overweight or obesity is a very common disorder which can be corrected without dieting."

When I telephoned the office of Dr. C. C. Mendenhall in Gardena, California, the first thing the girl said was that visit and medication would cost $15. That's cash; no personal checks, she said. When I arrived, a girl led me to a small room with an ankle-jerk machine, this one called a "Photomotograph." While the machine was warming up, she quizzed me about my physical condition, even about how my liver and spleen were doing, as if a layman could know. She said I looked slim and asked what I wanted to weigh. I had just hit 132¼; the cheesecake obviously had gotten to me. I said I wanted to weigh 120 to 125. She tapped my Achilles tendon, measured me and took my pulse and blood pressure. (Later, Dr. Mendenhall's services to new patients were expanded to include a physical exam, electrocardiogram, urinalysis and blood tests.) The girl gave me a brochure which urged patients to follow a high-protein, low-fat diet, and she told me not to eat fried foods, salad oils or soft drinks.

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Dr. Mendenhall appeared, looking tired, perhaps because he sees 60 or more patients a day. He reviewed my medical history, put a stethoscope to my heart in two places, felt the front and back of my neck and checked my ankles for possible swelling. I asked how much a person of my height and build should weigh.

"It wouldn't do any good to tell you because you people aren't going to get down to the weight you should weigh anyhow," he said.

You people?

He said he was just trying to get people down to a weight where they would be happy. "I'm not trying to reform the world. Very few fat people get down to their ideal weight and stay there."

I asked about medication, and he told me I would be getting an appetite depressant, a laxative to take if I needed it, some protein, thyroid and something for my hips (which I said I wanted to reduce). I asked what the hip medication was. "My own preparation." It turned out to be prednisone, an anti-inflammation hormone.

I left Dr. Mendenhall with 364 pills to consume in a *month*, and the next day, after a visit with Dr. Myron F. Babcock in the Los Angeles office of Raymond A. Landis, D.O., I had 84 more pills, including amphetamines. After several tests (weight, measurements, ankle jerk, blood), Dr. Babcock said, "You're not overweight, honey," then congratulated me on "catching the problem in time." The pills? "Things to make you lose weight." And, after I persisted: "This one's a thyroid-acting substance—something you could put young children on."

From there I went to San Diego, where Dr. Orville J. Davis' patients receive a 10-page mimeographed notebook which begins, "WELCOME ABOARD! . . . FIRST, if you are NOT overweight by average standard I DO NOT WANT YOU TO WASTE YOUR MONEY AND MY TIME WITH EVEN AN INITIAL VISIT" and concludes, "I do not consider you to have ANY medical overweight problem at all unless you are 15% or more over your average weight."

My average standard was 125. That day I was 130 with my clothes on, only 4% over—an honest-to-God test case for Dr. Davis. Technicians first put me through a physical exams procedure—urinalysis, blood drawn from the vein in my left arm, weight, measurements, blood pressure, pulse and electrocardiogram—and then I saw Dr. Davis. He said, "You're in great shape, kid. You have no weight problem." then he prescribed progesterone, which is a sex hormone, and 234 pills, including diuretics, thyroid and appetite suppressants. I paid $40 and wondered how many pills Dr. Davis would give someone *with* a medical overweight problem.

In Denver I saw Dr. Charles William Breitenstein, and after being weighed and measured—nothing else—paid $12 for a 28-day supply of appetite suppressants and tablets containing thyroidlike material. Then I went to the office of Chester M. Rasmussen and Duane A. Thompson, D.O.s, in Hillsboro, Oregon, where a brown-haired woman with glasses, a white dress and the sweetest of voices told me she wanted to check my hemoglobin count. She jabbed the side of my third finger, right hand, but couldn't draw enough blood, then rubbed my finger, trying to push something, anything, out of the capillary. She apologized, gave up and tried the third finger, left hand. Only an insignificant drop or two came. As she kept rubbing and apologizing, her hands got sweaty and so did mine. Now very flustered and very contrite, she attacked my middle finger, right hand. Same result. She kept saying, "You just don't know how sorry I am." She had no idea just how sorry *I* was.

Finally, she called in another woman who noted that jabbing should be done at the tip of the finger, not the side. She demonstrated on me, and she was right: there was all kinds of blood.

The first woman, still apologizing, resumed the testing—urinalysis, ankle jerk, pulse, blood pressure, measurements, weight. In a heavy suit and shoes I came to 131¾ pounds.

Then she posed a medical history quiz, replying, "Real good," whenever I indicated I had no problem. She asked if I had any swollen extremities—hands, feet. I told her I had some swollen fingers.

After she left, Dr. Thompson discussed my diet, said, "We don't want to make you look like Twiggy. Ha. Ha. Ha." but nevertheless prescribed the sex hormone, progesterone, and other pills, including digitalis, thyroid, amphetamine—268 in all for the month.

My next stop was the Manhattan office of Gordon L. Green, M.D., one of the most prosperous "fat doctors" in the country. He has 19 offices and grosses just under a million dollars a year. Here, I encountered machine-age medicine. The receptionist told me to listen to a tape recording, which said that the pills I'd receive would not affect any illness I might get one way or the other. You can lose weight without pills, said the voice, but you came to me for an easy way to reduce.

After listening to the tape, I asked the receptionist where Dr. Green was. She said he was not in any of the 19 offices. "He just runs the business." I asked if that voice on the tape was his. "Oh, no. We got a disc jockey to do that."

She weighed me (129 with clothes on), took measurements and asked about my medical history. She took a plastic box of capsules and tablets off a shelf and directed me to the doctor's office, where she put the pillbox on his desk. Then Dr. Sam Provenzano checked my blood pressure, listened to my heart, asked some questions about my medical history and explained how I should take the pills—46 for the week, including amphetamine-thyroid combinations.

In Falls Church, Virginia, Dr. Julius Seymour Siegel said I weighed 129 pounds and that he could tell, "by the size of your arm," that I ought to weigh 115. "Eat and drink anything you want," he said. "All you have to do is take the pills I'm going to give you"—three a day until I got down to 115, then one a day as "maintenance medicine." He took my blood pressure and pulse rate, listened to my heart, said, "Ah, perfect," asked no questions about medical history, current illnesses or allergies to medicine. Then he picked up a wall phone that was a direct line to a pharmacy, said he wanted pills for, uh, "Hey, what's your name?" and, hanging up, gave me directions to the Falls Church Drug Center. "Can I get the prescription filled at my own pharmacy?" I asked the secretary-nurse. "Oh, no," she answered. "You *must* go to the Drug Center." I paid her $3 and left to pick up 150 amphetamine-barbiturate-thyroid combinations for $7.50. I had spent three minutes with Dr. Siegel.

Dr. Siegel set the record for short office calls, and my next doctor, Harry Needelman, M.D. of Miami Beach, Florida, the record for long ones. Dr. Needelman holds another record. In 1957 he was convicted of illegal sales of narcotics, was later *pardoned*, and is still battling the Dade County Medical Association for reinstatement.

Despite his legal difficulties, Dr. Needelman has a booming weight-control practice, seeing, according to one report, 750 patients a week. When I joined the ranks, I brought along a LIFE photographer who said he was my husband and asked if he could watch. "Sure," said the receptionist, "we'll be glad to let him go through the factory, too."

I was weighed (130¼), measured and tested (blood pressure, temperature, hemoglobin, urine), then directed through a door that said "Doctor's Office" and opened into a small auditorium. The room was remarkable. The doctor's elaborate, crescent-shaped desk was on a platform a step higher than where the patients, or audience, sat on 11 large black leatherette chairs arranged in three rows.

The thick carpet was Kelly green, with standing ashtrays sunk into it. The doctor's desk had a camera (for taking before-and-after pictures of patients), a tape recorder and a rotary slide projector.

Three of us "fatties" had settled into the audience chairs by the time Dr. Needelman, a small, overweight man in his mid-fifties, bounced into the room, smiling frequently and talking very much like Eddie Cantor, though with a slight lisp. He took his place onstage, at his desk, and for an opener told us we could, if we wanted, eat six turkey sandwiches a day. "Doesn't that sound like a fairy tale?" All we had to do was to follow his advice on eating the right foods and we would lose five to seven pounds the first week and three to five pounds a week thereafter.

Then, amazingly enough, he called each of us up to his desk, one by one, and discussed our individual cases in front of the other patients. I listened, for example, as he interviewed one woman who loses weight under his program but gains it back when she returns home to New York. She had been going, off and on, to Dr. Needlelman for four years. When she first came, her weight was 128; it was now 148. I asked her later about her downhill progress, and with the loyalty fat patients characteristically have for their "fat doctors," she said huffily, "Dr. Needelman can't help it because I'm a pig."

It was my turn. "You're a young woman," he told me. "Would you like to get

down to 120?" He promised to get me down to that in two weeks, then put me on a maintenance program of one pill a day for a month. In front of everyone, he reviewed the state of my kidneys, hemoglobin and blood pressure. He listened briefly to my heart and asked about any swelling. But he took no medical history.

He proudly proclaimed that we were about to see "the longest-running show in the world," that he had been giving the same lecture, with variations, for 14 years. "Now," he said, "we'll put our little show on the road." He flicked on the tape recorder and sat silently as his voice came down at us from a loudspeaker in the ceiling.

The tape went on and on and on as the slide projector flashed "before-and-after" pictures of patients. The voice would name the patients and tell where they worked. It mentioned a local lawyer, shoe salesman, grocer, hotel employe, even a local bookie. "You see, I give all the local businesses a little plug," explained the voice. "With my pills, you can eat 3,000 to 4,000 calories a day and lose weight."

After an hour or more, Dr. Needelman, in person, allowed questions from the audience, even asked himself questions, answered them and reviewed what he had already said. "Aren't we having fun this afternoon?" he beamed. He kept calling himself the "talkingest doctor in the world."

Finally it was time for our weekly shot, which he explained only by saying it was the first gear in revving up the body machinery. I was reluctant, but he overwhelmed me with, "Try it this time. If you don't like it, you won't have to take it next time." I took it. I also received 26 pills for the week—diuretics, barbiturates and a combination of amphetamine, laxative and thyroid—and paid $15. A sign at the desk advised that after Jan. 1 prices were going up: $20 for the first visit and $10 a week thereafter. Dr. Needelman told us our capsules contained thyroid, adding that he would be able to determine the following week if we were getting the correct dosage. The "show" was over. It had run three hours, 15 minutes.

Among the "fat doctors" I visited, there was no consensus on diet—some said eat anything you want; others offered elaborate programs. They did not agree on exercise, or on liquor consumption. Their physical examinations ranged from several tests to merely a weight and measurement check. There was consensus, though, on one point: pills, pills, pills.

[From Life, Jan. 26, 1968]

MAKING MILLIONS OUT OF THE OBESITY BUSINESS

Many drug manufacturing firms are involved in the booming diet pill industry, but the obesity business is particularly lucrative for a dozen or so small companies that distribute their products almost exclusively to "fat doctors." The records of 10 of these firms have been subpoenaed by the Senate Antitrust Subcommittee for the current hearings and one company, the Western Research Laboratories, Inc., already has been charged by the government with misleading labeling. The drugs themselves are produced very cheaply and some can be sold to doctors in wholesale lots at a cent apiece. A few of the "fat doctors" charge as much as $75 for a first visit and some gross nearly $1 million annually. In one case a doctor had to hire a carpenter to reinforce the floor of his waiting room—it had sagged under the weight of his burgeoning practice.

Some companies actually recruit doctors for the weight-control business and dispense copious money-making advice, a practice deplored by the major U.S. pharmaceutical manufacturers. Several times a year the Lanpar Company of Dallas—whose two top officials were convicted in 1966 of violating drug manufacturing standards—conducts symposia on weight control which are attended by scores of doctors. Until four years ago Lanpar provided the participants with round-trip air fare and free lodging at such resorts as Disneyland in return for agreeing to purchase at least $400 in diet pills.

LIFE asked Dr. Leonard J. Flohr, an associate clinical professor of internal medicine at the University of Texas Southwestern Medical School, to attend a Lanpar symposium in Dallas last November. The speaker at the three-day meeting was Dr. Orville J. Davis *(right)*, who maintains a thriving weight control practice in San Diego. In his report on the symposium, Dr. Flohr said the speaker had advocated dangerously high doses of thyroid and the use of digitalis, which can seriously damage the heart.

"During the symposium three Lanpar salesmen approached me," Dr. Flohr

reported, "and asked if I wanted to buy their drugs. The selling of products at a supposedly scientific gathering is unethical. The program obviously was organized to sell Lanpar products. There was not one bit of documentation to substantiate the claims of Lanpar drugs. This program was simply hucksterism, and it ought to be discontinued."

[From Life, Jan. 26, 1968]

FIVE CASE HISTORIES WHERE THE REDUCERS DIED

Even before Oregon's Dr. Henry pointed to diet pills in the death of Cheryl Oliver, suspicious cases began turning up elsewhere in the U.S. Here are a few of them:

Mrs. Norma Jo Hill of New Braunfels, Texas died in 1965 of "toxic myocarditis." She was just 38 and had been a weight-control patient. Her widowed husband is suing the doctor for $342,000, alleging that he gave her a variety of drugs without adequate examination or proper supervision. In a deposition the doctor denied the charges.

In New Jersey, John Napoliello of Sayreville received a substantial out-of-court settlement from three Newark obesity-control doctors—Walter Sherman, Mordecai Schwartz and Herbert Allen—in the death, two years ago, of Napoliello's wife Rose, 50. According to her husband she went to the doctors for obesity treatment, and despite her long history of rheumatic heart disease they prescribed a variety of diet drugs. Later she developed embolisms leading to heart and brain damage, amputation of both legs and incapacitation for three years before her death.

In Illinois, Mrs. Frances Eleanor Espenschied of Springfield died in 1966 at 51. She was 5'5" and weighed 233 pounds. For a year she had been taking a large number of diet pills. She had heart trouble, and the autopsy showed digitalis in her system. Though a toxicology study indicated that no one drug was present in a toxic quantity, the report raised the question: "Could the combination have been important?"

Coroner Darrell Holland of Effingham County, Ill. cited digitalis intoxication as the cause of death of Mrs. Helen Bailey, who had been on diet pills and who died in 1966 at the age of 43.

In the death of Roger E. Schaefer, an Elmhurst, Ill. policeman, DuPage County Coroner Dr. Samuel K. Lewis listed two possible causes of death: auricular fibrillation (heart spasms) and "alergic reaction to medication." Schaefer had been taking diet pills before he died in 1964 at 28. Positive proof is difficult, but Dr. Lewis says, "I see about one case every six weeks in which I suspect that death was due to diet pills."

S. STATEMENT OF DR. JOHN D. GRIFFITH, ASSOCIATE PROFESSOR OF PSYCHIATRY AND PHARMACOLOGY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.*

At issue before this committee is a proposal to assign both amphetamine and amphetamine-like drugs to Schedule II of the Controlled Substances Act. Such legislation is long overdue and its thrust is in keeping with the public interest and safety. However, the committee should be aware of certain medical and pharmacological issues that deserve consideration.

1. USEFULNESS AND TOXICITY OF AMPHETAMINE DRUGS

The Controlled Substances Act defines drugs in Schedule II as having a) high potential for abuse; b) currently accepted medical use with severe restrictions and, c) abuse (which) may lead to severe psychic or physical dependence. At the present time, only opiate drugs; cocaine; and injectable methamphetamine are assigned to this category. However, it is my opinion and many of the physicians who gave testimony during hearings on the Controlled Dangerous Substances Act that amphetamines were misassigned to Schedule III and more properly belonged in Schedule II.[1] The medical literature supporting this opinion is voluminous and conclusive. An analysis of this topic was prepared for the House Select Committee on Crime and is included (Appendix I). To summarize this report, it is evident that amphetamines are of very limited medical usefulness

*Statement before the Subcommittee on Juvenile Delinquency, U.S. Senate, the Honorable Birch E. Bayh, Chairman, July 16, 1971.

except in the treatment of certain rare diseases. Too, these drugs have a very high potential for abuse which equals, and probably exceeds that of opiate drugs. Lastly, psychosis and physical illness can be complications of high-dose amphetamine abuse. For these reasons, assignment of amphetamine and methamphetamine to Schedule II is in keeping with the definition of the Schedule.

2. ARGUMENTS IN DEFENSE OF AMPHETAMINE

Various arguments have been raised in the past that amphetamines are "not addicting," are abused only by maladjusted people, and are psychotomimetic only if the subject has a pre-existing mental disease. These arguments have been cited to oppose the ban on nasal inhalers containing large quantities of amphetamine and methamphetamine; to oppose legislation restricting the refilling of prescriptions for amphetamines; and to oppose quotas on the manufacture of amphetamine. None of these arguments have stood the test of time. The history of these encounters between those who would protect the public interest and those who would sell amphetamine drugs is referenced in my paper "Amphetamines: Addiction to a Non-Addicting Drug" (Appendix II). Nevertheless, despite stringent restrictions on drug prescription refilling, drug sales, and record keeping, almost all amphetamine drugs seized in police raids bear the trademark of a legitimate manufacturer. This supports the view that eight billion amphetamine tablets is in excess of the current needs of the U.S. public.

3. DRUGS WITH AMPHETAMINE-LIKE EFFECTS

Serious consideration should be given to assigning methylphenidate and phenmetrazine to Schedule II. However, for two reasons this matter should be given further attention. First, methylphenidate and phenmetrazine are but two of several compounds with amphetamine-like action. Other agents include benzphetamine, phentermine, diethylpropion, phendimetrazine, and mepthentermine. To isolate two drugs from this list and subject only these to controls would only promote abuse of the others as well as work an unfair advantage to the manufacturers. Second, methylphenidate and phenmetrazine are both marketed by large and responsible drug firms who have shown due care in their manufacturing and wholesaling practices. The manufacturer of methylphenidate has even refused to advertise the drug in this country as an anti-obesity agent. Consequently, these drugs are not usually identified in large quantities in drug raids as are the amphetamine preparations.

Nevertheless, there is much evidence that the general class of amphetamine-like drugs are powerful stimulants and are abused. This has been especially evident in European countries. To quote Oswald:

". . . experience leads to scepticism when claims are made that a new appetite-reducing drug does not affect alertness or mood.

One may take the example of diethylpropion, reported by Seaton et al from Edinburgh to be an effective appetite reducer with "no evidence of undue central nervous stimulation or insomnia. . . . No important side effect." Time, however, showed that diethylpropion, like dexamphetamine and phenmetrazine, was a pep-pill, causing elevation of mood and of the pace of thinking. Despite spirited defense (Roebuck) it has become recognized as a drug which can lead to tolerance, dependence, abuse, and psychotic manifestations, selling in the illicit market at a slightly lower price than amphetamine and being included in the Drugs (Prevention of Misuse) Act, 1964." [2]

Other investigators have come to similar conclusions for drugs of this class.[3 4 5 6 7 8] Although it may be argued that amphetamine-like drugs may show variations in pharmacological mechanism of action and duration of action, the general effect of these compounds is similar to amphetamine.

4. PROBLEM OF AMPHETAMINE-BARBITURATE COMBINATIONS

The committee should also be aware that a very special problem exists in terms of drug combinations which consist of amphetamine or methamphetamine compounded with either a barbiturate or a minor tranquilizer. The older pharmacology texts stated that this combination of drugs was more effective in that the sedative or tranquilizer neutralized the stimulant effect of amphetamine. It is now recognized that the barbiturate only increases the addiction potential of

amphetamine. Indeed, amphetamine addicts rarely take only amphetamine but prefer an amphetamine-barbiturate combination. Perhaps the U.S. should follow the lead of Norway and ban amphetamine-barbiturate combinations. This could be accomplished by FDA regulation or legislative assignment of the combination to Schedule I. To my knowledge there is no clinical syndrome in which an amphetamine-barbiturate combination is either essential or more effective than amphetamine alone. If such cases do exist they may easily be handled by the writing of two prescriptions.

5. NEED FOR INFORMED CONSENT TO TREATMENT

Many individuals have been prescribed amphetamine and amphetamine-like drugs and learn, only after they are addicted, that they have been prescribed an addicting drug. Existing law provides for labeling of dangerous drugs. It is my opinion that this committee should hear testimony as to the adequacy of precautionary statements now included in prescription bottles for amphetamine drugs. Legislative guidelines are needed, also, to precisely define the tort liability of a drug vendor who contributes to the addiction of a client.

6. SPECIFIC DANGERS WHICH MAY RESULT FROM ASSIGNING AMPHETAMINE DRUGS TO SCHEDULE II

Although the preponderance of evidence suggests that amphetamine and amphetamine-like drugs should be assigned to Schedule II, it should be recognized that certain problems may be introduced that should be solved before these drugs are restricted. One vexing dilemma has been observed by Lars M. Gunne, Professor and Chairman of the Department of Psychiatry at the University of Uppsala, Sweden. He noted that a number of patients in Sweden, as in the U.S., have been given small but regular amounts of amphetamines for periods ranging up to years. When an almost total ban was placed on the prescription of amphetamine drugs in Sweden, many of these patients experienced a depression which did not improve with time or treatment. Suicide was also seen. Dr. Gunne points out that these individuals should not have been given amphetamines in the first place, but now that the damage was done, some provisions should be made for them to receive small doses of amphetamine from some competent medical source. Dr. P. H. Connell, Director of the Drug Addiction Treatment Unit, Maudsley Hospital, London, supports this view and adds that most such patients take small, regular doses, do not develop tolerance, and lead normal, acceptable lives. To incapacitate them by withdrawing them from amphetamine would not be acceptable until some working alternative can be found.

Dr. John Kramer, University of California, Irvin, has also pointed out that withdrawal from amphetamine, although not as dramatic as withdrawal from opiates, can be a rather long-lasting syndrome. He feels that it should be permissible for a physician to prescribe, with difficulty, amphetamine to certain patients even though the specific indication may not be generally recognized. He cites a case of a patient with extra-pyramidal symptoms who responded to amphetamine but not to other forms of therapy.

By assigning amphetamines to Schedule II, these drugs could not be used "except for medical purposes." Historically, the Bureau of Narcotics and Dangerous Drugs has not recognized the administration of a drug to an addict as a "medical" purpose. A similar bias exists in the Food and Drug Administration. The law should make itself clear as to whether treatment of amphetamine addicts is a legitimate medical objective.

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Proposed Ban of Amphetamine Drugs[1] by John D. Griffith, M.D.[2]

PROPOSED BAN OF AMPHETAMINE DRUGS

Mr. Chairman, members of the Select Committee, I am Dr. John Griffith, an assistant professor in the Department of Psychiatry and Pharmacology at Vanderbilt University School of Medicine. My colleagues and I conduct research in the field of addicting drugs. Our activities are quite broad and include surveys into the sales and distribution of illicit drugs, the treatment of drug addiction, the effects of drugs on human behavior, and the basic pharmacology of these drugs in animals. Drugs of the amphetamine class are now under our scrutiny, and it is my purpose to present to you as succinct and pertinent an evaluation of the amphetamines as our present state of knowledge allows. So that I may be brief, I will reference my remarks rather than present a detailed discussion.

To evaluate any drug one must first understand a basic principle of pharmacology: that is, every drug, however innocuous, has some degree of toxicity. A drug, therefore, is a type of poison, and its poisonous qualities must be carefully weighed against its therapeutic usefulness. A problem now being considered in most of the capitals of the free world is whether the benefits derived from amphetamine drugs outweigh their toxicity. It is the consensus of the world scientific literature that the amphetamines are of very little benefit to mankind; they are, however, quite toxic. I would now like to discuss these points, then conclude by suggesting that your committee take a new tack and explore certain unusual solutions to the problem of drug addiction. In this discussion the term, amphetamines, will be used in a general sense to designate the d- and dl-isomers of amphetamine, methamphetamine, and the piperidine derivatives, methylphenidate and piprandrol. These drugs have very similar effects in man.

USEFULNESS OF AMPHETAMINE DRUGS

The bulk of amphetamine drugs sold in the U.S. are prescribed for the treatment of obesity. Studies show that these drugs will suppress appetite and that subjects will lose an average of 6.75 pounds more during an eight-to-twelve week period than will matched subjects on placebos (sugar-pills). At the end of this time, the patient becomes resistant to the effects of the amphetamine and derives little or no further benefit.[1,2,3,4,5] The cosmetic and health advantages derived from a 6.75 pound weight loss are quite minor. For this reason, responsible physicians are of the opinion that amphetamines should *not* be prescribed for appetite suppression. This view becomes even more pertinent now that at least one appetite suppressant has been discovered that is not a stimulant (Fenfluramine).

Amphetamine drugs are also advertised and prescribed for the treatment of emotional depression.[6,7] After many years of clinical trials it is now evident that the anti-depressant effect of amphetamines is very brief—on the order of days. If the patient attempts to overcome his tolerance to the drug by increasing the dose, he runs the risk of becoming even more depressed. Evidence obtained in our laboratories suggests that initial doses of amphetamine will turn a

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[1] Statement before the Select Committee on Crime, U.S. House of Representatives, Hon. Claude Pepper, Chairman, November 18, 1969.

[2] Department of Psychiatry, Vanderbilt University School of Medicine, 1105 Baker Building, 110 21st Avenue, South, Nashville, Tennessee 37203.

patient "on", but metabolites formed from amphetamine will turn a patient "off" again.[8] Therefore one must conclude that amphetamine is a poor treatment for mild depressions. It is absolutely contraindicated in more severe depressions.[9] I might add parenthetically that mild depressions could also be treated with cocaine, morphine, and alcohol with approximately the same degree of success and very little additional risk of addiction.

Narcolepsy is a disease of unknown cause in which the patient will fall asleep unexpectedly—even while standing up and engaged in conversation. Because amphetamines cause wakefulness, these drugs have long been used to treat this condition.[10] Some patients appear benefited; others are refractory to this approach.[11] Fortunately, the disease is so rare that a specialist in neurology will see only a handful of these patients during his entire career. Commercial interest in this condition, therefore, is quite small.

No reputable drug company suggests that amphetamine be given to normal individuals so that they might stay awake or perform unusual physical tasks. As a practical matter, however, some physicians do prescribe amphetamines for this purpose, even for themselves and their college-student children.[12] Other physicians will prescribe amphetamines for weight reduction to patients who are obviously thin or have not lost weight since a previous visit. It is tacitly understood in this relationship that the drug is being used as a stimulant. The armed services also provide stimulant drugs to their military personnel.[13] These drugs, which are part of an "emergency kit" are often raided by the airmen who are assigned to guard airplanes. Several military physicians have suggested that amphetamines actually reduce the efficiency of a military unit.[14] Airmen addicted to amphetamines are being identified in our VA case files.

Some drug companies suggest that amphetamines be used in the treatment of alcoholism.[6] Since the alcoholic is especially prone to amphetamine addiction, this use is contraindicated and should not be advertised for this purpose. Neither is it of use in the treatment of barbiturate overdosage.

Amphetamines are useful, however, in the treatment of hyperkinetic children.[15] Children who manifest this condition are frequently brain-damaged and exhibit such a high degree of pathological hyperactivity that they cannot learn, be disciplined, or allowed to play with normal children. If treated with amphetamines, many of these children will normalize their behavior—especially after the short-term effects of the drug have subsided.[16] The long-term toxicity of this form of treatment has not yet been established; neither is it clear whether amphetamines are superior to other drugs.[17] Physicians by and large agree that if amphetamine were to disappear from the market tomorrow, almost all patients would benefit except these children.

We may conclude, therefore, that amphetamine are of little benefit in the treatment of obesity and emotional depressions. These drugs are of some benefit in certain rare disorders such as narcolepsy and quite useful in the treatment of certain brain-damaged children. Now let us consider the toxicity of these drugs.

TOXICITY OF AMPHETAMINE

The medical profession has been slow to accept the dangers of amphetamine use. Since 1938, when the drug was first introduced, reports of amphetamine abuse have appeared in the medical literature each year. Nevertheless, many other papers have described amphetamine abuse as either nonexistent;[7] impossible, because withdrawal symptoms do not occur;[18] as occurring only in antisocial and maladjusted individuals;[19] as a minor problem;[7] and as late as 1959 as a major problem, but on the decrease.[20] During the last decade, however, the profession has now identified and recognized amphetamine abuse as being a major health problem—many times more serious than narcotic addiction.[21-29] Amphetamine abuse is also of interest in that an illicit market in the drug sprang up even though the drug had been "legalized." At one stage in its sales, amphetamines could be purchased without prescription.

Admittedly, not every person in the United States who has been exposed to amphetamine—my guess, 9 million adults[24] become addicted. However, the widespread availability of the drug on the illicit market plus its availability as a stimulant and appetite suppressant has resulted in many cases of drug abuse.

Not all of these cases of drug abuse are severe. Perhaps the mildest form is committed by students who use the drug as an imagined study aid. Dr. Stanley N. Smith, who investigated this practice at the University of Oregon Medical

School, found that slightly less than one-half of the students had used amphetamines. It is interesting that 38 percent of these students obtained their drugs from licensed physicians.[24] This seemingly innocuous practice is not without its hazards.

Dr. Smith points out that he became interested in the problem after observing a senior medical student became psychotic while using amphetamines. Sadusk, also, has pointed out that the use of amphetamines by students may lead to more serious consequences.[25]

However, amphetamine abuse is not confined to students. Our case files indicate that the most likely occupational group to be represented are medical personnel; housewives are next, and those engaged in nocturnal occupations follow. Our research, and the studies of others have identified amphetamine abuse, too, among various underworld characters such as petty thieves, convicts, and prostitutes.[21] "Successful" criminals do not use amphetamines as a rule.

Addiction to amphetamine also occurs. The older medical literature suggested that this was not so, however, direct observations of amphetamine addicts now make it clear that amphetamine addiction is more widespread, more incapacitating, more dangerous and socially disrupting than narcotic addiction. Intravenous use of amphetamine is common and Kramer [22] has pointed out that this abuse is indistinguishable from cocaine addiction. The problem is compounded, both literally and figuratively, by the availability of amphetamine-barbiturate combinations. It is easy to dismiss the amphetamine addict as a criminal or useless derelict of society. The committee should recognize, however, that many were once useful professional people of great promise. For example, the first case I observed (1960) was a young psychiatrist who had been confined on a locked ward. The second, an award-winning Air Force tanker pilot.

The psychological and physical penalties for amphetamine abuse are severe. Individuals who abuse this drug have great difficulties following occupational, domestic, or social pursuits: they risk damage to body organs; and they may experience a severe mental illness. We have observed some of these adverse mental effects of amphetamine under laboratory conditions and have established that the drug will cause a psychosis—even in normal individuals.[26]

It should also be noted that amphetamines are physically toxic. Because these drugs elevate blood pressure and have a direct action on the heart, they can aggravate preexisting diseases.[27] Deaths of children from accidental ingestion of their mothers' prescriptions have also been reported as have intentional suicides.[28]

Theoretically, most of these dangers of amphetamine abuse could be avoided, given a fool-proof system of distribution and controls. As you will notice in the following paragraphs, this system does not exist.

LEGITIMATE SALE AND DISTRIBUTION OF AMPHETAMINE DRUGS

Amphetamine drugs are inexpensive, simple to manufacture, and patent rights on the basic drugs, d- and dl-amphetamine have long since expired. For this reason, most drug houses realize profits of less than a 1/10¢ a tablet on the sales of these drugs. Because of this small profit margin, companies simply cannot afford to scrutinize their sales.

Some companies do hold patents on amphetamine-like drugs and advertise them as superior to amphetamine. There is little scientific evidence that this is so. However, this position allows them to market these drugs at a considerably higher price than generic brands of d-amphetamine. These companies do not want their drugs to acquire the reputation for abuse. Nevertheless, most advertise their product as a weight-control item. This is where the money is.

Another marketing technique is to heavily advertise a brand name. Once this name is well-recognized it can be used to promote a drug that can then be sold for several times the cost of its generic equivalent. In reality, these drugs can be nothing more than warmed over items from the 1930's.

Another practice is to sell a tablet which contains an amphetamine plus some other drug, usually a barbiturate or a minor tranquilizer. The rationale offered by the company is that the drugs tend to neutralize one another. Evidence obtained from addicts and from laboratory studies indicate that these combinations are much more attractive and, therefore more addicting. It has been our experience that addicts offered amphetamine alone (without barbiturates and/or alcohol) find that amphetamines are quite unpleasant in large doses.

By-and-large, the drug industry has not shown a great deal of restraint in selling addicting drugs unless required by law. Exceptions do occur, however. Ciba Pharmaceutical Company, for example, has not advertised their product, Ritalin®, as an appetite suppressant in this country even though it is as effective in this regard as d-amphetamine. Smith, Kline, and French Laboratories once sold an inhaler containing large quantities of dl-amphetamine and inadvertently supplied many young people with an unrestricted supply of this stimulant drug. The company withdrew the inhaler from the market before being required to do so by the FDA. This responsible behavior should be contrasted with a practice of a St. Louis company that sold a nasal inhaler containing 150 mgm of meth-amphetamine (about 30 times a therapeutic oral dose) until around 1965. Our research prior to that time showed that the inhaler was being widely abused and young adults would "shoot" the contents of this inhaler intravenously. The Food and Drug Administration (since under new management) did not respond to my plea that the inhaler be restricted to prescription sales and pointed out that consideration should be given to public need for non-prescription drugs. Only after a Congressional hearing was this practice changed. Other forms of irresponsible behavior by legitimate drug companies have been documented by your staff and us.

The conclusion that might be drawn from these observations is that the legitimate drug industry cannot, as a group, always move together to protect the public good. It should be added that many individuals in drug companies recognize this problem but are frequently hamstrung by their marketing department which points out that objective statements about drugs or restrictions on drug sales will cut into profits.

Until Congress enacted legislation requiring that prescriptions on amphetamines expire at the end of a fixed time, many legitimate pharmacists, whose aim was not to offend their customers, would refill amphetamine prescriptions promiscuously. We now find that pharmacists have become very careful with these drugs, check with physicians before refilling, and refuse to refill out-dated prescriptions. Except for the occasional bad apple in any barrel of professionals, this problem has improved considerably.

Many physicians, too, have changed their prescribing practices. A small survey of medical specialists in our area indicated that only one out of three prescribed amphetamine. Some were vehement and would answer the survey with "hell, no!" etc. Psychiatrists, as a rule do not prescribe amphetamines. Some physicians continue to exercise poor judgment in prescribing this drug. The legal problem here is that criminal convictions are almost impossible to obtain against these physicians. Alternative methods of enforcing patient-oriented conduct should be explored by this committee.

The patient cannot be relied on to show good judgment in the use of drugs. Some lie to their physicians to obtain drugs; others lie to themselves that they need drugs in large quantities. The problem here is that once an individual is prescribed amphetamine his judgment about continued drug use is seriously impaired. The patient, therefore, should not be made to bear the responsibility for drug abuse since this is largely beyond his control. Therefore, arguments that the drug is safe if "taken as directed" ignores the fact that a large number of patients will ignore directions.

Summary

It appears, therefore, that amphetamine drugs are of little benefit except to a very small segment of the ill in our society. On the other hand, making these drugs available for the treatment of obesity and depression has proved to be quite harmful to the public. Although a fool-proof system of regulations might alleviate some of these harmful consequences, existing controls such as are now practiced, are inadequate. It is evident that the present system of controls places the major risk, pain, and financial burden of amphetamines directly on the consumer. In addition, those who do not use drugs must be taxed to control the social disruption resulting from drug abuse.

Recommendations

Congress has wrestled with the problem of public drug abuse for many decades. Although some isolated improvements have occurred, it is evident that drug abuse, as a total problem, is now worse than ever. Neither can a spontaneous "cure" be expected. Indeed, historians may someday compare our problems with drugs to the ravages of the Black Death during the Middle Ages.

A careful analysis of solutions proposed for drug problems in the past shows why these did not work. Most were too expensive or cumbersome to be carried out. For this reason, I would plead with you that, whatever is done, that it be inexpensive. Let me suggest some examples:

One action the committee might take is to prohibit the sales of amphetamine-barbiturate or amphetamine-tranquilizer drug combinations. Most physicians would not write two prescriptions, and some potential addicts would find amphetamine, alone, to be unpleasant.

The committee might also ask the FDA to consider restricting the treatment indications for amphetamine to the treatment of narcolepsy and certain childhood behavior disorders. This would prompt lawsuits by several major drug companies, however, and sales would continue for two years or more. For this reason, direct congressional legislation should be considered. The implication of this proposal is that prescribing amphetamines as stimulants would become medical malpractice.

The committee should consider legislation that would require the vendor of a drug—whether a legal vendor or an illegal peddler—to be *financially responsible* for careless or promiscuous distribution to customers. The problem is this: Fines are small, convictions are rare, large corporations can tie up matters in courts for years, the district attorney's offices are saturated with a backlog of cases, and the prisons are overcrowded. Therefore, one has little to fear in the way of a jail sentence for violating the drug laws. On the other hand, if a vendor knows that supplying or prescribing a drug to a student, teenager, housewife might make him liable to damages, he would dispense these drugs with utmost care. You will notice that most private swimming pools are surrounded by a high fence. The fence is not there because the owner is good-hearted. It is there because he fears being sued by the father of a child who might drown in the pool. We are all children where drugs are concerned—as the observation of any cocktail party will attest—and the vendor of drugs should either erect his own walls or risk the financial consequences. As matters now stand, our laws require the addict to bear the consequences of his addiction unaided.[29]

Congress should also consider making the manufacture, sale, and distribution of addicting drugs an absolute government monopoly. This is not a suggestion that drugs be "legalized"; neither is it a plea for prohibition. However, it would be a system in which the distribution of addicting drugs would be determined by public need and bureaucratic inefficiency—both useful in this instance.

Lastly, there is a need for research in the field of drug addiction and alcoholism. It may come as a surprise to some of you that we do not know how drugs and alcohol act; where they act (except somewhere in the brain); or how to treat addiction to these substances. Until more research is done, programs which propose to treat and prevent drug addiction and alcoholism are likely doomed to failure.

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Amphetamines: Addiction to a Non-Addicting Drug[1]

By John Griffith, M.D.,[2] and John Davis, M.D.,[2] and John Oates, M.D.[3]

Young school children receive lessons in ecology. Their teacher points to a small aquarium and explains that the fish breathe oxygen generated by plants in the water; the plants, in turn, breathe the carbon dioxide given off by the fish. This, the teacher explains, is a "balanced" aquarium. Young students are spared the grim observation that this balance can be established by death of both organisms. This lesson is learned when the school child attempts to swim among the dead fish that drift ashore from Lake Michigan.

Human beings, in their own fishbowl, are finding that they must come to terms with similar ecological issues. Just as an abundance of phosphates has given plants in the Great Lakes a sudden advantage over fish life, some drugs have suddenly made man more durable. Antibiotics keep young men from dying of pneumonia; a young woman with diabetes, thanks to insulin, can now have children; some arthritics can work if given steroids, and analgesics have made

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[1] Presented at the International Congress of Neuro-Psychiatry, Prague, Czechoslovakia, August 11–15, 1970.
[2] Departments of Psychiatry and Pharmacology.
[3] Departments of Medicine and Pharmacology.

surgical operations bearable. Indeed, man has become such a hardy specie that his proliferation threatens to destroy the biosphere. Nevertheless, it is the general consensus that we will keep these drugs and solve the problem of pollution and overpopulation by other techniques.

However, man expects more from life than comfort and survival. This has led him to use other drugs as sources of pleasure—a practice greatly emphasized in a technological culture where other pleasures are on the decline (Kerr, 1963). These drugs, too, are effective. Properly medicated, most individuals can be transformed into a specie of carp that can endure extremes of environmental pollution ranging from a boring cocktail party to abject poverty. However, this advantage, if it may be termed such, carries with it the risk of drug and alcohol dependence. In this instance society is less sure that it is getting a bargain.

One may speculate that society might be improved if pleasure-producing drugs were either eliminated or better controlled. As a practical matter, however, drugs are rather easily introduced into a society and controlling influences rarely come into play. This point will be illustrated by describing amphetamine abuse in the U.S.—a logical example because these drugs entered the U.S. without historic preamble; were for many years considered harmless, and, to date, have escaped effective controls.

SOURCES OF AMPHETAMINES

1932 was a bad year for the U.S. public. Unemployment was at an all-time high; the great experiment with prohibition had left organized crime in its wake; 21,000 people committed suicide and 1,166 banks failed. News was not very cheerful. However, the public was encouraged by two bits of information. Their police promised that, given time and support, they would wipe out narcotic addiction. On a lighter note, those with colds were promised relief from nasal congestion by a new device, the amphetamine inhaler.

Even these bits of cheer, however, proved later to have rather dismal consequences. Despite 38 years, billions of dollars, and hundreds of thousands of arrests, the police are beginning to understand that they alone cannot control drug abuse. As for the amphetamine inhaler, it launched a new type of drug abuse that grew into a problem even greater than narcotic addiction.

In retrospect, little else could have happened. Amphetamine inhalers were placed in every drug store, sold without prescription and aggressively advertised. Each contained massive amounts of stimulants. One brand, for example, contained 250 mgm of racemic amphetamin; another 239 mgm of methamphetamine. The stimulant properties of these drugs was soon learned by a wide range of persons from students to prisoners. In short order, songs were being written about amphetamines; abuse of these drugs was being denounced in the popular literature. In 1947, Monroe and Drell, in their now classic study, reported that one out of four military prisoners was abusing amphetamines obtained from inhalers.

In the years that followed the Monroe and Drell report, abuse of amphetamine inhalers became such a problem that many of the more reputable drug houses withdrew such products from the market. Those that did not were forced to do so by an FDA ban in 1959. Unfortunately, this action did not eliminate the problem. For reasons that are not altogether clear, the FDA ban applied only to amphetamine. This left a loophole that was seized upon by at least one Midwest drug firm that manufactured an inhaler (Valo$^{(R)}$) that contained 150 mgm of methamphetamine. This led to the ultimate in inhaler abuse—injection of an extract of the contents intravenously (Griffith, 1959). At the same time, Greenberg and Lustig (1966), and Angrist, Schweitzer, Gershon and Friedhoff (1970) have described abuse of inhalers containing mephentermine. Although abuse of stimulant inhalers is fading, the practice has left its mark. Thousands of young persons from a variety of social classes were introduced to a potent stimulant drug.

The U.S. public was introduced to a second source of amphetamine drugs when prescription tablets generally became available in 1937. Originally, the drug was prescribed for narcolepsy. Soon, however, amphetamines were also being recommended for such conditions as emotional depression, obesity, chronic alcoholism, barbiturate overdose, fatigue, and hyperkinetic childhood disorders. Military physicians recommended their use in wartime. The important issue

here is that some of these conditions affect nearly everyone; at the same time, problems such as obesity are difficult to treat. For these reasons, amphetamine drugs were soon being overprescribed. By the 1960's, for example, the annual U.S. production of amphetamines was being manufactured in tons. Six percent of all prescriptions written were for these drugs. Manheimer (1968) reported that one out of every five adults in California had experienced stimulants. Surveys of students indicated an even higher incidence of use and abuse.

Undoubtedly, most individuals who received amphetamines while under the care of a physician did not experience significant difficulties. However, there is little doubt that this brisk legitimate market soon became the base for an illegal market. Even today, most amphetamines confiscated by the police are tablets manufactured under legitimate conditions. Techniques used to pervert the legal distribution of amphetamines are countless. These include bogus mail order sales, orders from fake companies established by the underworld, so-called "diet clinics", forged prescriptions, use of outdated prescriptions intended for others, thefts, and deception of doctors as to the actual use to be made of the drug. Even veterinary supplies (amphetamines apparently encourage chickens to lay more eggs) have not gone untouched. At the present time, diversion of amphetamines from legitimate distribution is so efficient that illegal tablets are available in almost every American city and cost little more than if the item were to be bought through a pharmacy. This is in sharp contract to illegal narcotic sales.

A third source of amphetamine drugs—illegal manufacture—gradually developed as more and more individuals have demanded a methamphetamine preparation which can be administered intravenously in larger doses. Roger Smith and others have identified this practice and found that directions for Methamphetamine synthesis to be fairly well disseminated among members of the Haight-Asbury drug culture. This has created additional problems in that the compounds prepared are of unknown dose and purity.

Thus, one may identity a gradual evolution of amphetamine abuse. Amphetamine inhalers made the drug available to a very wide base of individuals which included members of all social classes. As this source was gradually terminated, amphetamine tablets were diverted from legitimate sources. Finally, in an era when amphetamine abuse may actually be on the decline, a subculture of amphetamine-dependent individuals, the so-called "speed freak," has evolved that is being supplied, in part, by illicit manufacture.

At the same time, the response of regulatory agencies has been quite sluggish. Mr. Ainslinger, speaking for the Bureau of Narcotics in 1951, minimized problems of amphetamines. The time lag between the first medical report of amphetamine inhaler abuse (1947) and an FDA ban (1959) was twelve years. Even then, loopholes in the regulation were not plugged until 1965 and even in that instance only partially. A similar lag was noted in response to amphetamine tablet abuse. Amphetamines were not declared prescription items by Federal law until 1951—despite medical and drug industry reports dating from 1944 that amphetamines had effects similar to cocaine. Now, in 1970, "tough new legislation" has been suggested to control amphetamine drugs. Ironically, this move, which might have been quite beneficial in 1939, may not be effective now. As Cohen (1969) has pointed out, such legislation may well force the illegal manufacture of amphetamine. In addition, the FDA has promised to limit the indications for amphetamine to narcolepsy, hyperkinetic impulse disorders, and "shortterm appetite reduction." However, this last item may prove to be another disastrous loophole.

MEDICAL VIEWS ON AMPHETAMINES

If the response of regulatory agencies to amphetamine problems may be described as sluggish, the response of scientific and political arms of medicine can be described as both ambivalent and highly polarized. Three questions that have been hotly debated were: 1) are amphetamines addicting; 2) are these drugs useful, and 3) do they have significant psychotogenic properties.

Ironically, the first reported misuse of amphetamine in the U.S. occurred in Minneapolis while the psychological effects of the drug were being evaluated at the University of Minnesota. Students, learning by word of mouth about this new stimulant, surreptitiously obtained amounts as a supposed study aid. This practice evoked a critical editorial in the Journal of the American Medical

Association (1937), and, later, when the drug was included in the NNR, amphetamines were specifically "not recommended for developing a sense of increased energy or capacity" (Council on Pharmacy and Chemistry, 1937). Waund (1938) warned that addiction to amphetamines was a possibility; "a possibility true of any drug with psychological effects." Guttmann (1938) pointed out that maladjusted individuals might find the use of the drug attractive, as did Reifenstein and Davidoff (1940) who used the drug in the treatment of alcoholism. Case histories of amphetamine abuse that followed usually concluded with similar warnings.

It is a historical irony that almost every drug now being abused by the U.S. public has been vouchsafed by certain members of the medical profession as useful and non-addicting (whatever that term may mean). Amphetamines were no exceptions. Indeed, the same statements that are now being made about marijuana were once used to defend amphetamines: Amphetamines cause no serious impairment of muscular coordination (one writer advocated their use by airplant pilots and nocturnal drivers); amphetamines were not addicting because cessation of use did not lead to withdrawal symptoms; amphetamines were useful in the treatment of alcoholism and drug addiction, and excessive amphetamine use is a reflection of abnormal personality factors. As late as 1958, one writer stated that "no clear case of addiction to d-amphetamine has been reported." Other authorities admitted that amphetamine abuse did occur but there was no real hazard if the drug was used in moderation—a statement that would apply, with equal accuracy, to any drug, even heroin. Another opined that amphetamine abuse was a significant problem, but on the decrease.

Connell's (1958) classic monograph on the amphetamine psychosis, plus descriptions of the Japanese experience with methamphetamine, changed these views dramatically. U.S. investigators, afterwards, had little difficulty locating cases and the trend became one of reporting larger series, more precise clinical and biochemical data, and an ever-escalating range of doses. Nevertheless, the argument was still advanced that amphetamine dependence was a very rare phenomenon (Grahn, 1958).

This speculation was refuted by a second generation of amphetamine studies which looked at subjects in their "natural habitat" instead of jails or hospitals. To our knowledge, the first such study was done by one of us (Griffith, 1966) in Oklahoma City, and the second by Rawlin (1968) in St. Louis. In both studies, drug peddlers and drug users were interviewed and the behavior of individuals self-administering massive doses of amphetamine was observed.

Kramer (1967) complimented these studies by reporting a large series of hospitalized patients who used amphetamine intravenously. In each of these three studies a characteristic pattern was observed: gradual introduction to drug use; escalation of dose; tolerance; periods of withdrawal ("crashing"); occupational incapacitation; concept of self as an addict—"speed freak," "fiend;" and pursuit of criminal activities for financial support. Indirect evidence suggested that there were at least 5,000 such cases in Oklahoma City (population 300,000); Kramer estimated 5,000 such cases in one San Francisco neighborhood. Although one might think of amphetamine abuse as a criminal activity, it should be remembered that many case reports described physicians and nurses—reminiscent of those who first studied cocaine and later became drug-dependent.

Reports of amphetamine dependence have caused the clinical usefulness of amphetamines to be reevalnated. Contemporary views on the drug are that it may be of help to some individuals who suffer from: 1) narcolepsy; 2) hyperkinetic impulse disorders of childhood, and 3) short-term treatment of obesity. This last indication is somewhat tenuous. We examined five studies, randomly selected from the medical literature, which described the effectiveness of amphetamine as appetite suppressants. Subjects (most of whom were quite obese) lost an average of 6.75 pounds more during a 12-week period that did subjects on the placebo. After that time, there was no statistical differences between groups. Since the cosmetic and health advantages of a 6.75 pound weight loss are quite minor, and the consequences of drug-dependence great, then, perhaps, even this indication should be reconsidered.

A last issue which pertained to the amphetamine psychosis was whether these drugs were psychotomimetic. Actually, the phenomenon was examined from two directions. Clinicians were interested because a drug which produces a psychosis should be dispensed with greater care than a drug that does not;

too, patients with amphetamine psychosis were proving to be a challenging diagnostic problem. From another direction, scientific interest was voiced because the amphetamine psychosis might represent the long-sought-after paradigm for schizophrenia.

The first report of an amphetamine psychosis was by Young and Scoville (1938), who described two patients (narcoleptics) who developed a paranoid psychosis while taking large doses of amphetamine. Monroe and Drell (1947) also reported a psychosis as complication of amphetamine abuse by federal prisoners. The Boston physicians, Norman and Shea (1945), editorializing that their patient was of Irish descent, described clear-cut parnoid symptoms in a patient who used amphetamines and alcohol. Similar cases were also being reported in other parts of the world. Initially, authors tended to think of these cases as representing either an idiosyncratic drug reaction or an incipient psychosis. However, Connell's (1958) large series made this view difficult to maintain. There remained only the possibility that the psychosis was limited to those with a predisposition to mental illness or that the psychosis was more related to some extraneous factor in the drug culture such as sleep deprivation. However, these possibilities were excluded, to a reasonable degree, by a number of experimental studies (Griffith, Cavanaugh, and Oates, 1958, 1970; Jonsson and Gunne, 1970; Angrist, 1970). These left little doubt that amphetamines were psychotomimetics in their own right. The role this property of the drug might play in irrational violence has been explored by Smith (1970) and Ellinwood (1970).

In summary, 38 years of amphetamine abuse in the U.S. has proved these drugs to be of limited medical value, to have important dependence-producing properties, and, in large doses, to be psychotomimetic. The history of these drugs also underlines the failure of society to come to terms with compounds with significant abuse potential. Ironically, some future writer may look back on amphetamines and conclude that these drugs were of no real value except, perhaps, as pharmacological tools used to explore the physiological mechanisms underlying pathological mood alterations and paranoid distrust.

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9. LETTER AND ATTACHMENTS OF DRS. O'BRIEN, STARK, AND MLADICK, SUBMITTED BY RAYMOND J. O'BRIEN, M.D., MICHIGAN CITY, INDIANA, SEPTEMBER 10, 1971

MICHIGAN CITY, IND.,
September 10, 1971.

SENATE JUVENILE DELINQUENCY SUBCOMMITTEE,
Senate Annex, Washington, D. C.

Attn: Liz Martin

DEAR MISS MARTIN: Thank you very much for your phone call September 9, 1971.

In the early part of 1971 a number of our Doctors became concerned about the growing abuse and misuse of amphetamines in our area. It was brought vividly to my attention that amphetamines were being sold in the corridors of the local school system by students who had "borrowed" from their parents medicine cabinets. As we investigated this problem further it appeared that the use of amphetamines was a starting point in some instances for the use of hard narcotics. This was also the expression of the local law enforcement authorities. Further it was found out that the country of Ireland had banned the use of amphetamines and in November, 1970 a resolution was passed in the state of Utah, that the Internal Medicine Society as well as the Utah State Medical Society, placed a ban on amphetamines and they no longer would be used in the treatment of obesity.

Therefore a program was worked out whereby the LaPorte County Medical Society would establish a program to try to combat this problem in the County. In addition to an educational program within the school systems and through the various news media we felt it imperative to bring some harsh facts directly back to the doctors. It was also felt a closer cooperation with the pharmaceutical Society and Law Enforcement Authorities including local, county, and state was absolutely necessary. Along with this, a resolution was passed by the Executive Committee of LaPorte County Medical Society that a three month moratorium be established on the prescription of amphetamines and at the conclusion of the three months that a definite program of evaluation be established (at the onset of the moratorium.)

In February and early March a written survey was conducted of the membership and 75% of the practicing doctors were for the three month moratorium. At the conclusion of this three month period, the effectiveness of the moratorium was judged on three basis. 1. whether the law enforcement people would see a definite decline of the illicit drugs on the street. 2. Whether the general public was positive, neutral, or negative toward the program. 3. Whether the pharmacist and law enforcement authorities felt that this should be continued.

The results of this three month moratorium were evaluated in June of 1971. We received many letters and phone calls from the community, from lay people. They were positive for this program and thanked us for it. The LaPorte County Pharmaceutical Association endorsed the program unanimously and 3. The local chief of police of Michigan City as well as the County Sheriff as well as the State Police also encountered the program and gave us some factual information. Therefore it was decided by the Executive Committee of LaPorte County Medical Association early in July, 1971 that a continued moratorium of 1 year of the writing of amphetamine prescriptions with the exception of the cases of narcolepsy, hyperkinesis and certain psychiatric conditions. This survey now has been conducted again of the above named moratorium and the results to date show 95% of the membership for this.

The same resolution is being proposed at the Indiana State Medical Association by our County Medical Society.

In the course of obtaining further information about this general problem considerable valuable material can be obtained from the U.S. Department of Justice, Bureau of Narcotics and Dangerous Drugs, Washington D.C. 20537 and from Donald K. Fletcher, Manager Distribution Protection of Smith, Kline and French Laboratories in Philadelphia.

Hoping this answers your questions, I remain,

Very truly yours,

DOCTORS O'BRIEN, STARK AND MLADICK
RAYMOND J. O'BRIEN, M.D.

MICHIGAN CITY, IND.
June 24, 1971.

RAYMOND J. O'BRIEN, M.D.
President of LaPorte County Medical Society,
1801 Franklin Street,
Michigan City, Ind.

DEAR DR. O'BRIEN: We recognize that the moratorium on Amphetamines has been a deterrent, the price on Amphetamines has gone up to about $3.00 as compared to approximately 50¢. Since the moratorium the activity and complaints are less. Since this problem has been handled more discreetly and from reading newspapers and other news media, other State and Federal Government supporting this type of program. I do also.

From talking with State and County law enforcement people and other people in law enforcement, early support has been a great deterrent in Michigan City and LaPorte County.

Control of this matter has assisted greatly the availability of Amphetamines in Michigan City. Amphetamines have become rather scarce in Michigan City, the traffic has been going to Gary to obtain their drugs. As our more recent arrests have disclosed the facts that addicts must go out of town to obtain their supply.

With the current employment problem, the addict can't borrow and/or buy from one another, but they are able to buy in small quantities only.

We are still using selective enforcement in curtailing narcotics and dangerous drugs.

On behalf of the Michigan City Police Department and myself, you are to be congratulated in your effort in assisting all law enforcement agencies in the abuse of these drugs. I remain,

Very truly yours,

LEON C. SHIPARSKI,
Superintendent of Police.

INDIANA STATE POLICE,
DUNES PARK DISTRICT NO. 11
Chesterton, Ind., June 30, 1971.

RAYMOND J. O'BRIEN, M.D.,
Michigan City, Ind.

DEAR DOCTOR O'BRIEN: I would like to take this opportunity to comment on the recent moratorium called on amphetamines in LaPorte County. We feel that this program has much merit.

In our opinion, the moratorium should be continued and also carried out in the surrounding counties if at all possible. The response from the physicians in LaPorte County was most favorable.

It is the feeling of our department that the moratorium did much to curb the drug problem in our area, and would appreciate its continuance.

Thank you for your future consideration.

Respectfully yours,

ALBERT D. HARTMAN,
Lieutenant Commander, Dunes Park District No. 11.

LAPORTE, IND., *July 6, 1971.*

DR. RAYMOND J. O'BRIEN, M.D.,
LaPorte County Medical Society,
Michigan City, Ind.

DEAR DR. O'BRIEN: We in Law Enforcement want to thank your organization for your co-operation in helping us combat the deadly drug traffic of our community.

I personally know that the ban placed on the amphetamines has been a big help to our community and it is my recommendation that this ban be continued, with the exception of serious cases that the drug is necessary for the patients' treatment.

Today the abuse of amphetamines is a major medical and social problem, thus any step taken by your organization to halt the administration of such dangerous drugs will be a great help to our community.

I want you to know that we welcome these opportunities to cooperate with you on this difficult drug problem and if I can be of assistance, please contact me.

Sincerely yours,

RODGER L. NICKELL,
Sheriff of LaPorte County.

LAPORTE COUNTY PHARMACEUTICAL ASSOCIATION, INC.

DEAR DOCTOR: On Wednesday, March 24, 1971, the pharmacist-members of the LaPorte County Pharmaceutical Association called a special meeting in order to fully discuss—and vote upon—an issue of your resolution of March 16, 1971, in which you approved and adopted a three month moratorium on the prescribing of amphetamine prescriptions in LaPorte County.

After lengthy deliberation, the following motion was proposed: " . . . That the LaPorte County Pharmaceutical Association adopt a resolution offering our unanimous cooperation to the LaPorte County Medical Society in jointly accomplishing a successful moratorium on the prescribing and compounding of amphetamine prescriptions during the next three months."

We are pleased to announce that the approval by our group was unanimous; said moratorium will be in effect concurrently with that adopted by your society.

We project successful results in not only this resolution—but also those which may result from future joint endeavors of both organizations.

Very truly yours,

STAN SMITH, R.P.
ANTHONY DARGIS, R.P.
JOHN KAHN, R.P.
LAPORTE COUNTY PHARMACEUTICAL
ASSOCIATIONAL RESOLUTION COMMITTEE.

NOTE: This formal notification is also being sent to individual pharmacists, pharmacy owners, chain pharmacy managers, and to chain pharmacy district offices.

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10. STATEMENT OF MILTON GORDON, M.D., CHAIRMAN, EDUCATION, DRUG ABUSE TASK FORCE, SUFFOLK COUNTY MEDICAL SOCIETY, LONG ISLAND, N.Y., BEFORE THE COMMITTEE ON THE JUDICIARY, SUBCOMMITTEE TO INVESTIGATE JUVENILE DELINQUENCY HEARINGS ON S. 674, "AMPHETAMINE LEGISLATION 1971," JULY 15, 1971

THE SUFFOLK COUNTY MEDICAL SOCIETY,
Hauppauge, N.Y., July 6, 1971.

TESTIMONY TO THE COMMITTEE ON THE JUDICIARY SUBCOMMITTEE TO INVESTIGATE JUVENILE DELINQUENCY

To: Hon. Birch Bayh.
From: Milton Gordon, M.D., Chairman,
Education, Drug Abuse Task Force,
Suffolk County Medical Society.

A recent study concluded by the Research Director, Dr. Carl Cambers of the New York State Narcotic Addiction Control Commission, uncovered the following:

Pep pills, amphetamines, and amphetamine-like compounds, are the most abused drugs in the State and that more than half the 110,000 users in New York State obtained them without prescription.

Other statistical evidence uncovered by the survey showed:

1. More than 361,000 people in New York State use barbiturates on a regular basis, and 10% of them are obtained without a legal prescription.

2. Some 525,000 people in the State of New York regularly use minor tranquilizers (i.e., Librium, Milltown.)

3. Some 222,000 people regularly use diet pills and 19% of them are obtained without a prescription.

4. Some 203,000 have used LSD in the past six months, and 45,000 of them used it on a regular basis.

5. Some 110,000 persons have used Methedrine ("speed") in the past six months and 35,000 of them do so on a regular basis.

6. Some 64,000 persons have used heroin during the past six months and 32,000 of them do so on a regular basis.

What is even more surprising is that nearly half of the users were high school seniors or college students and 70% were under 25 years of age. More than 76% were white and most were from the middle class, or more affluent classes.

There is no question in anyone's mind that many Americans were placing undue dependence on drugs and what is even more distressing is that tens of thousands of people from all walks of life are using a wide variety of potentially harmful drugs without prescription or medical supervision. These people rely on pills to get them up in the morning, to prevent them eating too much during the day, to prevent anxiety at the office, and to lull them to sleep at night.

Without realizing that we were the first community in the nation to organize a voluntary ban on prescribing and dispensing amphetamines, our local Narcotic Guidance Council and the Drug Abuse Task Force of Suffolk County agreed that a drug education program was in urgent need. Physicians were asked to sign their names to a pledge and join the attack on amphetamines in the interest of the welfare of both the adult and youth community. The doctors were asked to pledge and support the campaign to ban the prescription of amphetamines unless the drug is needed in the treatment of narcolepsy and hyperkinesis.

The results obtained were most satisfying. 260 pledges were mailed to physicians in the Huntington Township. Over 60% of the doctors agreed to support the idea not to prescribe amphetamines. This study was even more impressive if one were to realize that 20% of the physicians in the township have no need to prescribe any of the amphetamines, i.e., Dermatologists, ENT, Ophthalmogists, Pathologists, Radiologists, etc.

Based mainly on the tremendous response of the media to this endeavor, the program was expanded to include the entire physician population of Suffolk County.

In addition to the physicians, 28 pharmacists signed the pledge, with only 5 declining to sign, and 9 abstaining.

This campaign should be characterized as being educational in nature. The drug abuse problem within the community was not any more severe than in most communities throughout the United States.

The doctors of Huntington were concerned and felt that the use and abuse of amphetamines required stricter control on production, distribution, prescribing and dispensing. It was also felt that a voluntary program as this one would cut down the base that the Justice Department would use in determining production and would thus further limit the supply available.

As we look back over the action taken, it has been brought to our attention that for the first time the adult population was given an opportunity to relate to their children. Must a pill be taken to pep us up in the A.M., relieve anxiety and depression, lull us to sleep? Are we adults completely dependent on drugs for our daily existence?

It seemed reasonable that if we could focus the physician's attention on one drug that has been abuseed like amphetamines, we might motivate him to set an example for the rest of his community. We must call the physician's attention to the need of re-evaluating and re-examining his prescription and dispensing of amphetamines. If the doctors throughout the nation refuse to prescribe drugs manufactured by pharmaceutical companies that also put out stimulants like amphetamines, the industry would cease its widespread production of amphetamines.

The course of events included the following:

1. Initial letter and pledge to the physicians of the Huntington Township.
2. Follow-up letter and pledge to physicians not responding.
3. Letter and pledge to balance of physician members of the Suffolk County Medical Society.
4. Statistical evaluation: 260 pledges were mailed to physicians in Huntington Township. 26 of those were Dermatologists, Ophthalmologists, Otolaryngologists, Pathologists, Proctologists, Radiologists. 234 were those who might be using amphetamines in their practice. 152 pledges were received agreeing and 7 disagreed. Based mainly on the tremendous response of the media to this endeavor, the program was expanded to include the entire county, witness the letter of June 9, 1971. In this latter endeavor, 874 pledges were mailed with the following results. 110 of those were of the above specialties who would not be using amphetamines in their practice. Total response 372; signed pledges 359 (96.5%); in disagreement 13 (3.5%).

5. All press reports concerning action taken in Huntington and Suffolk County as well as the action of the Honorable Pepper.

6. Resolution to the AMA and the action taken by the House of Delegates. "In separate action as related to drug dependence, the House went on record as favoring measures to urge physicians to limit their use of amphetamines and other stimulant drugs to specific medical indications. The House supported the Bureau of Narcotics and Dangerous Drugs proposal to establish manufacturing quotas for amphetamines and methamphetamines."

7. Accumulating statistical evidence relating to number of prescriptions written by physicians for amphetamines prior to the campaign and comparing that number with prescriptions that have been written as of July 1, 1971.

Enclosures.

MAY 19, 1971.

AMPHETAMINES

DEAR DOCTOR: On May 5, 1971, I wrote to you on the subject, indicating that a number of physicians in Huntington Township would like to see the Huntington Medical Community pioneer in the effort to voluntarily abandon the prescription of amphetamines, except for medical necessities such as: (1) narcolepsy, (2) the hyperkinetic child, (3) certain types of epilepsy, (4) some aggressive psychopaths, (5) hypersomnia.

The response has not lived up to expectations, but I can report that of a total of 92 responses, 88 have pledged support to the program described.

Our records indicate that you have not responded and in order to obtain a clear reading of the desires of the professional in this matter, we again request that you reread my letter of May 5 and if so motivated return the attached pledge form signed, which is enclosed for your convenience.

Sincerely yours,

MILTON GORDON, M.D.,
Chairman,
Education, Drug Abuse Task Force.

Enclosure.

PROPOSED PLEDGE

I _____ M.D., a physician practicing in the Town of Huntington *join the attack on amphetamines* in the interests of the welfare of both the adult and youth community of Huntington, and do hereby pledge to support the campaign to ban the prescription of amphetamines by not prescribing amphetamines for any of my patients *unless* the drug is needed in the treatment of narcolepsy and hyperkinesis.

DATED: _____ 1971.

JUNE 9, 1971.

DEAR DOCTOR: The Suffolk County Medical Society has completed a pilot study in the Township of Huntington for the prime purpose of calling to the physicians' attention the critical problems arising in the drug field, particularly in the use and abuse of amphetamines. There is no doubt in anyone's mind that the production in excess of four billion amphetamines per year (or about 40 pills per person in the nation) is greatly in excess of the known medical need.

This pilot study has revealed the following results:

1. 60% of all Huntington Township physicians agreed to support the idea not to prescribe amphetamines, except for a few medical indications. This would constitute a voluntary embargo on these drugs, as well as a concerted effort by the physicians to attempt to cope with the problem.

2. In addition, the study was even more impressive if one were to realize that 20% of our physicians (i.e. dermatologists, ENT, ophthalmologists, etc.) have no need to prescribe any of the amphetamines.

Your Task Force on Drug Abuse and Addiction would like to see the entire Suffolk County Medical Community continue to pioneer in this effort to voluntarily abandon the prescription of amphetamines, except for medical necessities such as: 1) narcolepsy, 2) the hyperkinetic child, 3) certain types of epilepsy 4) some aggressive psychopaths, 5) hypersomnia.

To turn the pages back for just a brief moment, amphetamines were first introduced into medicine in the middle 1930's—in 1935 by Prinzmetal and

Bloomberg, who found "Benzedrine" of value in narcolepsy, and in 1936 by Peoples and Guttman, for its euphoric effect. In 1937, Guttman and Sargent described a controlled study of "Benzedrine" in Mansley Hospital, Edinburgh, England. Drugs of this type have been used therapeutically for their euphoric effect ever since. However, owing to the addictive or dependency-producing property of these drugs, Time (1969 had commented as follows: "Psychologically more destructive than heroin—and now more available than marijuana—amphetamines are in many ways the most treacherous of all abused drugs".

The position has now been reached where many clinicians are all but prepared to jettison the amphetamines from the therapeutic armamentarium. Swanton had the following to say: (Swanton, C. 1967 Med. J. of Australia—2:625).

"I would suggest—that the amphetamines have little if any place or value in medicine. There are, I believe, alternatives equally useful and less hazardous drugs which may be used in place of the amphetamines and for similar purposes and that, apart from the drug companies, perhaps few if any would suffer if the amphetamines were removed from the pharmacopia."

Amphetamines have *no place* in treatment for 1) obesity, 2) depression, 3) fatigue, 4) as a pressor drug, 5) in Narcotic poisoning, 6) nocturnal enuresis, premenstrual tension, dysmenorrhea and migraine. (Fulton, 1969).

Those persons becoming involved with amphetamines on a fairly regular basis tend to be more severely disturbed personalities and often take a whole variety of different drugs at different times—largely in relation to availability. By and large, the treatment for this group at the present time is very far from satisfactory and "cures" are few and far between.

One is, therefore, left with the only alternative—prevention. It may be worthwhile to try to ban the drug completely. However, it is well accepted in medicine by law-enforcement bodies and by Government Departments of drugs and food that the illicit manufacture of amphetamines exceeds by three to ten times the commercial legal production in this country and in many other parts of the world. In Toronto, for example, there are at least four "meth factories", two of them in the bathrooms of apartments. In addition, controls restricted to amphetamines have had only limited effect partly because the addict has usually been able to turn to other stimulants that are freely available.

Knowing full well our limitations, the medical profession will have to accept their real responsibility for the creation and maintenance of a considerable amount of abuse of the amphetamines. We know that they cause behavioral toxicity, physical damage and dependency. If it were possible, amphetamines should be sharply curtailed and probably limited to one or two pharmaceutical companies.

An opinion form has been sent to you and to every physician in the county, enlisting their agreement to cooperate in this novel attack on the problem. Won't you help support this very worthy effort?

Respectfully yours,

MILTON GORDON, M.D.,
Chairman,
Education, Drug Abuse Task Force.

Enclosure.

JUNE 9, 1971.

OPINION POLL

I am a physician practicing in Suffolk County. I agree ( )/disagree ( ) to *join the attack on amphetamines* in the interests of the welfare of both the adult and youth community of Suffolk County, and do hereby pledge to support the campaign to ban the prescription of amphetamines by not prescribing amphetamines for any of my patients *unless* the drug is needed in the treatment of narcolepsy and hyperkinesis.

(Signed)_____,

(Specialty)_____

JUNE 9, 1971.

RESOLUTION—AMPHETAMINES

WHEREAS: The amphetamines have been found to be psychologically more destructive than heroin, and

WHEREAS: Amphetamines are now more available than marijuana and in many ways more treacherous than all abused drugs, and

WHEREAS: The production of amphetamines per year has reached the astronomical figure of four billion pills (or 40 pills for every person in the nation), and

WHEREAS: Pilot studies in Suffolk County, New York, have indicated that the majority of physicians are interested in placing a temporary embargo on the use of amphetamines except for a few medical necessities, be it therefore

RESOLVED: That the medical profession will accept its real responsibility in the use and abuse of amphetamines and sharply curtail and limit the prescription of amphetamines, and be it further

RESOLVED: That the medical profession will lend its full support behind the Justice Department's plans to set production quotas and tighten distribution of amphetamines.

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11. REPORT OF PROCEEDINGS ON CURRENT STATUS OF DRUG ABUSE, BY THE AMERICAN MEDICAL ASSOCIATION, HOUSE OF DELEGATES, JUNE 20–24, 1971

PROCEEDINGS, AMA HOUSE OF DELEGATES

June 20–24, 1971

House Action: Filed.

Following is a report from the Council on Mental Health and its Committee on Alcoholism and Drug Dependence which summarizes the current status of drug abuse in the United States. One statement pertaining to insurance coverage for alcoholism and drug dependence has been deleted from the report as submitted to the Board and has been referred to the Council on Medical Service for study and report at a later time.

STATUS REPORT ON DRUG ABUSE

INCIDENCE AND PREVALENCE OF DRUG ABUSE AND DEPENDENCE

There can be no accurate measure of the overall extent of drug abuse and dependence in the United States: there is lack of agreement on definition and relatively few drug abusers come to the attention of medical, law enforcement and other authorities.

Some 85 to 90 million Americans drink alcoholic beverages. About 10 percent are severely dependent on alcohol, and an additional undetermined percentage, although not severely dependent, abuse the drug frequently by drinking to a state of intoxication.

The widespread use of marihuana has had some, but by no means an appreciable, effect on the consumption of alcoholic beverages by young people. It can be safely assumed that alcoholism and alcohol abuse will continue to constitute the major drug problem in this country for all age groups.

According to a Gallup Poll survey in 1969, marihuana had been smoked on one or more occasions by 10 million persons in this country, most of them teenagers and young adults. How many are one-time or infrequent experimenters, or how many are regular users, is not known. Also unknown is the accuracy of data on self-incriminating behavior, such as marihuana use, gathered through public opinion poll techniques.

The use of marihuana appears to be increasing among adults as well as young people, cutting across all economic and social strata. That its possession and sale are illegal in every political jurisdiction—a factor which some believe serves as an incentive for youth to use the drug—apparently has as little deterrent effect on adult users as on young people. A good deal of proselytizing is evident in the distribution of marihuana. Those who are users, especially confirmed users, often will share their supply with others without remuneration. The use of marihuana also is typically a "social" affair and with the young constitutes a part of an inter-personal subculture which displays other forms of shared behavior, beliefs and attitudes.

The 1969 Gallup Poll reported that four of every 100 college students had taken LSD. Since then, the abuse of LSD reportedly has been falling off, partly because of research reports associating LSD with chromosomal damage and possible teratogenic effects and partly because of "bad trips" and other unpleasant experiences. No estimates have been made of the abuse of other hallucinogenic substances such as STP, DMT, morning glory seeds and peyote.

Fewer than 100,000 persons dependent on heroin are known to the Federal Bureau of Narcotics and Dangerous Drugs, but the number of such persons in New York City alone has been estimated to be in excess of that figure.

Most heroin-dependent persons start their abuse of drugs with marihuana, amphetamines, or alcohol. This does not mean, however, that most drug abusers "progress" to heroin or other opiates. Yet, the number of persons becoming dependent on heroin has been increasing in recent years and white middle-class youth are being found among their ranks in greater proportion than before. Of significance in this regard may be the "downer" use of heroin among amphetamine abusers. This practice can lead to a state of morphine-type dependence.

Persons who incur a primary dependence on methadone, although relatively few in number, represent a recent phenomenon frequently associated with diversion of this drug from some programs using oral methadone maintenance in the management of heroin-dependent persons. Methadone administered intravenously by a heroin-dependent person can produce euphoric effects comparable to those of heroin; and methadone taken either orally or intravenously by a non-dependent person can, with repeated self-administration, produce drug dependence in that individual.

Those narcotics, such as morphine, which have a place in medical practice are abused by heroin-dependent persons when heroin is not available, and also by persons who have relatively easy access to these drugs. Included in this latter group are physicians, nurses, laboratory technicians and others in the health profession. It has been claimed that the rate of drug abuse in this occupational field is higher than in any other, but substantiating data are lacking.

It is estimated that at least 400,000 persons abuse barbiturates and other sedative drugs, principally the so-called minor tranquilizers. A significant proportion of persons abusing these drugs obtain them originally through legitimate medical channels and for legitimate medical reasons. But dependence on the drug's effects, including tolerance, can result from abuse of the drug by the patient, and can compel the patient to take more of the drug, and at a greater frequency, than prescribed. Because the number of refills of prescriptions for such drugs are limited by law, the patient eventually may find it necessary to go to more than one physician or even into the illicit market to secure his supply.

Because barbiturates have cross-tolerance with alcohol, some alcoholics use them as substitutes or supplements in their dependence patterns. This type of substitution also may take place when heroin-dependent persons are temporarily unable to get heroin or any other narcotic drugs.

Large quantities of amphetamine preparations are known to be diverted from legitimate manufacturers through the illicit market to drug abusers. In pill form, amphetamines are abused by persons of all age groups and classes. Some persons are introduced to these drugs in a therapeutic regimen, such as a program for weight control, and then continue to take them beyond the short-term prescribed by a physician.

In injectable form, amphetamines, particularly methamphetamine, are taken by the so-called "speed shooters" or "speed freaks" who are mainly young people. Shooting speed is a rapidly growing practice and it is involving many of the younger adolescents who have had no previous drug experience. The past two years have seen a marked rise in the abuse of all types of amphetamines and other stimulant substances.

Whatever the actual incidence of drug abuse in its various forms may be, most observers agree that the practice still is on the increase. Along with the mounting abuse of drugs, there has been a noticeable shift toward multiple drug use, with two or more drugs being taken in combination or in sequence. Those who shoot speed, for example, and achieve a high through the administration of amphetamine or methamphetamine, will often take a narcotic or a barbiturate to "come down." Multiple drug use has particular implications for treatment: the diagnostician must be alert to the possibility that more than one drug may still be pharmacologically active and that each may have to be dealt with in a different way.

TRENDS IN TREATMENT

The most notable trend in treatment of alcoholism and drug dependence is toward community-based facilities and services. This trend has been given ex-

pression in public policy with the passage of amendments to the Community Mental Health Center Act providing for neighborhood programs of treatment and rehabilitation. The new Federal law on alcoholism, passed in 1970, also emphasized the importance of local services.

With respect to alcoholism, more and more general hospitals are admitting alcoholic persons under that diagnosis. The entire optimum range of services, from detoxification through hospitalization and after-care, has been given impetus in a few states with the adoption of new legislation recognizing alcoholism as a complex illness.

In the treatment of heroin dependence, the use of oral methadone with maintenance techniques has been seen in several programs to enhance the personal and social productivity of certain dependent persons and to reduce criminal behavior, especially among patients not amenable to abstinence programs. The Council on Mental Health and the Committee on Alcoholism and Drug Dependence, together with the National Research Council, earlier this year recognized this technique as an acceptable form of medical practice if used as part of a total program that includes facilities for urine testing, general medical and psychiatric services, hospital facilities as needed, adequate staff, and measures to prevent diversion of the drug to illicit use.

The proliferation of drug abuse, especially multiple drug abuse and abuse of hallucinogens and "speed," has resulted in the formation of so-called "street clinics" and "crash pads," many of which lack professional medical direction or supervision. Those who abuse drugs often are reluctant to seek proper medical attention even if it happens to be available because of a fear of being turned over to the police; instead they choose non-professional help with its attendant health hazards.

TRENDS IN PREVENTION AND CONTROL

Efforts to prevent and contain the abuse of drugs have taken the form of legal controls, treatment programs, educational programs in the schools, and informational campaigns and material directed to the public.

The new Federal law to control drug abuse (PL 91–513) has gone a long way toward eliminating legal inconsistencies and reducing inequities in the law which had existed previously. Many of these previous defects were caused by the fact that new substances had been abused subsequent to the passage of the former drug control acts. Such substances then had to be controlled *ad hoc* by regulation. One example was the regulatory placement of control of THC (tetrahydrocannabinol), one of the active principles of marihuana, under the Dangerous Drugs Control Amendments. Illegal possession under that law was a misdemeanor, whereas illegal possession of marihuana itself, under another law, was a felony.

The new Federal law treats first-offense illegal possession of controlled substances for personal use as misdemeanors, whatever the drugs may be, and gives the Courts discretion to grant probation and expunge the arrest record of first offenders. Although states are beginning to change their drug abuse control laws to conform with the new Federal act, young first-offenders in many jurisdictions still risk incurring a criminal record which can stay with them for life and prove especially damaging to those about to embark on a career.

The chief drawback of PL 91–513 is its relative lack of emphasis on drug dependence as an illness and its failure to recognize the fact that many drug abusers who are apprehended are sick individuals who should be medically evaluated and treated. The regulatory thrust of this law is in contrast with the new Federal alcoholism act which encourages the implementation of comprehensive treatment and educational programs on national, state and local levels.

Nearly all states require public schools to give instruction in alcoholism and drug abuse. Few of these laws, however, specify what type and how much information should be presented, who should present it, and how it should be financed. While such courses are mandatory for school children, instruction in these subjects is rarely compulsory for teachers.

The National Education Association has compiled an excellent curriculum guide for teachers, and several school systems have developed comprehensive instructional programs. A number of state and county medical societies have cooperated with educational groups in providing basic information to teachers.

Yet, the value of formal educational efforts, particularly in the high schools, has been questioned. With this age group, peer pressure has been seen to be far more influential than the presentations and preachments of teachers and parents. In fact, in some cases peer group influence has been utilized in a positive way and incorporated into the school system. Most educators emphasize the need to reach children in elementary school at a time when drug abuse is not widespread among their friends.

Many groups are now providing public information on drug abuse. To evaluate their efforts and to provide a forum and clearinghouse for ideas and experiences, the National Coordinating Council on Drug Abuse Education and Information was organized in 1968. The AMA is one of more than 100 organizations represtnted in the Council. Other constructive public information programs have been conducted by the National Institute of Mental Health and the U.S. Office of Education.

RESEARCH NEEDS AND ISSUES

Multi-faceted research on a broad scale is needed on nearly every aspect of drug abuse and drug dependence.

With respect to the drugs themselves, while much is known about their properties, relatively little is known about their precise mode of action in the human organism and the exact nature of the long-term effects of their regular use by man.

While some of the factors which lead individuals to abuse drugs are understood, science is not yet able to predict who may be vulnerable to drug dependence. The role of drug abuse within the context of a total life style also needs to be more clearly delineated.

Much work remains to be done in developing new, and evaluating existing, treatment modalities in terms of the therapeutic needs and psycho-social makeup of the individual patient. Physicians can treat the acute effects of drug abuse and drug dependence, often preventing serious physical and psychological consequences; but medical and sociological management techniques have not been developed to insure that a significant number of patients will not return to abuse of drugs and to their patterns of dependence, after the acute symptoms have been abated through treatment.

Methods of "reaching out" to the young drug abuser must be tested to ascertain the most effective courses that educators, physicians and others in the helping professions can pursue..

Finally, a great deal more work should be carried out with human subjects. Especially needed are longitudinal studies encompassing etiology, diagnosis, treatment and after-care, even though such studies would require an extended period of years.

RECOMMENDATIONS FOR MEDICINE

The Council and Committee suggest that the following issues are ones to which organized medicine, on national, state and local levels, can respond and make a contribution:

1. Increased attention should be given to alcoholism and drug abuse in the curriculum of medical schools, and to the identification of these problems within a unifying concept of psychology and physiology. Physicians of the future must be prepared to deal knowledgeably with drug abuse and drug dependence as complex problems.

2. Medical students, interns and residents should be encouraged to associate themselves with "street clinics" so that medical input and guidance can be made available, and so that links can be established between the medical profession and the population of young drug abusers.

3. For physicians and other health professionals already in practice, there should be continued development and dissemination of reliable information through publications, seminars and other avenues of postgraduate education. New diagnostic and treatment techniques, properly tested and verified, should be recommended as indicated. Attention should be called to any new substances that are being abused and their effects and dependence-liability should be explained.

4. Laws and regulations should be modified insofar as possible to give adequate recognition to alcoholism and drug dependence as illnesses and to provide for the medical handling of offenders who are alcoholic or drug dependent or

who have other medical problems associated with their abuse of alcohol and other drugs.

5. Medical societies should effect close liaison with law enforcement and licensure bodies to deal jointly with the problem of the practicing physician who is suspected of professionally misusing or personally abusing narcotics or other controlled substances.

6. There is a need for continually up-dated factual material for public consumption, particularly the type of material that a physician can give to his patients and that he can utilize in his contacts with lay organizations.

7. There should be increased emphasis on the responsible use of drugs for therapeutic purposes; on the part of both the public and members of the medical profession.

The Council and Committee will continue working toward these objectives both independently and, where appropriate, in conjunction with other groups within the AMA and with other national organizations.

RESOLUTIONS

No. 4. Increase private practitioners' participation in narcotic addiction control programs, particularly methadon maintenance therapy.

Introduced by Oregon delegation. (Reference Committee E, page 343).

House action: Referred to Board of Trustees and its Council on Mental Health.

Resolved, That the American Medical Association, together with state and county medical societies, become more deeply and actively involved in supporting and extending present medical programs concerned with drug abuse and narcotic addiction, including Methadon maintenance therapy for narcotic addiction under less rigid legal restrictions; and be it further

Resolved, That the American Medical Association immediately take steps to recommend that restriction on the use of Methadone be modified and revised to permit the private practitioner to employ Methadone maintenance therapy.

No. 5. FDA practices of removing drugs from the market.

Introduced by Oregon delegation. (Reference Committee E, page 340).

House action: Following substitution Resolution 5 referred to Board of Trustees and its Council of Legislation in lieu of Resolutions 5, 12, 14, 45, and 87).

Resolved, That the American Medical Association urgently press for the establishment of mechanisms to assure the early dissemination of information to and participation by practicing physicians in the regulatory activities of the Food and Drug Administration that directly affect the prescribing practices of physicians.

No. 6. Restrictions on use of stimulant drugs.

(Introduced by Missouri delegation. (Reference Committee E, page 344).

House action: Following substitute Resolution 6 adopted in lieu of Resolutions 6, 29, and 85.

Resolved, That the American Medical Association urge all physicians to limit their use of amphetamines and other stimulant drugs to specific, well-recognized medical indications; and be it further

Resolved, That the American Medical Association support the proposal of the Bureau of Narcotics and Dangerous Drugs to transfer Amphetamine and Methamphetamine and their Salts, Optical Isomers and Salts of their Optical Isomers, from Schedule III to Schedule II published in the May 26, 1971 Federal Register.

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12. Selections From, "An Assessment of Drug Use in the General Population"

Carl D. Chambers, Ph. D., Director, Division of Research, New York State Narcotic Addiction Control Commission, May 1971

(Introduction, pp. 1–10, Pep Pills, pp. 61–68; Diet Pills, pp. 69–74; and, Methedrine, pp. 118–124.)

INTRODUCTION

During 1968–1969, the Narcotic Addiction Control Commission designed and completed a general assessment of the public's knowledge of the effects of various drugs, knowledge of the prevalence of drug use and attitudes concerning durg users and their treament (Glaser and Snow, "Public Knowledge and

Attitudes on Drug Abuse in New York State," *New York State Narcotic Addiction Control Commission Research Monograph*, 1969). While this major research effort provided a frame of reference wherein meaningful preventive education efforts could be directed, the study had not been designed as a direct assessment of drug use. During 1970, the Commission scientists began designing a second major interview survey. The new design strategy was to include a determination of the types and an assessment of the extent of drug use within the general population throughout New York State. Such a statewide epidemiological assessment of drug use was without precedent. While this second survey was to establish the dimensions of *drug use*, it was not designed to document the incidence of current *drug abuse* in New York State. Methodologists and epidemiologists responsible for the survey strategy were in agreement that such a determination would be a logical third phase survey which could only occur after the accumulation of experiences from the first two surveys. The design of interview schedules which will systematically elicit valid data whereby measurements of personal and social dysfunctioning are possible can only occur after the strategists have accurate attitudinal data and comprehensive statistics relevant to who is involved, the drugs of involvement and the dimensions of frequency, duration and amount of use. This third survey, the determination of *drug abuse*, will be conducted when sufficient research monies become available. A grant was provided by the New York State Office of Crime Control Planning (Grant No. 343) to partially support this current project. This financial support permitted the Commission to secure the collaborative assistance of a leading private research organization during the conducting of the survey. Special Report No. 1 is the first report in a series which will be released by the Narcotic Addiction Control Commission to share the results of this epidemiological survey. The survey results for the total State are the subject for this first report. Other reports in the series will reference the survey results from various geographical regions within the State.

METHODOLOGY

The primary focus of the study was to assess the prevalence, incidence, frequency and situational content of all types of drug use within the general population. At the same time, the study was designed to include three secondary assessments an assessment of the accuracy of beliefs relative to the adverse effects of certain forms of drug misuse and abuse, an assessment of the visibility of persons who misuse or abuse drugs as reflected in the awareness of other persons of this misuse and, finally, an assessment of the general population's attitudes toward various types of drug abuse and abusers. These data were to be obtained by face-to-face interviews with selected persons aged 14 and above.

The sample

Extensive consultations involving the behavioral scientists and epidemiologists within the N.A.C.C. Division of Research and the senior custom market researchers of Daniel Starch and Staff, Inc. and their subsidiaries, one of the leading independent research organizations, resulted in a mutual agreement on the following sample considerations and decisions.

1. Reliability and projectability to the base population could be obtained with approximately 7,500 actual interviews.

2. Sampling and analytical objectivity could best be accomplished by the rational collapsing of the base population into five age groups. As near as possible, these five age groups were defined in accordance with the social, psychological maturation phases within an individual's life which were most likely to produce variability in patterns of drug use. The age groups were established as follows:

Age	Phase	Percentage distribution in the total population
14 to 17	Late adolescence	9.3
18 to 24	Early adulthood	14.6
25 to 34	Adulthood	14.9
35 to 49	Mature adulthood	24.5
50 and over	Senior adulthood	36.7

For maximum reliability of projection, the sample of 7,500 should be disproportionately allocated in terms of age. Although each successively older age group contained numerically more people, the interview allocation for each age group was the same, 1,500 interviews. This disproportionate allocation insured sufficient numbers in the two youngest and numerically smallest age groups for meaningful analyses. Appropriate weights were applied during data processing to represent ages in their true proportions.

3. For maximum efficiency, equal numbers of males and females could be interviewed in each age group. Appropriate weights were applied during data processing to represent the two sexes in their true proportions.

4. In order to provide utilitarian data for addressing the problems associated with prevention, education, control and treatment efforts, an independent cross-section of the State should be surveyed. Projectability could be served if the 7,500 interviews were allocated within 17 regions comprised of contiguous and demographically similar groups of counties. The number of actual interviews conducted within each region were weighted during data processing, to bring all regions into the true numerical proportion for the base population. The 17 regions and their interview allocations were as follows:

Region	Counties	Allocation
1	New York, Kings, Queens, Bronx, and Richmond	1,200
2	Nassau	400
3	Suffold	400
4	Westchester	400
5	Orange and Rockland	390
6	Columbia, Dutchess, and Putnam	390
7	Greene, Sullivan, and Ulster	390
8	Albany, Fulton, Montgomery, Rensselaer, Saratoga, and Schenectady	400
9	Clinton, Essex, Hamilton, Warren, and Washington	390
10	Franklin, Jefferson, Lewis, and St. Lawrence	390
11	Chenango, Delaware, Otsego, and Schoharie	390
12	Herkimer, Madison, Oneida, Onondaga, and Oswego	400
13	Broome, Chemung, Schuyler, Steuben, and Tioga	390
14	Cayuga, Cortland, Ontario, Seneca, Tompkins, and Yates	390
15	Monroe, Orleans, and Wayne	390
16	Erie and Niagara	400
17	Allegany, Cattaraugus, Chautauqua, Genesee, Livingston, and Wyoming	390
	Total, New York State	7,500

5. Efficiency, reliability and projectability could all be served with a sampling procedure which combined elements of both probability and quota techniques. Essentially, the procedure included the probability drawing of a residential block and then interviewing a quota of respondents residing on that block.

The full technique for respondent selection, accomplished in accordance with standard statistical procedures, included two stages as outlined below:

In the first stage, and within each region, communities were stratified according to size, based on U.S. Census data. Interviewer work loads or basic sampling units, i.e., 30 interviews, were allocated to each stratum, proportionate to population size.

In the second stage, those communities selected for interviewing were subdivided into areas of equal population, the number of areas dependent on the number of work loads. Three widely dispersed "female" interviewing blocks per work load were predesignated, on the basis of block statistics where available, and on the basis of equal probability elsewhere. Interviewing of males was done on three separate blocks, adjacent to the female blocks, with selection of these blocks done in a systematic manner. Thus, 15 female interviews were assigned to 3 blocks—5 per block, and a comparable assignment for males on the 3 male blocks. Actual respondent selection within blocks was done as follows:

On each of the blocks assigned for a given sex, and at a predesignated starting household, the interviewer asked if there was a person of that sex in residence age 14 to 17. If so, that person became the designated respondent. The interview took place then if the person was available at home otherwise, up to

three call backs were made before selecting a substitute respondent. If no one 14–17 was in residence, the person of appropriate sex in the next oldest age group who livd there became the designated respondent. Thus, houshold age composition was recorded in all cases—both to disproportionately interview younger people, and to interview those who tend to be away from home in the same proportions as "at home" people, and to have a pool of names available for substitute purposes or blocks that produced no one in residence of a given age and sex. Each interviewer work load of 15 female interviews (and 15 male) was spread across the three predesignated blocks, and three adjacent blocks with no more than two individuals of the same sex and age interviewed on the same block, to insure wide geographic dispersion. Only one interview was done per household, and in all cases interviewers were instructed to try to conduct it privately, away from any other members of the household.

In summary, this sampling procedure is believed to be a highly reliable one from a statistical sense, the only practical way to over-represent the younger age levels and unique in terms of geographical dispersion. Over 2,500 different blocks in the State of New York were preselected for interviewing purposes, located in 185 different incorporated and unincorporated places outside of New York City, and in each of the five borough within the City. At least one-third of each individual interviewer's work was validated, in most cases by postcard, but in many instances by telephone or in person by a regional supervisor where those interviewed had not returned the postcard.

The interviewers

In view of the sensitive nature of the study's subject, a series of criteria were imposed upon the selection of interviewers. Only after the various interviewing blocks had been isolated were interviewers selected. Wherever possible, interviewers were hired and trained to "fit" or match the demographic characteristics of their respective interviewing locations. Thus, in the great majority of cases, Blacks were interviewed by Blacks and Puerto Ricans were interviewed by persons fluent in Spanish, younger respondents by interviewers who were also young, and so on. A special attempt was made to recruit interviewers to interview within similar socioeconomic neighborhoods—interviewers who had been reared or currently resided in ghetto areas, for example, were trained to work in similar areas. Finally, in those areas where the use of illegal drugs was believed to be high, ex-addicts working for the N.A.C.C. and other agencies were hired and trained to conduct the interviews assigned such locations.

In addition to training the interviewers in the mechanics of the schedule, all the interviewers were instructed in the various drug names—generic, trade and slang—that they might subsequently encounter.

The interview schedule

The study was accomplished with a specially designed interview schedule (Appendix A). The schedule content was determined by the N.A.C.C. Division of Research with the format being a collaborative effort with the contracted market researchers. The interview schedule was designed to maximize validity of response and the questions were proposed in a manner leading up to respondent's own use of the drug. The schedule was divided into sections:

(1) The first part dealt with general use of drugs for nonspecific reasons.

(2) The second part related knowledge and attitudes about specific drug use, drug users and laws regarding drug use.

(3) The third section dealt with respondent's use of the 17 classes of drugs, and knowledge of use of others using drugs. Data indicating frequency of use were also collected. The criteria for classifying frequency of use was as follows:

(a) Non-user—has never taken or used the drug.

(b) Former user—has taken or used the drug but not within the previous 6 months.

(c) User—has taken or used the drug within the previous 6 months but not as much as six times during the previous 30 days.

(d) Regular user—has taken or used the drug at least six times during the previous 30 days.

Finally, this section probed as to the way in which the drug was obtained (physician's prescription), where it was used (social gathering, etc.), and in the

case of a legal drug, whether the drug was used as it had been prescribed. The respondents were provided with a card (Appendix B) which listed the drugs or drug group as well as appropriate examples of each. If the respondent asked about a drug not indicated, the interviewer categorized the drug referencing a drug listing guide provided by the Division. When a compound or "combination" drug was reported, the Division edited the response into the drug or drug class represented by the most important component, to avoid over-reporting of use.

(4) The final section of the schedule contained those questions necessary to establish demographic profiles, i.e., education status, marital status, employment/school characteristics, ethnicity, neighborhood characteristics, and so on. This determination was necessary in order to assess any differential patterns of drug use. The present report focussed upon six respondent distributions—sex, employment/school status, age grouping, ethnicity, socioeconomic status and formal education. Projections to various base populations were made in relation to the following distributions of 13,784,000 New York State residents age 14 and above:

	Percent
1. Sex distribution:	
a. Males	47
b. Females	53
2. Employment/school status distribution:	
a. Male high school students	6
b. Female high school students	5
c. Male college students	3
d. Female college students	2
e. Males employed	29
f. Females employed	14
g. Males unemployed	9
h. Females unemployed	31
3. Age distribution:	
a. 14–17	9
b. 18–24	15
c. 25–34	15
d. 35–49	24
e. 50 and over	37
4. Ethnicity distribution:	
a. White	81
b. Black	11
c. Puerto Rican	7
d. Other	1
5. Socioeconomic status distribution (neighborhood):	
a. Upper and upper middle	7
b. Middle	42
c. Lower middle and lower	51
6. Formal education distribution:	
a. Less than high school	42
b. High school graduate	32
c. More than high school	26

An elaboration of the basis for determining the socioeconomic status of a respondent is contained in Appendix C.

RESULTS

The study design dictated the interviews be conducted during the period August 1 through September 5, 1970. Ninety-eight percent of the 7,500 assigned interviews were completed, with all interviews conducted in person, in the respondents' homes. The following indicates the completion level within each region.

Region	Interviews		Percent
	Assigned	Completed	
1. New York, Kings, Queens, Bronx, and Richmond	1,200	1,260	105
2. Nassau	400	378	95
3. Suffolk	400	420	105
4. Westchester	400	392	98
5. Orange and Rockland	390	374	96
6. Columbia, Dutchess, and Putnam	390	389	100
7. Greene, Sullivan, and Ulster	390	366	94
8. Albany, Fulton, Montgomery, Rensselaer, and Schenectady	400	406	101
9. Clinton, Essex, Hamilton, Warren, and Washington	390	358	92
10. Franklin, Jefferson, Lewis, and St. Lawrence	390	382	98
11. Chenango, Delaware, Otsego, and Schoharie	390	343	88
12. Onondaga, Madison, Herkimer, Oneida, and Oswego	400	392	98
13. Broome, Chemung, Schuyler, Steuben, and Tioga	390	389	100
14. Cortland, Tomkins, Cayuga, Seneca, Yates, and Ontario	390	379	97
15. Monroe, Orleans, and Wayne	390	372	95
16. Erie and Niagara	400	400	100
17. Allegany, Cattaraugus, Chautauqua, Genesee, Livingston, and Wyoming	390	378	97
Total, New York State	7,500	7,378	98

The number of actual interviews in each region was weighted during analysis to bring all regions into their true numerical proportions.

The results and the projections derived from them are presented in four sections:

Section one—Attitudes and knowledge.

Section two—General drug use.

Section three—Specific drug use.

Section four—Personal drug use compared with knowledge of drug users.

A detailed description of the estimating procedure and a table for determining the standard error associated with the estimating and projecting procedures are contained in appendix D.

PEP PILLS

General remarks

For the purposes of this survey pep pills were defined as those prescription amphetamines, excluding methamphetamine and the diet pills, which were taken for their stimulant effects on the central nervous system. Only two drugs were encountered with any regularity, amphetamine sulfate (Benzedrine) and dextroamphetamine (Dexedrine).

As with all the amphetamines, the pep pills have as their characteristic the excitation or stimulation of the central nervous system. In addition to stimulation usually perceived of as increased alertness, these drugs produce feelings of well-being and confidence. While the prevention of sleepiness and fatigue seems to be the reason the drugs are not commercialized, use to "feel better" or to reduce anxiety by making the individual feel "confident and secure," should not be minimized.

With the continued intake of the pep pills, tolerance develops and psychic dependence occurs. Although physical dependence has not been demonstrated, withdrawal of these agents from abusers may unmask symptoms of chronic fatigue followed by drowsiness and prolonged sleep. At high doses toxic psychosis may develop.

Incidence and prevalence of pep pill use

The *prevalence* of pep pill use in the State of New York is projected to be 6.3% of the population age 14 and above—approximately 865,000 persons have taken a pep pill at least once (Table 23). The *incidence* of the regular use of these drugs is .8% of the total base population—approximately 110,000 persons age 14 and above are using these pep pills at least 6 times per month.

Demographic characteristics of the regular users

There are an estimated 110,000 regular users of the pep pills of whom the majority—66,000—are females. *The major contributor to the population of regular pep pill users are unemployed females*—26.4% of all the regular users of

these drugs are unemployed females. Minor sex differences do exist in the use of these drugs. Among the some 66,000 females, the data indicate 21.2% (14,000) are students, 34.8% (23,000) are employed and 43.9% (29,000) are unemployed and presumed to be housewives. In contrast, 36.4% of the 44,000 male users are students, 21.3% are employed and some 36.4% report themselves as unemployed. These differences, however, are not statistically different.

The age distribution curve for these regular users of pep pills is bimodal, has two peaks. Of the projected 110,000 regular users, 31.8% (35,000) are between the ages of 18–24 and 27.3% (30,000) are in the age group 50 and over. The remainder of regular pep pill use is fairly evenly distributed throughout the other age groups.

With regard to ethnicity, Whites appear slightly overrepresented; Blacks appear to be underrepresented and Puerto Ricans proportionately represented within this population of regular users of pep pills.

The regular use of pep pills cannot be identified as associated with any one socioeconomic class. In fact, base population comparisons indicate the socioeconomic class. In fact, base population comparisons indicate the socioeconomic class distributions within the population of pep pill users is almost identical to the distribution within the general population (Table 24). For example, within the general population, 7.0% are members of the upper/upper middle classes as compared to 7.3% of the population of regular users of pep pills. Likewise, the middle class contributes 42.0% and 38.2% respectively to the general and regular pep pill using populations, as the lower middle/lower classes respectively contribute 51.0% and 54.5%.

The regular use of pep pills can be identified as associated with education. In this survey, some 77,000 of the total 110,000 regular users of pep pills were at least high school graduates—70.0% of all regular users of pep pills are high school graduates and 40.9% of all regular users have pursued education beyond high school. This association between education and this form of regular drug use was also found with the regular use of other "medicines," i.e., diet pills, antidepressants, tranquilizers and sedative-hypnotics.

Characteristics of use among regular users

A significant number of the regular users of pep pills obtain at least a portion of these drugs without the benefit of a legal prescription. Of the estimated 110,000 regular users of these drugs, 52.7% (58,000) indicated some of the drugs were not obtained with a legal prescription and 32.7% (36,000) reported none of their drugs were obtained with a legal prescription (Table 25). In addition, approximately 12.7% of the respondents refused to answer the question. One can assume a significant proportion of these "refusals" reflect sources other than legal prescriptions.

The finding of widespread use of these drugs without appropriate medical supervision was validated with the correlate findings that 48.2% did not take the drugs as prescribed and an additional 19.1% of the regular users refused to answer the question.

Probably indicative of the high rate of illicit use of pep pills, *40.9% of all the regular users report using the drugs at social gatherings.*

It should be noted, of the estimated 35,000 regular users of pep pills who are employed, 71.4% (25,000) report they use the drugs on the job. Of the 30,000 regular users of these drugs who are students, 20.0% (6,000) reports using the drugs while at school.

Concurrent regular use of other drugs

Regular users of pep pills are most frequently regular users of other drugs as well. The most common concurrent use involves an illicit drug, marihuana/hashish—*60.9% of all regular users of pep pills also regularly use marihuana/hashish.* In addition, the concurrent illicit use of methedrine and LSD is also high—14.5% and 11.8% of all regular users of pep pills respectively use these other drugs on a regular basis.

With regard to concurrent use of legally manufactured drugs, at least ten percent of all the regular users also regularly use relaxants/minor tranquilizers (28.2%), diet pills (26.4%), barbiturates (21.8%), non-amphetamine stimulants (17.3%) and non-barbiturate sedative-hypnotics (10.0%).

Workers in the drug abuse fields have asserted for some time there existed a large number of persons who regularly and concurrently used central nervous system stimulants and central nervous system depressants. This survey has at last provided empirical evidence of the dimensions of this group. For example, of the estimated 110,000 regular users of pep pills, at least 30,000 or a minimum of some 27.3% are regular users of one of the central nervous system depressants. There does appear, therefore, to be a rather sizeable population made up primarily of white middle class females who graduated high school but are not currently in the labor force, who have become cyclical users of drugs to stimulate and to relax them. Future analyses of the multiple drug users should more clearly define these cyclical users.

TABLE 23.—INCIDENCE AND PREVALENCE OF PEP PILL USE[1]

	Amount	Percent
Never used	12,663,000	91.9
Former users (no use in the past 6 months)	490,000	3.6
Infrequent users (fewer than 6 times per month)	265,000	1.9
Regular users (at least 6 times per month)	110,000	.8
No data	256,000	1.8
Total	13,784,000	100.0

[1] For example, dextroamphetamine (Dexedrine), amphetamine-sulfate (Benzedrine), etc.

TABLE 24.—DEMOGRAPHIC CHARACTERISTICS OF THE 110,000 REGULAR USERS OF PEP PILLS

	Amount	Percent
I. Sex distribution:		
a. Males	44,000	40.0
b. Females	66,000	60.0
II. Employment status distribution:		
a. Male high school students	8,000	7.3
b. Female high school students	10,000	9.1
c. Male college students	8,000	7.3
d. Female college students	4,000	3.6
e. Males employed	12,000	10.9
f. Females employed	23,000	20.9
g. Males unemployed	16,000	14.5
h Females unemployed	29,000	26.4
III. Age distribution:		
a. 14–17	12,000	10.9
b. 18–24	35,000	31.8
c. 25–34	15,000	13.6
d. 35–49	18,000	16.4
e. 50 and over	30,000	27.3
IV. Ethnicity distribution:		
a. White	96,000	87.3
b. Black	1,000	1.0
c. Puerto Rican	9,000	8.2
d. Other/No data	4,000	3.6
V. Socioeconomic status distribution:		
a. Upper or upper middle	8,000	7.3
b. Middle	42,000	38.2
c. Lower middle or lower	60,000	54.5
VI. Education distribution:		
a. Less than high school	14,000	12.7
b. High school	50,000	45.5
c. More than high school	45,000	40.9
d. No data	1,000	1.0

TABLE 25.—USE CHARACTERISTICS AMONG THE 110,000 REGULAR USERS OF PEP PILLS

	Amount	Percent
I. How the pep pills were obtained:		
a. All with a legal prescription	38,000	34.5
b. Some with a legal prescription	22,000	20.0
c. None with a legal prescription	36,000	32.7
d. No data	14,000	12.7
II. How the pep pills were used:		
a. Exactly as prescribed	36,000	32.7
b. All other	53,000	48.2
c. No data	21,000	19.1
III. Where the pep pills were used:[1]		
a. At home	85,000	77.3
b. At a social gathering	45,000	40.9
c. At work	25,000	22.7
d. At school	6,000	5.5
e. All other	13,000	11.8

[1] Totals are in excess due to the use of the drugs in more than 1 location.

TABLE 26.—INCIDENCE OF THE REGULAR USE OF OTHER DRUGS AMONG 110,000 REGULAR USERS OF PEP PILLS

	Amount	Percent
I. Legal drugs:		
Relaxants/minor tranquilizers	31,000	28.2
Diet pills	29,000	26.4
Barbiturates	24,000	21.8
Other stimulants	19,000	17.3
Nonbarbiturate sedative-hypnotics	11,000	10.0
Antidepressants	10,000	9.1
Major tranquilizers	4,000	3.6
Noncontrolled narcotics and prescription nonnarcotic analgesics	4,000	3.6
Controlled narcotics (nonheroin)	1,000	1.0
II. Illegal drugs:		
Marihuana/Hashish	67,000	60.9
Methedrine	16,000	14.5
LSD	13,000	11.8
Heroin	6,000	5.5
Solvents/Inhalants	6,000	5.5
Psychotogens other than LSD	5,000	4.5
Cocaine	4,000	3.6

DIET PILLS

General remarks

The diet pills most often consist of an amphetamine-like substance alone or in combination with a central nervous system depressant. When combined this way, the stimulant acts to reduce appetite and the depressent serves to counteract any overstimulation which might otherwise occur.

The effect of amphetamine containing diet pills appears to be related to their ability to create a sense of well being. As such they may be useful when applied for short periods of time. However, their long term effectiveness in weight control may be properly questioned.

A variety of other compounds have been used in the treatment of overweight patients. These include thyroid, diuretics, antispasmodics and digitalis. All of these are considered to be without indication when so applied.

Incidence and prevalence of diet pill use

The *prevalence* of diet pill use in the State of New York is projected to be 11.7% of the population age 14 and above—approximately 1,613,000 persons have taken a diet pill at least once (Table 27). The *incidence* of the regular use of these drugs is 1.6% of the total base population—approximately 222,000 persons age 14 and above are using these diet pills at least 6 times per month.

Demographic characteristics of the regular users

The overwhelming majority of the regular users of diet pills are females—80.2% of all the regular users are females (Table 28). Among the some 178,000 females who are regularly using diet pills, 10.7% are high school students, 3.4% are college students, 33.3% are employed and 52.5% are unemployed. One can logically assume the majority in this last group are housewives who are not in the labor force. Of the some 44,000 males who are regularly using diet pills, most of them (28,000) are employed.

The regular use of diet pills is distributed throughout the various age groups. In this survey, 29.3% were younger than 25, 18.9% were in the age group 25–34, 32.9% were in the age group 35–49 and 18.9% were 50 or older.

Whites, members of the middle socioeconomic classes and persons with at least high school educations are most frequently the regular users of diet pills. As shown in Table 28, 80.2% of the regular users are Whites, 48.6% are in the middle class and 97.3% have at least high school educations.

Characteristics of use among regular users

The regular use of diet pills without medical supervision appears to be very high. Of the estimated 222,000 regular users, the data indicate at least 46,000 (20.8%) obtain at least a part of their drugs without a legal prescription with 41,000 (18.5%) reporting they had never had a legal prescription.

Of those with legal prescriptions, 76.1% of the regular users, most did follow the regimen which had been prescribed.

While most diet pill use occurs at home, 7.2% of the regular users do report use at social gatherings. It seems reasonable to assume a significant portion of this use at social gatherings would be for the stimulating or euphoric effects rather than appetite depression.

Concurrent regular use of other drugs

Probably indicative of the number of regular diet pill users who use the drugs for other than appetite control, 13.1% of all these users also regularly use pep pills, 15.8% regularly use marihuana/hashish and 5.0% regularly use L.S.D. Significant numbers also regularly use relaxants/minor tranquilizers (8.6%) and the barbiturates (5.4%). It is less likely, however, that these concurrent users use the drugs for their euphoric effects.

TABLE 27.—INCIDENCE AND PREVALENCE OF DIET PILL USE[1]

	Amount	Percent
Never used	11,955,000	86.7
Former users (no use in the past 6 months)	1,070,000	7.8
Infrequent users (fewer than 6 times per month)	321,000	2.3
Regular users (more than 6 times per month)	222,000	1.6
No data	216,000	1.6
Total	13,784,000	100.0

[1] For example, dextroamphetamine plus amobarbital (Dexamyl), dextroamphetamine plus meprobamate (Appetrol), phenmetrazine (Preludin), etc.

TABLE 28.—DEMOGRAPHIC CHARACTERISTICS OF THE 222,000 REGULAR USERS OF DIET PILLS

	Amount	Percent
I. Sex distribution:		
a. Males	44,000	19.8
b. Females	178,000	80.2
II. Employment status distribution: [1]		
a. Male high school students	7,000	3.2
b. Female high school students	19,000	8.6
c. Male college students	2,000	.9
d. Female college students	6,000	2.7
e. Males employed	28,000	12.7
f. Females employed	59,000	26.7
g. Males unemployed	7,000	3.2
h. Females unemployed	93,000	42.1
III. Age distribution:		
a. 14 to 17	19,000	8.6
b. 18 to 24	46,000	20.7
c. 25 to 34	42,000	18.9
d. 35 to 49	73,000	32.9
e. 50 and over	42,000	18.9
IV. Ethnicity distribution:		
a. White	173,000	80.2
b. Black	20,000	9.0
c. Puerto Rican	20,000	9.0
d. Other/no data	4,000	1.8
V. Socioeconomic status distribution:		
a. Upper or upper middle	22,000	9.9
b. Middle	108,000	48.6
c. Lower middle or lower	92,000	41.4
VI. Education distribution:		
a. Less than high school	6,000	2.7
b. High school	150,000	67.6
c. More than high school	66,000	29.7

[1] Based on 221,000 due to rounding error.

TABLE 29.—USE CHARACTERISTICS AMONG THE 222,000 REGULAR USERS OF DIET PILLS

	Amount	Percent
I. How the diet pills were obtained: [1]		
a. All with a legal prescription	169,000	76.1
b. Some with a legal prescription	5,000	2.3
c. None with a legal prescription	41,000	18.5
d. No data	6,000	2.7
II. How the diet pills were used:		
a. Exactly as prescribed	163,000	73.4
b. All other	51,000	23.0
c. No data	8,000	3.6
III. Where the diet pills were used: [2]		
a. At home	205,000	92.3
b. At a social gathering	16,000	7.2
c. At work	13,000	5.9
d. At school	9,000	4.1
e. All other	10,000	4.5

[1] Based upon 221,000 due to rounding error.
[2] Totals are in excess due to the use of the drugs in more than 1 location.

TABLE 30.—INCIDENCE OF THE REGULAR USE OF OTHER DRUGS AMONG 222,000 REGULAR USERS OF DIET PILLS

	Amount	Percent
I. Legal drugs:		
Pep pills	29,000	13.1
Relaxants/minor tranquilizers	19,000	8.6
Barbiturates	12,000	5.4
Noncontrolled narcotics and prescription nonnarcotic analgesics	10,000	4.5
Nonbarbiturate sedative-hypnotics	9,000	4.1
Antidepressants	6,000	2.7
Other stimulants	5,000	2.3
Controlled narcotics (nonheroin)	1,000	.5
II. Illegal drugs:		
Marihuana or hashish	55,000	15.8
LSD	11,000	5.0
Methedrine	10,000	4.5
Psychotogens other than LSD	5,000	2.3
Heroin	3,000	1.4
Cocaine	1,000	.5
Solvents and inhalants	1,000	.5

METHEDRINE

General remarks

Methedrine, a brand name for methamphetamine, is a central nervous system stimulant more potent but chemically related to the amphetamines (amphetamine sulfate (Benzedrine) and d-amphetamine sulfate (Dexedrine)). The drug was first used widely by the German army during World War II to counter fatigue among combatants. The drug is currently marketed for its appetite-suppressing effects, its potential for reducing mild symptoms of mental depression, its potential as a mood elevator, as an analptic in sedative overdose, and to raise abnormally low blood pressure, i.e., in anesthetized patients.

Unfortunately, the primary use of this drug is nonmedical, unsupervised illicit abuse by habitual high-dose amphetamine users. It is the drug of choice among those persons who use amphetamines by intravenous injection only for their euphoric effects.

Psychological dependence and tolerance have been well documented. High doses over extended periods of time engender acute or chronic psychoses, loss of memory and powers of concentration. Violent behavior is also commonly seen. There are reports to indicate that methedrine abusers may experience damage to their brains and arteries.

Incidence and prevalence of methedrine use

The *prevalence* of methedrine use in the State of New York is projected to be 1.9% of the population age 14 and above—approximately 249,000 persons are believed to have used methedrine on at least one occasion (Table 55). The *incidence* of regular use, however, is only .3% of the total base population—approximately 35,000 persons are believed to be using methedrine at least 6 times per month. *Some 111,000 persons are projected to have used methedrine at least once during the period March-August, 1970.*

Demographic characteristics of the regular users

Consistent with existing knowledge, the regular use of methedrine was found to be primarily a male phenomenon—*82.9% of all regular users* of methedrine are males (Table 56). Among these some 29,000 males, 24.1% (7,000) are currently in high school, 34.5% (10,000) are currently enrolled in college, 13.8% (4,000) are employed and the remaining 27.6% (8,000) report themselves as unemployed. An equal number of the same 6,000 females who regularly use methedrine were found to be in school or employed.

Reflecting the large number of students, the regular use of methedrine was found to be concentrated in the younger age groups—*80.0% of all regular users of methedrine are under the age of 25.* Of the users under age 25, 75.0% are in the age group 18–24.

Both the ethnic group composition of the population of regular users of methedrine and the socioeconomic class distribution within this population are proportionate to the composition and distribution within the general population (Table 56). The regular use of methedrine is not disproportionately associated with any ethnic group of any socioeconomic class.

At least in this survey, *the regular use of methedrine is associated with formal education.* No users were located who had dropped out of high school. Of those regular users who were identified, 25.7% (9,000) were currently in high school, 40.0% (14,000) had terminated their educations after graduating from high school, 31.4% (11,000) were currently in college and the remaining 2.9% (1,000) had begun college before terminating their education.

Characteristics of use among regular users

The social content of this form of drug use is exemplified in *85.7% of all the regular users reported using methedrine at social gatherings.* Of the estimated 20,000 regular users who are students, 6,000 (30.0%) reported they had used the methedrine while at school. Of the estimated 7,000 regular users who are employed, 6,000 (85.7%) reported they had used the methedrine while at work.

Concurrent regular use of drugs

The poly-drug use among persons who regularly use methedrine encompasses the legally manufactured and distributed drugs as well as the illicit drugs (Table 58). Almost all (91.4%) of the regular users of methedrine are also regular users of marihuana/hashish and almost half (45.7%) are regular users of the psychedelics and the amphetamines. The incidence of concurrent use of the barbiturates and of heroin were also found to be high (25.7% and 17.1% respectively).

Special comment

N.A.C.C. scientists believe the prevalency figure of 249,000 persons and the incidence figure of 35,000 persons to be minimal projections. An unknown number of persons who regularly use large quantities of this drug were not available for interview. The use of this drug as well as those which they concurrently use has resulted in their becoming personally and socially dysfunctional. Such persons were not selected for interview in this current design.

TABLE 55.—INCIDENCE AND PREVALENCE OF METHEDRINE USE

	Amount	Percent
Never used	13,270,000	96.3
Former users (no use in past 6 months)	138,000	1.0
Infrequent users (fewer than 6 times per month)	76,000	.6
Regular users (at least 6 times per month)	35,000	.3
No data	265,000	1.9
Total	13,784 000	100.0

*Total does not equal 100 percent due to a rounding error.

TABLE 56.—DEMOGRAPHIC CHARACTERISTICS OF THE 35,000 REGULAR USERS OF METHEDRINE

	Amount	Percent
I. Sex distribution:		
a. Males	29,000	82.9
b. Females	6,000	17.1
II. Employment status distribution:		
a. Male high school students	7,000	20.0
b. Female high school students	2,000	5.7
c. Male college students	10,000	28.6
d. Female college students	1,000	2.9
e. Males employed	4,000	11.4
f. Females employed	3,000	8.6
g. Males unemployed	8,000	22.9
h. Females unemployed		
III. Age distribution:		
a. 14 to 17	7,000	20.0
b. 18 to 24	21,000	60.0
c. 25 to 34	7,000	20.0
d. 35 to 49		
e. 50 and over		
IV. Ethnicity distribution:		
a. White	30,000	85.7
b. Black	3,000	8.6
c. Puerto Rican	2,000	5.7
V. Socioeconomic status distribution:		
a. Upper or upper middle	1,000	2.9
b. Middle	15,000	42.9
c. Lower middle or lower	19,000	54.3
VI. Education distribution:		
a. Less than high school		
b. High school	23,000	65.7
c. More than high school	12,000	34.3

TABLE 57.—USE CHARACTERISTICS AMONG THE 35,000 REGULAR USERS OF METHEDRINE

	Amount	Percent
I. Where the methedrine was used:[1]		
a. At home	11,000	31.4
b. At a social gathering	30,000	85,7
c. At work	6,000	17.1
d. At school	6,000	17.1
e. All other	3,000	8,6

[1] Totals are in excess due to the use of the drugs in more than 1 location.

TABLE 58.—INCIDENCE OF THE REGULAR USE OF OTHER DRUGS AMONG 35,000 REGULAR USERS OF METHEDRINE

	Amount	Percen
I. Legal drugs:		
Pep pills	16,000	45.7
Diet pills	10,000	28.6
Barbiturates	9,000	25.7
Non-Barbiturate sedatives	3,000	8.6
Relaxants and minor tranquilizers	3,000	8.6
Antidepressants	3,000	8.6
Noncontrolled narcotics	2,000	5.7
Controlled narcotics (nonheroin)	1,000	2.9
II. Illegal drugs:		
Marihuana or hashish	32,000	91.4
LSD	16,000	45.7
Heroin	6,000	17.1
Psychotogens other than LSD	5,000	14.3
Cocaine	3,000	8.6

13. Differential Drug Use Within the New York State Labor Force

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Interpretations or viewpoints stated in this document do not necessarily represent the official position or policy of the U.S. Department of Labor.

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Introduction

During 1968-1969, the Division of Research for the New York State Narcotic Addiction Control Commission designed and completed a general assessment of the public's knowledge of the effects of various drugs, knowledge of the prevalence of drug use and attitudes concerning drug users and their treatment. This assessment was accomplished utilizing standard survey techniques. Some 6,100 persons were scientifically selected to be a representative sample of all New York State household members age 13 or older. Each person was interviewed in the home by trained interviewers using a specially designed questionnaire. The Commission made the results of this benchmark study available in 1969 (Glaser and Snow, "Public Knowledge and Attitudes on Drug Abuse in New York State," *New York State Narcotic Addiction Control Commission Research Monograph*, 1969). While this original research effort did provide a frame of reference whereln meanlngful preventive education could be directed, it had not been designed as a direct assessment of drug use.

During 1970, Commission scientists began developing the strategies to assess this use. This new study was also to be a survey within the general population. Some 7,500 persons were selected to be a representative sample of all New York State household members age 14 or older. Again, each person was interviewed in the home by specially trained interviewers utilizing a questionnaire specifically designed to systematically elicit information about the use of a wide variety of both legal and illegal drugs. Such a statewide epidemiological assessment of actual drug use was without precedent. The Commission made the results of this second survey available in 1971 (Chambers, "An Assessment of Drug Use in the General Population," *New York State Narcotic Addiction Control Commission Research Monograph*, 1971). Commission scientists reported these drug use results as the minimal number of persons using the various drugs. Under-representations of use were anticipated due to a respondent's natural forgetfulness, some reluctance to discuss illegal or socially disapproved drug taking and by drawing samples from household members thereby excluding persons in institutions, hotels, rooming houses and other non-permanent residences.

During the analyses of these original drug use data, it became apparent that significant numbers of employed persons were regular users of both legal as well as illegal drugs. In order to more completely document the use of drugs by members of the labor force, and to ascertain any differences in types of use among the various occupational groups, it was desirable to pursue a specialized supplementary analysis of these data. Such a supplementary reanalysis required the regrouping and reweighting of the original data, to reflect as accurately as possible the New York State labor force. Except for these regroupings and reweightings, the basic methdological strategies and techniques of the original field survey remained intact.

While the second survey was designed to establish the dimensions of *drug use*, it was not an attempt to document the incidence of *drug abuse*. Commission methodologists and epidemiologists responsible for the survey were in agreement that such a determination would be a logical third phase survey which could only occur after the accumulation of experiences from the first two surveys. Designs are in progress whereby an assessment of the social costs and personal difficulties attendant to the various types of drug use could be obtained.

Highlights of Report

The data secured through the study indicate that of the estimated 13,690,000 people in New York State age 14 and older:

1. some 377,000 people use barbiturates, e.g., Seconal, Tuinal, etc., on a regular basis (at least six times per month) and 205,000 of these people are employed ....among these employed users, sales workers have the highest rate of regular use (1,230 per 10,000) and some 11.3% report using the drugs while on the job;
2. some 173,000 people regularly use the non-barbiturate sedative/hypnotics, e.g., Doriden, Noludar, etc., and 72,000 of these people are employed....among these employed users, the unskilled workers have the highest rates of regular use (180 per 10,000) but *none* of these workers report using the drugs while on the job;
3. some 525,000 people regularly use the minor tranquilizers, e.g., Librium, Miltown, Valium, etc., and 157,000 of these people are employed....among these employed users, the clerical and other white collar workers have the highest rate of regular use (570 per 10,000) and some 3.7% of these workers report using these drugs while on the job;
4. some 85,000 people regularly use major tranquilizers, e.g., Thorazine, Mellaril, Stelazine, etc., and 55,000 of these people are employed....among these employed users, sales workers have the highest rate of regular use (210 per 10,000) but *none* of these workers report using the drugs while on the job;
5. some 37,000 people regularly use antidepressants, e.g., Tofranil, Elavil, etc., and 13,000 of these people are employed....among these employed people, the rate of regular use is the same for clerical, skilled, semi-skilled and unskilled workers (30 per 10,000) but *none* of these workers report using the drugs while on the job;
6. some 110,000 people regularly use prescription pep pills, e.g., Dexedrine, Benzedrine, etc., and 51,000 of these people are employed....among these employed people, sales workers have the highest rate of regular use (140 per 10,000) and *all* of these workers report using the drugs while on the job;
7. some 225,000 people regularly use prescription diet pills usually containing amphetamines, e.g., Dexamyl, etc., and 117,000 of these people are employed.... among these employed people, sales workers have the highest rate of regular use (360 per 10,000) and some 28.6% of these workers report using the drugs while on the job;
8. some 21,000 people regularly use controlled narcotics other than heroin, e.g., Demerol, Morphine, Dilaudid, etc., and 19,000 of these people are employed.... among these employed people, sales workers have the highest rate of regular use (90 per 10,000) but *none* of these workers report using the drugs while on the job
9. some 485,000 people regularly use marihuana and 293,000 of these people are employed....among these employed people, sales workers have the highest rate of regular use (860 per 10,000) and some 44.0% of these workers report using marihuana while on the job;
10. some 50,000 people regularly use LSD and 25,000 of these people are employed....among these employed people, sales workers have the highest rate of regular use (260 per 10,000) and some 26.7% of these workers report using LSD while on the job;
11. some 34,000 people regularly use methedrine and 10,000 of these people are employed....among these employed users, sales workers have the highest rate of regular use (70 per 10,000) and *all* of them report using the drug while on the job;
12. some 41,000 people regularly use heroin and 34,000 of these people are employed....among these employed users, sales workers have the highest rate of regular use (210 per 10,000) and *all* of them report using the drug while on the job.

These highlighted figures are a numerical projection of the more "stable" of the drug users and consequently constitute minimums. Anyone who has become personally and socially dysfunctional as the result of drug use, e.g., "heroin street addicts," "speed freaks," "acid heads," etc., generally were not available for interview. Thus, only those drug users with a place of residence or routine "at home" hours were located. In some cases these minimal figures should be multiplied by 3 or 4 in order to project maximum involvement. Since these dysfunctional drug users are not part of the employed labor force, the projections of use within the various occupational groupings are reliable as they are reported

Results

The survey results and projections contained in this report are presented in four sections:

1. The prevalence (ever used), incidence (current use) and rates of use of specific drug groups throughout the labor force.
2. The demographic characteristics of the regular drug users within each occupational group.
3. The summary distributions of all the regular drug users within each occupational group.
4. The attitudes towards drug use and drug users within each occupational group.

This labor force supplementary analysis was designed to assess the use of *twelve* separate drugs or drug groups within *nine* occupational groupings. The drugs and occupational groupings are as follows:

Drugs and Drug Groups

A. Legal Drugs
   1. Barbiturates
   2. Non-Baributrate Sedative/Hypnotics
   3. Relaxants/Minor Tranquilizers
   4. Major Tranquilizers
   5. Antidepressants
   6. Pep Pills (Amphetamine)
   7. Diet Pills (Amphetamine)
   8. Controlled Narcotics (Non-Heroin)

B. Illegal Drugs
   9. Marihuana
   10. LSD
   11. Methedrine
   12. Heroin

Base Population: 13,649,000

Occupational Groups

A. Currently Employed (7,389,000 Persons)
   1. Professionals, Technical Workers, Managers and Owners
   2. Clerical and Other White Collar Workers
   3. Skilled and Semi-skilled Workers
   4. Unskilled Workers
   5. Service and Protective Workers
   6. Sales Workers
   7. Farmers

B. Currently Not Employed (6,260,000 Persons)
   1. Housewives
   2. Other Not Employed

The patterns of use which form the content of this report result from the dependent-independent manipulation of these two sets of variables.

I. The Prevalence and Incidence of the Use of a Drug Throughout the Labor Force

1. Barbiturates

General Remarks

The barbiturates are central nervous system depressants which when taken in small doses have a sedating effect and at higher doses have a hypnotic effect. That is, through their action they quiet the user or put him to sleep. As such the barbiturates are applied in the management of a number of medical conditions where these results are desired. However, with the advent of the newer antianxiety and antipsychotic agents, they are now less widely used in the treatment of minor psychiatric disturbances.

Psychic dependence to the barbiturates can occur, at any dose level, but physical dependence normally does not when prescribed doses are taken. At higher or abuse dosage levels, drunkenness, not unlike that seen with alcohol, and toxic psychosis, occur. With continued high dose utilization, tolerance and physical dependence emerge.

The withdrawal syndrome associated with barbiturate addiction is considered more life threatening than that associated with addiction to the opiates and can include convulsions, delirium and psychosis. The withdrawal process requires close medical supervision and chemotherapeutic assistance.

Toxic overdose with the barbiturates can result in death. Indeed, barbiturates are a leading cause of accidental poison death as well as one of the main vehicles for committing suicide.

A danger associated with barbiturate use is that barbiturates and alcohol potentiate one another's actions. Accidental overdose can occur under these circumstances.

Prevalence and Incidence

The number of persons estimated to have used a barbiturate on at least one occasion is 2,720,000. This *prevalency* figure represents some 19.6% of the population age 14 and above. The *incidence* of the use of these drugs is projected to be 2.8% of this base population . . . an estimated 377,000 persons who are using these drugs at least six times a month. *Of all the 2,720,000 persons who have ever used the barbiturates, 13.9% currently use them on a regular basis.*

Some regular use of the barbiturates is detected within all of the occupational groupings except the farmers. The highest incidence rate for barbiturate use is among the sales workers (12.3%). The incidence rate for this drug use is some three times greater among sales workers than any other occupational group. Sales workers, service and protective workers and not employed persons (excluding housewives) are the only groups having individual incidence rates greater than the total population.

PREVALENCE AND INCIDENCE OF THE USE OF BARBITURATES

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,254,000 (74.1)	288,000 (17.0)	68,000 (4.0)	44,000 (2.6)	38,000 (2.2)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,096,000 (77.1)	187,000 (13.2)	86,000 (6.0)	23,000 (1.6)	30,000 (2.1)	1,422,000 (100.0)
3. Skilled, Semi-skilled Workers	2,035,000 (84.1)	211,000 (8.7)	90,000 (3.7)	27,000 (1.1)	58,000 (2.4)	2,421,000 (100.0)
4. Unskilled Workers	272,000 (83.4)	18,000 (5.5)	19,000 (5.8)	7,000 (2.1)	10,000 (3.1)	326,000 (100.0)
5. Service & Protective Workers	748,000 (84.5)	80,000 (9.0)	22,000 (2.5)	33,000 (3.7)	2,000 (.2)	885,000 (100.0)
6. Sales Workers	391,000 (67.5)	107,000 (18.5)	7,000 (1.2)	71,000 (12.3)	3,000 (.5)	579,000 (100.0)
7. Farmers	60,000 (93.8)	3,000 (4.7)	1,000 (1.6)	–	–	64,000 (100.0)
Total Employed	5,856,000 (79.3)	894,000 (12.1)	293,000 (4.0)	205,000 (2.8)	141,000 (1.9)	7,389,000 (100.0)
8. Not Employed Housewives	2,203,000 (72.6)	560,000 (18.5)	139,000 (4.6)	73,000 (2.4)	58,000 (1.9)	3,033,000 (100.0)
9. Other Not Employed	2,629,000 (81.5)	294,000 (9.1)	163,000 (5.1)	99,000 (3.1)	42,000 (1.3)	3,227,000 (100.0)
Total Not Employed	4,832,000 (77.2)	854,000 (13.6)	302,000 (4.8)	172,000 (2.7)	100,000 (1.6)	6,260,000 (100.0)
Total	10,688,000 (78.3)	1,748,000 (12.8)	595,000 (4.4)	377,000 (2.8)	241,000 (1.8)	13,649,000 (100.0)

RATE OF USE PER 10,000 BARBITURATES

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	2,360	260
Clerical and Other White Collar Workers	2,080	160
Skilled, Semi-skilled Workers	1,350	110
Unskilled Workers	1,340	210
Service and Protective Workers	1,520	370
Sales Workers	3,200	1,230
Farmers	630	–
Total Employed	1,890	280
Not Employed Housewives	2,550	240
Other Not Employed	1,730	310
Total Not Employed	2,110	270
Total	2,000	280

2. Non-Barbiturate Sedative/Hypnotics

General Remarks

What can be said about the barbiturates is generally also appropriate for the non-barbiturate sedative/hypnotics. This would be the case whether the examples were for legitimate medical use or the effects of misuse.

While most of these drugs are indeed physically addicting when misused, available evidence suggests this addiction will occur only at dose levels considerably in excess of those therapeutically prescribed. Once addiction has occurred, the abstinence syndrome can include convulsions, delirium, psychoses and even death unless the detoxification is medically managed.

Prevalence and Incidence

The number of persons estimated to have used a non-barbiturate sedative/hypnotic on at least one occasion is 1,173,000. This *prevalency* figure represents some 8.6% of the population age 14 and above. The *incidence* of the use of these drugs is projected to be 1.3% of this base population . . . an estimated 173,000 persons who are using these drugs at least six times a month. *Of the 1,173,000 persons who have ever used these non-barbiturate sedative/hypnotics, 14.7% currently use them on a regular basis.*

Some regular use of these drugs was detected within all of the occupational groupings. The highest incidence rates were recorded for the unskilled workers (1.8%) and the housewives who were not employed (1.8%).

PREVALENCE AND INCIDENCE OF THE USE OF NON-BARBITURATE SEDATIVE/HYPNOTICS

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,455,000 (86.0)	116,000 (6.9)	52,000 (3.1)	21,000 (1.2)	48,000 (2.8)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,253,000 (88.1)	69,000 (4.9)	43,000 (3.0)	12,000 (.8)	45,000 (3.2)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,168,000 (89.5)	91,000 (3.8)	70,000 (2.9)	21,000 (.9)	71,000 (2.9)	2,421,000 (100.0)
4. Unskilled Workers	297,000 (91.1)	4,000 (1.2)	6,000 (1.8)	6,000 (1.8)	13,000 (4.0)	326,000 (100.0)
5. Service & Protective Workers	801,000 (90.5)	48,000 (5.4)	25,000 (2.8)	10,000 (1.1)	1,000 (.1)	885,000 (100.0)
6. Sales Workers	523,000 (90.3)	36,000 (6.2)	2,000 (.3)	1,000 (.2)	17,000 (2.9)	579,000 (100.0)
7. Farmers	62,000 (96.9)	1,000 (1.6)	–	1,000 (1.6)	–	64,000 (100.0)
Total Employed	6,559,000 (88.8)	365,000 (4.9)	198,000 (2.7)	72,000 (1.0)	195,000 (2.6)	7,389,000 (100.0)
8. Not Employed Housewives	2,647,000 (87.3)	128,000 (4.2)	80,000 (2.6)	55,000 (1.8)	123,000 (4.1)	3,033,000 (100.0)
9. Other Not Employed	2,893,000 (89.6)	163,000 (5.1)	66,000 (2.0)	46,000 (1.4)	59,000 (1.8)	3,227,000 (100.0)
Total Not Employed	5,540,000 (88.5)	291,000 (4.6)	146,000 (2.3)	101,000 (1.6)	182,000 (2.9)	6,260,000 (100.0)
Total	12,099,000 (88.6)	656,000 (4.8)	344,000 (2.5)	173,000 (1.3)	377,000 (2.8)	13,649,000 (100.0)

RATE OF USE PER 10,000 NON-BARBITURATE SEDATIVE/HYPNOTICS

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	1,120	120
Clerical and Other White Collar Workers	870	80
Skilled, Semi-skilled Workers	760	90
Unskilled Workers	480	180
Service and Protective Workers	930	110
Sales Workers	670	20
Farmers	320	160
Total Employed	860	100
Not Employed Housewives	860	180
Other Not Employed	850	140
Total Not Employed	850	160
Total	860	130

3. Relaxants/Minor Tranquilizers

General Remarks

Considerable professional disagreement exists as to classification distinctions between the relaxants/minor tranquilizers and the sedative/hypnotics. For the purpose of this study, the following drugs were categorized as relaxants/minor tranquilizers:

Generic Name	Brand Name
Chlorodiazepoxide	Libritabs
Chlorodiazepoxide hydrochloride	Librium, Librax
Diazepam	Valium
Hydroxyzine hydrochloride	Atarax
Meprobamate	Miltown, Equanil, Meprotabs, Meprospan

The relaxants/minor tranquilizers can be viewed as agents which reduce the less severe manifestations of anxiety and tension. They do not possess analgesic or anesthetic properties but do potentiate the effects of opiates, sedative/hypnotics and alcohol. Physical despendence occurs with the abuse of these drugs; however, only at dose levels considerably in excess of those therapeutically prescribed. The withdrawal illness resembles that seen with the barbiturates and the sedative/hypnotics.

Prevalence and Incidence

The number of persons estimated to have used a relaxant/minor tranquilizer on at least one occasion is 2,714,000. This *prevalency* figure represents some 19.8% of the population age 14 and above. The *incidence* of the use of these drugs is estimated at 3.8% of this base population....some 525,000 persona who are using these drugs a minimum of six times a month. *Of the 2,714,000 persons who have ever used the relaxants/minor tranquilizers, 19.3% currently use them on a regular basis.*

Except for farmers, some regular use of the relaxants/minor tranquilizers was detected in all the occupational groups. Four groups had incidence rates in excess of that recorded for the total population: clerical and other white collar workers (5.7%); not employed housewives (5.3%); service and protective workers (4.3%); and sales workers (4.3%).

PREVALENCE AND INCIDENCE OF THE USE OF RELAXANTS/MINOR TRANQUILIZERS

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,257,000 (74.3)	226,000 (13.4)	114,000 (6.7)	50,000 (3.0)	45,000 (2.7)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,065,000 (74.9)	129,000 (9.1)	119,000 (8.4)	81,000 (5.7)	28,000 (2.0)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	1,995,000 (82.4)	190,000 (7.8)	149,000 (6.2)	36,000 (1.5)	51,000 (2.1)	2,421,000 (100.0)
4. Unskilled Workers	273,000 (83.7)	16,000 (4.9)	20,000 (6.1)	10,000 (3.1)	7,000 (2.1)	326,000 (100.0)
5. Service & Protective Workers	721,000 (81.5)	91,000 (10.3)	26,000 (2.9)	38,000 (4.3)	9,000 (1.0)	885,000 (100.0)
6. Sales Workers	417,000 (72.0)	61,000 (10.5)	59,000 (10.2)	25,000 (4.3)	17,000 (2.9)	579,000 (100.0)
7. Farmers	62,000 (96.9)	1,000 (1.6)	1,000 (1.6)			64,000 (100.0)
Total Employed	5,790,000 (78.4)	714,000 (9.7)	488,000 (6.6)	240,000 (3.2)	157,000 (2.1)	7,389,000 (100.0)
8. Not Employed Housewives	2,150,000 (70.9)	386,000 (12.7)	251,000 (8.3)	161,000 (5.3)	85,000 (2.8)	3,033,000 (100.0)
9. Other Not Employed	2,694,000 (83.5)	214,000 (6.6)	136,000 (4.2)	124,000 (3.8)	59,000 (1.8)	3,227,000 (100.0)
Total Not Employed	4,844,000 (77.4)	600,000 (9.6)	387,000 (6.2)	285,000 (4.6)	144,000 (2.3)	6,260,000 (100.0)
Total	10,634,000 (77.9)	1,314,000 (9.6)	875,000 (6.4)	525,000 (3.8)	301,000 (2.2)	13,649,000 (100.0)

RATE OF USE PER 10,000 RELAXANTS/MINOR TRANQUILIZERS

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	2,310	300
Clerical and Other White Collar Workers	2,320	570
Skilled, Semi-skilled Workers	1,550	150
Unskilled Workers	1,410	310
Service and Protective Workers	1,750	430
Sales Workers	2,500	430
Farmers	320	–
Total Employed	1,950	320
Not Employed Housewives	2,630	530
Other Not Employed	1,460	380
Total Not Employed	2,040	460
Total	1,980	380

4. Major Tranquilizers

General Remarks

The major tranquillizers modify the symptoms of psychosis and are important drugs used in the treatment of acute and chronic psychosis. In the psychotic patient, they reduce panic, fear, hostility, agitation, and the patient's adverse reactions to hallucinations and delusions. They also serve to regularize thinking and ameliorate disorganized behavioral patterns.

The major tranquilizers have not demonstrated a significant tendency to cause psychic dependence and become drugs of abuse. The abuse potential and addiction liability for these drugs are undoubtedly reduced because of the unpleasant side effects readily discernible by nonpsychotic individuals.

The major tranquilizers potentiate the actions of the central nervous system depressants. They may also impair the mental and physical skills required to perform coordinated tasks such as driving, machine operation and so on.

Prevalence and Incidence

The number of persons estimated to have used a major tranquilizer on at least one occasion is 437,000. Thia *prevalency* figure represents some 3.2% of the population age 14 and above. The *incidence* of the use of these drugs is projected as .6% of this base population...an estimated 85,000 persona who use these drugs at least six times a month. *Of the 437,000 persons who have ever used a major tranquilizer, 18.6% currently use them on a regular basis.*

Only two occupational groups have higher rates of regular use of major tranquilizers than that for the general population....some 2.1% of all sales workers and 1.4% of all the clerical and other white collar workers regularly use these drugs. No regular use waa detected among the farmers.

PREVALENCE AND INCIDENCE OF THE USE OF MAJOR TRANQUILIZERS

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,674,000 (93.0)	53,000 (3.1)	17,000 (1.0)	3,000 (.2)	45,000 (2 7)	1,692,000 (100 0)
2. Clerical and Other White Coller Workers	1,324,000 (93.1)	35,000 (2.5)	10,000 (.7)	20,000 (1.4)	33,000 (2.3)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,294,000 (94.8)	33,000 (1.4)	14,000 (.6)	15,000 (.6)	65,000 (2.7)	2,421,000 (100.0)
4. Unskilled Workers	307,000 (94.2)	8,000 (2.5)	3,000 (.9)	1,000 (.3)	7,000 (2.1)	326,000 (100.0)
5. Service & Protective Workers	851,000 (96.2)	11,000 (1,2)	4,000 (.5)	4,000 (.5)	15,000 (1.7)	885,000 (100.0)
6. Sales Workers	539,000 (93.1)	—	—	12,000 (2.1)	28,000 (4 8)	579,000 (100.0)
7. Farmers	62,000 (96.9)	2,000 (3.1)	—	—	—	64,000 (100.0)
Total Employed	6,951,000 (94.1)	142,000 (1.9)	48,000 (.6)	55,000 (.7)	193,000 (2.6)	7,389,000 (100.0)
8. Not Employed Housewives	2,861,000 (94.3)	67,000 (2.2)	11,000 (.4)	11,000 (.4)	83,000 (2.7)	3,033,000 (100.0)
9. Other Not Employed	3,074,000 (95.3)	58,000 (1.8)	26,000 (.8)	19,000 (.6)	50,000 (1.5)	3,227,000 (100.0)
Total Not Employed	5,935,000 (94.8)	125,000 (2.0)	37,000 (.6)	30,000 (5)	133,000 (2.1)	6,260,000 (100.0)
Total	12,886,000 (94.4)	267,000 (2.0)	85,000 (.6)	85,000 (6)	326,000 (2 4)	13,649,000 (100.0)

RATE OF USE PER 10,000 MAJOR TRANQUILIZERS

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	430	20
Clerical and Other White Collar Workers	460	140
Skilled, Semi-skilled Workers	260	60
Unskilled Workers	370	30
Service and Protective Workers	220	50
Sales Workers	210	210
Farmers	310	—
Total Employed	320	70
Not Employed Housewives	300	40
Other Not Employed	320	60
Total Not Employed	310	50
Total	320	60

5. Antidepressants

General Remarks

The introduction of antidepressants, generally known as mood elevators, has greatly facilitated the management of a wide variety of depressive states. These drugs have chemical structures quite different from the amphetamines and have largely replaced them in the treatment of depression.

In clinical practice antidepressants are continued for three to six months after optimal improvement in the patient's condition has been attained. They are then gradually withdrawn. Tolerance and physical dependence to these substances have yet to be documented.

A wide variety of undesirable effects have been reported with the use of antidepressant drugs. The type of reaction tends to depend upon the compound used. Adverse reactions most commonly reported include blurred vision, dizziness, hypotension, dry mouth and increased sweating. Some of these effects would, of course, retard the individual's physical performance capability.

The antidepressants potentiate the effects of alcohol, amphetamines, sedatives, and a number of other substances. Care must be exercised when such compounds and the antidepressants are used concurrently. Some mixtures are contraindicated.

Prevalence and Incidence

The number of persons estimated to have used an antidepressant on at least one occasion is 336,000. This *prevalency* figure represents some 2.5% of the population age 14 and above. The *incidence* of the use of these drugs is estimated at .3% of this base population....some 37,000 persons who use an antidepressant a minimum of six times a month. *Of the 336,000 persons who have ever used an antidepressant, 11.0% currently use them on a regular basis.*

Only one group was found to have a higher rate of regular use than that for the general population....some 6% of the not employed housewives reported themselves as regular users of antidepressants. No regular use of these drugs was detected among the professionals, technical workers, managers and owners, service and protective workers, sales workers and farmers.

PREVALENCE AND INCIDENCE OF THE USE OF ANTIDEPRESSANTS

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,613,000 (95.3)	16,000 (.9)	20,000 (1.2)		43,000 (2.5)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,363,000 (95.9)	18,000 (1.3)	7,000 (.5)	4,000 (.3)	30,000 (2.1)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,305,000 (95.2	28,000 (1.2)	20,000 (.8)	8,000 (.3)	60,000 (2.5)	2,421,000 (100.0)
4. Unskilled Workers	313,000 (96.0)	3,000 (.9)	1,000 (.3)	1,000 (.3)	8,000 (2.5)	326,000 (100.0)
5. Service & Protective Workers	872,000 (98.5)	4,000 (.5)	2,000 (.2)	—	7,000 (.8)	885,000 (100.0)
6. Sales Workers	554,000 (95.7)	10,000 (1.7)	—	—	15,000 (2.6)	579,000 (100.0)
7. Farmers	64,000 (100.0)	—	—			64,000 (100.0)
Total Employed	7,084,000 (95.9)	79,000 (1.1)	50,000 (.7)	13,000 (.2)	163,000 (2.2)	7,389,000 (100.0)
8. Not Employed Housewives	2,844,000 (93.8)	57,000 (1.9)	38,000 (1.3)	17,000 (.6)	77,000 (2.5)	3,033,000 (100.0)
9. Other Not Employed	3,088,000 (95.7)	43,000 (1.3)	32,000 (1.0)	7,000 (.2)	57,000 (1.8)	3,227,000 (100.0)
Total Not Employed	5,932,000 (94.8)	100,000 (1.6)	70,000 (1.1)	24,000 (.4)	134,000 (2.1)	6,260,000 (100.0)
Total	13,016,000 (95.4)	179,000 (1.3)	120,000 (.9)	37,000 (.3)	297,000 (2.2)	13,649,000 (100.0)

RATE OF USE PER 10,000 ANTIDEPRESSANTS

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	210	–
Clerical and Other White Collar Workers	210	30
Skilled, Semi-skilled Workers	230	30
Unskilled Workers	150	30
Service and Protective Workers	70	–
Sales Workers	170	–
Farmers	–	–
Total Employed	200	20
Not Employed Housewives	380	60
Other Not Employed	250	20
Total Not Employed	310	40
Total	250	30

6. Pep Pills

General Remarks

For the purposes of this survey, pep pills were defined as those prescription amphetamines, excluding methamphetamine and the diet pills, which were taken for their stimulant effects on the central nervous system. Only two drugs were encountered with any regularity, amphetamine sulfate (Benzedrine) and dextroamphetamine (Dexedrine).

As with all the amphetamines, the pep pills have as their characteristic, the excitation or stimulation of the central nervous system. In addition to stimulation usually perceived of as increased alertness, these drugs produce feelings of well-being and confidence. While the prevention of sleepiness and fatigue seems to be the reason the drugs are not commercialized, use to "feel better" or to reduce anxiety by making the individual feel "confident and secure," should not be minimized.

With the continued intake of the pep pills, tolerance develops and psychic dependence occurs. Although physical dependence has not been demonstrated, withdrawal of these agents from abusers may unmask symptoms of chronic fatigue followed by drowsiness and prolonged sleep. At high doses, toxic psychosis may develop.

Prevalence and Incidence

The number of persons estimated as having used a prescription pep pill on at least one occasion is 856,000. This *prevalence* figure represents some 6.3% of the population age 14 and above. The *incidence* of the use of these stimulants is projected at .8% of this base population ....as estimated 110,000 persons who are using these drugs a minimum of six times a month. *Of the 856,000 persons who have ever used a prescription pep pill, 12.9% currently use them on a regular basis.*

Only two of the groups have higher rates of regular use than that for the general population....some 1.6% of the not employed persons (excluding housewives) and 1.4% of the sales workers regularly use these drugs. No regular use of prescription pep pills was detected among the farmers.

PREVALENCE AND INCIDENCE OF THE USE OF PRESCRIPTION PEP PILLS

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,509,000 (89.2)	90,000 (5.3)	37,000 (2.2)	14,000 (.8)	42,000 (2.5)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,291,000 (90.8)	64,000 (4.5)	24,000 (1.7)	12,000 (.8)	31,000 (2.2)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,228,000 (92.0)	74,000 (3.1)	55,000 (2.3)	9,000 (.4)	55,000 (2.3)	2,421,000 (100.0)
4. Unskilled Workers	296,000 (90.8)	13,000 (4.0)	6,000 (1.8)	1,000 (.3)	10,000 (3.1)	326,000 (100.0)
5. Service & Protective Workers	798,000 (90.2)	46,000 (5.2)	28,000 (3.2)	7,000 (.8)	6,000 (.7)	885,000 (100.0)
6. Sales Workers	536,000 (92.6)	11,000 (1.9)	15,000 (2.6)	8,000 (1.4)	9,000 (1.6)	579,000 (100.0)
7. Farmers	62,000 (96.9)	1,000 (1.6)	1,000 (1.6)	–	–	64,000 (100.0)
Total Employed	6,720,000 (90.9)	299,000 (4.0)	166,000 (2.2)	51,000 (.7)	153,000 (2.1)	7,389,000 (100.0)
8. Not Employed Housewives	2,853,000 (94.1)	79,000 (2.6)	41,000 (1.4)	8,000 (.3)	52,000 (1.7)	3,033,000 (100.0)
9. Other Not Employed	2,974,000 (92.2)	101,000 (3.1)	60,000 (1.9)	51,000 (1.6)	41,000 (1.3)	3,227,000 (100.0)
Total Not Employed	5,827,000 (93.1)	180,000 (2.9)	101,000 (1.6)	59,000 (.9)	93,000 (1.5)	6,260,000 (100.0)
Total	12,547,000 (91.9)	479,000 (3.5)	267,000 (2.0)	110,000 (.8)	246,000 (1.8)	13,649,000 (100.0)

RATE OF USE PER 10,000 PEP PILLS

	Prevelence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	830	80
Clerical and Other White Collar Workers	700	80
Skilled, Semi-skilled Workers	580	40
Unskilled Workers	610	30
Service and Protective Workers	920	80
Sales Workers	590	140
Farmers	320	–
Total Employed	690	70
Not Employed Housewives	430	30
Other Not Employed	660	160
Total Not Employed	540	90
Total	630	80

7. Diet Pills

General Remarks

The diet pills most often consist of an amphetamine-like substance alone or in combination with a central nervous system depressant. When combined this way, the stimulant acts to reduce appetite and the depressant serves to counteract any overstimulation which might otherwise occur.

The effect of amphetamine containing diet pills appears to be related to their ability to create a sense of well being. As such they may be useful when applied for short periods of time. However, their long term effectiveness in weight control may be properly questioned.

A variety of other compounds have been used in the treatment of overweight patients. These include thyroid, diuretics, antispasmodics and digitalis. All of these are considered to be without indication when so applied.

Prevalence and Incidence

The number of persons estimated to have used a prescription diet pill on at least one occasion is 1,587,000. This *prevalency* figure represents some 11.5% of the population age 14 and above. The *incidence* of the use of these drugs is estimated to be 1.6% of this base population....some 225,000 persons who use these drugs at least six times a month. *Of the 1,587,000 persons who have ever used these prescription diet pills, 21.6% currently use them on a regular basis.*

Four groups have incidence rates greater than that for the general population....3.6% of all sales workers; 2.7% of all not employed housewives; 2.5% of all clerical and other white collar workers; and, 2.0% of all professionals, technical workers, managers and owners regularly use diet pills. No regular use was detected among the farmers.

PREVALENCE AND INCIDENCE OF THE USE OF PRESCRIPTION DIET PILLS

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,469,000 (86.8)	134,000 (7.9)	24,000 (1.4)	34,000 (2.0)	31,000 (1.8)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,196,000 (84.1)	125,000 (8.8)	44,000 (3.1)	35,000 (2.5)	22,000 (1.5)	1,422,000 (100.)
3. Skilled & Semi-skilled Workers	2,180,000 (90.0)	108,000 (4.5)	63,000 (2.6)	21,000 (.9)	49,000 (2.0)	2,421,000 (100.0)
4. Unskilled Workers	296,000 (90.8)	14,000 (4.3)	9,000 (2.8)	2,000 (.6)	5,000 (1.5)	326,000 (100.0)
5. Service & Protective Workers	814,000 (92.0)	46,000 (5.2)	15,000 (1.7)	4,000 (.5)	6,000 (.7)	885,000 (100.0)
6. Sales Workers	481,000 (83.1)	48,000 (8.3)	8,000 (1.4)	21,000 (3.6)	21,000 (3.6)	579,000 (100.0)
7. Farmers	63,000 (98.4)	1,000 (1.6)	–	–	–	64,000 (100.0)
Total Employed	6,499,000 (88.0)	476,000 (6.4)	163,000 (2.2)	117,000 (1.6)	134,000 (1.8)	7,389,000 (100.0)
8. Not Employed Housewives	2,421,000 (79.8)	405,000 (13.4)	84,000 (2.8)	81,000 (2.7)	42,000 (1.4)	3,033,000 (100.0)
9. Other Not Employed	2,922,000 (90.5)	163,000 (5.1)	71,000 (2.2)	27,000 (8)	44,000 (1.4)	3,227,000 (100.0)
Total Not Employed	5,343,000 (85.4)	568,000 (9.1)	155,000 (2.5)	108,000 (1.7)	86,000 (1.4)	6,260,000 (100.0)
Total	11,842,000 (86.8)	1,044,000 (7.6)	318,000 (2.3)	225,000 (1.6)	220,000 (1.6)	13,649,000 (100.0)

RATE OF USE PER 10,000 DIET PILLS

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	1,130	200
Clerical and Other White Collar Workers	1,440	250
Skilled, Semi-skilled Workers	800	90
Unskilled Workers	770	60
Service and Protective Workers	740	50
Sales Workers	1,330	360
Farmers	160	–
Total Employed	1,020	160
Not Employed Housewives	1,890	270
Other Not Employed	810	80
Total Not Employed	1,330	170
Total	1,150	160

8. Controlled Narcotics (Non-Heroin)

General Remarks

The controlled narcotics are very potent analgesics that are generally classified as "natural" or "synthetic." the natural narcotics include opium, two alkaloid components of opium-morphine and codeine, and semi-synthetic derivatives of them such as heroin, oxymorphone (Numorphan), hydromorphone (Dilaudid). The synthetic narcotics are related compounds that are morphine-like in their effects, i.e., methadone (Dolophine). meperidine (Demerol), anileridine (Leritine), etc.

All of these drugs produce euphoria, analgesia, respiratory depression, tolerance, psychic dependence, and physical dependence. In addition, they exhibit cross-tolerance, the ability of one drug to substitute for another in a tolerant individual. Tolerance develops rapidly and occurs within therapeutic dose ranges. The severity of withdrawal is positively related to the amount of drug taken.

Increased awareness among physicians prescribing these medications has greatly reduced the number of medical addicts — persons accidentally addicted to these drugs during a therapeutic regimen. Predictability in this area is limited, however. The degree to which levels of euphoria are perceived and the extent to which this sensation or feeling becomes defined as pleasurable and desirable to recapture appears to vary widely among persons exposed to these drugs. Within limits, the perception of withdrawal distress and the reaction to this distress during detoxification from these drugs also appears to vary widely even among persons who have been on very high dose regimens.

Prevalence and Incidence

The number of persons estimated to have used a controlled narcotic other than heroin on at least one occasion is 1,006,000. This *prevalency* figure represents some 7.4% of the population age 14 and above. The *incidence* of the use of these drugs is projected as .2% of this base population....an estimated 21,000 who use these drugs at least six times a month. *Of the 1,006,000 persons who have ever used a controlled narcotic other than heroin, only 2.8% currently use them on a regular basis.*

Three occupational groups have higher incidence rates than that for the general population....some .9% of all the sales workers; .3% of the service and protective workers, and, .3% of the unskilled workers regularly use these drugs. No regular use was detected among the farmers.

PREVALENCE AND INCIDENCE OF THE USE OF CONTROLLED NARCOTICS (NON-HEROIN)

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers & Owners	1,431,000 (84.6)	174,000 (10.3)	21,000 (1.2)	4,000 (.2)	62,000 (3.7)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,319,000 (92.8)	49,000 (4.1)	8,000 (.6)	1,000 (.1)	35,000 (2.5)	1,422,000 (100.0)
3. Skilled, Semi-skilled Workers	2,234,000 (92.3)	106,000 (4.4)	12,000 (.5)	5,000 (.2)	64,000 (2.6)	2,421,000 (100.0)
4. Unskilled Workers	306,000 (93.9)	9,000 (2.8)	2,000 (.6)	1,000 (.3)	8,000 (2.5)	326,000 (100.0)
5. Service & Protective Workers	818,000 (92.4)	43,000 (4.9)	15,000 (1.7)	3,000 (.3)	6,000 (.7)	885,000 (100.0)
6. Sales Workers	523,000 (90.3)	36,000 (6.2)	1,000 (.2)	5,000 (.9)	14,000 (2.4)	579,000 (100.0)
7. Farmers	63,000 (98.4)	1,000 (1.6)	–	–	–	64,000 (100.0)
Total Employed	6,694,000 (90.6)	428,000 (5.8)	59,000 (.8)	19,000 (.3)	189,000 (2.6)	7,389,000 (100.0)
8. Not Employed Housewives	2,637,000 (86.9)	274,000 (9.0)	39,000 (1.3)	1,000 (.0)	82,000 (2.7)	3,033,000 (100.0)
9. Other Not Employed	2,986,000 (92.5)	131,000 (4.1)	54,000 (1.7)	1,000 (.0)	55,000 (1.7)	3,227,000 (100.0)
Total Not Employed	5,623,000 (89.8)	405,000 (6.5)	93,000 (1.5)	2,000 (.0)	137,000 (2.2)	6,260,000 (100.0)
Total	12,317,000 (90.2)	833,000 (6.1)	152,000 (1.1)	21,000 (.2)	326,000 (2.4)	13,649,000 (100.0)

RATE OF USE PER 10,000 CONTROLLED NARCOTICS (NON-HEROIN)

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	1,170	20
Clerical and Other White Collar Workers	480	10
Skilled, Semi-skilled Workers	510	20
Unskilled Workers	370	30
Service and Protective Workers	690	30
Sales Workers	730	90
Farmers	160	–
Total Employed	690	30
Not Employed Housewives	1,030	0
Other Not Employed	580	0
Total Not Employed	800	0
Total	740	20

9. Marihuana

General Remarks

The various Cannabis sativa preparations (marihuana, hashish, dagga, charas, bhang, etc.) are the most widely used illegal drugs in the world. Likewise, in the United States the use of marihuana exceeds the use of any other illegal drug and quite probably the abuse of the legally manufactured drugs.

For the purposes of this survey, any use of a Cannabis preparation was recorded as the use of marihuana. This was done when it became apparent that some respondents used the terms interchangeably or were at times uncertain as to which preparation had been used. This is, of course, consistent with our awareness that the marihuana grown, sold and used is not a single uniform substance. It contains varying mixtures of the seeds, flowers, leaves and stems of the plant. The drug subsequently produces a wide variation of hallucinogenic effects.

While it is obvious the hallucinogenic effects of the marihuana are related to the amount and potency of the drug ingested, individual reactions are also manipulated by the setting in which the use occurs, the emotional and intellectual maturity of the user and the previous use experience of the user. These combine to prevent meaningful prediction of either harmful psychological or physiological effects of use. At the present time and with our current state of knowledge, it is apparent there are some psychological and physiological "costs" which accompany marihuana use. The extent of these "costs" remains to be documented.

The primary usage pattern in the United States appears to be long-term infrequent use of low-potency marihuana.

Prevalence and Incidence

The number of persons estimated to have used marihuana on at least one occasion is 1,433,000 of whom 889,000 (62.0%) are currently employed. The total *prevalence* figure represents 10.5% of the population age 14 and above. The *incidence* of the use of marihuana is projected as 3.6% of this base population or an estimated 485,000 persons who use marihuana at least six times a month.... some 293,000 (60.4%) of these regular users are currently employed. *Of the 1,433,000 persons who have ever used marihuana, 33.8% currently use the drug on a regular basis.* Among the 889,000 employed persons who have ever used marihuana, 33.0% are current regular users.

Six groups have higher rates of regular marihuana use than that for the general population. In their rank order, 8.6% of all sales workers, 5.8% of the persons not employed (excluding housewives), 5.2% of all the unskilled workers; 4.0% of all the service and protective workers, and, 4.0% of all the clerical and other white collar workers are current regular users of marihuana. There was no regular use of this drug among the farmers.

PREVALENCE AND INCIDENCE OF THE USE OF MARIHUANA

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,469,000 (86.8)	62,000 (3.7)	64,000 (3.8)	48,000 (2.8)	49,000 (2.9)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,217,000 (85.6)	50,000 (3.5)	69,000 (4.9)	57,000 (4.0)	29,000 (2.0)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,040,000 (84.3)	112,000 (4.6)	127,000 (5.2)	86,000 (3.6)	56,000 (2.3)	2,421,000 (100.0)
4. Unskilled Workers	271,000 (83.1)	12,000 (3.7)	19,000 (5.8)	17,000 (5.2)	7,000 (2.1)	326,000 (100.0)
5. Service & Protective Workers	391,000 (92.1)	22,000 (5.2)	24,000 (5.7)	16,000 (3.8)	5,000 (1.2)	424,000 (100.0)
6. Sales Workers	456,000 (85.3)	6,000 (1.0)	25,000 (4.6)	46,000 (8.6)	8,000 (1.5)	535,000 (100.0)
7. Farmers	63,000 (98.4)	–	1,000 (1.6)	–	–	64,000 (100.0)
Total Employed	6,344,000 (85.9)	265,000 (3.6)	331,000 (4.5)	293,000 (4.0)	156,000 (2.1)	7,389,000 (100.0)
8. Not Employed Housewives	2,923,000 (96.4)	30,000 (1.0)	23,000 (.8)	5,000 (.2)	52,000 (1.7)	3,033,000 (100.0)
9. Other Not Employed	2,698,000 (83.6)	116,000 (3.6)	183,000 (5.7)	187,000 (5.8)	43,000 (1.3)	3,227,000 (100.0)
Total Not Employed	5,621,000 (89.8)	146,000 (2.3)	206,000 (3.3)	192,000 (3.1)	95,000 (1.5)	6,260,000 (100.0)
Total	11,965,000 (87.7)	411,000 (3.0)	537,000 (3.9)	485,000 (3.6)	251,000 (1.8)	13,649,000 (100.0)

RATE OF USE PER 10,000 MARIHUANA

	Prevalance Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	1,030	280
Clerical and Other White Collar Workers	1,240	400
Skilled, Semi-skilled Workers	1,340	360
Unskilled Workers	1,470	520
Service and Protective Workers	980	400
Sales Workers	1,360	860
Farmers	160	-
Total Employed	1,210	400
Not Employed Housewives	200	20
Other Not Employed	1,510	580
Total Not Employed	870	310
Total	1,050	360

General Remarks

LSD — D-lysergic acid diethylamine — is a semi-synthetic derivative from one of the ergot alkaloids whose hallucinogenic properties were accidentally discovered in 1943. Ergot is a fungus which grows as a rust on rye and other cereals. The drug is relatively easy to manufacture in clandestine laboratories and has become one of the most widely used illegal drugs. With the exception of federally approved research projects, all use of LSD is unlawful.

To date, neither the mode nor site of action of LSD are completely known. Drug induced activity, i.e., distortions of perception, emotionality and rationality, generally lasts for eight to twelve hours. The most intense and bizarre changes apparently occur during the first half of the experience with the latter part being characterized by introspection and hypersuggestibility.

LSD is not physically addicting in the sense of barbiturates and opiates. The dependence is psychological not physical. Tolerance develops rapidly after a few days of repeated use, but is usually lost in two or three days. Some users reportedly have built up their LSD doses to 1000 and 2000 mcg. over a period of days. The first or threshold dose is about 25 mcg. and an average dose is 200 to 400 mcg. Paradoxically, some users report a state of increased sensitivity to LSD once they have lost their tolerance.

Unexpected return of the drugged state without ingestion of LSD for months or even a year later has been reported.

The literature reports three different kinds of experiences under LSD: (1) *the good trip* — a predominantly pleasant experience; (2) *the bad trip* — a dysphoric experience characterized by anxiety, panic, feelings of persecution, fears of loss of ego boundaries, loss of control and time perception, and impaired performance; and (3) an *ambivalent state* where the subject may simultaneously experience contrasting feelings as of happiness and lightness, relaxedness and tenseness.

Prevalence and Incidence

The number of persons estimated to have used LSD on at least one occasion is 329,000 of whom 191,000 (58.1%) are currently employed. The total *prevalency* figure represents 2.5% of the population age 14 and above. The *incidence* of the use of LSD is estimated to be .4% of this population base....some 50,000 persons who are using LSD at least six times a month. Half or 25,000 of these regular users of LSD are currently employed. *Of the 329,000 persons who have ever used LSD, 15.2% currently use the drug on a regular basis.* Among the 191,000 employed persons who report histories of LSD use, 13.2% are current regular users.

Only two groups have higher rates of regular LSD use than that found in the general population....some 2.6% of all the sales workers and .7% of the persons not employed (excluding housewives) are regular users of LSD. No farmer was detected who had ever used LSD.

PREVALENCE AND INCIDENCE OF THE USE OF LSD

Occupational Group	Never Used	Former User (No use in 8 months)	Infrequent User (1 but not 8 times per month)	Regular User (At least 8 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,624,000 (96.0)	10,000 (.6)	12,000 (.7)	2,000 (.1)	44,000 (2.6)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,357,000 (95.4)	24,000 (1.7)	13,000 (.9)	--	28,000 (2.0)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,298,000 (94.9)	27,000 (1.1)	38,000 (1.5)	4,000 (.2)	58,000 (2.3)	2,421,000 (100.0)
4. Unskilled Workers	307,000 (94.2)	4,000 (1.2)	9,000 (2.8)	1,000 (.3)	5,000 (1.5)	326,000 (100.0)
5. Service & Protective Workers	853,000 (98.4)	4,000 (.5)	18,000 (2.0)	3,000 (.3)	7,000 (.8)	885,000 (100.0)
6. Sales Workers	548,000 (94.6)	4,000 (.7)	5,000 (.9)	15,000 (2.8)	7,000 (1.2)	579,000 (100.0)
7. Farmers	64,000 (100.0)	–	–	..	–	64,000 (100.0)
Total Employed	7,051,000 (95.4)	73,000 (1.0)	93,000 (1.3)	25,000 (.3)	147,000 (2.0)	7,389,000 (100.0)
8. Not Employed Housewives	2,958,000 (97.8)	7,000 (.2)	–	2,000 (.1)	58,000 (1.8)	3,033,000 (100.0)
9. Other Not Employed	3,055,000 (94.7)	50,000 (1.5)	56,000 (1.7)	23,000 (.7)	43,000 (1.3)	3,227,000 (100.0)
Total Not Employed	6,023,000 (96.2)	57,000 (.9)	56,000 (.9)	25,000 (4)	99,000 (1.6)	6,260,000 (100.0)
Total	13,074,000 (95.8)	130,000 (1.0)	149,000 (1.1)	50,000 (4)	246,000 (1.8)	13,649,000 (100.0)

RATE OF USE PER 10,000 LSD

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	140	10
Clerical and Other White Collar Workers	260	–
Skilled, Semi-skilled Workers	280	20
Unskilled Workers	430	30
Service and Protective Workers	280	30
Sales Workers	420	260
Farmers	–	
Total Employed	260	30
Not Employed Housewives	30	10
Other Not Employed	390	70
Total Not Employed	220	40
Total	250	40

11. Methedrine

General Remarks

Methedrine, a brand name for methamphetamine, is a central nervous system stimulant more potent but chemically related to the amphetamines - amphetamine sulfate (Benzedrine) and d-amphetamine sulfate (Dexedrine). The drug was first used widely by the German army during World War II to counter fatigue among combatants. The drug is currently marketed for its appetite-suppressing effects, its potential for reducing mild symptoms of mental depression, its potential as a mood elevator, as an analeptic in sedative overdose, and to raise abnormally low blood pressure, i.e., in anesthetized patients.

Unfortunately, the primary use of this drug is nonmedical, unsupervised illicit abuse by habitual high-dose amphetamine users. It is the drug of choice among those persons who use amphetamines by intravenous injection only for their euphoric effects.

Psychological dependence and tolerance have been well documented. High doses over extended periods of time engender acute or chronic psychoses, loss of memory and powers of concentration. Violent behavior is also commonly seen. There are reports to indicate that methedrine abusers may experience damage to their brains and arteries.

Prevalence and Incidence

The number of persons estimated to have used methedrine on at least one occasion is 247,000 of whom 147,000 (59.5%) are currently employed. The total *prevalency* figure represents 1.7% of the population age 14 and above. The *incidence* of the use of methedrine is estimated at .2% of this base population....some 34,000 persons who are using methedrine a minimum of six times a month. An estimated 29.4% of these regular users of methedrine are currently employed. *Of the 247,000 persons who have ever used methedrine, 9.8% currently use the drug on a regular basis.* Of the 147,000 employed persons reporting a history of use, some 6.8% are current regular users of the drug.

Three groups have higher rates of regular methedrine use than that found in the general population....some .7% of all the sales workers, .7% of those persons not employed (excluding housewives) and .3% of all the unskilled workers report the regular use of methedrine. No farmer was detected who had ever used methedrine.

PREVALENCE AND INCIDENCE OF THE USE OF METHEDRINE

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,627,000 (96.2)	15,000 (.9)	5,000 (.3)	2,000 (.1)	43,000 (2.5)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,364,000 (95.9)	25,000 (1.8)	6,000 (.4)	3,000 (.2)	24,000 (1.7)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,312,000 (95.5)	33,000 (1.4)	16,000 (.7)	–	60,000 (2.5)	2,421,000 (100.0)
4. Unskilled Workers	311,000 (95.4)	7,000 (2.1)	2,000 (.6)	1,000 (.3)	5,000 (1.5)	326,000 (100.0)
5. Service & Protective Workers	860,000 (97.2)	16,000 (1.8)	2,000 (.2)	–	7,000 (.8)	885,000 (100.0)
6. Sales Workers	558,000 (96.4)	6,000 (1.0)	4,000 (.7)	4,000 (.7)	7,000 (1.2)	579,000 (100.0)
7. Farmers	64,000 (100.0)	–				64,000 (100.0)
Total Employed	7,096,000 (96.0)	102,000 (1.4)	35,000 (.5)	10,000 (.1)	146,000 (2.0)	7,389,000 (100.0)
8. Not Employed Housewives	2,953,000 (97.4)	5,000 (.2)	3,000 (.1)		72,000 (2.4)	3,033,000 (100.0)
9. Other Not Employed	3,093,000 (95.8)	35,000 (1.1)	33,000 (1.0)	24,000 (.7)	42,000 (1.3)	3,227,000 (100.0)
Total Not Employed	6,046,000 (96.6)	40,000 (.6)	36,000 (.6)	24,000 (.4)	114,000 (1.8)	6,260,000 (100.0)
Total	13,142,000 (96.3)	142,000 (1.0)	71,000 (.5)	34,000 (.2)	260,000 (1.9)	13,649,000 (100.0)

RATE OF USE PER 10,000 METHEDRINE

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	130	10
Clerical and Other White Collar Workers	240	20
Skilled, Semi-skilled Workers	210	–
Unskilled Workers	300	30
Service and Protective Workers	200	–
Sales Workers	240	70
Farmers	–	–
Total Employed	200	10
Not Employed Housewives	30	–
Other Not Employed	280	70
Total Not Employed	160	40
Total	170	20

12. Heroin

General Remarks

Heroin is a highly addictive white crystalline powder prepared by acetylation from morphine. The drug was first produced in 1898 and marketed as a nonaddicting substitute for morphine and codeine. Subsequent experience has shown the drug to be twice as potent as morphine at any given quantity and tolerance develops very rapidly. In fact, there is considerable agreement that heroin has a higher addiction liability than morphine.

As tolerance increases, the heroin user typically uses the drug in increasingly greater amounts, and most of his waking hours are spent in drug centered behavior. With the exception of drug related phenomenon, the addicted user becomes insensitive to his environment and indifferent to his personal situations.

Our current knowledge suggests the use of heroin is rising throughout the country, and, increasingly, is becoming associated with younger individuals and all ethnic groups and socioeconomic classes.

Prevalence and Incidence

This survey detected some 149,000 persons who have used heroin on at least one occasion of whom 89,000 (59.7%) are currently employed. The total *prevalency* figure represents 1.1% of the population age 14 and above. The *incidence* of heroin use is estimated to be .3% of the total base population...some 41,000 persons who are currently using heroin at least six times a month. An estimated 82.9% of the regular users of heroin detected during this survey are currently employed. *Of the 149,000 persons who have ever used heroin, 27.5% currently use the drug on a regular basis.* Of the 89,000 employed persons who report a history of heroin use, 38.2% currently use the drug on a regular basis.

Only two occupational groups have higher rates of regular heroin use than that found in the general population....2.1% of all the sales workers and .6% of all the clerical and other white collar workers report the regular use of heroin. No farmer was detected who had ever used heroin and no current regular use was detected among any of the service and protective workers and not employed housewives

PREVALENCE AND INCIDENCE OF THE USE OF HEROIN

Occupational Group	Never Used	Former User (No use in 6 months)	Infrequent User (1 but not 6 times per month)	Regular User (At least 6 times per month)	No Data	Total
1. Professionals, Technical Workers, Managers and Owners	1,636,000 (96.7)	9,000 (.5)	–	4,000 (.2)	43,000 (2.5)	1,692,000 (100.0)
2. Clerical and Other White Collar Workers	1,378,000 (96.9)	2,000 (.1)	–	9,000 (.6)	33,000 (2.3)	1,422,000 (100.0)
3. Skilled & Semi-skilled Workers	2,335,000 (96.4)	23,000 (1.0)	3,000 (.1)	8,000 (.3)	52,000 (2.1)	2,421,000 (100.0)
4. Unskilled Workers	315,000 (96.6)	3,000 (.9)	2,000 (.6)	1,000 (.3)	5,000 (1.5)	326,000 (100.0)
5. Service & Protective Workers	865,000 (97.7)	13,000 (1.5)	–	–	7,000 (.8)	885,000 (100.0)
6. Sales Workers	560,000 (96.7)	–	–	12,000 (2.1)	7,000 (1.2)	579,000 (100.0)
7. Farmers	64,000 (100.0)	–	–	–	–	64,000 (100.0)
Total Employed	7,153,000 (96.8)	50,000 (.7)	5,000 (.1)	34,000 (.5	147,000 (2.0)	7,389,000 (100.0)
8. Not Employed Housewives	2,967,000 (97.8)	12,000 (.4)	2,000 (.1)	–	52,000 (1.7)	3,033,000 (100.0)
9. Other Not Employed	3,137,000 (97.2)	21,000 (.7)	18,000 (.6)	7,000 (.2)	44,000 (1.4)	3,227,000 (100.0)
Total Not Employed	6,104,000 (97.5)	33,000 (.5)	20,000 (.3)	7,000 (.1)	96,000 (1.5)	6,260,000 (100.0)
Total	13,257,000 (97.1)	83,000 (.6)	25,000 (.2)	41,000 (.3)	243,000 (1.8)	13,649,000 (100.0)

RATE OF USE PER 10,000 HEROIN

	Prevalence Rate (Ever Used)	Incidence Rate (Regular Use)
Professionals, Technical Workers, Managers and Owners	70	20
Clerical and Other White Collar Workers	70	60
Skilled, Semi-skilled Workers	140	30
Unskilled Workers	180	30
Service and Protective Workers	150	–
Sales Workers	210	210
Farmers	–	–
Total Employed	130	50
Not Employed Housewives	50	–
Other Not Employed	150	20
Total Not Employed	90	10
Total	110	30

Special Comments

N.A.C.C. epidemiologists and demographers wish to emphasize that the projected prevalency figure of 149,000 persons and the projected incidence figure of 41,000 persons are underrepresentations of the total heroin using population. This anticipated underrepresentation occurred naturally as the result of the sampling technique employed in the study. The sampling procedures, as outlined in the methodology section of this report, drew a study population from persons living in households and excluded those persons who were living in rooming houses, hotels, any residential institution and all others who did not have a regular residence. In addition, time and budget limitations did not permit more than two "call backs" to locate any one individual selected for interview. Therefore, even those persons who have a regular residence but who are seldom at home were also excluded. Because of this combination of excluding factors, a large number of heroin addicts were not available or "at risk" for interview. It is the user of heroin who is least likely to have a regular residence, or if he has a regular residence, to be absent from it frequently and for extended periods of time.

There are a number of factors which support this assumption of a sample bias underrepresentation. For example, although the age and ethnic group distributions are consistent with our knowledge of the demographic characteristics of this addict population, the education, employment and social class characteristics are not consistent with previously described populations. These data suggest the sampling procedure succeeded in isolating only the most stable of the regular heroin users. Some 82.9% of the respondents were legally employed and two out of three of those remaining reported themselves as students. Some two-thirds of all these regular heroin users are high school graduates or above. It is, therefore, apparent the less stable "heroin street addict" who is more likely to be uneducated, unemployed and without a stable residence, was not located with this sampling procedure.

An analysis of the drugs concurrently being used by these regular heroin users supports the above comments. The relatively high incidences of amphetamine, methedrine and LSD use suggest the respondents were not the "heroin street addict" typically described in the professional literature. Correspondingly, the relative infrequency of concurrent cocaine and other opiate use also indicate the underrepresentation of the "heroin street addict."

Certain arithmetic adjustments or rational projections are available for those who choose to correct for the sampling bias. (1) Some 14,000 plus *known* heroin users were in residential institutions, i.e., jails, prisons, N.A.C.C.'s own civil commitment facilities, etc., during this study period and were not available for selection as a respondent. (2) An extensive analysis of the educations of known contemporary heroin addicts in New York State indicate only about one third have completed high school. This compares with two-thirds in the surveyed population. (3) Studies of several metropolitan heroin addict populations indicate from 70% to 90% of the "heroin street addicts" cannot maintain employment after becoming regular users of heroin. This compares to an unemployed group of only 12.5% in the surveyed population.

In summary, while it would not be conclusive, it would not be unreasonable to suggest the sampling technique employed for this survey was successful in identifying only some one-third of the actual population of regular heroin users – the figure most frequently projected from other data sources. No other drug using population has so many participants who are *not* at risk for being selected for interview, i.e., a known not at risk institutionalized population half as large as the projected total. Future surveys of heroin users should incorporate census enumeration techniques of calling back until a defined respondent is located, surveying transient populations and surveying institutionalized populations. N.A.C.C. scientists also believe the same comments on underrepresentation are appropriate for any sociopathic drug user who has become dysfunctional and without a stable residence, work role, and so on. This type of individual has a social profile similar to the "heroin street addict" whether his drug of choice is methedrine, LSD, barbiturates, and so on.

II. The Demographic Characteristics of the Regular Drug Users Within Each Occupational Group

The survey instrument was designed to provide selected demographic attributes for those persons who reported any use of the drugs. For this report, the age, ethnicity, sex, education and any use while at work are provided for the regular users (at least six times a month) within each occupational group.

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 1,692,000 PROFESSIONALS, TECHNICAL WORKERS, MANAGERS AND OWNERS

Drug	Number of Regular Users	Age Distribution -25	Age Distribution 25+	Ethnicity White	Ethnicity Nonwhite	Sex Males	Sex Females	High School Graduates Yes	High School Graduates No	Any Use of the Drug on the Job
Barbiturates	44,000	6.8	93.2	97.7	2.3	90.9	9.1	95.5	4.5	11.4
Other Sedative/Hypnotics	21,000	4.8	95.2	95.2	4.8	85.7	14.3	95.2	4.8	–
Minor Tranquilizers	50,000	6.0	94.0	100.0		58.0	42.0	96.0	4.0	36.0
Major Tranquilizers	3,000	-	100.0	100.0		100.0		100.0		-
Antidepressants	-	-	-	-	-	–	-	-	–	–
Pep Pills	14,000	21.4	78.6	92.9	7.1	28.6	71.4	85.7	14.3	28.6
Diet Pills	34,000	11.8	88.2	100.0	–	44.1	55.9	91.2	8.8	11.8
Narcotics (Non-Heroin)	4,000	25.0	75.0	100.0	–	–	100.0	75.0	25.0	75.0
Marihuana	48,000	27.1	72.9	87.5	12.51	58.3	41.7	93.8	6.2	20.8
LSD	2,000	50.0	50.0	100.0	–	50.0	50.0	100.0	–	50.0
Methedrine	2,000	50.0	50.0	100.0	–	50.0	50.0	50.0	50.0	50.0
Heroin	4,000	100.0	–	25.0	75.0	100.0	–	50.0	50.0	–

A. Most frequently used of the *legal* drugs
- 50,000 Regular Users ...Relaxants/Minor Tranquilizers
- 36%....report taking the drugs while at work
- 94%....are age 25 or above
- 100%....are whites
- 58%....are males
- 96%....are high school graduates

B. Most frequently used of the *illegal* drugs
- 48,000 Regular Users....Marihuana
- 20.8%... report using the drug while at work
- 72.9%... are age 25 or above
- 87.5%....are whites
- 58.3%....are males
- 93.8%....are high school graduates

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 1,422,000 CLERICAL AND OTHER WHITE COLLAR WORKERS

Drug	Number of Regular Users	Age Distribution -25	Age Distribution 25+	Ethnicity White	Ethnicity Nonwhite	Sex Males	Sex Females	High School Graduates Yes	High School Graduates No	Any Use of the Drug on the Job
Barbiturates	23,000	4.3	95.7	69.6	30.4	43.5	56.5	91.3	8.7	4.3
Other Sedative/Hypnotics	12,000	25.0	75.0	91.7	8.3	–	100.0	100.0	–	16.7
Minor Tranquilizers	81,000	14.8	85.2	87.7	12.3	14.3	85.2	84.0	16.0	3.7
Major Tranquilizers	20,000	–	100.0	100.0	–	30.0	70.0	60.0	40.0	15.0
Antidepressants	4,000	–	100.0	100.0	–	–	100.0	50.0	50.0	–
Pep Pills	12,000	25.0	75.0	100.0	–	50.0	50.0	100.0	–	–
Diet Pills	35,000	40.0	60.0	82.9	17.1	2.9	97.1	88.6	11.4	3.5
Narcotics (Non-Heroin)	1,000	100.0	–	100.0	–	100.0	–	100.0	–	–
Marihuana	57,000	63.2	36.8	50.9	49.1	71.9	28.1	87.7	12.3	35.1
LSD	–	-	-	–		-	-	-	-	-
Methedrine	3,000	-	100.0		100.0	100.0		100.0	-	–
Heroin	9,000	100.0	–		100.0	88.9	11.1	55.6	44.4	

A. Most frequently used of the *legal* drugs
- 81,000 Regular Users....Relaxants/Minor Tranquilizers
- 3.7%....report taking the drugs while at work
- 85.2%....are age 25 or above
- 87.7%....are whites
- 85.2%....are females
- 84.0%....are high school graduates

B. Most frequently used of the *illegal* drugs
- 57,000 Regular Users. ..Marihuana
- 35.1%....report using the drug while at work
- 63.2%....are younger than 25
- 50.9%... are whites
- 71.9%....are males
- 87.7%....are high school graduates

CHARACTERISTICS OF THE REGULAR DRUG USERS AMONG 2,421,000 SKILLED AND SEMI-SKILLED WORKERS

Drug	Number of Regular Users	Age Distribution -25	25+	Ethnicity White	Nonwhite	Sex Males	Females	High School Graduates Yes	No	Any Use of the Drug on the Job
Barbituretes	27,000	37.0	63.0	85.2	14.8	59.3	40.7	92.6	7.4	7.4
Other Sedative/Hypnotics	21,000	28.6	71.4	66.7	33.3	76.2	23.8	66.7	33.3	–
Minor Tranquilizers	36,000	13.9	86.1	100.0	–	72.2	27.8	69.4	30.6	13.9
Major Tranquilizers	15,000	60.0	40.0	100.0	–	100.0	–	100.0	–	–
Antidepressants	8,000	50.0	50.0	100.0	–	50.0	50.0	100.0	–	–
Pep Pills	9,000	88.9	11.1	88.9	11.1	44.4	55.6	100.0		22.2
Diet Pills	21,000	61.9	38.1	61.9	38.1	28.6	71.4	90.5	9.5	14.3
Narcotics (Non Heroin)	5,000	40.0	60.0	100.0		40.0	60.0	40.0	60.0	–
Marihuana	86,000	84.9	15.1	76.7	23.3	83.7	16.3	80.2	19.8	22.1
LSD	4,000	50.0	50.0	50.0	50.0	50.0	50.0	100.0		
Methedrine	–	–	–	–	–	–	–	–	–	–
Heroin	8,000	–	100.0	–	100.0	100.0	–	100.0	–	–

A. Most frequently used of the *legal* drugs
- 36,000 Regular Users....Relaxants/Minor Tranquilizers
- 13.9%....report taking the drugs while at work
- 86.1%....are age 25 or above
- 100.0%....are whites
- 72.2%....are males
- 69.4%....are high school graduates

B. Most frequently used of the *illegal* drugs
- 86,000 Regular Users....Marihuana
- 22.1%....report using the drug while at work
- 84.9%....are younger than 25
- 76.7%....are whites
- 83.7%....are males
- 80.2%....are high school graduates

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 326,000 UNSKILLED WORKERS

Drug	Number of Regular Users	Age Distribution -25	25+	Ethnicity White	Nonwhite	Sex Males	Females	High School Graduates Yes	No	Any Use of the Drug on the Job
Barbituretes	7,000	–	100.0	28.6	71.4	85.7	14.3	28.6	71.4	–
Other Sedative/Hypnotics	6,000	16.7	83.3	33.3	66.7	33.3	66.7	–	100.0	–
Minor Tranquilizers	10,000	30.0	70.0	50.0	50.0	40.0	60.0	40.0	60.0	30.0
Major Tranquilizers	1,000	100.0	–	100.0	–	100.0	–	–	100.0	–
Antidepressants	1,000	–	100.0	100.0	–	100.0	–	100.0	–	–
Pep Pills	1,000	100.0	–	100.0	–	–	100.0	–	100.0	–
Diet Pills	2,000	50.0	50.0	50.0	50.0	50.0	50.0	–	100.0	–
Narcotics (Non-Heroin)	1,000	–	100.0	100.0	–	–	100.0	100.0	–	–
Marihuana	17,000	88.2	11.8	76.5	23.5	76.5	23.5	52.9	47.1	35.3
LSD	1,000	100.0	–	–	100.0	100.0	–	–	100.0	–
Methedrine	1,000	100.0	–	100.0	–	100.0		100.0		100.0
Heroin	1,000	100.0	–		100.0		100.0	-	100.0	

A. Most frequently used of the *legal* drugs
- 10,000 Regular Users....Relaxants/Minor Tranquilizers
- 30.0%....report taking the drugs while at work
- 70.0%....are age 25 or above
- 50.0%....are whites
- 60.0%....are females
- 60.0%....are *not* high school graduates

B. Most frequently used of the *illegal* drugs
- 17,000 Regular Users....Marihuana
- 35.3%....report using the drug while at work
- 88.2%....are younger than 25
- 76.5%....are whites
- 76.5%....are males
- 52.9%....are high school graduates

The Demographic Characteristics of the Regular Drug Users Within Each Occupational Group

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 885,000 SERVICE AND PROTECTIVE WORKERS

Drug	Number of Regular Users	Age Distribution -25	25+	Ethnicity White	Nonwhite	Sex Males	Females	High School Graduates Yes	No	Any Use of the Drug on the Job
Barbiturates	33,000	–	100.0	100.0	–	42.4	57.6	84.8	15.2	–
Other Sedative/Hypnotics	10,000	–	100.0	100.0	–	20.0	80.0	80.0	20.0	–
Minor Tranquilizers	38,000	–	100.0	100.0	–	36.8	63.2	60.5	39.6	36.8
Major Tranquilizers	4,000	–	100.0	100.0	–	–	100.0	100.0	–	100.0
Antidepressants	–	–	–	–	–	–	–	–	–	–
Pep Pills	7,000	57.1	42.9	100.0	–	57.1	42.9	100.0	–	57.1
Diet Pills	4,000	50.0	50.0	100.0	–	50.0	50.0	100.0	–	–
Narcotics (Non-Heroin)	3,000	–	100.0	100.0	–	–	100.0	100.0	–	–
Marihuana	35,000	51.4	48.6	71.4	28.6	80.0	20.0	57.1	42.9	2.9
LSD	3,000	–	100.0	100.0	–	–	100.0	100.0	–	–
Methedrine	–	–	–	–	–	–	–	–	–	–
Heroin	–	–	–	–	–	–	–	–	–	–

A. Most frequently used of the *legal drugs*
38,000 Regular Users....Relaxants/Minor Tranquilizers
36.8%....report taking the drugs while at work
100.0%....are age 25 or above
100.0%....are whites
63.2%....are females
60.5%....are high school graduates

B. Most frequently used of the *illegal* drugs
35,000 Regular Users....Marihuana
2.9%....report using the drug while at work
51.4%....are younger than 25
71.4%....are whites
80.0%....are males
57.1%....are high school graduates

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 579,000 SALES WORKERS

Drug	Number of Regular Users	Age Distribution -25	26+	Ethnicity White	Nonwhite	Sex Males	Females	High School Graduates Yes	No	Any Use of the Drug on the Job
Barbiturates	71,000	9.9	90.1	88.7	11.3	57.7	42.3	69.0	31.0	11.3
Other Sedative/Hypnotics	1,000	–	100.0	100.0	–	100.0	–	100.0	–	100.0
Minor Tranquilizers	25,000	8.0	92.0	100.0	–	24.0	76.0	48.0	62.0	36.0
Major Tranquilizers	12,000	–	100.0	100.0	–	–	100.0	100.0	–	–
Antidepressants	–	–	–	–	–	–	–	–	–	–
Pep Pills	8,000	12.5	87.5	50.0	50.0	–	100.0	100.0	–	100.0
Diet Pills	21,000	23.8	76.2	100.0	–	28.6	71.4	61.9	38.1	28.6
Narcotics (Non-Heroin)	5,000	–	100.0	100.0	–	100.0	–	·	100.0	–
Marihuana	50,000	56.0	44.0	92.0	8.0	38.0	62.0	82.0	18.0	44.0
LSD	15,000	–	100.0	73.3	26.7	–	100.0	100.0	–	26.7
Methedrine	4,000	–	100.0	100.0	–	–	100.0	100 0	–	100.0
Heroin	12,000	41.7	58.3	100.0	–	16.7	83.3	83.3	16.7	100.0

A. Most frequently used of the *legal* drugs
71,000 Regular Users....Barbiturates
11.3%....report taking the drugs while at work
90.1%....are age 25 or above
88.7%....are whites
57.7%....are males
69.0%....are high school graduates

B. Most frequently used of the *illegal* drugs
50,000 Regular Users....Marihuana
44.0%....report using the drug while at work
56.0%....are younger than 25
92.0%....are whites
62.0%....are females
82.0%....are high school graduates

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 64,000 FARMERS

Drug	Number of Regular Users	Age Distribution 25	Age Distribution 25+	Ethnicity White	Ethnicity Nonwhite	Sex Males	Sex Females	High School Graduates Yes	High School Graduates No	Any Use of the Drug on the Job
Barbiturates	-	-	-							
Other Sedative/Hypnotics	1,000		100.0	100.0	-	100.0			100.0	-
Minor Tranquilizers	-	-	-	-	-	-		-		-
Major Tranquilizers	-	-	-	-	-	-	-			-
Antidepressants	-	-	-	-	-	-	-	-	-	-
Pep Pills	-	-	-	-	-	-	-	-	-	-
Diet Pills	-	-	-	-	-	-	-	-	-	-
Narcotics (Non-Heroin)	-	-	-	-	-	-	-	-	-	-
Marihuana	-	-	-	-	-	-	-	-	-	-
LSD	-	-	-	-	-	-	-	-	-	-
Methedrine	-	-	-	-	-	-	-	-	-	-
Heroin	-	-	-	-	-	-	-	-	-	-

For all intents and purposes, one can report virtually no regular use of any drug among farmers

CHARACTERISTICS OF REGULAR DRUG USERS AMONG 3,033,000 NOT EMPLOYED HOUSEWIVES

Drug	Number of Regular Users	Age Distribution -25	Age Distribution 25+	Ethnicity White	Ethnicity Nonwhite	Sex Males	Sex Females	High School Graduates Yes	High School Graduates No	Any Use of the Drug on the Job
Barbiturates	73,000	2.7	97.3	93.2	6.8	-	100.0	79.5	20.5	
Other Sedative/Hypnotics	55,000	-	100.0	96.4	3.6		100.0	69.1	30.9	
Minor Tranquilizers	161,000	2.5	97.5	80.7	19.3		100.0	67.7	32.3	
Major Tranquilizers	11,000		100.0	36.4	63.6		100.0	27.3	72.7	
Antidepressants	17,000		100.0	64.7	35.3		100.0	52.9	47.1	
Pep Pills	8,000	-	100.0	87.5	12.5		100.0	62.5	37.5	
Diet Pills	81,000	14.8	85.2	65.4	34.6	-	100.0	58.0	42.0	
Narcotics (Non-Heroin)	1,000	-	100.0	100.0	-	-	100.0	100.0	-	-
Marihuana	5,000	60.0	40.0	20.0	80.0	-	100.0	80.0	20.0	-
LSD	2,000	-	100.0	-	100.0	-	100.0	100.0	-	-
Methedrine	-	-	-	-	-	-	-	-	-	-
Heroin	-	-	-	-	-	-	-	-	-	-

A. Most frequently used of the *legal* drugs
161,000 Regular Users....Relaxants/Minor Tranquilizers
97.5%....are age 25 or above
80.7%....are whites
67.7%....are high school graduates

B. Most frequently used of the *illegal* drugs
5,000 Regular Users... Marihuana
60.0%....are younger than 25
80.0%....are nonwhites
100.0%....are high school graduates

CHARACTERISTICS OF THE REGULAR DRUG USERS AMONG 3,227,000 OTHER PERSONS NOT EMPLOYED

Drug	Number of Regular Users	Age Distribution -25	Age Distribution 25+	Ethnicity White	Ethnicity Nonwhite	Sex Males	Sex Females	High School Graduates Yes	High School Graduates No	Any Use of the Drug on the Job
Barbiturates	99,000	24.2	75.8	82.8	17.2	47.5	52.5	36.4	63.6	-
Other Sedative/Hypnotics	46,000	30.4	69.6	73.9	26.1	41.3	58.7	23.9	76.1	
Minor Tranquilizers	124,000	32.3	67.7	83.9	16.1	50.0	50.0	46.0	54.0	
Major Tranquilizers	19,000	26.3	73.7	73.7	26.3	47.4	52.6	73.7	26.3	
Antidepressants	7,000	85.7	14.3	85.7	14.3	71.4	28.6	42.9	57.1	
Pep Pills	51,000	51.0	49.0	88.2	11.8	49.0	51.0	49.0	51.0	-
Diet Pills	27,000	66.7	33.3	96.3	3.7	48.1	51.9	51.9	48.1	-
Narcotics (Non-Heroin)	1,000	100.0	-	100.0	-	-	100.0	100.0	-	-
Marihuana	187,000	80.2	19.8	78.1	21.9	62.6	37.4	51.3	48.7	-
LSD	23,000	82.6	17.4	91.3	8.7	87.0	13.0	26.1	73.9	-
Methedrine	24,000	91.7	8.3	87.5	12.5	87.5	12.5	50.0	50.0	-
Heroin	7,000	85.7	14.3	42.9	57.1	71.4	28.6	57.1	42.9	-

A. Most frequently used of the *legal* drugs
121,000 Regular Users....Relaxants/Minor Tranquilizers
67.7%....are age 25 or above
83.9%....are whites
50.0%....are males
54.0%....are *not* high school graduates

B. Most frequently used of the *illegal* drugs
187,000 Regular Users ... Marihuana
80.2%....are younger than 25
78.1%....are whites
62.6%....are males
51.3%....are high school graduates

III. The Summary Distributions of All the Regular Users Within Each Occupational Group

Summary analyses within each occupational group indicating the drugs most frequently being used on a regular basis are as follows:

Professionals, technical workers, managers and owners . . . . . Relaxants/Minor Tranquilizers
(50,000 Regular Users — 36.0% report taking them while at work)

Clerical and other white collar workers . . . . . Relaxants/Minor Tranquilizers
(81,000 Regular Users — 3.7% report taking them while at work)

Skilled and semi-skilled workers . . . Marihuana
(86,000 Regular Users — 22.1% report use while at work)

Unskilled workers . . . . . Marihuana
(17,000 Regular Users — 35.3% report use while at work)

Sales workers . . . . . Barbiturates
(71,000 Regular Users — 11.3% report taking them while at work)

Farmers . . . . . Other Sedative/Hypnotics
(1,000 Regular Users)

Not employed housewives . . . . . Relaxants/Minor Tranquilizers
(161,000 Regular Users)

Other not employed . . . . . Marihuana
(187,000 Regular Users)

Summary analyses within each drug group indicating which of the groups contribute to the greatest number of current regular users are as follows:

Barbiturate users . . . . . Not employed housewives
(73,000 or 19.1% of all Regular Users)

Other Sedative/Hypnotics . . . . . Not employed housewives
(55,000 or 31.8% of all Regular Users)

Relaxants/Minor Tranquilizers . . . Not employed housewives
(161,000 or 30.7% of all Regular Users)

Major Tranquilizers . . . . . Clerical or other white collar workers
(20,000 or 23.5% of all Regular Users)

Antidepressants . . . . . Not employed housewives
(17,000 or 45.9% of all Regular Users)

Pep Pills . . . . . Other not employed
(51,000 or 46.4% of the Regular Users)

Diet Pills . . . . . Not employed housewives
(81,000 or 36.0% of the Regular Users)

Narcotics (Non-Heroin) . . . . . Sales workers and skilled and semi-skilled workers
(5,000 or 23.8% each of the Regular Users)

Marihuana . . . . . Other not employed
(187,000 or 38.6% of the Regular Users)

LSD . . . . . Sales Workers
(15,000 or 30.0% of the Regular Users)

Methedrine . . . . . Sales Workers
(4,000 or 11.8% of the Regular Users)

Heroin . . . . . Sales Workers
(12,000 or 29.3% of the Regular Users)

SUMMARY TABLE – NUMERICAL AND PERCENTAGE DISTRIBUTION OF REGULAR DRUG USERS (AT LEAST SIX TIMES PER MONTH)

	Barbiturates	Other Sedatives	Minor Tranquilizers	Major Tranquilizers	Anti-depressants	Pep Pills	Diet Pills	Narcotics (Non-Heroin)	Marihuana	LSD	Methedrine	Heroin
1. Professionals, Technical Workers, Managers and Owners	44,000 (11.7)	21,000 (12.1)	50,000 (9.5)	3,000 (3.5)	–	14,000 (12.7)	34,000 (15.1)	4,000 (19.0)	48,000 (9.9)	2,000 (4.0)	2,000 (5.9)	4,000 (9.8)
2. Clerical and Other White Collar Workers	23,000 (6.1)	12,000 (6.9)	81,000 (15.4)	20,000 (23.5)	4,000 (10.8)	12,000 (10.9)	35,000 (15.6)	1,000 (4.8)	57,000 (11.8)	–	3,000 (8.8)	9,000 (22.0)
3. Skilled & Semi-skilled Workers	27,000 (7.2)	21,000 (12.1)	36,000 (6.9)	15,000 (17.6)	8,000 (21.6)	9,000 (8.2)	21,000 (9.3)	5,000 (23.8)	86,000 (17.7)	4,000 (8.0)	–	8,000 (19.5)
4. Unskilled Workers	7,000 (1.9)	6,000 (3.5)	10,000 (1.9)	1,000 (1.2)	1,000 (2.7)	1,000 (.9)	2,000 (.9)	1,000 (4.8)	17,000 (3.5)	1,000 (2.0)	1,000 (2.9)	1,000 (2.4)
5. Service & Protective Workers	33,000 (8.8)	10,000 (5.8)	38,000 (7.2)	4,000 (4.7)	–	7,000 (6.4)	4,000 (1.8)	3,000 (14.3)	35,000 (7.2)	3,000 (6.0)	–	–
6. Sales Workers	71,000 (18.8)	1,000 (.6)	25,000 (4.8)	12,000 (14.1)	–	8,000 (7.3)	21,000 (9.3)	5,000 (23.8)	50,000 (10.3)	15,000 (30.0)	4,000 (11.8)	12,000 (29.3)
7. Farmers	–	1,000 (.6)	–	–	–	–	–	–	–	–	–	–
Total Employed	205,000 (54.4)	72,000 (41.6)	240,000 (45.7)	55,000 (64.6)	13,000 (35.1)	51,000 (46.4)	117,000 (52.0)	19,000 (90.5)	293,000 (60.4)	25,000 (50.0)	10,000 (29.4)	34,000 (83.0)
8. Not Employed Housewives	73,000 (19.4)	55,000 (31.8)	161,000 (30.7)	11,000 (12.9)	17,000 (45.9)	8,000 (7.3)	81,000 (36.0)	1,000 (4.8)	5,000 (1.0)	2,000 (4.0)	–	–
9. Other Not Employed	99,000 (26.3)	46,000 (26.6)	124,000 (23.6)	19,000 (22.4)	7,000 (18.0)	51,000 (46.4)	27,000 (12.0)	1,000 (4.8)	187,000 (38.6)	23,000 (46.0)	24,000 (70.6)	7,000 (17.1)
Total Not Employed	172,000 (45.6)	101,000 (58.4)	285,000 (54.3)	30,000 (35.3)	24,000 (64.8)	59,000 (53.7)	108,000 (48.0)	2,000 (9.6)	192,000 (39.6)	25,000 (50.0)	24,000 (70.6)	7,000 (17.1)
Total	377,000 (100.0)	173,000 (100.0)	525,000 (100.0)	85,000 (100.0)	37,000 (100.0)	110,000 (100.0)	225,000 (100.0)	21,000 (100.0)	485,000 (100.0)	50,000 (100.0)	34,000 (100.0)	41,000 (100.0)

IV. The Attitudes Toward Drug Use and Drug Users Within Each Occupational Group

Significant attitudinal differences exist within the general population as to the role of freedom of choice in the use of drugs, the most effective means for preventing drug use, the treatment of drug users, and so on. In order to assess any relationship between attitudes and occupation, each respondent was asked to register his attitude with respect to a number of these specific issues. Six items are reported here.

Item: Drug use should be a matter of personal choice.
46.3% — agree
45.3% — disagree
8.4% — don't know/refused to answer

Item. A lot of people need drugs to cope with stress.
51.7% — agree
36.9% — disagree
11.4% — don't know/refused to answer

Item: Drug addicts should be treated as sick people and not as criminals.
86.8% — agree
7.1% — disagree
6.1% — don't know/refused to answer

Item: Strict and harsh punishment of drug abusers will keep others from using drugs.
37.1% — agree
52.8% — disagree
10.1% — don't know/refused to answer

Item: Education is the best way of preventing drug abuse.
77.5% — agree
16.3% — disagree
6.2% — don't know/refused to answer

Item: There is nothing wrong with smoking marihuana as long as a person does so in moderation.
20.1% — agree
71.1% — disagree
8.8% — don't know/refused to answer

Not unexpectedly, significant differences exist among the various occupational groups

DRUG USE SHOULD BE A MATTER OF PERSONAL DECISION

	Occupational Group	Agree	Disagree	DK/NA
1.	Professionals, Technical Workers, Managers and Owners	36.5	59.0	4.5
2.	Clerical and Other White Collar Workers	45.6	47.4	7.0
3.	Skilled and Semi-Skilled Workers	49.5	43.3	7.2
4.	Unskilled Workers	53.4	37.1	9.5
5.	Service and Protective Workers	45.8	42.3	11.4
6.	Sales Workers	35.6	58.4	6.0
7.	Farmers	48.4	48.4	3.2
8.	Not Employed Housewives	41.0	49.4	9.6
9.	Other Not Employed	55.5	34.1	10.4
10.	Total	46.3	45.3	8.4

A LOT OF PEOPLE NEED DRUGS TO COPE WITH STRESS

	Occupational Group	Agree	Disagree	DK/NA
1.	Professionals, Technical Workers, Managers and Owners	55.0	34.5	10.5
2.	Clerical and Other White Collar Workers	56.0	33.8	10.2
3.	Skilled and Semi-Skilled Workers	50.8	38.0	11.2
4.	Unskilled Workers	50.6	38.3	11.1
5.	Service and Protective Workers	51.4	38.1	10.5
6.	Sales Workers	52.2	39.6	8.2
7.	Farmers	37.5	51.6	10.9
8.	Not Employed Housewives	51.7	36.6	11.7
9.	Other Not Employed	49.0	37.7	13.3
10.	Total	51.7	36.9	11.4

DRUG ADDICTS SHOULD BE TREATED AS SICK PEOPLE AND NOT AS CRIMINALS

	Occupational Group	Agree	Disagree	DK/NA
1.	Professionals, Technical Workers, Managers and Owners	90.4	6.3	3.3
2.	Clerical and Other White Collar Workers	87.9	5.8	6.3
3.	Skilled and Semi-Skilled Workers	85.5	7.4	7.1
4.	Unskilled Workers	81.3	11.7	7.0
5.	Service and Protective Workers	83.4	11.1	5.5
6.	Sales Workers	93.1	5.7	1.2
7.	Farmers	93.8	4.7	1.5
8.	Not Employed Housewives	87.9	4.8	7.3
9.	Other Not Employed	84.6	9.0	6.4
10.	Total	86.8	7.1	6.1

STRICT AND HARSH PUNISHMENT OF DRUG ABUSERS WILL KEEP OTHERS FROM USING DRUGS

	Occupational Group	Agree	Disagree	DK/NA
1.	Professionals, Technical Workers, Managers and Owners	30.1	62.4	7.5
2.	Clerical and Other White Collar Workers	31.7	55.8	9.5
3.	Skilled and Semi-Skilled Workers	38.8	51.9	9.3
4.	Unskilled Workers	36.2	54.9	8.9
5.	Service and Protective Workers	38.5	53.6	7.9
6.	Sales Workers	27.5	66.3	6.2
7.	Farmers	46.9	39.1	14.0
8.	Not Employed Housewives	41.0	46.8	12.2
9.	Other Not Employed	38.2	50.3	11.5
10.	Total	37.1	52.8	10.1

EDUCATION IS THE BEST WAY OF PREVENTING DRUG ABUSE

	Occupational Group	Agree	Disagree	DK/NA
1.	Professionals, Technical Workers, Managers and Owners	81.9	13.6	4.5
2.	Clerical and Other White Collar Workers	76.4	19.0	4.6
3.	Skilled and Semi-Skilled Workers	78.6	15.7	5.7
4.	Unskilled Workers	68.7	20.2	11.1
5.	Service and Protective Workers	81.2	13.9	4.9
6.	Sales Workers	76.9	13.8	9.3
7.	Farmers	79.7	12.5	7.8
8.	Not Employed Housewives	83.0	11.7	5.3
9.	Other Not Employed	69.7	22.3	8.0
10.	Total	77.5	16.3	6.2

THERE IS NOTHING WRONG WITH SMOKING MARIHUANA AS LONG AS A PERSON DOES SO IN MODERATION

	Occupational Group	Agree	Disagree	DK/NA
1.	Professionals, Technical Workers, Managers and Owners	22.1	68.9	9.0
2.	Clerical and Other White Collar Workers	21.2	70.3	8.5
3.	Skilled and Semi-Skilled Workers	22.5	69.1	8.4
4.	Unskilled Workers	26.4	65.3	8.3
5.	Service and Protective Workers	19.2	73.9	6.9
6.	Sales Workers	35.9	58.0	6.1
7.	Farmers	9.1	79.7	10.9
8.	Not Employed Housewives	8.1	82.6	9.3
9.	Other Not Employed	25.2	65.3	9.5
10.	Total	20.1	71.1	8.8

Epilogue

This study was not designed to determine the incidence of *drug abuse* in New York State. Methodologists and epidemiologists responsible for the survey design were in agreement that such a determination would require a more sophisticated interview schedule and more experienced interviewers than budget and time limitations permitted. This decision reflects the assumption that the definition of drug abuse is more complex and difficult to ascertain than generally assumed. Drug abuse cannot be determined solely by the dimensions of frequency, duration and amount of use. For example, the context in which the use occurs and some measurement of personal and social dysfunctioning must also be considerations in this determination. This would be true especially when considering the use of the legally manufactured and prescribed drugs. Future surveys, building upon the experiences obtained during this current study, should address this issue directly.

Suggested Reading

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Kurtis, C.: Drug abuse as a business problem. *New York Chamber of Commerce* (September, 1970).

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Rush, H.M.F. and Brown, J.K.: The drug problem in industry. *The Conference Board Record* (March, 1971).

Sweeney, F.E.: Illegal drug abuse and industry. *American Association of Industrial Nurses Journal* (August, 1967).

Stewart, W.W.: *Drug Abuse In Industry*. Miami: Halos, 1970.

The Bureau of National Affairs: ASPA-BNA survey: the employee with problems. *Bulletin to Management* (December, 1970).

Note: The books and articles listed above are presented because they are representative of the materials currently available. The listing of a reference does not necessarily imply a professional endorsement of the contents of the material.

Technical Appendices

Methodology

The primary focus of the original field survey was to assess the prevalence, incidence, frequency and situational content of all types of drug use within the general population. At the same time, the study was designed to include a number of secondary assessments; an assessment of the accuracy of beliefs relative to the adverse effects of certain forms of drug misuse and abuse; an assessment of the general population's attitudes toward various types of drug abuse and abusers, and so on. These data were to be obtained by face-to-face interviews with selected persons age 14 and above.

The Sample

Extensive consultations involving the behavioral scientists and epidemiologists with the N.A.C.C. Division of Research and the senior custom market researchers of Daniel Starch and Staff, Inc., one of the leading independent research organizations, resulted in a mutual agreement on the following sample considerations and decisions.

1. Reliability and projectability to the base population could be obtained with approximately 7,500 actual interviews.
2. Sampling and analytical objectivity could best be accomplished by the rational collapsing of the base population into five age groups. As near as possible, these five age groups were defined in accordance with the social, psychological and physiological maturation phases within an individual's life which were most likely to produce variability in patterns of drug use. The age groups were established as follows:

Age	Phase	Percentage Distribution in the Total Population
14-17	Late Adolescence	9.3%
18-24	Early Adulthood	14.6%
25-34	Adulthood	14.9%
35-49	Mature Adulthood	24.5%
50 and over	Senior Adulthood	36.7%

For maximum reliability of projection, the sample of 7,500 should be disproportionately allocated in terms of age. Although each successively older age group contained numerically more people, the interview allocation for each age group was the same...1,500 interviews. This disproportionate allocation insured sufficient numbers in the two youngest and numerically smallest age groups for meaningful analyses. Appropriate weights were applied during data processing to represent ages in their true proportions.

3. For maximum efficiency, equal numbers of males and females could be interviewed in each age group. Appropriate weights were applied during data processing to represent the two sexes in their true proportions.
4. In order to provide general population data, a cross-section of the State would be surveyed. Projectability could be served if the 7,500 interviews were allocated within 17 regions comprised of contiguous and demographically similar groups of counties. The number of actual interviews conducted within each region were weighted during data processing, to bring all regions into the true numerical proportion for the base population. The 17 regions and their interview allocations were as follows:

Region	Counties	Allocation
1.	New York, Kings, Queens, Bronx, Richmond	1,200
2.	Nassau	400
3.	Suffolk	400
4.	Westchester	400
5.	Orange, Rockland	390
6.	Columbia, Dutchess, Putnam	390
7.	Greene, Sullivan, Ulster	390
8.	Albany, Fulton, Montgomery, Rensselaer, Saratoga, Schenectady	400
9.	Clinton, Essex, Hamilton, Warren, Washington	390
10.	Franklin, Jefferson, Lewis, St. Lawrence	390
11.	Chenango, Delaware, Otsego, Schoharie	390
12.	Herkimer, Madison, Oneida, Onondaga, Oswego	400
13.	Broome, Chemung, Schuyler, Steuben, Tioga	390
14.	Cayuga, Cortland, Ontario, Seneca, Tompkins, Yates	390
15.	Monroe, Orleans, Wayne	390
16.	Erie, Niagara	400
17.	Allegany, Cattaraugus, Chautauqua, Genesee, Livingston, Wyoming	390
	Total New York State	7,500

5. Efficiency, reliability and projectability could all be served with a sampling procedure which combined elements of both probability and quota techniques. Essentially, the procedure included the probability drawing of a residential block and then interviewing a quota of respondents residing on that block.

The full technique for respondent selection, accomplished in accordance with standard statistical procedures, included two stages as outlined below:

In the first stage, and within each region, communities were stratified according to size, based on U.S. Census data. Interviewer work loads or basic sampling units, i.e., 30 interviews were allocated to each stratum, proportionate to population size.

In the second stage, those communities selected for interviewing were subdivided into areas of equal population, the number of areas dependent on the number of work loads. Three widely dispersed "female" interviewing blocks per workload were predesignated, on the basis of block statistics where available, and on the basis of equal probability elsewhere. Interviewing of males was done on three separate blocks, adjacent to the female blocks, with selection of these blocks done in a systematic manner. Thus, 15 female interviews were assigned to 3 blocks – 5 per block, and a comparable assignment for males on the 3 male blocks. Actual respondent selection within blocks was done as follows:

On each of the blocks assigned for a given sex, and at a predesignated starting household, the interviewer asked if there was a person of that sex in residence age 14 to 17. If so, that person became the designated respondent. The interview took place then if the person was available at home; otherwise, up to three call backs were made before selecting a substitute respondent. If no one 14-17 was

in residence, the person of appropriate sex in the next oldest age group who lived there became the designated respondent. Thus, household age composition was recorded in all cases — both to disproportionately interview younger people, and to interview those who tend to be away from home in the same proportion as "at home" people, and to have a pool of names available for substitute purposes or blocks that produced no one in residence of a given age and sex. Each interviewer work load of 15 female interviews (and 15 males) was spread across the three predesignated blocks, and three adjacent blocks with no more than two individuals of the same sex and age interviewed on the same block, to insure wide geographic dispersion. Only one interview was done per household, and in all cases interviewers were instructed to try to conduct it privately, away from any other members of the household.

In summary, this sampling procedure is believed to be a highly reliable one from a statistical sense, the only practical way to over-represent the younger age levels and unique in terms of geographical dispersion. Over 2,500 different blocks in the State of New York were preselected for interviewing purposes, located in 185 different incorporated and unincorporated places outside of New York City, and in each of the five boroughs within the City. At least one-third of each individual interviewer's work was validated, in most cases by postcard, but in many instances by telephone or in person by a regional supervisor where those interviewed had not returned the postcard.

Sample Limitations

N.A.C.C. scientists were aware of certain limitations inherent in the sampling strategy. For example, the strategy would not isolate those drug users who had become so dysfunctionally involved with the drugs that they were not maintaining a stable residence or were not maintaining any predictable "time at home." These users would not be selected for interview or if selected would not be available ... most "heroin street addicts," "speed freaks," "acid heads," "pot heads," etc., would not normally be interviewed. In addition, any drug users who resided in hotels, rooming houses and other transient facilities or who were institutionalized were not included in the sample selection. These limitations would not, however, inflate the projected figures within the various categories of employed persons contained in this report. These dysfunctional drug users are not members of the working labor force.

The Interviewers

In view of the sensitive nature of the study's subject, a series of criteria were imposed upon the selection of interviewers. Only after the various interviewing blocks had been isolated were interviewers selected. Wherever possible, interviewers were hired and trained to "fit" or match the demographic characteristics of their respective interviewing locations. Thus, in the great majority of cases, Blacks were interviewed by Blacks, Puerto Ricans were interviewed by interviewers fluent in Spanish, younger respondents by interviewers who were also young, and so on. A special attempt was made to recruit interviewers to interview within similar socioeconomic neighborhoods — interviewers who had been reared or currently resided in ghetto areas, for example, were trained to work in similar areas. Finally, in those areas where the use of illegal drugs was believed to be high, ex-addicts working for the N.A.C.C. and other agencies were hired and trained to conduct the interviews assigned such locations.

In addition to training the interviewers in the mechanics of the schedule, all the interviewers were instructed in the various drug names — generic, trade and slang — that they might subsequently encounter.

The Interview Schedule

The study was accomplished with a specially designed interview schedule (Attachment A). The schedule content was determined by the N.A.C.C. Division of Research with the format being a collaborative effort with the contracted market researchers. The interview schedule was designed to maximize validity of response and the questions were proposed in a manner leading up to respondent's own use of the drug. The schedule was divided into sections:

1. The first part dealt with general drug use for nonspecific reasons.
2. The second part related knowledge and attitudes about specific drug use, drug users and laws regarding drug use.
3. The third section dealt with respondent's use of the 17 classes of drugs, and knowledge of use of others using drugs. Data indicating frequency of use were also collected. The criteria for classifying frequency of use was as follows:

a. Non-user . . .	has never taken or used the drug.
b. Former User .	has taken or used the drug but not within the previous 6 months.
c. Infrequent User	has taken or used the drug within the previous 6 months but not as much as six times during the previous 30 days
d Regular User .	has taken or used the drug at least six times during the previous 30 days.

Finally, this section probed as to the way in which the drug was obtained (physician's prescription), where it was used (social gathering, etc) and in the case of a legal drug, whether the drug was used as it had been prescribed.

The respondents were provided with a card (Attachment B) which listed the drugs or drug group as well as appropriate examples of each. If the respondent asked about a drug not indicated, the interviewer categorized the drug referencing a drug listing guide provided by the Division. When a compound or "combination" drug was reported, the Division edited the response into the drug or drug class represented by the most important component, to avoid over-reporting of use.

Even though the design strategy included (1) matching the interviewers and respondents; (2) providing each respondent with written assurances of anonymity and confidentiality from both the Narcotic Addiction Control Commission and the custom research firm; and (3) the using of a carefully designed interview schedule which led each respondent through progressive drug using patterns, N.A.C.C. scientists were aware that the reported drug use would probably be under-representative of actual use. It was anticipated at least three factors would produce an unknown amount of under-representation....the natural forgetfulness of some people in recalling such a wide variety of drugs, the inability of some people to identify drugs prescribed for them and the understandable reluctance of some people to discuss their personal involvement in a socially unacceptable or illegal activity.

The last section of the schedule contained those questions necessary to establish demographic profiles, i.e., education status, marital status, employment/school characteristics, ethnicity, neighborhood characteristics, and so on.

The study design dictated the interviews be conducted during the period August 1 through September 5, 1970. Ninety-eight percent of the 7,500 assigned interviews were completed, with all interviews conducted in person, in the respondents' homes. The following indicates the completion level within each region.

Region		Interviews Assigned	Completed
1.	New York, Kings, Queens, Bronx, Richmond	1,200	1,260 (105%)
2.	Nassau	400	378 (95%)
3.	Suffolk	400	420 (105%)
4	Westchester	400	392 (98%)
5.	Orange, Rockland	390	374 (96%)
6.	Columbia, Dutchess, Putnam	390	389 (100%)
7.	Greene, Sullivan, Ulster	390	366 (94%)
8	Albany, Fulton, Montgomery, Rensselaer, Saratoga, Schenectady	100	406 (101%)
9	Clinton, Essex, Hamilton, Warren, Washington	390	358 (92%)
10.	Franklin, Jefferson, Lewis, St. Lawrence	390	382 (98%)
11	Chenango, Delaware, Otsego, Schoharie	390	343 (88%)
12.	Herkimer, Madison, Oneida, Onondaga, Oswego	100	392 (98%)
13	Broome, Chemung, Schuyler, Steuben, Tioga	390	389 (100%)
14.	Cayuga, Cortland, Ontario, Seneca, Tompkins, Yates	390	379 (97%)
15.	Monroe, Orleans, Wayne	390	372 (95%)
16.	Erie, Niagara	400	400 (100%)
17.	Allegany, Cattaraugus, Chautauqua, Genesee, Livingston, Wyoming	390	378 (97%)
	Total New York State	7,500	7,378 (98%)

The number of actual interviews in each region was weighted during analysis to bring all regions into their true numerical proportions.

During the supplementary analysis, the data were reweighted and projected to bring all the occupational groups into their true numerical proportions as enumerated in the 1969 edition of Marketing Statistics, Inc.

Estimating Procedure and Standard Error of Percentage

Estimating Procedure

A weight was developed for each person interviewed such that all respondents' weights jointly reflected the population age 14 years and over of New York State.

As described in the methodology section, within each of the seventeen regions into which the State was divided, a selection of communities and blocks for interviewing was made employing standard probability sampling methods. Age and sex quotas were assigned for each block.

Within the seventeen regions, the most current population estimates by age, sex, race and occupation were obtained from 1969 Marketing Statistics, Inc. data. Differential individual weights were applied according to the sex, age, race and occupation of the respondents so that the aggregate composition agreed with the MSI projections.

All tabulations of this study employ these weights, and percentages were obtained by division of weighted numbers.

All tables are reported with one standard error or deviation which means at a 68% confidence level.

Standard Error of Percentage

SURVEY PERCENTAGE

Sub Sample Size	5/95	10/90	20/80	30/70	40/60	50/50
100	2.2	3.0	4.0	4.6	4.9	5.0
300	1.3	1.8	2.3	2.7	2.8	2.9
500	1.0	1.3	1.8	2.1	2.2	2.2
700	0.8	1.1	1.5	1.7	1.9	1.9
1,000	0.7	1.0	1.3	1.5	1.6	1.6
3,000	0.4	0.5	0.7	0.8	0.9	0.9
5,000	0.3	0.4	0.6	0.6	0.7	0.7
6,000	0.2	0.3	0.5	0.6	0.6	0.6

For example, the survey estimates some 3.8% of total New York State population age 14 and older....525,000 people.... are regularly using minor tranquilizers. The chances are 68 in 100 that this figure is within 0.2 percentage points of the value that would have been obtained by a complete census utilizing the same survey procedures. Another illustration of the standard error of percentage, 78.3% of all the people in the base population....10,688,000 people ... report never having used a barbiturate. The chances are 68 in 100 that this figure is within 0.5 percentage points of the value one would obtain by a complete census using the same techniques.

Attachment A

Interview Instrument

AGE

14 - 17.....	1	35 - 49.....	4	
18 - 24.....	2	50 and over...	5	
25 - 34.....	3			15/

1. Almost everyone uses different kinds of drugs and medicines for various reasons throughout their lives. I'm going to read you a list of some things people take drugs or medicine for. For each one, would you tell me if you have ever used any drug or medicine for each one I call out?

a. To cure or prevent a serious illness of any kind?

Yes..... 1
No..... 2
Don't know or no answer..... 3

b. To relieve a headache, backache or muscular pain?

Yes..... 4
No..... 5
Don't know or no answer..... 6

c. To help you get to sleep?

Yes..... 7
No..... 8
Don't know or no answer..... 9 16/

d. To lose weight or control your weight?

Yes..... 1
No..... 2
Don't know or no answer..... 3

e. To relieve a tired feeling or pep you up when you have to keep going?

Yes..... 4
No..... 5
Don't know or no answer..... 6

f. To calm you down or relieve nervous tension?

Yes..... 7
No..... 8
Don't know or no answer..... 9 17/

2. Now I would like to read you some statements about drugs--their effects and the laws governing their use. After each statement, please tell me your own confidential opinion about the statement--whether you basically agree or disagree with it:

	Agree	Disagree	Don't know	Refused, No Answer	
a. There is nothing wrong with smoking marihuana as long as a person does so in moderation.....	1	2	3	4	18
b. Once an addict, always an addict.....	1	2	3	4	19
c. Everyone should try drugs at least once to find out what they are like.....	1	2	3	4	20
d. Most people who smoke marihuana use it for a long time but never try anything else.....	1	2	3	4	21

2. CONTINUE TO ASK ABOUT EACH STATEMENT. (Please tell me your own confidential opinion about the statement---whether you basically agree or disagree with it:)

	Agree	Disagree	Don't know	Refused, No Answer	
e. Sniffing glue can damage the brain.....	1	2	3	4	22/
f. Education is the best way of preventing drug abuse.....	1	2	3	4	23/
g. Drug addicts should be treated as sick people and not as criminals.....	1	2	3	4	24/
h. Current laws regarding marihuana use are too severe.....	1	2	3	4	25/
i. People can use drugs to find out more about themselves.....	1	2	3	4	26/
j. Current laws regarding heroin use are too severe.....	1	2	3	4	27/
k. Most people who smoke marihuana try it a few times and then never use any other drugs...	1	2	3	4	28/
l. Drug use should be a matter of personal decision.....	1	2	3	4	29/
m. Amphetamines--"pep" or "diet pills," can produce psychological dependence.....	1	2	3	4	30/
n. Marihuana is addictive.....	1	2	3	4	31/
o. A lot of people need drugs to cope with stress.....	1	2	3	4	32/
p. All drug abusers are pretty much alike.....	1	2	3	4	33/
q. Strict and harsh punishment of drug abusers will keep others from using drugs.....	1	2	3	4	34/
r. Addicts will do anything to get more drugs	1	2	3	4	35/
s. Most people who abuse drugs do so because their friends do.....	1	2	3	4	36/
t. Smoking marihuana is no more harmful than drinking liquor.....	1	2	3	4	37/
u. Barbiturates--prescription sleeping pills, can lead to physical as well as psychological dependence.....	1	2	3	4	38/
v. L.S.D. can cause chromosome change--birth defects.....	1	2	3	4	39/
w. One of the difficulties in treating most addicts is that they appear to enjoy the drug way of life.....	1	2	3	4	40/
x. The medical benefits from most prescription drugs outweigh the risk that they might be misused.....	1	2	3	4	41/
y. Most people who smoke marihuana use it for a while and then go to something stronger..	1	2	3	4	42/

3,4. Here is a card listing 17 numbered classes of drugs--with some examples shown of each kind in most cases. (HAND RESPONDENT CARD) (ASK Q.3 ABOUT ALL 17 DRUGS. FOR EACH "YES" TO Q.3, ALSO ASK Q.4. THEN ASK ABOUT NEXT DRUG ON LIST)

	Q.3 Do you personally know anyone who has ever taken or used:				Q.4 I don't want to know who they are, but do any of them live in this neighborhood:			
	DK,NA	NO	YES		DK,NA	NO	YES	
1. BARBITURATES (phenobarbital, seconal, tuinal, amytal, amobarbital, prescription sleeping pills, etc.).....	1	2	3	-->	4	5	6	43/
2. OTHER SEDATIVES (doriden, bromides, noludar, etc.).....	1	2	3	-->	4	5	6	44/
3. RELAXANTS--MINOR TRANQUILIZERS (librium, equanil, valium, etc.)	1	2	3	-->	4	5	6	45/
4. MAJOR TRANQUILIZERS (thorazine, stelazine, mellaril, etc.).....	1	2	3	-->	4	5	6	46/
5. ANTI-DEPRESSANTS (elavil, tofranil, marplan, etc.).....	1	2	3	-->	4	5	6	47/
6. DIET PILLS (dexamyl, preludin, etc.).....	1	2	3	-->	4	5	6	48/
7. PEP PILLS (dexedrine or benzedrine).....	1	2	3	-->	4	5	6	49/
8. METHEDRINE - METHAMPHETAMINE ("speed," desoxyn, desbutal, etc.)	1	2	3	-->	4	5	6	50/
9. COCAINE.....	1	2	3	-->	4	5	6	51/
10. OTHER STIMULANTS (ritalin, novacaine, procaine, etc.).....	1	2	3	-->	4	5	6	52/
11. MARIHUANA OR HASHISH.....	1	2	3	-->	4	5	6	53/
12. L.S.D.....	1	2	3	-->	4	5	6	54/
13. OTHER PSYCHOTOGENS (psilosybin, mescaline, D.M.T., etc.).....	1	2	3	-->	4	5	6	55/
14. SOLVENTS OR INHALANTS (glue, amylnitrate, etc.).....	1	2	3	-->	4	5	6	56/
15. HEROIN.....	1	2	3	-->	4	5	6	57/
16. OTHER OPIATES (morphine, paregoric, demerol, etc.).....	1	2	3	-->	4	5	6	58/
17. NON-CONTROLLED NARCOTICS (codeine cough syrups, darvon, talwin, etc.)	1	2	3	-->	4	5	6	59/
18. OTHER: _____ (write in and ask Q.4)			60/	-->	4	5	6	61/

5. Starting from the top of that list again, have you yourself ever taken or used any (ASK ABOUT ALL 17 DRUGS AND RECORD. FOR EACH "YES," ALSO CIRCLE DRUG NAME AT TOP RIGHT ON FACING PAGES):

	YES	NO	DK,NA
1. BARBITURATES?.....	1	2	3
2. OTHER SEDATIVES?.....	1	2	3
3. RELAXANTS OR MINOR TRANQUILIZERS?.....	1	2	3
4. MAJOR TRANQUILIZERS?.....	1	2	3
5. ANTI-DEPRESSANTS?.....	1	2	3
6. DIET PILLS?.....	1	2	3
7. PEP PILLS?.....	1	2	3
8. METHEDRINE OR METHAMPHETEMINE?.....	1	2	3
9. COCAINE?.....	1	2	3
10. OTHER STIMULANTS?.....	1	2	3
11. MARIHUANA OR HASHISH?.....	1	2	3
12. L.S.D.?.....	1	2	3
13. OTHER PSYCHOTOGENS?.....	1	2	3
14. SOLVENTS OR INHALANTS?....	1	2	3
15. HEROIN?.....	1	2	3
16. OTHER OPIATES?.....	1	2	3
17. NON-CONTROLLED NARCOTICS?	1	2	3

15/31

18. OTHER

_____ 32/
(Write in and circle 18 "Other")

INSTRUCTION: ASK QUESTION SERIES 6-14 ABOUT EACH DRUG CIRCLED AT TOP OF PAGES 5 AND 7. START WITH LOWEST NUMBER DRUG. IF NONE CIRCLED, SKIP TO QUESTION 15, PAGE 8.

6. You said you have used (call off circled drug). Have you used or taken any of these in the last 6 months?

7. Have you used or taken any in the last 90 days--3 months?

8. Have you used or taken any in the last 30 days--1 month?

9. Have you used it 6 or more times in the last month?

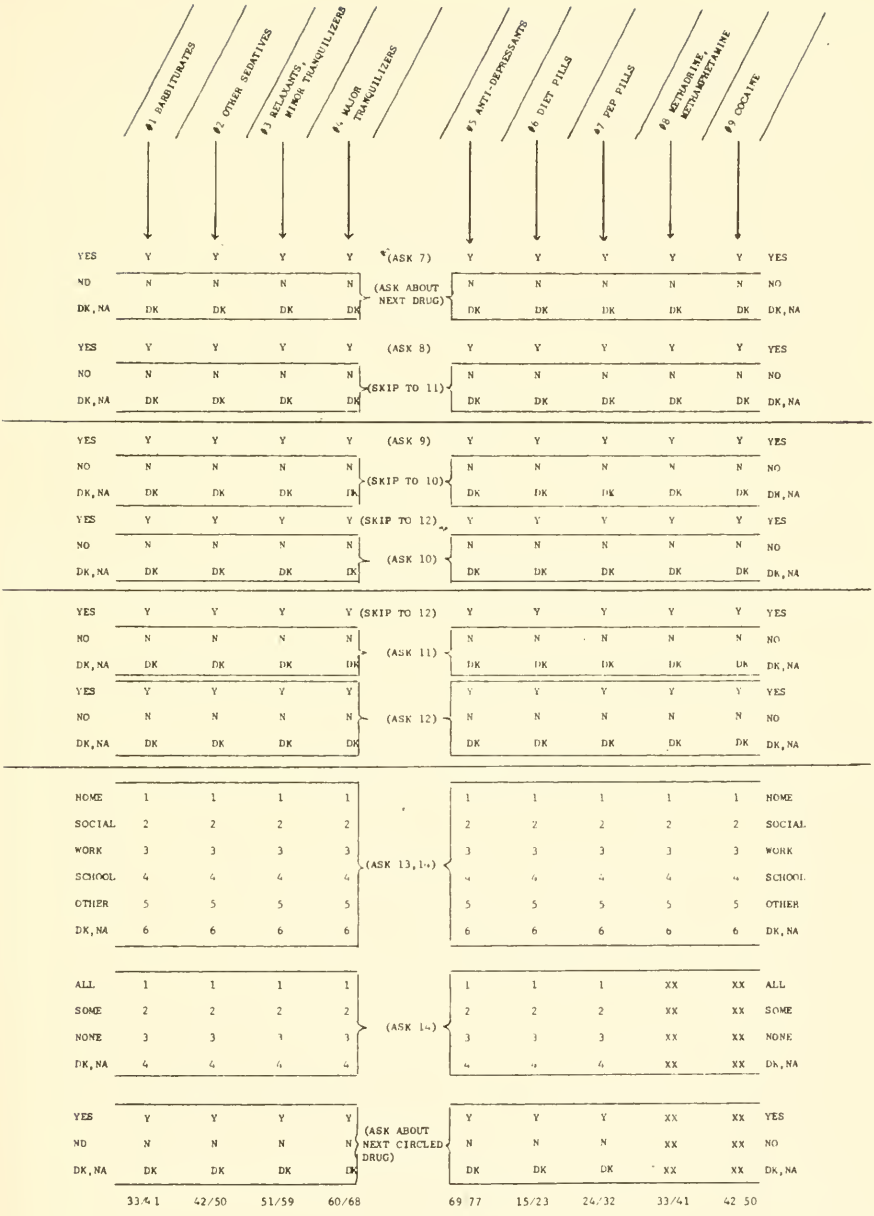
10. Have you used it 6 or more times in the last 3 months?

11. Have you used it 6 or more times in the last 6 months?

12. Where do you usually take or use it--at home, or at a social gathering or going to and from one, or at work (or at school)?

13. Have all of the ones you have taken recently been obtained under your doctor's prescription, or some of them, or none of them?

14. Have you taken them just the way your doctor ordered--or not--like more than he prescribed, or more often than directed, or for different reasons?


#1 BARBITURATES
#2 OTHER SEDATIVES
#3 RELAXANTS, MINOR TRANQUILIZERS
#4 MAJOR TRANQUILIZERS
#5 ANTI-DEPRESSANTS
#6 DIET PILLS
#7 PEP PILLS
#8 METHADRINE, METHAMPHETAMINE
#9 COCAINE
YES Y Y Y Y (ASK 7) Y Y Y Y Y YES
NO N N N N (ASK ABOUT NEXT DRUG) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK
YES Y Y Y Y (ASK 8) Y Y Y Y Y YES
NO N N N N (SKIP TO 11) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK
YES Y Y Y Y (ASK 9) Y Y Y Y Y YES
NO N N N N (SKIP TO 10) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK
YES Y Y Y Y (SKIP TO 12) Y Y Y Y Y YES
NO N N N N (ASK 10) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK
YES Y Y Y Y (SKIP TO 12) Y Y Y Y Y YES
NO N N N N (ASK 11) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK
YES Y Y Y Y Y Y Y Y Y YES
NO N N N N (ASK 12) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK
NONE 1 1 1 1 1 1 1 1 1 NONE
SOCIAL 2 2 2 2 2 2 2 2 2 SOCIAL
WORK 3 3 3 3 (ASK 13,14) 3 3 3 3 3 WORK
SCHOOL 4 4 4 4 4 4 4 4 4 SCHOOL
OTHER 5 5 5 5 5 5 5 5 5 OTHER
DK,NA 6 6 6 6 6 6 6 6 6 DK,NA
ALL 1 1 1 1 1 1 1 XX XX ALL
SOME 2 2 2 2 (ASK 14) 2 2 2 XX XX SOME
NONE 3 3 3 3 3 3 3 XX XX NONE
DK,NA 4 4 4 4 4 4 4 XX XX DK,NA
YES Y Y Y Y Y Y Y XX XX YES
NO N N N N (ASK ABOUT NEXT CIRCLED DRUG) N N N XX XX NO
DK,NA DK DK DK DK DK DK DK XX XX DK,NA
33/41 42/50 51/59 60/68 69 77 15/23 24/32 33/41 42 50

6. You said you have used (call off circled drug). Have you used or taken any of these in the last 6 months?

7. Have you used or taken any in the last 90 days--3 months?

8. Have you used or taken any in the last 30 days--1 month?

9. Have you used it 6 or more times in the last month?

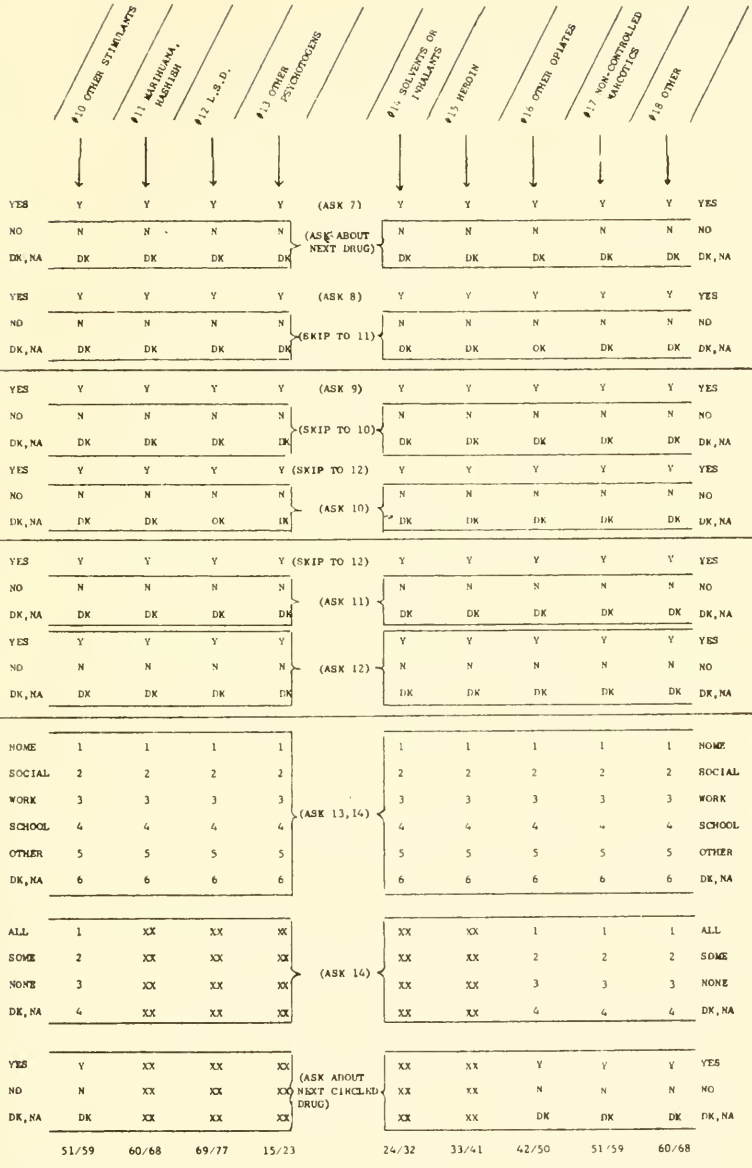
10. Have you used it 6 or more times in the last 3 months?

11. Have you used it 6 or more times in the last 6 months?

12. Where do you usually take or use it--at home, or at a social gathering or going to and from one, or at work (or at school)?

13. Have all of the ones you have taken recently been obtained under your doctor's prescription, or some of them, or none of them?

14. Have you taken them just the way your doctor ordered--or not--like more than he prescribed, or more often than directed, or for different reasons?


#10 OTHER STIMULANTS
#11 MARIJUANA, HASHISH
#12 L.S.D.
#13 OTHER PSYCHEDELICS
#14 SOLVENTS OR INHALANTS
#15 HEROIN
#16 OTHER OPIATES
#17 NON-CONTROLLED NARCOTICS
#18 OTHER
YES Y Y Y Y (ASK 7) Y Y Y Y Y YES
NO N N N N (ASK ABOUT NEXT DRUG) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK,NA
YES Y Y Y Y (ASK 8) Y Y Y Y Y YES
NO N N N N (SKIP TO 11) N N N N N NO
DK,NA DK DK DK DK DK DK OK DK DK DK,NA
YES Y Y Y Y (ASK 9) Y Y Y Y Y YES
NO N N N N (SKIP TO 10) N N N N N NO
DK,NA DK DK DK DK DK DK DK DK DK DK,NA
YES Y Y Y Y (SKIP TO 12) Y Y Y Y Y YES
NO N N N N (ASK 10) N N N N N NO
DK,NA DK DK OK DK DK DK DK DK DK DK,NA
YES Y Y Y Y (SKIP TO 12) Y Y Y Y Y YES
NO N N N N (ASK 11) N N N N N NO
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YES Y Y Y Y Y Y Y Y Y YES
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SOCIAL 2 2 2 2 2 2 2 2 2 SOCIAL
WORK 3 3 3 3 (ASK 13,14) 3 3 3 3 3 WORK
SCHOOL 4 4 4 4 4 4 4 4 4 SCHOOL
OTHER 5 5 5 5 5 5 5 5 5 OTHER
DK,NA 6 6 6 6 6 6 6 6 6 DK,NA
ALL 1 XX XX XX XX XX 1 1 1 ALL
SOME 2 XX XX XX (ASK 14) XX XX 2 2 2 SOME
NONE 3 XX XX XX XX XX 3 3 3 NONE
DK,NA 4 XX XX XX XX XX 4 4 4 DK,NA
YES Y XX XX XX (ASK ABOUT NEXT CIRCLED DRUG) XX XX Y Y Y YES
NO N XX XX XX XX XX N N N NO
DK,NA DK XX XX XX XX XX DK DK DK DK,NA
51/59 60/68 69/77 15/23 24/32 33/41 42/50 51/59 60/68

(ASK EVERYONE)

Now, just a few questions for tabulating purposes.

15. Are you married, single, widowed, divorced, or separated?

Married..... 1

Single..... 2

Widowed.... 3

Divorced.... 4

Separated... 5 64/

16. Do you live alone, by any chance?

Yes... 1 (SKIP TO 18)

No.... 2 (ASK 17) 65/

17. Who are the other members of your household living here with you? (RECORD ALL APPROPRIATE CATEGORIES)

Spouse..... 3

Dependent children..... 4

Roommate (or other unrelated individuals)... 5

Parents..... 6

Other relatives..... 7

18. Are you employed, either full or part time, at the present time?

Full time..... 1 } (SKIP TO 20)

Part time..... 2 }

Not employed... 3 (ASK 19) 66/

19. Are you (SINGLE RECORD ONLY):

Housewife..... 4

Retired..... 5

Unemployed but looking for work..... 6 } (SKIP TO 21)

Unemployed, not looking for work..... 7

Student..... 8

20. What is your occupation?

a. Top management, top talent, and major professional...	1	
b. Executive, administrative, lesser professional.....	2	
c. Owner--small retail store or business.....	3	
d. Technicians, minor administrative, and low supervisory.....	4	
e. White collar, clerical (non-supervisory).....	5	
f. Skilled and semi-skilled labor.....	6	
g. Unskilled labor.....	7	
h. Service and protective workers.....	8	
i. Salesman.....	9	
j. Farmers (owners and managers).....	0	
k. Military personnel.....	X	67/

21. What was the last year of regular school that you completed--not counting specialized schools like secretarial, art or trade schools?

No school.....	1	
Some grade (1-7).....	2	
Graduated grade (8).....	3	
Some high (9-11).....	4	
Graduated high (12).....	5	
Some college (13-15).....	6	
Graduated college (16+)...	7	
Graduate school.....	8	68/

22. Would you mind telling me your age? _____ 69/70-
(write in exact age)

INSTRUCTION: ASK 23 ONLY OF PEOPLE 25 YEARS OF AGE OR UNDER. OTHERS SKIP TO 27.

23. Have you been a full time student during the last year, that is during the spring of this year?

Yes...	1 (ASK 24)	
No....	2 (SKIP TO 27)	71/

24. Is the school you attended during the last year a high school, or prep school, or a junior college, or a four year college or university?

High school.....	3 (SKIP TO 27)	
Prep school.....	4	(ASK 25)
Junior college.....	5	
College, university	6	

25. Is your school <u>within</u> New York State, or <u>outside</u> the State?

Within New York State.... 1 (ASK 26)

Outside New York State... 2 (SKIP TO 27) 72/

26. Do you commute to your school from home, or live away from home--at or near your school?

Commute..... 3

At, near school... 4

27. What is your religion?

Protestant..... 1

Roman Catholic.... 2

Jewish..... 3

None..... 4

Other _____ 5 73/
(write in)

F A C T U A L

28. Type of dwelling unit in which this respondent lives:

Single family house..... 1

Multifamily dwelling unit without elevator..... 2

Elevator apartment building..... 3

Garden apartment..... 4

Trailer or mobile home... 5

Other..... 6 74/

29. Is the home of the respondent part of a public housing project?

Yes... 1

No.... 2 75/

30. Location description:

Indicate the type of neighborhood covered in this location by circling one of the seven categories listed below. This should be done ONLY in terms of how this ENTIRE location looks in the eyes of the people in the community. Those people you spoke to PLUS your own opinions, based on your awareness of the location's characteristics, must be considered. Circle more than one category if such is necessary to accurately describe this location.

1. A wealthy, or "Society" type neighborhood; big business officials, very rich lawyers and doctors, and people with large, inherited incomes live here..... 1

2. An excellent white-collar neighborhood--doctors, highly-paid managers, strictly a professional and executive neighborhood..... 2

3. A better white-collar neighborhood--not many executives or doctors live here, but there are probably no blue-collar people, either..... 3

4. Predominantly white-collar neighborhood, though a lot of fairly well-paid blue-collar families live here also 4

5. Predominantly a blue-collar neighborhood--though some office workers might live here also..... 5

6. Strictly a working-class neighborhood--not slummy, but a few shacks and very poor housing mixed in; probably no white-collar workers live here..... 6

7. A slum neighborhood, the people here are common laborers or people on relief..... 7 76/

31. Sex:

Male..... 1

Female... 2 77/

32. Race:

White..... 1

Negro..... 2

Puerto Rican or other Spanish speaking..... 3

Oriental..... 4

Other..... 5 78/

----------DETACH----------

Name_____

Address_____ Apt. #_____

Phone number_____ Date_____

Respondent #_____

Interviewer's Initials_____

Attachment B

Drug Card for Respondents

1. BARBITURATES (phenobarbital, seconal, tuinal, amytal, amobarbital, etc.)
2. OTHER SEDATIVES (doriden, bromides, noludar, etc.)
3. RELAXANTS/MINOR TRANQUILIZERS (librium, equanil, valium, etc.)
4. MAJOR TRANQUILIZERS (thorazine, stelazine, mellaril, etc.)
5. ANTIDEPRESSANTS (elavil, tofranil, marplan, etc.)
6. DIET PILLS (dexamyl, preludin, etc.)
7. PEP PILLS (dexedrine or benzedrine)
8. METHEDRINE/METHAMPHETAMINE ("speed," desoxyn, desbutal, etc.)
9. COCAINE
10. OTHER STIMULANTS (ritalin, novacaine, procaine, etc.)
11. MARIHUANA/HASHISH
12. LSD
13. OTHER PSYCHOTOGENS (psilocybin, mescaline, DMT, etc.)
14. SOLVENTS/INHALANTS (glue, amyl nitrite, etc.)
15. HEROIN
16. OTHER OPIATES (morphine, paregoric, demerol, etc.)
17. NONCONTROLLED NARCOTICS AND PRESCRIPTION NONNARCOTIC ANALGESICS (codeine cough syrups, darvon, talwin, etc.)

14. CRIME IN AMERICA—WHY 8 BILLION AMPHETAMINES?

HEARINGS

BEFORE THE

SELECT COMMITTEE ON CRIME
HOUSE OF REPRESENTATIVES

NINETY-FIRST CONGRESS

FIRST SESSION

PURSUANT TO

H. Res. 17

A RESOLUTION CREATING A SELECT COMMITTEE TO CONDUCT STUDIES AND INVESTIGATIONS OF CRIME IN THE UNITED STATES

NOVEMBER 18, 1969, WASHINGTON, D.C.

Printed for the use of the Select Committee on Crime

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SELECT COMMITTEE ON CRIME

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THOMAS F. McBRIDE, *Deputy Chief Counsel*
LARRY REIDA, *Associate Chief Counsel*
ARTHUR E. CAMERON, *Associate Counsel and Assistant to the Chairman*

CONTENTS

CRIME IN AMERICA—WHY 8 BILLION AMPHETAMINES?

TUESDAY, NOVEMBER 18, 1969

HOUSE OF REPRESENTATIVES,
SELECT COMMITTEE ON CRIME,
Washington, D.C.

The committee met, pursuant to recess, at 10:10 a.m., in room 311, Cannon House Office Building, Hon. Claude Pepper (chairman) presiding.

Present: Representatives Pepper (chairman), Nix, Waldie, and Wiggins.

Also present: Albert W. Overby, Jr., associate counsel and Andrew Radding, assistant counsel.

Mr. PEPPER. The committee will come to order, please.

We are here today to hear several witnesses who have responded to our request to give information on the medical uses of amphetamines and methamphetamines.

In other hearings, particularly those held in San Francisco from October 23 through October 27, we have heard expert testimony on the abuses of the amphetamines and methamphetamines. We know there is a great deal of abuse of these drugs, that they involve more people than those using heroin, and that their effects upon the personality can be as dangerous as the effects of heroin.

This committee is concerned with the kind of legislative action which may be necessary to deal with the threat which these drugs present. It appears that over half of the production of amphetamines goes into illegal or irregular channels for distribution. It seems clear that new legislation is needed to stop such dispersion into unsupervised channels.

It has been suggested that, because the amphetamines and methamphetamines are of relatively minor value in medical practice, their production should be banned or very rigorously controlled.

The handbook[1] on drug dependence published by the American Medical Association lists eight uses for amphetamine-type drugs, but says that, "With the exception of the first two items, the indications for the proper medical use of stimulants are subject to varying de-

[1] "Drug Dependence, a Guide for Physicians, 1969," copyright American Medical Association, Chicago, Ill., 60610. The eight uses for which the amphetamines are prescribed are listed by the handbook (p. 114) as follows:
(1) Control the symptoms of narcolepsy.
(2) Control certain hyperkinetic behavioral disorders of children.
(3) Relieve or prevent fatigue in individuals with deteriorated psychomotor performance.
(4) Treat mild depression.
(5) Antagonize the pharmacological actions of depressant drugs (e.g., barbiturates, alcohol).
(6) Control appetite.
(7) Induce insomnia and counteract fatigue in persons occasionally required to perform mental or physical tasks of long duration.
(8) Enhance the action of analgesic drugs.

grees of professional controversy." The handbook says, "The debate, waged on both scientific and ethical grounds, is focused on the efficacy of these drugs as well as on the hazards involved * * *"

The members of this committee regard it as essential that we gather additional information in this controversial area of the use of amphetamines and methamphetamines. We have with us today experts from various parts of the Nation and from different aspects of medical practice. I believe they can give us testimony which will help the committee and Congress make a determination as to whether the beneficial medical uses of these drugs outweigh the hazards of their misuse.

Our first witness today will be Dr. Sidney Cohen.

Dr. Sidney Cohen is Director of the Division of Narcotic Addiction and Drug Abuse, National Institute of Mental Health. He was formerly Chief, Psychiatric Service, Wadsworth VA Hospital, and associate professor of medicine of the University of California at Los Angeles.

He is editor of "Drug Dependence" and associate editor of "Psychosomatics." He has been involved in research on drugs which affect mental processes for the past 20 years. Over a hundred research articles have been published by him. He has spoken in this country and abroad on every aspect of the drug issues. Three of his popular books have been "The Beyond Within: The LSD Story," "LSD," and "The Drug Dilemma."

We are very pleased to have you here, Dr. Cohen.

STATEMENT OF SIDNEY COHEN, M.D., DIRECTOR, DIVISION OF NARCOTIC ADDICTION AND DRUG ABUSE, NATIONAL INSTITUTE OF MENTAL HEALTH

Dr. COHEN. Thank you, Mr. Chairman.

Mr. Chairman, because of the brief period between your invitation to appear and the date of this hearing, it has not been possible for me to obtain clearance for this statement from the National Institute of Mental Health or from the Department of Health, Education, and Welfare. Therefore, it must not be considered either as a statement of policy, or as a representation of any viewpoint but my own.

It is really a pleasure to be here as one who may be qualified to assist in your consideration of the stimulant use-abuse pattern. I know that you have had a number of experts testify before you on this issue. Therefore, it is unnecessary for me to include in my remarks much of what already has been said. In order not to be misunderstood, however, it is desirable to note briefly some points upon which my position is based.

Mr. PEPPER. Doctor, we recall very gratefully your valuable appearance before us on marihuana some time ago.

Dr. COHEN. Thank you, sir.

We are observing the misuse of the many amphetamines today. These drugs belong to the larger class of stimulants. Certain other stimulants which are not amphetamines are also capable of abuse so that the nonamphetamine stimulants should be included in your deliberations.

I am referring to drugs such as methyphenidate, Ritalin. These, too, have potential for abuse.

Mr. PEPPER. What are they?

Dr. COHEN. Ritalin.

Mr. WIGGINS. Are they used by any other trade name?

Dr. COHEN. Ritalin is the trade name. Methyphenïdate is the generic name. I would estimate, that at least in some parts of the country, a certain degree of abuse of a drug like Ritalin.

Another point which must be made is that a broad spectrum of the abuse pattern of amphetamines is obvious. At one end is the person who will infrequently take an amphetamine to temporarily exceed his physiologic limits: to stay awake, to study for an exam, to drive through the night, to excel in an athletic contest. This sort of misuse is trivial in comparison to what is happening at the other end of the scale, but it must be mentioned since a rare disaster has occurred even under this minimal type of misuse.

I am referring here to the fact that there have been occasional deaths reported in connection with the use of amphetamines during athletic contests.

A second form of abuse is that of the person who regularly takes amphetamines without supervision. The amount used is either within average limits or is gradually increased to more than ordinarily prescribed amounts. A typical example of such an instance is the person who is given amphetamines for obesity, but who continues to use them long after any attempt to lose weight has been abandoned.

A third, and most extreme abuse of amphetamines is the swallowing of handfuls of pills, the "snorting" of amphetamine powder, or its injection into a vein in the form of a solution. Generally, the progression is from swallowing and sniffing to intravenous injection. The drug most frequently used in this country for this purpose is methamphetamine—speed, crystal, and meth. Other amphetamines can be similarly used; in fact, the one popular in Sweden for this purpose is phenmetrazine, also known as Preludin. You have already heard testimony concerning the effects of injecting huge amounts of "speed" and of the "speed-freak." I will simply mention that in certain respects it is, as you said in your opening statement, a more ominous practice than "mainlining" heroin. Furthermore, the use of hundreds of times the average dose of amphetamines is physically addicting, meaning that tolerance builds up, and definite withdrawal symptoms occur when the drug is discontinued.

You have already heard enough of the horror stories about the "speed-freak." Unfortunately, they are true. The panic and the paranoid states, the malnutrition, the prolonged nervous breakdowns, the infections that occur—all of these are well documented. I would like to mention one other complication that has been largely ignored—the possibility that the use of very high doses of amphetamines over long periods of time may lead to brain cell changes. This has been demonstrated in animals, and from the Japanese experience, in man. I have seen a few heavy users who, while not on any drug, were confused, had memory gaps, were apathetic, and partially disoriented. These are signs of organic brain damage. These are not features associated with a psychotic breakdown. That condition produces other kinds of symptoms.

It is my understanding that this committee is particularly interested in questions dealing with the relationship between the legiti-

mate medical use and the illicit use of amphetamines, questions of control of supplies, diversion, and whether sufficient medical indications exist to permit their retention in view of our abuse problems. Others are better qualified than I to deal with some of these matters. I would prefer to contribute in those particular areas in which I may have some special knowledge.

One item that requires an answer is: How much of the licit supplies manufactured in this country find their way into illicit channels? I believe a real distinction must be made at this point between the ethical pharmaceutical firms who strictly control their amphetamine preparations, and the many other firms who make little or no effort to be sure that their products do not leak out into nonmedical channels. Although amphetamines originating from the plants of ethical manufacturers are occasionally seen on the street, most often the products of the dozens of less-than-scrupulous manufacturers, wholesalers, and distributors are on sale there—meaning the street. Barrels of amphetamines can be purchased today from these supply houses. In general, a considerable tightening up of the controls for the distribution of amphetamines and barbiturates is required at this time.

The physician who does not carefully supervise the patient for whom he has prescribed stimulants may be producing more trouble than he set out to cure. Good medical practice requires that the amphetamines not be given for prolonged periods except in the treatment of such infrequent patients as the narcoleptic or the hyperkinetic child.

Mr. PEPPER. What does that mean, Doctor?

Dr. COHEN. Narcolepsy?

Mr. PEPPER. Yes.

Dr. COHEN. Narcolepsy is an infrequent condition in which the individual has a compulsion to fall asleep during his so-called waking period. He may fall asleep hundreds of times a day, and this is irresistible, and it can be successfully treated with amphetamines.

Mr. PEPPER. What is a hyperkinetic?

Dr. COHEN. The hyperkinetic child is usually a youngster, perhaps with brain damage, perhaps not, who is behaviorally disordered, very hyperactive. For some strange reason, although you would think amphetamines would make him worse, it does improve the behavior of some of these children.

Mr. PEPPER. Thank you.

Dr. COHEN. The ethical pharmacist should comply with the physician's refilling instructions and with the statutory regulations regarding refilling prescriptions for amphetamines. The interminable honoring of an old prescription for stimulants can be a source of abused supplies.

The medicine cabinet may be a Pandora's box which can be opened by young and old alike to enter into a career of drug abuse. It should not become a medical stockpile; rather, it should be regularly inspected to remove no longer needed medications.

Should the medical use of the stimulants be restricted only to special cases? I would be in favor of this if I were convinced that it would decrease the abuse of these drugs. It must be kept in mind, however, that the crystalline methamphetamine which is sniffed or injected intravenously is almost invariably made in clandestine labo-

ratories. The manufacture of methamphetamine and dextroamphetamine is not difficult from precursors that are obtained in chemical supply houses. I hope that the sale of these precursors is being checked.

Clandestine laboratories which manufacture methamphetamine capsules and tablets have been detected during the past 3 years. If the entire licit production were curtailed, then more of these laboratories will spring up. Many foreign countries continue to be an easy source of supply for smugglers. Unless international regulation of the amphetamines can be initiated, this substance will remain in good supply even if medical uses of amphetamines were limited by law.

One type of amphetamine abuse might be decreased by restriction of the drug in the practice of medicine. This is exemplified by the patient who comes to depend upon her weight reduction pills. Unless the entire health profession regulates itself, then compulsory legislation of the amphetamines will come to pass.

Mr. PEPPER. Doctor, somebody told me before I came out here, that there is a meeting of the diet doctors in Washington today. Maybe we should invite them to appear here. I wonder what their discussions will disclose?

Dr. COHEN. I would hope that these gentlemen would think about alternatives to weight reduction, which is an important medical problem, other than the use of pills, especially the overuse of pills. This is certainly, I think, a part of good medical practice.

Mr. PEPPER. What is the physical impact, what does the amphetamine contribute to weight reduction? What does it do?

Dr. COHEN. The amphetamines alter the appetite-regulating center in the brain. It gives the individual a feeling of nonhunger, and in that way, appetite is reduced.

Mr. PEPPER. Thank you.

Dr. COHEN. To carelessly prescribe amphetamines for trivial reasons by a few will result in the enactment of restrictive laws for all physicians.

Perhaps we can learn something about our amphetamine problem from the Japanese and Swedish experiences. After World War II in Japan stocks of methamphetamine were dumped on the open market. Because of the postwar mental depression, and the need to work exceedingly long hours, an epidemic of amphetamine abuse swept over the country. This culminated 15 years ago when as many as 4 percent of the adult population in Japan's large cities were dependent on amphetamines. Strict controls over the availability of the stimulants, education of the populace and increased punitive action against those involved in the traffic produced considerable improvement in the situation. However, Japan is right now experiencing a resurgence in excessive amphetamine and other drug taking.

Ten years ago an amphetamine called phenmetrazine was introduced into Sweden as a nonhabit forming, antiobesity pill. Its use was taken up by thousands, and eventually some crushed the tablets, dissolved them and injected them into their veins. It is estimated that 10,000 people in Sweden during 1968 used intravenous amphetamines. Sweden has a population of 8 million people.

During the past decade, the laws were made more and more stringent but without significant effect. Early in 1968 patients could have

amphetamines prescribed only if their doctors applied to a special medical group for approval. This has not yet controlled the use of phenmetrazine because it is being illegally manufactured in that country, and because it is being smuggled in from other lands.

I know of no simple and easy answer to the amphetamine abuse problem. Before amphetamines and other abused substances can come under control, a number of fundamental changes must occur among our children and among citizenry.

1. We must gain a new respect for all drugs and transmit this respect to our children. Surely, we are childlike in our thinking if we believe that chemicals will ever be a solution to our personal problems. They can temporarily dissolve them, but never resolve them.

2. We must make these drugs as unavailable as possible, and deter major dealers with prompt and appropriate penalties.

3. Better goals which are relevant to the person, especially the young person, must be discovered. Much amphetamine taking is due to boredom, lack of purpose, and existential alienation.

4. We must fight fire with fire. The ex-amphetamine abusers should be mobilized to "turn off" the users and prevent the spread of this epidemic. The person who has gone through the shattering life of the "speed-freak" is well equipped to understand and communicate with those who are involved with amphetamines.

5. An expanded education-information program will help deter many from amphetamine excesses. Today we have sufficient reliable information about the dangers at hand to deter all but the very disturbed person from becoming caught in the amphetamine orbit that has as many downs as it has ups, and it all too often ends nowhere.

Thank you, Mr. Chairman.

Mr. PEPPER. Thank you.

Doctor, I heard over the radio this morning that the District of Columbia was trying to get some additional funds in its budget, among other things, to provide treatment centers for—I understood it to mean narcotics users. Would such a treatment center include also the abusers of drugs like the amphetamines and methamphetamines? And if so, what are the techniques of treating people who have been abusing the use of those kinds of drugs?

Dr. COHEN. The funds for the District are primarily for heroin addiction. However, I would think it reasonable that the people who run these centers would treat other drug abusers, including amphetamine abusers, because it is really unusual for a person to stay on any single drug. He samples others and may wander from amphetamines to heroin or heroin to amphetamines. So I would think it would be very appropriate for such centers to treat all sorts of drug abuse.

Mr. PEPPER. Doctor, you have told us what some of the medical uses of amphetamines are, reducing obesity. Are there other medical uses that are legitimate?

Dr. COHEN. Yes, sir. I would think most medical doctors use amphetamines not only for the treatment of obesity, the narcoleptic individual, or the hyperkinetic child, but also for the fatigued person and for the individual with a mild depression. We know now that amphetamines are not effective in the treatment of severe or even moderate depressions, but for mild depressions, they may sometimes give enough of a

lift to help a person through. Whether these are very realistic indications for their use, I hesitate to say. I think they do help some people. Other people are not helped, and still others get overinvolved in the use of their stimulant prescription.

Mr. PEPPER. It may be that we should stimulate the drug industry to create new drugs that would not have the bad effects of these amphetamines but would still have a similar medicinal purpose. Is that a good suggestion?

Dr. COHEN. I think your suggestion is a very rational one. For example, I can visualize from a neurophysiologic point of view—that is, from my understanding of how the brain functions, I can visualize that we can obtain a substance which reduces the feeling of hunger and yet will not stimulate. So that, yes, this would be a possibility for our pharmaceutical firms to work on.

Mr. PEPPER. Doctor, what's the approximate incidence of narcolepsy and of hyperkinetic problems?

Dr. COHEN. It is very low, very low.

Mr. PEPPER. So there is not a great demand?

Dr. COHEN. No, the billions of tablets that have been manufactured go elsewhere. When I was in Sweden, just 1 year ago, I asked the same question and they said that in Stockholm, they have only approved six prescriptions for this purpose. So this is a minimal use of the drug.

Mr. PEPPER. Now, does tolerance develop during the use of amphetamines for weight control?

Dr. COHEN. It can. It does not necessarily have to, but it can. I know of incidences where people kept increasing the dose not so much for weight control, but because they did not get a lift out of the drug, and they increased the amount over and above what the doctor ordered.

Mr. PEPPER. Have you noticed any higher incidence of requests for amphetamines at student health services with which you have been in contact?

Dr. COHEN. I have spoken to people who work at the student health services and there is some degree of interest and desire to obtain supplies of these drugs.

Mr. PEPPER. What is your observation as to whether doctors are becoming more or less disposed to prescribe these methamphetamines and amphetamines?

Dr. COHEN. I am not qualified to answer that, but my impression is that I think they are beginning to realize that these are not trivial drugs. Perhaps some of the other witnesses can help with that question.

Mr. PEPPER. Just for the record, will you describe what is methamphetamine and what is an amphetamine?

Dr. COHEN. Yes, sir. Amphetamines are a group of drugs which, as I mentioned in my remarks, are called stimulants. There are other drugs which are stimulants—cocaine, Ritalin—but amphetamines are the largest group of stimulants.

Now, amphetamines are many drugs. There may be dozens of amphetamines. One is methamphetamine, another is dextroamphetamine, another one is Benzedrine. These are three and there are still others. When we speak of methamphetamine, we are speaking of an amphetamine.

Mr. PEPPER. Besides the contribution that they make, perhaps, to the reduction of obesity by diminishing the appetite, and besides the narcoleptic and the hyperkinetic instances, and their use, you said, perhaps for mild depression, are there other legitimate medical uses for these drugs?

Dr. COHEN. One that comes to mind is the treatment of the tired person, the person who is always worn out, can't get going in the morning, and so forth, or the person who is overfatigued. This is one use to which the amphetamines are not infrequently put.

Mr. PEPPER. You mentioned a while ago the tendency to take a handful of these drugs. I heard the other day somebody telling about it becoming more and more the habit of truckdrivers to take a handful of these things and swallow them with water, sometimes without knowing the strength of the particular drug that they took. Have you heard of instances like that?

Dr. COHEN. Yes. This is so common that the source of supply of many of these amphetamines is at truck stops, where they can be purchased. One of these drugs is called the Los Angeles turnaround. If you take enough of them, you can drive from New York to Los Angeles and back without stopping.

Now, it is pretty obvious that if one does not sleep for a period of days, keeps awake on pills, his judgment is going to be impaired, and this has happened. There have been more truck accidents occurring because people either dozed off for a moment while driving, trying to keep going, or actually had hallucinations as a result of taking a lot of amphetamines. This is one of the complications of amphetamines.

Mr. PEPPER. Can the person who takes a large quantity of these drugs experience a high?

Dr. COHEN. Yes, sir. This is why it is a drug of abuse among many people. It is for the experience of the high. And this is more particularly the reason why it is being injected, because the high is a tremendous, as they call it, a "rush" or "flash." It is a high very reminiscent of the cocaine high.

Mr. PEPPER. How many of these tablets would ordinarily be required for one to experience a high?

Dr. COHEN. That depends on the individual. I recall taking a single 5 milligram tablet of dextroamphetamine and I was high and jittery for about 8 hours.

On the other hand, other individuals, especially if they have been taking them over a period of time, can take hundreds of milligrams at a time in order to get that same high.

Mr. PEPPER. Now, do you happen to know what these drugs sell for, if they sell in the street, these tablets?

Dr. COHEN. No; I am not familiar with the current quotations on them. Actually, they should be very inexpensive. They are easily made and I heard awhile back that one could pick them up for a dime or so, but maybe the price has gone up.

Mr. PEPPER. In our hearings in San Francisco, there were 13 bins of amphetamines somewhat like Benzedrine, as I recall, that had 1,200,000 of them, and they were consigned by a manufacturer in Chicago to a consignee in Tijuana, Mexico. The FBNDD acting on information furnished by our committee staff checked up on it, and they found

that the address of the so-called consignee was the 11th hole of the golf course at Tijuana and that a customs broker had diverted these amphetamines at the border into the black market. As I recall the hearing, the figure was 25 cents apiece that they were being sold for in the black market.

You did say that amphetamines and methamphetamines are hallucinogenic?

Dr. COHEN. They can, especially when taken in the large amounts that they are taken in today, produce hallucinations, delusions, and, what is very ominous, a state of suspiciousness, of oversuspiciousness, called paranoia, which leads them into activities that can harm themselves and others.

Mr. PEPPER. Is the effect of taking these amphetamines by injection different from taking them orally? I mean is the effect different?

Dr. COHEN. Yes, not only do the effects start quicker, but the high is higher and one loses control more easily.

Now, as soon as one feels oneself coming down, then one reinjects, so that one is really going on a speed binge. This can go on for days, perhaps over a week. During this period, one does not eat. You see, it is an appetite suppressant. And one rarely sleeps because it is used as an antifatigue substance.

Mr. PEPPER. That is what we popularly know as "speed"?

Dr. COHEN. Methamphetamine.

Mr. PEPPER. And LSD is——

Dr. COHEN. That is a little different group. It is in the group of hallucinogens, although I would like to clear up one point, namely, that the large doses of methamphetamine can produce all the hallucinations and all the strange illusions and delusions that LSD can do, even though they are two different groups of chemicals.

Mr. PEPPER. Under the Narcotics Rehabilitation Act, can persons be treated who have become abusers of methamphetamine and amphetamines, or is the treatment under that act limited to heroin users?

Dr. COHEN. The legislation says those who are addicted to narcotics or potentially addicted to narcotics, and I would interpret that as meaning people who are involved, overinvolved with drugs like methamphetamine and who are——

Mr. PEPPER. You think they could be treated?

Dr. COHEN. They could.

Mr. PEPPER. Along with the heroin addict?

Dr. COHEN. Although perhaps the legislation could be more specifically written.

Mr. PEPPER. Doctor, according to your observation, who are the principal abusers of these amphetamines and methamphetamines, by sex and race and age, if you have any knowledge of them?

Dr. COHEN. The present epidemic, especially the use of injectable amphetamines, is a white middle class-upper class phenomenon. These are people who are bored, frustrated, have no particular requirement to support themselves, and so forth. These are the ones who are getting into trouble.

Mr. PEPPER. You commented in your prepared statement about the possibility of banning all production of amphetamines. Would you care to comment any further on that?

Dr. COHEN. Yes, I have given it a lot of thought since I knew I was coming here. I think that we should get advice on this from every possible source before we make this move. As I suggest in my statement, if it would cure this abuse problem, I would be for it, but I am not at all sure that it would, sir.

Mr. WIGGINS. Excuse me, Mr. Chairman.

At this point, what other sources would you recommend that we consult on this question?

Dr. COHEN. I think that many practicing physicians, representatives of the American Medical Association, of the American Psychiatric Association, the American Academy of Medical Practice—these are people who are on the firing line, writing prescriptions. They would have an opinion to provide you, and I think it should be heard.

Mr. PEPPER. Doctor, are there other restrictions that you would suggest if we do not come to banning it?

Dr. COHEN. Well, when you tell me that over a million tablets go to the 11th hole of a golf course, it seems to me that this is ridiculous, and that we must regulate the entire procedure, from the precursor to the manufacturer of the amphetamine to its final disposition to the patient. This has to be regulated.

Mr. PEPPER. One of the large drug houses, Eli Lilly, through its representatives, testified before our San Francisco hearings that they thought it quite appropriate for the Federal Government to license the manufacturers of these dangerous drugs. Then when I suggested that those licenses might also be renewable periodically, they did not seem to object to that. That would give an opportunity to check on their performance. It would also make them very much more aware of the necessity of exercising some care in the sale of these drugs, would it not?

Dr. COHEN. Yes. There are two points I would like to make: Firms like Eli Lilly and Smith Kline & French are probably monitoring their supplies as carefully as you would like to see them right now. It is these dozens of other firms that do not even belong to the American Pharmaceutical Manufacturing Association that are giving us trouble.

The other point is that it is not enough to supervise the manufacturer or even the wholesaler, because the wholesaler then sells to jobbers and to pharmacists and the whole procedure has to be more closely supervised, or else there is diversion.

Mr. WALDIE. Will you yield, Mr. Chairman?

Mr. PEPPER. Yes.

Mr. WALDIE. It perhaps is not analogous, and I recognize there is specific legislation, but in your view as a health person, is the danger to the American populace as great from the use of cyclamates as it is from the use of amphetamines?

Dr. COHEN. I do not know. I really wish I could answer that, but I cannot, because I do not know what the dangers of the cyclamates are.

Mr. WALDIE. Without that knowledge, at least, we banned the use of cyclamates. Is it irrational to conclude that, without similar knowledge but suspicions that are at least as dark, with the use of amphetamines by the American public, that supply ought to be denied them? Are the medical advantages to the use of cyclamates, in the terms of

a basic, I believe, medical advantage, is that greater than the medical advantage to the American public from the use of amphetamines?

Dr. COHEN. The cyclamates are hardly used in medicine. They are used as food additives.

Mr. WALDIE. But their medical purposes, I assume, are restricted to use in obesity; is that correct?

Dr. COHEN. Yes.

Mr. WALDIE. And the use of these drugs, to all intents and purposes, they are almost exclusively used, today at least, for obesity; are they not? The other uses are so minimal that they really are, in terms of total production, the pills for narcolepsy or a hyperkinetic child, the uses are phenomenally minimal; are they not?

Dr. COHEN. Yes, sir.

Mr. WALDIE. We are talking about 99 percent of the total production goes for weight control, production by the legitimate producers?

Dr. COHEN. Weight control and fatigue; yes, sir.

Mr. WALDIE. In your view as a doctor, is weight control and fatigue so drastic a condition for American society today that recourse to amphetamines for treatment of those conditions ought to be continued?

Dr. COHEN. I would think that judicious use of amphetamines for the treatment of obesity is an aid——

Mr. WALDIE. I know it is an aid, but that really was not what I asked you. Is it so important for the treatment of those conditions that this drug be kept on the market in view of the consequences of misuse of this drug?

Dr. COHEN. No; we can do without these drugs except in those rare instances. But the question in my mind is will it solve our problem.

Mr. WALDIE. Well, it may not solve our problem, but the response I would give to you in that respect is it would not enhance our problem by withdrawing the drugs. The only person that would be injured by the withdrawal of these drugs is the manufacturer. Is that essentially correct?

Dr. COHEN. It would make a lot of obese men and women struggle a little harder to lose weight, but this is no big——

Mr. WALDIE. Which would be a positive thing, would it not, health-wise?

Dr. COHEN. Yes.

Mr. WALDIE. I have no further questions.

Mr. PEPPER. Just two other questions, Doctor.

Is it feasible to make these amphetamines and amphetamine pills in such a form that they cannot be injected into the body?

Dr. COHEN. First of all, the people who are using these amphetamines in an injectable form are usually buying the powder from black market sources. However, the pills can also be dissolved, filtered, and injected, too. It may be technically possible to put them in a form in which they cannot be injected. However, I would guess that over 90 percent of all the injected amphetamines these days are coming from black market sources, so that the manipulation of a pill to make it more difficult to inject would not be an answer to this problem.

Mr. WALDIE. Let me intrude here again.

Mr. PEPPER. Yes.

Mr. WALDIE. My hometown, Antioch, Calif., a small town, never heard of a drug problem until this generation. Now it is the primary issue of the whole community. It has about a 20,000 population. The whole community is deeply involved in this problem. The greatest source of supply of the pills in that community, it has been determined just recently, has been from the druggists and the kids working in drugstores diverting supplies from the drugstores into the schools. I just do not think controls of these drugs in the fantastic quantities that they are being manufactured in the legitimate market can really be imposed. If we can get the legitimate production out of circulation in America, and I would like to know the percentage of legitimate production over illegitimate production, we can concentrate on illegitimate production, it seems to me, with more certainty and more clarity.

May I ask you one more question? What would be the total value, in your rough estimate if you could give me this, of the amount of pills we would need to treat the rare instances of narcolepsy or the kinetic child?

Dr. COHEN. It would be in the thousands of pills rather than the billions.

Mr. WALDIE. In a year?

Dr. COHEN. Yes, sir.

Mr. PEPPER. How many are being produced a year? Do you recall that figure?

Dr. COHEN. It would seem to me that I remember a figure somewhere between 8 or 10 billion a year. This is only a guess.

Mr. PEPPER. One other question, Doctor. In Sweden, I understand, they have prohibited doctors from prescribing these drugs except in the case of a few patients, and, in the case of those patients, the prescription has to be approved by a commission. Now, would you think that we should try to impose some limitation upon the freedom of doctors in this country to prescribe these drugs, one, by law, and second, by the Department of Health, Education, and Welfare, for example, making a public appeal to doctors and trying to develop public opinion, calling upon the doctors in some cases not to profit.

A good while ago, I met two gentlemen in a certain part of this country. They told me that one of them, up to a few months ago, had been making a lot of money from prescribing these amphetamines for obesity. Then he got in trouble with the Government some way or other, so he was not doing so well thereafter. So evidently, there was a very large profit motive behind this doctor's specialization.

Could we work through either of those two methods—by legal prohibition or legal limitation of the authority—through the States, if we could not do it through the Federal Government, and, second, through a Government-sponsored and Government-supported effort to dissuade the medical prescription of these drugs except in proper cases?

Dr. COHEN. Well, I think both should be done. First of all, we must reeducate our health professionals to the relatively new dangers of amphetamine abuse.

I might tell you that we have one public information television spot which speaks to this point. It shows a number of women lined up getting their bags full of pills and the doctor just ringing up the money on the register. We call them "fat doctors." The president of that association to which you referred threatened to sue us because

we were defaming the "fat doctors" because we wanted to point out that this sort of medicine is not good practice.

Now, as to the barring of amphetamines, if it comes to pass, and I do not know whether this is the course that you will advocate; whether this is the wisest course or not, I am really not sure in my own mind—but if it should come to pass, then certainly certain uses of amphetamines should be permitted, maybe by a special commission.

I neglected to mention that sometimes, amphetamines are used to counteract the effects of sedative poisoning. This is another rather small use of amphetamines.

But in general, I would hope that we will explore every possible avenue in order to deal with this problem.

Mr. PEPPER. Mr. Waldie, do you have any other questions?

Mr. WALDIE. No, Mr. Chairman.

Mr. PEPPER. Mr. Wiggins?

Mr. WIGGINS. Just one.

Doctor, as far as you know, does statutory authority now exist to outlaw the use of amphetamines? May it be done administratively at the present time?

Dr. COHEN. I am not qualified to answer that, but if you forced me to, I would say I do not think we have any statutory capability to do this. That would have to be answered by a lawyer, I believe.

Nor, by the way, would I recommend that it be a State matter, because then we are only going to get into bringing it across State lines. It has to be done on a rather large scale if it has to be done.

Mr. WIGGINS. Does administrative authority now exist to require that the drug manufacturers code each individual tablet in order to determine the source of that tablet?

Dr. COHEN. I know of one firm that does this, but I do not believe it is in the regulations.

Mr. PEPPER. Thank you very much, Dr. Cohen.

Dr. COHEN. Thank you, gentlemen.

Mr. PEPPER. Dr. Griffith is our next witness.

Dr. John D. Griffith is assistant professor of psychiatry at Vanderbilt University School of Medicine. Born in 1931, Dr. Griffith received his B.A. from the University of Chattanooga in 1951, and his M.D. from the University of Tennessee School of Medicine in 1955.

From 1959 to 1961, he was Chief of Psychiatry at U.S. Air Force Hospital at Keesler Air Force Base in Mississippi. From 1961 to 1963, Dr. Griffith was director of the Harriet Cohn Guidance Center in Clarksville, Tenn. From 1962 to 1963, Dr. Griffith was also a clinical instructor in psychiatry at Vanderbilt Medical School. From 1963 to 1965, he was a research associate in the speech and hearing center at the University of Oklahoma Medical Center, and also an assistant professor in the university's department of psychiatry. Since 1965, Dr. Griffith has been assistant professor of psychiatry at Vanderbilt Medical School, and since 1968, an instructor in its department of pharmacology.

Dr. Griffith's publications include: "The Use of Amphetamines by Individuals in Critical Occupations," Proceedings of the 13th Annual Air Force Behavioral Science Symposium, 1966; "Psychiatric Implications of Amphetamine Abuse," Law Enforcement and Dangerous Drug Abuse, edited by T. Murton, 1966; "A Study of Illicit Ampheta-

mine Drug Traffic in Oklahoma City," American Journal of Psychiatry, November 1966; and "The Physician's Potential Liability for Prescribing Diet Pills," Oklahoma Law Review, May 1965.

Dr. Griffith, we are pleased to have you before us.

STATEMENT OF DR. JOHN D. GRIFFITH, ASSISTANT PROFESSOR OF PSYCHIATRY AND INSTRUCTOR OF PHARMACOLOGY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.

Dr. GRIFFITH. Thank you, Mr. Chairman, members of the committee. I would like to identify myself further as a member of a research team at Vanderbilt University which conducts research in the field of addicting drugs. Our activities are quite broad and include surveys into the sales and distribution of illicit drugs, the treatment of drug addiction, the effects of these drugs on human behavior and the basic pharmacology of these drugs in animals. The drugs of the amphetamine class are under our scrutiny and it is my purpose to present to you as succinct and pertinent an evaluation of the amphetamines as our present state of knowledge allows. In the interest of brevity, I will reference my remarks rather than present a detailed discussion.

I would first like to point out that every drug, however innocuous, has some degree of toxicity. A drug, therefore, is a type of poison and its poisonous qualities must be carefully weighed against its therapeutic usefulness. A problem now being considered in most of the capitals of the free world is whether the benefits derived from amphetamines outweigh their toxicity. It is the consensus of the world scientific literature that the amphetamines are of very little benefit to mankind. They are, however, quite toxic. I would like to discuss these points, then conclude by suggesting that this committee take a new tack and explore certain unusual solutions to the problem of amphetamine abuse.

In this discussion the term, amphetamine, will be used in a general sense to designate the d- and l-isomers of amphetamine, methamphetamine, and the piperdine derivatives, piprandrol and methylphenidate.

USEFULNESS OF AMPHETAMINE DRUGS

The bulk of amphetamine drugs sold in this country are prescribed for the treatment of obesity. Good studies show that subjects will lose an average of 6.75 pounds more during a course of treatment while using amphetamines than they will if given a placebo.

Mr. PEPPER. This many pounds each week or what?

Dr. GRIFFITH. No. 6.75 pounds total weight loss during an entire 6–20 week period.

At the end of 6 weeks, usually, the patient becomes resistant to the effects of the amphetamine and derives little or no further benefit. This is extremely well documented.[2 3 4 5 6]

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[2] Patel, Natoo et al. Comparison of benzphetamine, phenmetrazine, d-amphetamine and placebo. Clin. Phar. Ther., 4 :330–333, 1963.

[3] Seaton, D. A., et al.: Diethylpropion in the treatment of "refractory" obesity. Brit. Med. J., ———: 1009. Apr. 8, 1961.

[4] Seaton, D. A.: Sustained-action chlorphentermine in the correction of refractory obesity. Practioner, 193 : 698, Nov. 11, 1964.

[5] Simkin, B. and Wallace, L.: A controlled clinical comparison of benxphetamine and d-amphetamine in the management of obesity. Clin. Nutrition, 9 :632, September–October 1961.

[6] Hampton, J. et al.: Phenmetrazine and d-amphetamine in the management of obesity. Lacent 1 :1265, June 11, 1960.

The cosmetic and health advantages derived from a six and three quarters pounds weight loss is quite minor. For this reason, most responsible physicians are of the opinion that amphetamines should not be prescribed for appetite suppression. This view is even more pertinent now that at least one appetite suppressant has been discovered that is not a stimulant drug. (Fenfluramine)

The amphetamine drugs are also advertised and prescribed for the treatment of emotional depression.[7] [8] I might point out that we all get depressed from time to time. So if you go to a doctor because you feel bad, he is quite likely to give you a pill, and this pill is likely to be an amphetamine.

Mr. PEPPER. Are they used in mental hospitals where there is a serious mental disturbance?

Dr. GRIFFITH. Very rarely by competent physicians. After many years of clinical trials, it is now evident that this antidepressant effect of amphetamines is very brief—on the order of days. If the patient attempts to overcome this tolerance to the drug, he runs the risk of becoming addicted and even more depressed. Evidence obtained in our laboratories on human patients suggests that initial doses of amphetamine turn the patient "on," but metabolites formed from the amphetamine will turn the patient "off" again.[9] Therefore, it is generally concluded that amphetamine is a very poor treatment for mild depression. It is absolutely contraindicated in more severe depressions.[10] I might add parenthetically that mild depressions could be treated with cocaine, morphine, and alcohol with approximately the same degree of success and with very little additional risk of addiction.

Another disease which has been mentioned before is narcolepsy. I would just like to say that specialists in the treatment of narcolepsy will spend their entire career and maybe see a handful of these patients, a dozen or more. Amphetamines are used in the treatment of this condition with mixed success.[11] [12]

No reputable drug company suggests that amphetamines be given to normal individuals so that they might stay awake or perform unusual physical tasks. In fact, the NNR has specifically prohibited their use in that context. As a practical matter, however, some physicians do prescribe amphetamines for this purpose, for themselves, and even for their college student children.[13] Other physicians will prescribe amphetamines for weight reduction when it is perfectly obvious that the patient is not using the drug to lose weight.

The armed services also provide stimulant drugs to military personnel.[14] These drugs, which are part of "emergency kits" are often stolen by military personnel assigned to guard airplanes. Airmen addicted to amphetamine are being identified in our VA case files. Several mili-

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[7] Physicians' Desk Reference, 22d ed. Medical Economics, Oradell, N.J., 1968.
[8] Leake, C. D.: The Amphetamines. Charles C. Thomas, Springfield, Ill., 1958, pp. 67, 113.
[9] Cavanaugh, J., et al.; The effect of acute and chronic amphetamine administration on adrenergic neuron function in man. Garattini, S. and Costa, M. D. eds. Aphetamines and Related Compounds, Raven Press, 1969.
[10] Treatment of depression, Brit. Med. J. 2:164, Apr. 20, 1968.
[11] Merritt, H. H.: Textbook of Neurology. Lea and Febinger, Philadelphia, 1963, p. 753.
[12] Adams, R. D. in Principles of Internal Medicine, 5th ed. McGraw-Hill, New York, 1966, p. 1293.
[13] Smith, Stanley N.: Amphetamine usage by medical students. J. of Med. ed., 41:167, Feb. 1966.
[14] Benzedrine (amphetamine) alert. Air Surgeons Bull. (No. 2), 1:10–21, Feb. 1944.

tary physicians have suggested that amphetamines actually reduce the efficiency of a military unit.[15]

Other uses for amphetamines have been mentioned. For instance, in the Physicians' Desk Reference, amphetamines are suggested as a treatment for alcoholism. Since the alcoholic is especially prone to amphetamine addiction, this use is contraindicated. Amphetamines should not be advertised for this purpose. Neither are amphetamines of any use in the treatment of barbiturate overdosage.

Dr. Cohen has said, and I support him, that amphetamines are used in the treatment of hyperkinetic impulse disorders.[16] Children who manifest this condition are frequently brain damaged and exhibit such a high degree of pathological hyperactivity that they cannot learn, be disciplined, or allowed to play with normal children. If treated with amphetamines, many of these children will normalize their behavior—especially after the short term effects of the drug have worn off.[17] The long-term toxicity of this form of treatment has not yet been established; neither is it clear whether amphetamines are superior to other drugs.[18] Physicians by and large agree that if amphetamine were to disappear from the market tomorrow, almost all patients would benefit except these children.

We may conclude, therefore, that amphetamines are of little benefit in the treatment of obesity and emotional depressions. These drugs are of some benefit in certain rare disorders such as narcolepsy and quite useful in the treatment of certain brain-damaged children. Now let us consider the toxicity of these drugs.

Mr. Pepper. While you are at that point, what do you estimate would be the proper number of those tablets to be put on the market in the United States, if they were to be used only for legitimate and proper medical purposes?

Dr. Griffith. Well, for narcoleptics, it would just be a handful, enough to supply several hundred patients in the United States. The treatment of hyperkinetic children would require more, but not much more.

Mr. Pepper. Is it your opinion also that a billion or more of these tablets are being produced every year?

Dr. Griffith. Oh, yes.

Mr. Pepper. So you say a few hundred or a few thousand tablets would be enough to meet all the proper medical needs of this country?

TOXICITY OF AMPHETAMINE

Dr. Griffith. Absolutely. There is no doubt about it.

The medical profession has been slow to accept the dangers of amphetamine use. Since 1938, when the drug was first introduced, reports of amphetamine abuse have appeared in the medical literature each year. Nevertheless, many other papers have described amphetamine

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[15] Somerville, W.: On mental or physical fatigue in soldiers. Canad. M.A.J. 55:470, November 1946.

[16] McGraw, R. B. and Oliven, J. F., in Arieti, S., ed., American Handbook of Psychiatry. Basic Books, New York, 1959, p. 1560.

[17] Laufer, M. W.: ed. Freedman, A. M. and Kaplan, H. I., Comprehensive Textbook of Psychiatry, Williams & Wilkins, Baltimore, 1967, pp. 1446–1447.

[18] Aleandris, A.: Effect of thioridazine, amphetamine and placebo on the hyperkinetic syndrome and cognitive area in mentally deficient children. Canad. M.A.J. 98:92, Jan. 13, 1968.

abuse as either nonexistent;[19] impossible, because withdrawal symptoms do not occur;[20] as occurring only in antisocial and maladjusted individuals;[21] as a minor problem,[19] and as late as 1959 as a major problem, but on the decrease.[22] During the last decade, however the profession has now identified and recognized amphetamine abuse as being a major health problem—many times more serious than narcotic addiction.[23] [24] [25] Amphetamine abuse is also of interest in that an illicit market in the drug sprang up even though the drug had been "legalized." At one stage in its sales, amphetamines could be purchased without a prescription.

Admittedly, not every person in the United States who has been exposed to amphetamine—my guess, 9 million adults [26] become addicted. However, the widspread availability of the drug on the illicit market plus its availability as a stimulant and appetite suppressant has resulted in many cases of drug abuse.

Not all of these cases of drug abuse are severe. Perhaps the mildest form is committed by students who use the drug as an imagined study aid. Dr. Stanley N. Smith, who investigated this practice at the University of Oregon Medical School, found that slightly less than one-half of the students had used amphetamines. It is interesting that 38 percent of these students obtained their drugs from licensed physicians.[27] This seemingly innocuous practice is not without its hazards.

Dr. Smith points out that he became interested in the problem after observing a senior medical student become psychotic while using amphetamines. Sadusk, also, has pointed out that the use of amphetamines by students may lead to more serious consequences.[28]

However, amphetamine abuse is not confined to students. Our case files indicate that the most likely occupational group to be represented are medical personnel; housewives are next, and those engaged in nocturnal occupations follow. Our research, and the studies of others, have identified amphetamine abuse, too, among various underworld characters such as petty thieves, convicts, and prostitutes.[29] "Successful" criminals do not use amphetamines, as a rule.

Addiction to amphetamine also occurs. The older medical literature suggested that this was not so; however, direct observations of amphetamine addicts now make it clear that amphetamine addiction is more widespread, more incapacitating, more dangerous and socially disrupting than narcotic addiction. Intravenous use of amphetamine is common and Kramer [30] has pointed out that this abuse is indistinguishable

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[19] Leake, C. D.: The Amphetamines. Charles C. Thomas, Springfield, Ill., 1958, pp. 67, 113.
[20] Knapp, P. H.: Amphetamine and addiction. J. Ner. Ment. Dis. 115:406–432, 1952.
[21] Guttman, E.: Benzedrine: Uses and abuses. Proc. Roy. Soc. Med. 32:388, 1938.
[22] Nyswander, M.: "Drug Addiction." Arieti S., ed. American Handbook of Psychiatry, vol. 1. New York: Basic Books, 1959, pp. 614–622.
[23] Griffith, J.: A Study of illicit amphetamine drug traffic in Oklahoma City. Amer. J. Psychiat. 123:560, 1966.
[24] Kramer, J. C.: Amphetamine abuse. JAMA 201:89, July 31, 1967.
[25] Monroe, R. R. and Drell, H. J.: Oral use of stimulants obtained from inhalers. JAMA 135:909, 1947.
[26] Manheimer, D. I.: Psychotherapeutic drug use among adults in California. Calif. Med. 109:445, Dec. 1968.
[27] Smith, Stanley N.: Amphetamine usage by medical students. J. of Med. Ed., 41:167, Feb. 1966.
[28] Sadusk, J. F.: Nonnarcotic addiction: size and extent of the problem. JAMA 196:119, May 23, 1966.
[29] Griffith, J.: A study of illicit amphetamine drug traffic in Oklahoma City. Amer. J. Psychiat. 123:560, 1966.
[30] Kramer, J. C.: Amphetamine abuse. JAMA 201:89, July 31, 1967.

from cocaine addiction. The problem is compounded, both literally and figuratively, by the availability of amphetamine-barbiturate combinations. It is easy to dismiss the amphetamine addict as a criminal or useless derelict of society. The committee should recognize, however, that many were once useful professional people of great promise. For example, the first case I observed—1960—was a young psychiatrist who had been confined in a locked ward. The second, an award-winning Air Force tanker pilot.

The psychological and physical penalties for amphetamine abuse are severe. Individuals who abuse this drug have great difficulties following occupational, domestic, or social pursuits; they risk damage to body organs; and they may experience a severe mental illness. We have observed some of these adverse mental effects of amphetamine under laboratory conditions and have established that the drug will cause a psychosis—even in normal individuals.[31]

It should also be noted that amphetamines are physically toxic. Because these drugs elevate blood pressure and have a direct action on the heart, they can aggravate preexisting diseases.[32] Deaths of children from accidental ingestion of their mothers' prescriptions have also been reported as have intentional suicides.[33]

Theoretically, most of these dangers of amphetamine abuse could be avoided, given a foolproof system of distribution and controls. As you will notice in the following paragraphs, this system does not exist.

LEGITIMATE SALE AND DISTRIBUTION OF AMPHETAMINE DRUGS

Amphetamine drugs are inexpensive, simple to manufacture, and patent rights on the basic drugs, d- and dl-amphetamine have long since expired. For this reason, most drug houses realize profits of less than one-tenth of 1 cent a tablet on the sales of these drugs. Because of this small profit margin companies simply cannot afford to scrutinize their sales.

Some companies do hold patents on amphetamine-like drugs and advertise them as superior to amphetamines. There is little scientific evidence that this is so. However, their position allows them to market these drugs at a considerably higher price than generic brands of d-amphetamine. These companies do not want their drugs to acquire the reputation for abuse. Nevertheless, most advertise their product as a weight-control item. This is where the money is.

Another marketing technique is to heavily advertise a brand name. Once this name is well-recognized it will be widely prescribed and can be sold for several times the cost of its generic equivalent. In reality, these drugs can be nothing more than warmed over items from the 1930's.

Another practice is to sell a tablet which contains an amphetamine plus some other drug, usually a barbiturate or a minor tranquilizer. The rationale offered by the company is that the drugs tend to neutralize one another. Evidence obtained from addicts and from labora-

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[31] Griffith, J. D.: "Experimental Psychosis Induced by the administration of d-amphetamine" Garattini, S. and Costa, M.D. Ed.s, Amphetamine and Related Compounds. Raven Press, 1969.

[32] Wilson, D. R.: Drugs for obesity. Canad. M.A.J. 91:1369, Dec. 26, 1964.

[33] Zalis, E. G.: Fatal amphetamine poisoning, Arch. Int. Med. 112:60, December 1963.

tory studies indicates that these combinations are much more attractive and, therefore more addictive. It has been our experience that addicts offered amphetamine alone—without barbiturates and/or alcohol—find the amphetamines quite unpleasant in large doses.

By and large, the drug industry has not shown a great deal of restraint in selling addicting drugs unless required by law. Exceptions do occur, however, Ciba Pharmaceutical Co., for example, has not advertised their product, Ritalin, as an appetite suppressant in this country even though it is as effective in this regard as d-amphetamine. Smith Kline & French Laboratories once sold an inhaler containing large quantities of dl-amphetamine and inadvertently supplied many young people with an unrestricted supply of this stimulant drug. The company withdrew the inhaler from the market before being required to do so by the FDA. This responsible behavior should be contrasted with a practice of the Pfeiffer Co., St. Louis, Mo., that sold a nasal inhaler containing 150 milligrams of dl-amphetamine—about 30 times a therapeutic oral dose—until around 1965. Our research prior to that time showed that the inhaler was being widely abused and young adults would "shoot" the contents of this inhaler intravenously. The Food and Drug Administration—since under new management—did not respond to my plea that the inhaler be restricted to prescription sales and pointed out that consideration should be given to public need for nonprescription drugs. Only after a congressional hearing was this practice changed. Other forms of irresponsible behavior by legitimate drug companies have been documented by us and by your staff.

The conclusion that might be drawn from these observations is that the legitimate drug industry cannot, as a group, always move together to protect the public good. It should be added that many individuals in drug companies recognize this problem but are frequently hamstrung by their marketing department which points out that objective statements about drugs or restrictions on drug sales will cut into profits.

Until Congress enacted legislation requiring that prescriptions on amphetamines expire at the end of a fixed time, many legitimate pharmacists, whose aim was not to offend their customers, would refill amphetamine prescriptions promiscuously. We now find that pharmacists have become very careful with this drug, check with physicians before refilling, and refuse to refill outdated prescriptions. Except for the occasional bad apple in any barrel of professionals, this problem has improved considerably.

Many physicians, too, have changed their prescribing practices. A small survey of medical specialists in our area indicated that only one out of three prescribe amphetamine. Some were vehement and would answer the survey with "hell, no!" et cetera. Psychiatrists, as a rule do not prescribe amphetamines. Some physicians continue to exercise poor judgment in prescribing this drug. The legal problem here is that criminal convictions are almost impossible to obtain against these physicians. Alternative methods of enforcing patient-oriented conduct should be explored by this committee.

The patient cannot be relied on to show good judgment in the use of drugs. Some lie to their physician to obtain drugs; others lie to themselves that they need drugs in large quantities. The problem here is that once an individual is prescribed amphetamine his judgment

about continued drug use is seriously impaired. The patient, therefore, should not be made to bear the responsibility for drug abuse since this is largely beyond his control. Therefore arguments that the drug is safe if "taken as directed" ignore the fact that a large number of patients will ignore directions.

SUMMARY

It appears, therefore, that amphetamine drugs are of little benefit except to a very small segment of the ill in our society. On the other hand, making these drugs available for the treatment of obesity and depression has proved to be quite harmful to the public. Although a foolproof system of regulations might alleviate some of these harmful consequences, existing controls such as are now practiced are inadequate. It is evident that the present system of controls places the major risk, pain, and financial burden of amphetamines directly on the consumer. In addition, those who do not use drugs must be taxed to control the social disruption resulting from drug abuse.

Mr. PEPPER. Doctor, how important to the principal drug manufacturers of the country is the manufacture and distribution of these methamphetamines and amphetamines? How important is it to them? What proportion of their business is represented by this kind of manufacture and distribution?

Dr. GRIFFITH. Approximately 8 percent of the prescriptions written in this country are written for amphetamine drugs. That is a lot of prescriptions. You can see that the drug is extremely popular.

RECOMMENDATIONS

Congress has wrestled with the problem of public drug abuse for many decades. Although some isolated improvements have occurred, it is evident that drug abuse, as a total problem, is now worse than ever. Neither can a spontaneous "cure" be expected. Indeed, historians may someday compare our problems with drugs to the ravages of the Black Death during the Middle Ages when a third of the population was struck down.

A careful analysis of solutions proposed for drug problems in the past shows why these did not work. Most were too expensive or cumbersome to be carried out. For this reason, I would plea with you that, whatever is done, that it be inexpensive. Let me suggest some examples:

One action the committee might take is to prohibit the sales of amphetamine-barbiturate or amphetamine-tranquilizer drug combinations. Most physicians would not write two prescriptions, and some potential addicts would find amphetamine, alone, to be unpleasant.

The committee might also ask the FDA to consider restricting the treatment indications for amphetamine to the treatment of narcolepsy and certain childhood behavior disorders. This would prompt lawsuits by several major drug companies, however, and sales would continue for 2 years or more. For this reason, direct congressional legislation should be considered. The implications of this proposal is that prescribing amphetamines as stimulants would become medical malpractice.

The committee should consider legislation that would require the vendor of a drug—whether a legal vendor or an illegal peddler—to be financially responsible for careless or promiscuous distribution to customers. The problem is this: Fines are small, convictions are rare, large corporations can tie up matters in courts for years, the district attorneys' offices are saturated with a backlog of cases, and the prisons are overcrowded. Therefore, one has little to fear in the way of a jail sentence for violating the drug laws. On the other hand, if a vendor knows that supply or prescribing a drug to a student, teenager, housewife might make him liable to damages, he would dispense these drugs with utmost care. You will notice that most private swimming pools are surrounded by a high fence. The fence is not there because the owner is goodhearted. It is there because he fears being sued by the father of a child who might drown in the pool. We are all children where drugs are concerned—as the observation of any cocktail party will attest—and the vendor of drugs should either erect his own walls or risk the financial consequences. As matters now stand, our laws require the addict to bear the consequences of his addiction unaided.[34]

Congress should also consider making the manufacture, sale, and distribution of addicting drugs an absolute Government monopoly. This is not a suggestion that drugs be "legalized"; neither is it a plea for prohibition. However, it would be a system in which the distribution of addicting drugs would be determined by public need and bureaucratic inefficiency—both useful in this instance.

Lastly, there is a need for research in the field of drug addiction and alcoholism. It may come as a surprise to some of you that we do not know how drugs and alcohol act; where they act (except somewhere in the brain); or how to treat addiction to these substances. Until more research is done, programs which propose to treat and prevent drug addiction and alcoholism are likely doomed to failure.

Mr. Pepper. You do not recommend legislation banning the manufacture or the distribution into interstate commerce, for example, of these drugs?

Dr. Griffith. I think that the sale, the manufacture and sale of amphetamine-barbiturate amphetamine-tranquilizer drug combinations should be banned.

Mr. Pepper. Should be banned?

Dr. Griffith. They should be banned. There is no place, in my opinion, for these drugs.

Mr. Pepper. In other words, the medical uses that are made of them properly do not, in any sense of the word, in your opinion, equate with or counterbalance the injury done to the people of this country?

Dr. Griffith. Not even on a 1,000 to 1 ratio. I think, too, consideration should be given to restricting these drugs to the treatment of narcolepsy and to the treatment of hyperkinetic children. Legislation of this sort would make it malpractice to prescribe these drugs for any other purpose. I think that the people who are injured by this drug—that is, the noncriminal user—would have recourse to damages if he were sold this drug promiscuously.

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[34] Griffith, J.: Physicians' potential liability for prescribing "diet pills." Okla. Law Rev. 18:1–2, May 1965.

Mr. PEPPER. Doctor, one other question. Does the abuse of these drugs contribute to the kind of behavior that we call criminal?

Dr. GRIFFITH. The user of drugs is frequently so incapacitated that the only way he can make money is to engage in crime. For women, it is usually prostitution and for men, in my experience, it has been petty theft such as shoplifting.

Mr. PEPPER. Thank you.

Mr. Waldie?

Mr. WALDIE. I would certainly think, Mr. Chairman, that the testimony of the witness is confirmed by additional testimony—I would believe it to be—that it is rather peculiar that the Federal Government participates in a situation that contributes to the use of these drugs.

How widespread is its use in these armed services?

Dr. GRIFFITH. I can see how my testimony would give the impression that the Armed Forces, by having these drugs in "emergency kits" contribute to drug addiction. However, I would think having emergency kits kept in airplanes is only a small factor. On the other hand, the Air Force weight reduction program, in which it has been advocated that weight can be controlled by the use of amphetamines, and the sales of these drugs in VA hospitals and in the military services, where they are prescribed to military personnel and to their dependents for weight reduction, is a major source of drug dependency problems.

Mr. WALDIE. So that the Federal Government is a major purchaser of the drugs is your testimony, I presume.

Dr. GRIFFITH. I do not have any figures to substantiate this, but I would, I am quite certain that the Federal Government is a major purchaser.

Mr. WALDIE. I gather one of your recommendations is that we simply then ban or make it illegal to produce amphetamines for any purposes other than narcolepsy or the hyperkinetic child, which is a minimum production?

Dr. GRIFFITH. Yes. I think, too, that the committee should consider making the vendor responsible, financially, for damages caused by drugs that are promiscuously prescribed. We, as taxpayers, have to bear the responsibility for the drug users antisocial behavior and his treatment. I think if the vendor of a drug were made financially responsible, the situation would alter drastically.

Mr. WALDIE. Well, if it were banned for any use other than treatment of the narcoleptic case or the hyperkinetic child, prescribing for any other use would be malpractice?

Dr. GRIFFITH. Right.

Mr. WALDIE. Which would accomplish the result that you suggest.

Dr. GRIFFITH. Yes.

Mr. WALDIE. I have no further questions.

Mr. PEPPER. Mr. Wiggins?

Mr. WIGGINS. Doctor, you are a psychiatrist and a medical doctor as well, I take it?

Dr. GRIFFITH. Yes.

Mr. WIGGINS. Are the views you have expressed here this morning shared by most psychiatrists, if you are in a position to tell the views of most psychiatrists?

Dr. GRIFFITH. I think they are shared by most psychiatrists who are not taking amphetamines themselves. I do not mean this in any facetious sense, because it does happen.

I think if you were to poll the chairmen of the departments of medicine at our medical schools, you would find that these gentlemen would agree with what I have stated, especially since my statement is referenced and based on fact.

Mr. WIGGINS. The recognized association of psychiatrists is called what?

Dr. GRIFFITH. The American Psychiatric Association.

Mr. WIGGINS. Has the American Psychiatric Association taken a position in this case?

Dr. GRIFFITH. Yes, they have. Their position is that the problem exists, it is severe, and that something needs to be done about it. But what should be done about it is something else again.

I should point out as a reality of the matter that you might be forced to write off this present generation of drug users, because conventional treatment techniques are too expensive—on the order of $10,000 per patient—and even then, few recover.

Mr. WIGGINS. Thank you, Doctor.

Mr. PEPPER. Doctor, one other question. I understood you to say that you believe that the manufacture and distribution of these drugs should be banned except in the treatment of these two diseases that you spoke about, these two conditions, the narcoleptic and the hyperkinetic types of illness. Now, how would you determine who should receive the drugs? Would you leave that to the doctor and make it malpractice when they do otherwise, or would you set up a commission to approve certain prescriptions the way Sweden has done?

Dr. GRIFFITH. I think the commission would be the best approach. I think we are coming to the point that we may have to insist that only specialists prescribe certain drugs. You might also consider a commission that would determine, especially since only a small number of patients are involved, who should receive the drug and who should not.

Mr. PEPPER. Thank you very much, Doctor. We appreciate your coming.

Dr. Benjamin Sheppard is our next witness today.

Dr. Sheppard is qualified both as a doctor and a lawyer. I am very proud of the fact that he comes from my city of Miami.

He holds a medical degree and a degree of jurisprudence from the University of Miami. From 1953 to 1956 he served as acting medical examiner in Dade County. He then served as director of the county jail from 1953 to 1958. He became a juvenile judge in 1960 and senior judge of domestic relations in Dade County from 1960 to 1966. In 1966 he took time off to take courses in adolescent psychiatry.

Dr. Sheppard is presently the executive director of the Catholic Services Welfare Bureau for the Archdioceses of Florida (Miami). He supervises the drug clinics.

Dr. Sheppard has been one of the meaningful citizens in Dade County and of Miami, for many years. We all respect and admire and are grateful for his immensely valuable services to Miami out of his large experience. We are very pleased to have him give his testimony today.

Dr. Sheppard?

STATEMENT OF DR. BENJAMIN J. SHEPPARD, EXECUTIVE DIRECTOR OF THE CATHOLIC SERVICES WELFARE BUREAU FOR THE ARCHDIOCESES OF FLORIDA

Dr. SHEPPARD. Thank you, Senator. I will not read my statement, but I do say that out of 30 years of active medical practice, and I practiced medicine while I did the law work, I have seen one and a half cases of narcolepsy. This was a very active practice. I say "half" because I was half sure. One case I was sure.

As far as the use of Dexedrine for the child with a little bit of behavior disorder, I have been exposed to it more because I have the job of being the consultant to the two reading academies in Miami where they treated the hyperkinetic child. Now I do say, and I do not think anyone knows, why Dexedrine does help the hyperkinetic, short-attention-span child, the child who will get up out of the seat and walk around, disrupt the whole classroom. They do not seem to have any electroencephalogram changes, but they do seem to help in the classwork. But the duration of Dexedrine is never very long. It is for a few months and then we tend to swing toward the milder tranquilizers rather than to use anything, to continue our use of Dexedrine.

I personally can see no use for amphetamine whatsoever. I would be in favor, very definitely, of banning it completely or giving the few people who need the Dexedrine in this type of school some supervision. I do not know how you are going to do it. It will be difficult.

I would say very definitely that running a drug clinic, as I do down in Miami, speed is getting more and more common. The children are mainlining speed much more than they are dropping it. They find that it is a cheaper way to get a rush. They find that it is a cheaper way to escape from whatever they are escaping from than anything else.

As far as I am concerned, the best remedy for fatigue is a bed. I would not use any stimulant.

It has been proven experimentally that a placebo for weight reduction works just as well as the Dexedrine or as the amphetamine. I mean it has been proven in controlled experiments that by giving these placebos to different people, they lose just as much weight and the loss of appetite is just as great as in those individuals who take the true amphetamine products.

I think strong consideration should be given to the use of amphetamine in combination. By that, I mean the Dexamyls, the Desoxyns, Desbutal and all. I think those combinations are bad because they are misleading, they give a person a sense of euphoria.

But I am also on the school board of Dade County, which has the seventh largest school system. Being on the school board down there, I am in charge of the drug program. I feel very definitely that speed has gone down to our sixth and fifth grades, both taking it orally and mainlining it. Sometimes these kids will repeat that speed. The tolerance goes until they crash. And when they crash, they go into a paranoiac state—a catatonic state, rather, where they lie and you cannot arouse them for anything. They are so drowsy when they wake up that they just have to go out and find some more speed so that they can go on with their normal functioning.

As I say, I treat these children clinically. My work is mostly with the adolescent. But I have never seen more than one and a half cases of narcolepsy and outside of the hyperkinetic child, where it does have a beneficial effect, I see no reason for the use of amphetamine, for the manufacture of amphetamine. I see no reason for it whatsoever.

(The prepared statement of Dr. Sheppard follows:)

PREPARED STATEMENT OF DR. BENJAMIN J. SHEPPARD, EXECUTIVE DIRECTOR OF THE CATHOLIC SERVICES WELFARE BUREAU FOR THE ARCHDIOCESES OF FLORIDA

Drugs of the amphetamine type have been used for many years. We have come to find, however, they can in some produce a marked dependence which can produce varied problems. We have come to realize that the cause lies with the person himself more than with the drug. The answer, to the question why do some people "turn on" and others do not has not been found as yet—it rests with the psychological structure and functioning of the person. The medical profession and the psychologists have come to understand that we are dealing with sick people—psychologically, rather than what has the drug done to the individual and until we find the psychological reason we cannot win.

The worst effect of the drug is that it tunes out discomfort, there comes a time when any decisionmaking which may bring about some discomfort is circumvented by the use of any drug. This is most important because of the age bracket we have seen using the drug—the adolescent, and the young adult. At a time when they should be making the foundation for future life, this is the time when he must learn to develop his own capacities and learn to cope with future problems.

The drug dependent person is suffering from a serious mental or emotional disorder and shows it by craving the drug as a crutch. Drug dependence has been seen to serve many different psychoneurotic disorders, from anxiety to character disorders. Practically every phase is served.

Most drug dependent people will vocalize that they hate the drug—but they have great doubts as to their ability to perform without the drug. To suddenly take it away is a form of cruelty; no matter what we think of them we must show them the same degree of compassion as we would with any severe mental or physical disorder.

No matter what we do or say striving as we do for full normal and psychological development—there is going to be a small group who will not respond to our procedures and it is to this group we must address ourselves realizing that each individual is entitled to the acknowledgment that he is a human being and the best help in line with his own problems should be afforded.

We cannot say that all people who are dependent on drugs fit into a certain capsule for treatment. This is not medically true. This is a community problem and must be under central authority. All resources of the community must be considered in the planning for the individual and there must be a preliminary screening by a knowledgeable individual who through consultation will decide what color capsule will best fit the needs of this dependent and will go on from there.

AMPHETAMINE STUDIES

The FDA has determined that in 1962 over 100,000 pounds of amphetamine and methamphetamine products were available in the United States. The amount in this 1 year inventory is enough to supply 250 milligrams of these stimulants or 25 to 50 doses to every person in this country.

These drugs are prescribed for a few valid medical reasons; that is, to control narcolepsy and to control certain hyperkinetic disorders of children. They may have some use in treating mild depressions, and to help these people who have taken overdoses of barbiturates or alcohol. Too often the drug is used to control appetite.

For narcolepsy treatment and for the treatment of children with hyperkinetic disorders there is no argument, but with the others in susceptible people the dangers are too great because it can induce psychic dependence and tolerance. Medical use must not bring on medical misuse and we must carefully supervise the patient. I have seen people who have gone to several doctors who unknown to each other are giving the amphetamine to the same patient.

With the amphetamines we do not have physical dependence but the psychological dependence does develop. With some they produce a euphoria and excitatory effect and this is the danger.

Too often the patient will present himself as a person who wants to reduce—that he cannot control his weight which is basically a psychological problem and will start with his amphetamines to help with his weight reduction. Narcolepsy and the hyperkinetic will take small amounts of the drug and there is no fear here because the use is supervised—not like weight reduction where sometimes this amphetamine is given for years.

Black market sales are the thing which should bother us. There is a marked rise in the unsupervised use of the drug. There is lack of understanding that the therapeutic action can constitute misuse. We are concerned with the misuse which is where the professional enters the picture and abuse, where there is self-administration. Self-administration means as a rule a path to increased need because of the tolerance factors, sometimes very abnormal behavior and psychological dependence.

The amphetamines were introduced in 1920. Small doses can lead to a feeling of well being and as this is increased, fears, tremors, and excitement come in. We have come to realize that the amphetamines should be a prescription item—not a thing for inhalants as was before sold over the counter or appetite depressant which should never be sold over the counter.

A book called "Drug Dependence", which has been published by the Council of Mental Health, reported that in Japan during the years 1940–50—500,000 to 1 million people were abusing the drug regularly, that many cases of toxic psychoses developed and that in 1954—55,000 abusers of amphetamine were arrested by the Japanese police for crimes. This same book quotes the fact that Great Britain has a great problem with the abusers of amphetamines.

The use of amphetamine for weight reduction is of questionable value—some experiments have produced the same effects with placebos. With milder depression where it is used sometimes as a stop gap—the basic reason should be sought.

In acute drug overdosage it has its values. To increase performances either in the athletic or social world is dangerous as a routine measure.

Large quantities of these drugs are available in the black market—for example in lower socioeconomic neighborhoods and in "Bohemian" gathering places.

There has been an alarming increase in the number of speed amphetamine abusers, usually teenagers or young adults who use the drug for kicks—speed-freaks are not uncommon as a result, "mainlining" for a greater kick. Very often they use a barbiturate to bring them down. The pattern we worry about is self-administration—where increasing amounts are used to produce the desired euphoria. This leads to chronic abuse and sometimes death.

A report from the California Rehabilitation Center in Corona written by Dr. Kramer and coworkers, published in the AMA, stated that in San Francisco there were 4,000 individuals regularly taking amphetamine intravenously.

All their patients used the Dexedrines orally at first—going up to 150–250 mgm. per day then went on to mainlining. Intravenously 40–50 mg. were the initial dose as a rule, but as tolerance increased they needed more.

From a psychological viewpoint they noted disorganization and compulsive behavior, paranoia patterns, etc. Paranoia develops in the mainlining people.

It is evident that there is an extensive use of amphetamine intravenously, a form of drug abuse with addictive and relapse potential comparable to that of opiates or cocaine and some prefer this to heroin. This form of drug abuse is extremely disabling from a social and psychological standpoint, may lead to prolonged psychosis or brain damage. Because of the relative ease of illicit manufacturing and the less urgent need to maintain uninterrupted use, the users will not be involved in crimes against property as are the oplate users. But crimes

of violence are greater because of the uncertainty and the paranoic fears which develop.

The abuse of amphetamine is a medical problem, some behavioral disorders preceding and predisposing the drug abuse. The people must be studied independently to find out why and then treatment can be perfected, and this treatment must be continuous—even though there is relapse—and with understanding.

Mr. PEPPER. Doctor, then you would favor, out of your experience, a ban on the manufacture of these drugs, because they are not needed and they are very harmful to people?

Dr. SHEPPARD. I favor a complete ban and a complete regulation of these drugs.

Mr. PEPPER. And you have found substitutes for the legitimate uses that are claimed for these drugs?

Dr. SHEPPARD. I do not know enough about narcolepsy, because as I have said——

Mr. PEPPER. At least in the treatment of obesity?

Dr. SHEPPARD. Obesity, that is a joke. Those fat doctors you have heard about, as they are called over in Miami Beach, where they see a patient once and come over and get their pills and play a record, a sort of self-hypnosis, have these fat mamas waiting out in the streets to take their pills—this is ridiculous. You cannot do anything with them. The medical society can't do anything with them because they are not members of the AMA. They have a Florida State license and try to get that license removed.

Mr. PEPPER. Has it come to your knowledge, and I am not speaking now of Dade County, has it come to your knowledge or reached your understanding that a lot of doctors are making a racket out of these so-called weight reduction pills?

Dr. SHEPPARD. Let me put it this way: Having sat across the table from many patients, they come in and say, give me a pill for weight reduction. You have to make a choice. You have to tell that patient to go jump or you are going to give him something. It is up to the individual doctor. If you are trying to maintain your ethical standards, you tell him to go jump and tell him it is nonsense, because most compulsive eating is a psychological problem. The individual weighing 300 pounds needs psychological attention. It is as you said before or somebody said—are you a psychiatrist, no—to a M.D. That is very true. They need psychological help more than they need anything else.

You cannot just give them the pill. I bet you if you take 20 overweight people, give 10 placebos, 10 of the so-called amphetamine products, of these 10, they will equal in their rate.

I also want to emphasize one thing, that crimes of violence are severe with your amphetamines, because these kids are mainlining. When they are mainlining, they go out and hunt. It is not so much a crime against property with your speed as it is crimes of violence, because they become completely disoriented, especially if they are on a rush. And some of those kids will stay up 10 or 12 days.

Mr. PEPPER. So the prevalence of these drugs is not only causing physical injury to a lot of people, but it is also promoting crime among the younger people using these drugs?

Dr. SHEPPARD. Yes. I feel very strongly about that because I have seen so many. We have a drug prevention information clinic to which the schools and the juvenile courts refer their children. We see a

great deal of it, much more. It is cheaper to buy speed, it is just as addictive as heroin, just as addictive. There are withdrawal signs with speed, do not let anybody tell you differently. There are withdrawal signs from speed and it is dangerous.

Now, I have worked with them clinically. I have not written books but I have worked with them on the bedside.

Mr. PEPPER. You have seen some tragic cases from the use of these drugs by young people?

Dr. SHEPPARD. Yes. Since I started working with drugs in 1953, I have seen some severe tragedies.

Mr. PEPPER. A professor at the University of California told me in San Francisco recently, he assumed that, in his acquaintance, among his circle of friends, there are about 1,000 people. He said, "Out of those people that I know, I personally know of nine people who have been killed or lost their lives or committed suicide by the taking of these dangerous drugs, and I know of two who have committed murder because of being under the influence of these drugs."

Dr. SHEPPARD. I would buy that and I think that these pills like No Doz, which you can buy over the counter, which have a stimulant in them, and the fact that the bus driver has to have a fistful of "bennies" in his pocket before he takes off on a trip is ridiculous. He does not have to have it.

Mr. PEPPER. Mr. Waldie?

Mr. WALDIE. Just one question.

I thought your testimony was extremely credible, Doctor, and helpful. Is a hyperkinetic child also the neurologically handicapped child? Is that the same thing?

Dr. SHEPPARD. No. These children, 95 or 98 percent out of 100 will have a good IQ, as we use that term, their electroencephalogram will be normal. For some unknown reason, Dexedrine does increase their attention span, it does help them coordinate better with their classes, and they do better. I do not think it has ever been determined why.

Mr. WALDIE. Thank you.

Mr. PEPPER. Mr. Wiggins?

Mr. WIGGINS. What is the chemical composition, if you know, Doctor, in No Doz?

Dr. SHEPPARD. I tried to find out before I came up here, but it is related to one of the amphetamines. Those bennies and the Wyamine; fortunately, the Wyamine inhalers and the Benzedrine inhalers have been taken off the market.

We had a kid the other day, a speed-freak—if you have had experience with these kids, a speed-freak will shoot anything, I kid you not—from peanut butter, which they have melted down. The question was asked before, can they get the Dexedrine from the pill? Yes, they will soak it, just like they took the darned paragoric. Any kid who knows anything knows you can take three ounces of paragoric and boil it down and strain it and you have a good fix. They will do the same with any Dexedrine pill, they will soak it and shoot it. The body can take a lot of insult. They will soak the coat off and shoot it.

Mr. WIGGINS. Let's go back for a moment to No Doz.

Dr. SHEPPARD. I could not tell you too much. I tried to find out. It must be in the amphetamine range.

Mr. WIGGINS. Have you observed in your practice any person who has abused the use of No Doz and had an adverse effect?

Dr. SHEPPARD. Yes.

Mr. WIGGINS. Can you describe what you found out?

Dr. SHEPPARD. You will find a very excitable individual. You will find a young adolescent who cannot sit in a chair, will walk around, can't fall asleep and you are going to have to give him a down to bring him down.

Mr. WIGGINS. And you have attributed that to cases of abuse of No Doz?

Dr. SHEPPARD. Yes. I had a kid walk in the office, the clinic, the other day who had taken six of those Compoz tablets; taken six at one time. You are supposed to take one twice a day. She was a walking zombie, a 17-year-old girl.

I think the suggestion that was just made that the manufacturer should be held liable—it has long been my opinion that the advertiser who makes a profit from the ad should be made liable as much as the manufacturer for putting these drugs either on the air or in the paper.

Mr. WIGGINS. Thank you, Doctor.

Mr. PEPPER. Doctor, just one question. What's the treatment for the abusive use of this kind of drug?

Dr. SHEPPARD. It is just as hard as heroin. It is just as difficult to treat a speed-freak as it is to treat a heroin addict. The only treatment is mild tranquilization and total abstinence and psychological treatment at the same time. As you mentioned before, no withdrawal ward or no addiction center should be without beds for the use of speed-freaks or speed users or the LSD youngsters. It should be all inclusive. I mean we are focusing too much on our heroin addicts and forgetting that the younger people are using the other stuff.

Mr. PEPPER. Thank you very much, Doctor. We appreciate your coming up.

Our next witness is Dr. David C. Lewis. Dr. David C. Lewis is an associate in medicine at Beth Israel Hospital in Boston and at Harvard Medical School. Born in 1935, Dr. Lewis received his A.B. from Brown University in 1957, and his M.D. from Harvard Medical School in 1961.

Dr. Lewis is involved with numerous community activities related to drug treatment, education, and adolescent problems. He is director of the Medical Service, a free clinic in Boston that offers medical, psychiatric, and social services to young people and acts as a referral agency to the other existing facilities in Boston. He is chairman of the Drug Treatment and Drug Education Committee of the United Community Services of Metropolitan Boston. In addition, Dr. Lewis is an adviser to the study of the Rehabilitation of Drug Dependent Persons for the New England Governors Conference, and a member of the Massachusetts Attorney General's Advisory Committee on Drug Problems.

His numerous publications include "Narcotics Usage: A Spectrum of a Difficult Medical Problem," New England Journal of Medicine (1964) and "Narcotic Usage: The Doctor-Patient Relationship," United Nations—Bulletin on Narcotic Drugs (1967), he coauthored both articles with Dr. Norman Zinberg. Dr. Lewis is the author,

with M. Freedman and A. Stolow, of "Utilizing Drug-Experienced Youth in Drug Education Programs," Journal of National Association of Secondary School Principals (September, 1969). Dr. Lewis has an article entitled "Drug Education" that is in press for the same journal for December 1969. Also in press is "The Drug Experience: Data for Decisionmaking. A Comprehensive Drug Education Curriculum for Secondary Schools, Churches, and Community Groups," Boston: City Schools Curriculum Service, Inc. (February, 1970).

We are very pleased to have Dr. Lewis honor us with his presence and we welcome his statement.

STATEMENT OF DR. DAVID C. LEWIS, ASSOCIATE IN MEDICINE AT BETH ISRAEL HOSPITAL AND HARVARD MEDICAL SCHOOL, BOSTON, MASS.

Dr. LEWIS. We have only recently understood the spectrum of amphetamine abuse and indiscriminate amphetamine use. Other speakers have spoken about intravenous amphetamine use among young people and the oral use of amphetamines among young people. I think I should also say that many adults use excessive amounts of amphetamines and that these are often prescribed by physicians initially for weight control and for fatigue.

To say that there are no indications for these prescriptions, I think is to be really unfair to many of the patients who receive these drugs and to many physicians who prescribe them. I do feel, as some of the previous witnesses have testified, that these drugs are overused. I do not feel that they are worthless for the problems of depression, fatigue, and overweight. They are effective in some patients.

The question is, how do you regulate the "some patients"? Do you regulate by legislation or do you regulate by education and letting the doctor and patient make the decision?

I would really choose the latter course, not the legislation. I am not in favor, as a practicing physician, of having my medical judgment regulated. I am in favor of the Food and Drug Administration determining whether a drug is efficacious for the purpose that it is issued. I am not in favor of having someone tell me that I cannot use my clinical judgment in a particular patient to use amphetamines for the treatment of overweight. I have done so, and I have found amphetamines effective in some cases where other drugs have not been effective. While I do not use the drug frequently, I would like to retain the option of use in selective patients.

Mr. PEPPER. How can abuse be prevented, Doctor?

Dr. LEWIS. It makes quite a difference whether you are considering intravenous amphetamine abuse or whether you are talking about a housewife taking amphetamines continuously because it helps her get through the day. I would like to make some of those distinctions, because I think they are important when you consider legislation.

I am not sure how much restriction on medical amphetamine use will affect intravenous amphetamine abuse. In my statement, I cite a survey that I conducted in an adolescent free clinic which would support the fact that the widespread use of amphetamines is related to it abuse and in a specific way; namely, that most intravenous amphetamine users had used oral amphetamines before they used in-

travenous amphetamines and interestingly enough, they did not buy these illicitly on the street but often obtained them in their homes. In that way, use and abuse is connected.

To restrict amphetamine availability in the home might affect abuse patterns but I do not think it is going to wipe out abuse by young people any more than removing heroin from the medically available opiates in 1925 solved the heroin abuse problem for us.

In terms of the indiscriminate use connected with medical prescriptions, I think that some regulation is reasonable.

For instance, amphetamine prescriptions and records of such prescriptions, sales, supplies, and the like could be kept in somewhat the manner that opiates are now handled. I would consider that an acceptable regulation, not interfering with my personal decision about how to treat my patient, but making me better aware that this is a drug that I have to be thoughtful about the indications when I prescribe it to a patient and the patient has to realize this also.

Mr. PEPPER. Would you limit in any way the manufacture of these drugs by the drug company?

Dr. LEWIS. Manufacture should be very, very carefully controlled, since a large proportion of legally manufactured amphetamines are illicitly sold and used.

I am not sure I could place a number limit. I do not think that is sensible.

Mr. PEPPER. What about the Federal Government having to give a license to those who are manufacturing?

Dr. LEWIS. Yes.

Mr. PEPPER. Would you favor that?

Dr. LEWIS. Very definitely.

Mr. PEPPER. Would you favor the periodic renewal of that license?

Dr. LEWIS. Yes. This would go for all drugs that are prone to produce severe dependency. That is barbiturates, some tranquilizers, and amphetamines.

Let me say parenthetically in terms of banning a whole class of drugs or substances, in answer to a previous discussion that was held here this morning, that No Doz is caffeine and No Doz in fact can create problems, but this may not lead us to say we should ban caffeine. So I just would like to reiterate the point that there are certain kinds of controls that I feel would be more sensible at this time than others.

(The prepared statement of Dr. Lewis follows:)

PREPARED STATEMENT OF DR. DAVID C. LEWIS, ASSOCIATE IN MEDICINE AT BETH ISRAEL HOSPITAL AND HARVARD MEDICAL SCHOOL, BOSTON, MASS.

There is no debating that amphetamines are among the most widely used and abused classes of drugs in the United States. The estimated 8 billion doses produced annually represent a month's supply for every man, woman, and child. It is further estimated that approximately half of these 8 billion capsules and tablets find their way into illicit channels of distribution. During the last 5 years, amphetamine abuse has become more evident in the United States. This has largely been due to intravenous amphetamine use, particularly methamphetamine use, among young people. In recognizing the dependency producing liability of amphetamines and the risks involved in repeated amphetamine use, we have also become more aware of the numbers of middle-aged Americans who take excessive amounts of amphetamines. There now seems to be quite a spectrum of indiscriminate amphetamine use, including: (1) young people who experiment occasionally with amphetamine tablets and capsules; (2) intravenous amphetamine use, often in high doses, sometimes in association with barbiturates, LSD or

opiates; (3) spree amphetamine users, those who take amphetamines primarily on a weekend binge; and (4) adults who take excessive amounts of amphetamines, their drugs often having been initially prescribed for weight control or fatigue by a physician.

My own experience and interest in these drugs is from three viewpoints. First, as a practicing internist, I have prescribed amphetamines to my patients and have seen some of the benefits and complications of these drugs. Second, in an administrative capacity as director of a medical outpatient department and emergency unit, I have had the opportunity to observe how other physicians prescribe these drugs, and also ways in which medical patients can take these drugs indiscriminately. Lastly, I have had a special interest in drug abuse problems in the city of Boston and have seen approximately 50 amphetamine abusers, most of whom were young people using high dose intravenous amphetamines. It is on the basis of this experience that I will try to balance the medical usefulness of these drugs against their liabilities.

Current medical usage is summarized in a report by the American Medical Association Committee on Alcoholism and Addiction, published in the September 19, 1966 Journal of the American Medical Association. Rather than list all these medical uses and detail the evidence for each, I believe it would be fair to summarize the situation as follows:

There are some special situations in which amphetamines have been found to be extremely valuable in treatment. Examples are narcolepsy, a rare (a Mayo Clinic survey estimates one in 8,610 admissions to have this condition) disease, the symptoms of which consists of falling asleep at unpredictable times and another, the hyperkinetic disorder of children, in which these children are so hyperactive that they often are not able to participate in school. Amphetamine therapy is an important part of the treatment of these conditions.

The major medical usage of amphetamines is for three commonly encountered situations, first, for the treatment of overweight, using amphetamines as an appetite suppressant; second, for the treatment of fatigue states; and third, for the treatment of mild depression. There is no doubt in my mind that amphetamines can be extraordinarily effective in the treatment of each of these problems. The issue is one of selectivity of patients, or how frequently should they be prescribed for these conditions? Certain patients are afforded dramatic weight control through the aid of these drugs and in some patients, amphetamines seem to work where other drugs have failed. Furthermore, there are patients who have problems with fatigue and can be helped by amphetamines. It may be a short-term problem. For instance, I prescribed amphetamines to a night watchman who had a propensity to fall asleep on his job, and with a single 5-milligram dose was able to stay awake through the night and had no ill effects from the medication. More commonly, the fatigue for which amphetamines are prescribed is not so short-lived, and patients may become dependent on the drug, not in the sense of taking large daily doses, but in the psychological sense of feeling that the drug is necessary for them to get through a day's work.

Many patients in this category, in my experience, have been middle-aged housewives. In certain of these patients, amphetamines do, in fact, allow the individual to get through a day's work, where without the drug this would not take place. Such a situation could be compared with the daily use of tranquilizing drugs in other patients to allow them to function. The last indication, that of mild depression, is not as separate a category from the first two as it may seem, since depression is often an underlying force in overweight problems and in fatigue. Some patients with depressed states seem to benefit from the stimulatory effects of the amphetamines, but these are very few in my experience. I note the difference in prescribing patterns between my psychiatrist colleagues, who seem to hardly ever use amphetamines in the treatment of depression, even mild depression, and other physicians who seem to use the drug for this purpose more frequently.

In summary, amphetamines are valuable and powerful pharmacological agents, whose medical use can be very beneficial for some patients. For this reason I can see no persuasive argument for limiting their availability for the medical conditions in which they have proved to be efficacious. Within the realm of medical usage, I would feel that a physician should be free to use these drugs in whatever manner that is considered in the best interests of the patient. On the question of the frequency of the medical usage of amphetamines, I feel that these drugs are overprescribed by physicians for weight reduction, fatigue and depression, and overused by patients for these three conditions. The prob-

lems resulting from overuse are not just limited to untoward dependency occurring in patients under medical therapy, but that these drugs have become so widely dispersed in our society that their ready availability becomes a factor in their abuse by young people. Intravenous amphetamine use, which in my experience is as medically hazardous as heroin use, has been increasing in Boston over the past 3 years. In my survey of 50 young intravenous amphetamine users, over 90 percent had experimented with amphetamine tablets or capsules prior to their use of intravenous amphetamines. The majority of these tablets or capsules were not purchased illicitly on the street, but were obtained from home medicine cabinets, a testimony to their availability.

In considering methods of control, we already have strict regulations concerning illicit possession, distribution, and sale of amphetamines. Within the area of medical usage, we might now consider some regulation of the form of amphetamine prescription and the records that a physician is required to keep on these drugs. In the long run, though, it is my hope that education, rather than legal restraints, will be the primary factor in promoting the sensible use of drugs.

IN CONCLUSION

1. Amphetamines are valuable medical drugs and should be available to the physician for the therapies that have been proved to be efficacious.
2. Amphetamines are, in my opinion, overused in the United States today, and both doctor and patient should be more sensitive to the indications for which they are prescribed and taken.
3. Amphetamine abuse is encouraged by the ready availability of the drugs in the home.
4. Possible regulation of the type of prescription that can be issued for amphetamines and records that a pharmacist and physician must keep on amphetamine supplies should receive serious consideration.

Mr. PEPPER. Due to the wide experience you have had in the Boston area particularly, have you observed any connection between the abusive use of these drugs and the commission of crime?

Dr. LEWIS. In the sense of suicide, yes, and self-destructive activity, very, very much so, especially in methamphetamine users.

In terms of my observation that this leads directly to violent criminal activity because of the drug itself and not because of the person who takes it, I have not observed this and I am not sure that at the moment, there is any persuasive evidence that this is the case. It is a big fear, it is often quoted, it is often talked about. It has been documented with another stimulant, cocaine, so it is not out of the realm of possibility that this will be the case. But I think it is a very soft fact at present.

Mr. PEPPER. Do you find among the young a growing abuse of the use of these drugs?

Dr. LEWIS. I do, and I am terribly concerned, as are other physicians, about this. I feel that the intravenous amphetamines are medically at least as harmful as heroin and that controls in this regard are essential. They happen to be physically self-destructive in addition to their psychological side effects and all the various criminal problems that one gets not from the effect of the drug, but in the process of obtaining the drug and raising money to buy the drug and all the rest.

Mr. PEPPER. Are there treatment centers in the Greater Boston area for those who have become abusive users of these drugs?

Dr. LEWIS. Not specifically for amphetamines. In the sense that psychiatrists and physicians who are interested in drug dependency have tried to treat individual patients, this is going on. In terms of setting up a treatment center specifically for this purpose, it is not going on. I really think the fairest statement of the situation, having just sat

through a conference to try to discuss the treatment of drug dependency, we have little idea how to approach this problem.

Mr. PEPPER. Do you think the Federal Government should aid the States and the local communities in providing a sufficient number of treatment centers to treat drug addicts and narcotics addicts in the various communities of the country?

Dr. LEWIS. Yes, I feel this is a great need and that Federal support is essential in this area. One of the reasons we do not have alternatives for referral of young people is that this therapeutic resource is little supported at present.

Mr. PEPPER. Mr. Waldie?

Mr. WALDIE. Doctor, are you in private practice also?

Dr. LEWIS. Yes, I am a practicing internist.

Mr. WALDIE. Do you have any patients for whom you prescribe the amphetamines in terms of their obesity problems?

Dr. LEWIS. Yes, I do.

Mr. WALDIE. The percentage of your prescription of amphetamines in your practice would roughly be what?

Dr. LEWIS. It would be very tiny in relationship to the other pharmacologic agents that I use. Certainly much less than the 8 percent—amphetamines manufactured relative to other drugs—that was quoted before.

Mr. WALDIE. That perhaps was misphrased.

For all the patients for whom you prescribe amphetamines, what percentage of those patients is obesity cases? Is that the greatest use in your practice of amphetamines?

Dr. LEWIS. Yes.

Mr. WALDIE. And what percentage of your practice where amphetamines are prescribed is found for the obesity cases? Would it be 90 percent?

Dr. LEWIS. You mean is 90 percent of my practice in obesity? No.

Mr. WALDIE. No, 90 percent of the total volume of amphetamines that you prescribe, is that a proper figure to ascribe to obesity cases?

Dr. LEWIS. I think it would be fair. As an internist, I have seen one case of narcolepsy. It is rare. And I do not see the hyperkinetic children. So I encounter indications for chronic fatigue and specialized fatigue problems and obesity. I do occasionally prescribe amphetamines for this purpose. I cannot really give you exact percentages.

Mr. WALDIE. When you prescribe amphetamines, is it fair in describing your practice to say you prescribe amphetamines primarily for obesity?

Dr. LEWIS. In my practice, that is true, that the indication that I have used more amphetamines for has been obesity patients who seem not to respond to other means of therapy. This is not my firstline medication for these patients.

Mr. WALDIE. Of the amphetamines that you prescribe, the total, what percentage would be going to obesity patients? Are we talking of 100 percent or 99 percent?

Dr. LEWIS. We are probably talking in the order of 90 percent expressed in terms of the number of tablets that are prescibed. By the chronic nature of the obesity problem, one keeps up this therapy for a matter of weeks or months, looking for results, not years.

Mr. WALDIE. So the primary use of amphetamines in your practice is for the obese patient?

Dr. LEWIS. That is the indication for which I have used it the most.

Mr. WALDIE. Primarily in your practice, the amphetamines are prescribed for the obese patient. If you were to be deprived of the amphetamine, you would find your greatest deprivation would be in the treatment of the obese patient?

Dr. LEWIS. That is correct.

Mr. WALDIE. Thank you.

Mr. WIGGINS. You said this morning, Doctor, that you would object to the banning of amphetamines because that would deprive you of your option as a doctor to prescribe them in those cases where the prescription was indicated. Does it strike you as being wrong, does it similarly offend you, that the Food and Drug Administration can act against something like cyclamate, for example?

Dr. LEWIS. No, it really does not.

Mr. WIGGINS. In what way would you distinguish the cases?

Dr. LEWIS. Well, I really distinguish the difference between a Federal agency determining efficacy on scientific evidence and scientific grounds and requiring manufacturers and distributors of drugs to indicate in their advertising when indications have been proved efficacious. I distinguish that from laws that say this class of drugs will not be available for medical prescription or, if you prescribe these drugs because we feel there is drug abuse or because we feel this is a problem in our society, you are going to get into difficulty because we do not think that is the right thing to do. I think there is a difference between making the judgment on the basis of scientific evidence and efficacy and making the judgment on the basis of should we regulate medical practice in this way. I can see a difference, I can feel a difference as a physician.

Mr. WIGGINS. I suspect that there was no doubt about the efficacy of cyclamate being a sweetener, if that is indeed its function, that the judgment of the FDA was not on the basis of its efficacy for that purpose, but rather that it posed a risk of harm to human beings who consume it. The risk was not 100 percent, I speculate, but rather was much, much lighter than that. Nevertheless, it was sufficient to prompt the FDA to outlaw the drug.

Let's switch now to a recent announcement by the HEW banning the domestic use of a certain pesticide, DDT. I doubt that anyone would question the efficacy of DDT in killing bugs, but it posed a risk. The risk was not acceptable.

Do you not think that we might analogize and say that an amphetamine might be an efficacious drug in the treatment of obesity patients, but that it poses a risk and that the risk is not acceptable?

Dr. LEWIS. I think to make that kind of judgment, you would have to have the data which in fact, I do not think we have. For example, balancing the data that amphetamines help in the treatment of obesity—which incidentally is soft data—against the harm that is done to those individuals who in the course of medical practice take it for obesity.

The decision of whether taking amphetamines off the market for the treatment of obesity will affect drug abuse in other populations is a

much more subtle one and is of a different category than the showing of cyclamates producing direct harm or the showing of amphetamines producing direct harm in those medical uses of the drug. I think that is the distinction that I would make.

Mr. WIGGINS. If I understood your testimony correctly, you found that in your own practice, the abusers of amphetamines started with the oral pill rather than intravenous injections.

Dr. LEWIS. That is correct.

Mr. WIGGINS. I take it that in your experience, you have found that the tablet was of some legitimate manufacture.

Dr. LEWIS. Yes.

Mr. WIGGINS. We really get into the clandestine use when they started shooting it, as they say; is that so?

Dr. LEWIS. I do not——

Mr. WIGGINS. A typical clandestine product—a powder, for example, would go into the real abusing market, would it not?

Dr. LEWIS. I am not sure what you mean by the word "clandestine." It may be manufactured by a legitimate manufacturer and get into that market. I do not have the impression that amphetamines are being manufactured specifically for illegitimate sale on the street.

Mr. WIGGINS. What I am trying to get at is that pills that are originally manufactured for a proper medicinal purpose such as the treatment of obese patients seem to find their way into the hands of other than those who are suffering from that disability.

Dr. LEWIS. No question.

Mr. WIGGINS. And you can confirm that in your own practice?

Dr. LEWIS. Absolutely.

Mr. WIGGINS. And the prolonged use by those persons is followed by drug abuse which you have described as being as harmful as heroin.

Dr. LEWIS. I think that is true. I do not think it is inconsistent with my statement. I think the overuse of amphetamines in this country is a factor in drug abuse by young people, in indiscriminate use by young people. Their ready availability is a factor.

Mr. WIGGINS. If this committee wanted to accumulate additional evidence on the question of whether or not the pills should be outlawed, can you make any suggestions as to witnesses we might call?

Dr. LEWIS. I would look for those who have studied the relative harm of amphetamines in their medical-indicated use. I cannot suggest individuals, but I think I would seek evidence in that category, for I believe in that category that you could make your most cogent points.

Mr. WIGGINS. Thank you.

Mr. PEPPER. Thank you very much, Dr. Lewis. We appreciate your coming.

We have one more witness now, Dr. George R. Edison.

Doctor, would you come forward?

Dr. George R. Edison is the director of the student health service at the University of Utah and chairman of the board of trustees of the Community Drug Crisis Center. He received his M.D. in 1953 from Columbia University College of Physicians and Surgeons, and did residency work in internal medicine and psychiatry at the University of Utah Hospital and the University of Rochester.

The community drug crisis center in Salt Lake City serves as a free rehabilitation clinic, and through his work with the clinic Dr. Edison

has become acutely aware of the problems of drug abuse. Dr. Edison is in private practice in internal medicine also in Salt Lake City. He is also assistant clinical professor of internal medicine and associate clinical professor of preventive medicine at the University of Utah College of Medicine.

Doctor, you bring a valuable background to us today. We welcome your statement.

STATEMENT OF DR. GEORGE R. EDISON, DIRECTOR OF STUDENT HEALTH SERVICE, UNIVERSITY OF UTAH, AND CHAIRMAN OF THE BOARD OF TRUSTEES OF THE COMMUNITY DRUG CRISIS CENTER IN SALT LAKE CITY

Dr. EDISON. Thank you.

Mr. PEPPER. Do you have a prepared statement?

Dr. EDISON. I do.

Mr. PEPPER. Would you care to summarize it and put it in the record, or do you want to read it—which?

Dr. EDISON. I would feel more comfortable reading it, inasmuch as I have spent the last 15 hours trying to get here from Salt Lake.

Mr. PEPPER. We will be very glad to hear you, Doctor.

Dr. EDISON. Thank you. I beg your indulgence if I go over some repetitive material since, I am sorry, I do not know what preceded me. Thirty-nine years ago a drug called amphetamine was first described in the medical literature as a potent sympathomimetic agent with significant effects on blood pressure. Within 5 years it was also found to have actions as a bronchodilator and a respiratory stimulant, and to have potent effects on the central nervous system, specifically stimulation and reduction of appetite.

The use of this drug, and its numerous derivatives, such as dextroamphetamine and methamphetamine has grown remarkably in the last 30 years. They have been used for a wide variety of medical conditions, including obesity, mild depressive reactions, epilepsy, parkinsonism, narcolepsy, depression of the central nervous system due to intoxication by barbiturates and other drugs, and hyperkinetic reactions of children. They are also commonly used as stay-awake drugs—the truck driver's friend—and to increase physical performance.

The 1968 edition of the Physicians' Desk Reference (a compilation of package insert material) lists a total of 51 amphetamine preparations, either alone or in combination with sedatives, tranquilizers, and even vitamins, produced by 29 companies. In some cases the amphetamine is the company's only product.

The medical profession and the pharmaceutical industry have told us for years that these are very useful drugs in the practice of medicine but that they should be used only under medical supervision. The interesting thing to me is that in the last 10 years the quantity of these drugs produced and consumed has proliferated, while the list of legitimate medical indications has shrunk. In my opinion and in the opinion of a number of other physicians the list of legitimate medical indications has now shrunk virtually to zero. There are three reasons for this shrinkage:

1. Better drugs have become available for conditions like parkinsonism, epilepsy, and depressive reactions, and so amphetamines are no longer widely used for these conditions.

2. In the case of barbiturate intoxication there are no drugs which are as safe or effective as other nondrug methods of treatment, specifically artificial ventilation and artificial circulation support.

3. In the case of obesity, no better drugs have come along, but it has slowly become apparent that amphetamines are ineffective in the real treatment of obesity and quite unsafe because of their dependence-producing potential. It is true that most people can lose weight faster over a period of weeks or months while consuming amphetamines. Whether this is due to a direct effect on the appetite control center of the brain or to an antidepressant effect is not clear. But in almost all cases the weight is rapidly regained when the drug is stopped because proper methods of eating have not been developed. While I am not aware of any data to support this feeling, I do have the notion that rapid fluctuations in weight may be more harmful to the body than maintenance of a constant obesity.

The only remaining medical indications for amphetamines, therefore, are narcolepsy and hyperkinetic medical problems in children. Even for these two, there are other drugs, for example, methylphenidate—or Ritalin, the trade name—for narcolepsy and most recently imipramine—trade name Tofranil—has been described as a better drug for most behavior problems of children.

During this same period of time, there has been a tremendous growth in the illegal and casual use of amphetamines, strictly for their stimulant effect on the central nervous system. They are now recognized to be a group of drugs with a very high potential for producing psychological dependence. In addition to dependence there are major physical effects associated with the intravenous injection of these drugs (particularly infections), and they produce major behavioral toxicity. The behavioral toxicity with high doses often reaches the proportions of what has been described as the "amphetamine psychosis," a condition characterized by distortion of reality, impairment of judgment, and a hyperactive paranoid state with hallucinations.

This, then, is a group of drugs which produces serious toxic effects in all three of the major areas that we are concerned about in the field of drug abuse; that is, dependence, physical toxicity and behavioral toxicity. Virtually no other drug currently being abused has this wide a spectrum of hazards, and I would include here the opiates, the hallucinogens, and marihuana. Amphetamine abuse is the major drug abuse problem in the United States outside of the large cities where heroin addiction is so prevalent.

Amphetamines provide one of the major ironies of the whole field of drug abuse. We continue to insist that they are good drugs when used under medical supervision but their greatest use turns out to be frivolous, illegal, and highly destructive to the user. People who are working in the field of drug abuse are finding it most difficult to control the problem, partly because they have the reputation of being legal and good drugs.

In my personal experience as a practicing physician I find I have made errors in the prescription of amphetamines. In the case of a young man in a professional school who consulted me for sleepiness

and ineffective studying, my prescription of these drugs allowed both patient and physician to neglect the underlying depression which eventually caused him to flunk out of school. Had this depression been recognized, early treatment might have saved a career.

In another case of a young woman with a major emotional disturbance and a moderate depression, my prescription of amphetamines led to dependence on them, thereby complicating treatment.

Practically every physician in practice, almost every day, is asked by obese patients for a drug that will help them to lose weight. Often, the original purpose of the drug was forgotten while the long-term dependence developed. This has become known as the "tired housewife" syndrome. I frankly feel that most of the obese patients who are taking amphetamines are dependent on them. In an addendum I will cite authorities in the field to substantiate this. For my part, I have stopped prescribing them entirely except in the rare case of narcolepsy. My own experience with behavior problems in children is nil.

I feel very ambivalent about legislation or regulation in the area of personal behavior. As a physician, I feel particularly ambivalent about the regulation of my right to use a drug when I feel there is an indication for it. Furthermore, it puts the emphasis in the wrong place—on the drug rather than the user. I would prefer to see the medical and pharmaceutical professions voluntarily abandon the production and use of these drugs, but if this is not rapidly forthcoming, I feel that legislation may be necessary. Making amphetamines illegal will not solve the amphetamine abuse problem by any means. It will simply drive it underground and into illegal channels. What it will do is show the young people using drugs that we, the establishment, are at least a little less inconsistent in our attitude toward drugs than we are now. The bad model that adults are providing must be changed if we are ever to make inroads into the drug abuse problem.

I would like to respond to your questions and comments, but I have prepared a few more thoughts since preparing the statement. It turns out that amphetamines really do not conform, in my opinion, to the standards that we attempt to apply to every drug. That is, we need to show that there is a need for the drug, that the drug is effective, and that it is safe. On all three counts, I really do not feel that they qualify.

The drug companies, interestingly, themselves have shown their recognition of the poor performance of amphetamines by the constant introduction of new drugs that are related to amphetamine, but are proposed as being different and not carrying the side effects and the unfortunate dependence problems that amphetamine does. So far, to my knowledge, none of these drugs has panned out.

Then you ask why their production is continuing. I do not have the answer to that. But I was quite interested to learn most recently that one major drug company, Burroughs Wellcome & Co., has discontinued the production of the drug Methedrine. This is of great interest and irony, because Methedrine is Burroughs' trade name for methamphetamine. Methedrine has become, like aspirin, the generic term among kids, at least, and among the public, I think, for amphetamines, for speed. This brand of this drug will no longer be made, but the name Methedrine will, I am sure, continue. There are at least four other companies that I am aware of that have dropped

their amphetamine products out of the PDR from last year to this year. So the companies themselves, I believe, are beginning to see the problem. Burroughs and the other companies deserve our thanks and congratulations.

I frankly feel that if amphetamines remain legal, you almost have to legalize also heroin, LSD, and marihuana in order to remain consistent, because they also have therapeutic potentials and amphetamines just are not that much different from these apparently terribly dangerous drugs.

Mr. Pepper. Does heroin have some medical purpose that is legitimate?

Dr. Edison. It is an excellent pain killer, surely. In fact, in England, it has been used—I am not sure how widely, but there was a report about a year ago of its experimental use in heart attacks.[35]

Mr. Pepper. Doctor, suppose that the drug companies that manufacture these amphetamines did not respond to the public appeal made by the Food and Drug Administration or by the Department of Health, Education, and Welfare. Would you recommend any particular type of legislation to either limit or prohibit the manufacture of these drugs by them?

Dr. Edison. Well, I do not know that—I am not familiar enough with legislation. I do not believe any new legislation is really needed. I wonder if the Food and Drug Administration could not simply apply the standards that they apply to every drug, that it has to be shown to be effective and safe. We know that they are not safe—at least, I know that they are not safe. In an addendum I will cite evidence substantiating their ineffectiveness.

(The addendum referred to by Dr. Edison follows:)

Addendum Regarding Ineffectiveness and Danger of Certain Drugs

In my testimony to the House Select Committee on Crime I stated that we had witnessed a remarkable growth in the use of amphetamines for conditions in which they are now outmoded or ineffective, while at the same time we have only in the last 10 years really become aware of the serious hazards associated with the use of this drug both in "respectable abusers" and "speed-freaks."

I now wish to document the evidence which supports my position that these drugs are ineffective.

I will not detail their use in parkinsonism, epilepsy or central nervous system depression due to barbiturate intoxication because virtually no one questions their obsolescence in these conditions.

For narcolepsy and hyperkinetic behavior in children there may still be a legitimate use although in the former methylphenidate (Ritalin) has been found effective, and for the later imipramine (Tofranil) may be more effective than amphetamines (Journal of AMA, vol. 208: 1613, 1969 (June 2) in the medical news section).

For mild depressions I think you need a psychiatrist to argue the ineffectiveness and hazards of amphetamines. I would feel that it is dangerous and illogical to use a drug with an addictive potential for a condition like depression, in which we know the potential for dependence on many kinds of drugs including alcohol and barbiturates is quite high. Severe depression is indeed the underlying mood in most speed-freaks. Several excerpts from Goodman and Gilman, the Pharmacological Basis of Therapeutics, third edition. 1965, may be of interest:

1. "The dibenzazepine derivatives, imipramine and amitriptyline, are the most widely used drugs for the treatment of depression. They may be considered successors to the MAO inhibitors, which for several years were the only effective

[35] MacDonald et al. Circulatory Effects of Heroin in Patients With Myocardial Infarction. Lancet 1 :1072, 1967.

agents available for this condition. The sympathomimetic amines, such as amphetamine and phenmetrazine, and similarly acting CNS stimulants, such as methylphenidate and pipradrol, were tried in the treatment of depression and found wanting except in certain mild cases in which a drug-induced acute euphoric state would suffice" (p. 198).

2. In the section on Monoamine Oxidase (MAO) Inhibitors: "Sympathomimetic amines and other stimulant drugs had been tried, but with little success in most cases" (p. 191).

3. In the section on the treatment of depression: "Amphetamine and related substances capable of producing mood elevation in relatively normal individuals have not been proven effective in depressions" (p. 204).

Obesity deserves a lengthier documentation because this is the area in which the amphetamines have had the widest use. First we should remember that obesity is a complex, lifetime problem with immense social and psychological determinants. Key factors in the development of obesity are oral dependence, the need for oral gratification, and inability to tolerate frustration, all of which promote drug dependence as well. It seems both dangerous and illogical to treat a condition with such strong oral dependent overtones with an agent which in itself causes dependence.

SHORT-TERM EFFECTIVENESS OF AMPHETAMINES IN OBESITY

This is accepted, but irrelevant in my opinion because obesity is a long-term problem. In addition it is likely that the short-term effectiveness is due to its stimulant effect, according to Thorn and Bondy, article on obesity in the Harrison's Principles of Internal Medicine, fifth edition, 1966: "As a result of stimulation, or a lift, the patient's drive toward overeating may be significantly modified and as far as he is concerned, the overall effect of the drug is appetite depressing. Obviously drugs which create such a state of euphoria may lead to habituation in certain individuals."

Modell, Status and Prospect of Drugs for Overeating, a report to AMA Council on Drugs, JAMA volume 173:1131, 1960, states: "Central stimulation, not a specific central depressant effect on the appetite, is then the common mechanism through which these drugs act; it is clear, therefore, why undesirable central stimulant effects which have constituted their chief clinical limitation, have thus far appeared to be indivisible from their anorexigenic action."

Few people question the fact that amphetamines are effective in the short-term for appetite control (as we have seen, most likely from the very effect which attracts speed-freaks to them). However, there is some doubt whether they are effective even in the short term. Again, quoting from Modell's article that we cited above: "The amphetamines present special problems in the evaluation of their effectiveness. Patients often promptly recognize the drug by one or another of the central stimulant effects (usually the lift). Thus, they can distinguish between drug and placebo when these are used in what theoretically appears to be a well-designed clinical evaluation with a double-blind control. In patients with emotional disturbances particularly, who include most compulsive overeaters, the ability to distinguish medication from placebo by any effect other than the one under examination (weight loss) makes it exceedingly difficult to prevent bias and psychological factors from shaping the apparent effects of the drug. This tends to reduce the sensitivity of methods of clinical evaluation of these drugs as well as to make it especially difficult to design a study in which these factors do not bias results. In other studies in which doses are so small as not to induce recognizable lift, the doses are likely also to be too small to influence overeating by pharmacological action and hence either indicate a negative result for what might otherwise be an effective drug or produce effects due entirely to placebo action.

"This raises the question of the validity of reports in which drugs of this series are said to have induced weight loss in a series of patients without causing any disturbing psychic effects."

LONG-TERM EFFECTIVENESS

Thorn and Bondy, in Harrison's Principles of Internal Medicine: "Depression of appetite by a pharmacologic agent can facilitate weight loss although it is apparent that as soon as the pharmacologic effect wears off, or the medication is

discontinued, appetite will return and weight gain will recur unless the patient's inherent capacity to control his food intake has been altered fundamentally. That the pharmacologic agent used for these purposes be devoid of serious toxic side-effects is axiomatic.

"Unfortunately there is no pharmacologic agent available at this time which acts primarily by depressing the 'appetite center'."

Albrink's article on obesity in Cecil-Loeb's Textbook on Medicine, 12th edition, 1967: The following is the entire discussion of amphetamines in the treatment of obesity, in an article of 8,100 words in which Dr. Albrink devotes 3,600 words to treatment: "Drugs. Appetite-suppressant drugs of the amphetamine group are effective for only a few weeks. Dependence on their stimulatory effect occasionally makes withdrawal a problem. Such drugs have no demonstrated role in the long-term management of obesity."

Stunkard and McLaren-Hume, The Results of Treatment for Obesity, Archives of Internal Medicine, volume 103:79, 1959: "Summary: A review of the literature on out-patient therapy for obesity reveals that the ambiguity of reported results has obscured the relative ineffectiveness of such treatment. When the percent of patients losing 20 and 40 pounds is used as a criterion of success, the reports of the last 30 years show remarkably similar results. Although the subjects of these reports are grossly overweight persons, only 25 percent were able to lose as much as 20 pounds and only 5 percent lost 40 pounds.

"Routine treatment of a hundred consecutive obese outpatients in the nutrition clinic of a large teaching hospital (the New York Hospital) was even less successful. Only 12 percent were able to lose 20 pounds and only one patient lost 40 pounds. Furthermore, 28 percent of the patients never returned to either the nutrition clinic or the referring clinic after their first visit. Two years after the end of treatment only two patients had maintained their weight loss." It must be said that only a few of the 100 patients in this particular study were treated with drugs, but the review of the literature in this article covered all types of treatment.

Glennon, Weight Reduction—an Enigma, Archives of Internal Medicine, volume 118:1, 1966: "Review of the literature since 1958 did not reveal a successful long-term study using a diet regime by itself or in combination with drugs, psychologic treatment, or an exercise program."

Astwood, the Heritage of Corpulence, Endocrinology volume 71:337, 1962: "All of us know that we can't get fat people to become slim by suggesting a diet, so we conclude for the time being at least, that obesity is incurable. The people who know most about how to treat the condition, or so they say, are our friends in the pharmaceutical industry. In the mail that we throw away every day we see extolled one or another kind of pep-pill or goof-ball. Take this and the fat melts away." Needless to say, Astwood, a renowned authority in the field of endocrinology, does not promote such treatment.

Modell, again from the article cited above: "Summary: New and logical pharmacotherapy for persons who overeat will more likely come with understanding of the processes involved than through the current practice of developing more variations on old themes which have already been well exploited and have not satisfied the need. There is really nothing new on the scene. There are no anorexients to fit specific disturbances in eating patterns and there are no useful depressants of the appetite center, wherever it may be. Total therapy must consider the psychosocial aspects of eating patterns and the desire to lose weight, as well as the psychologic or physiologic disturbance which has brought on the hyperphagia. In virtually every instance, motivation for losing weight as well as the psychological reasons for overeating are important considerations in determining the therapeutic regimes which are likely to be effective and to lead to sustained benefits. Current pharmacotherapy for persons who overeat has limited use. Insofar as drugs are concerned, at the very best, their potential is secondary to the elimination of the cause of the hyperphagia. Drugs which give assistance along the lines now available provide short-lived symptomatic relief only. These seem to be useful only as adjuvants to a carefully controlled diet and in many cases, some type of psychotherapy."

Perhaps the most telling evidence against the long-term effectiveness of amphetamines in obesity is the continuing controversy over their place in the treatment of this disorder after 30 years of use. A good drug is known to work and is accepted within a much shorter period of time.

In addition the pharmaceutical industry itself has told us indirectly that these drugs are inadequate by their repetitive introduction of new variations on amphetamines, and by the five companies I cited at the hearing which have discontinued their production of amphetamines in the last year. I think we should congratulate these companies and urge the others to follow suit.

In summary, I think the Food and Drug Administration now has sufficient evidence of the ineffectiveness as well as the danger of these drugs to remove them from the pharmacopoeia without resort to legislation. If FDA action or voluntary curtailment by the pharmaceutical industry does not develop, legislation will be necessary.

Dr. EDISON. You could argue that penicillin, for example, is a wonderful drug, but it can be dangerous and has killed many people. But it has also saved lives. To my knowledge, amphetamines have never saved a life, so it is not in the same league with penicillin, cortisone, and so on.

Mr. PEPPER. In other words, the minor benefits are far outweighed by the major detriments which derive from the use of this drug?

Dr. EDISON. I would feel that, sir.

Mr. PEPPER. You would still, however, not want to take away from the doctors, if it is to be permitted at all, the right to determine whether it should be used or not by many?

Dr. EDISON. Well, I would feel badly if that were taken away.

Mr. PEPPER. Doctor, are you a member of the American Medical Association? I assume you are.

Dr. EDISON. Yes.

Mr. PEPPER. Has the American Medical Association taken any position on these amphetamines?

Dr. EDISON. Well, the position is that they are useful drugs when used under a physician's supervision.

Mr. PEPPER. Have they taken any steps to curb the abusive use of them, either by prescription or as used by the public and by the manufacturers?

Dr. EDISON. They have come out with pamphlets, with literature. They have taken some steps.

Mr. PEPPER. Would it not carry great weight with American public opinion if the American Medical Association, representing the doctors of the country, men in whom the people have confidence and for whom they have respect generally, if the AMA were to advise the people that these drugs have a very limited medicinal purpose of a genuine character and that the manufacture and use of them should be sharply curtailed? Would that not carry great weight with the public?

Dr. EDISON. I think it would. I think they have done that. I do not think they have suggested curtailing the manufacture of them, but I think they have said just what you said.

Mr. PEPPER. It would help us in any legislation if we had the support of the American Medical Association in curbing the use and manufacture of these drugs.

Dr. EDISON. I am sure it would.

Mr. PEPPER. Assuming there is any legitimate use, how many would you estimate would be properly needed in the United States a year? How many of these tablets?

Dr. EDISON. I would just give you a wild guess that less than 1 percent of all prescribed amphetamines is needed for these two rare conditions.

Mr. PEPPER. The billions that the manufacturers nowadays put on the market is a gross excess of production and distribution, is it not?

Dr. EDISON. I think it is very gross. The only way that I can explain it is that there are a large number of American people who are actually dependent in a subacute way on these drugs. When I told several of my friends the other day that I was coming to Washington to present this material, one of them almost went into shock and said, oh, you cannot take away these drugs, I need them to keep my weight down. Her real need is because they make her feel good.

Mr. PEPPER. How old was that person?

Dr. EDISON. A lady in her 40's.

There is very strong evidence, for example, that although they are effective in the short-term treatment of obesity, their effectiveness here relates not to a depression of the appetite control center but to the stimulant effect that they provide. In other words, fat people may be taking the drug for just the same reason that the young teenage speed-freak takes the drug—the stimulant effect, the euphoria effect.

Mr. PEPPER. Mr. Waldie?

Mr. WALDIE. No questions, Mr. Chairman.

Mr. WIGGINS. Doctor, are you aware of any studies to help us determine the question, whether or not fat people are taking them for their stimulant effect rather than to lose weight?

Dr. EDISON. Well, I can quote you one of the deans of American pharmacology, Walter Modell, of Cornell University Medical College who has an article in the Journal of the AMA, volume 173:1131, 1960. He says, "Undesirable, central stimulant effects which have constituted their chief clinical limitation have thus far appeared to be indivisible from anorexigenic action."

One of the two major textbooks of medicine, Harrison's Principles of Internal Medicine, fifth edition, 1966, in the article on obesity by a professor of medicine at Harvard, George Thorn, and a professor of medicine at Yale, Philip Bondy, states:

> Unfortunately, there is no pharmacologic agent available at this time which acts primarily by depressing the appetite center. Patients on amphetamines experience a sense of well being after the ingestion of these drugs and it is thought that the reduction in appetite is a consequence of distraction. As a result of stimulation or a lift, the patient's drive toward overeating may be significantly modified and as far as he is concerned, the overall effect of the drug is appetite depressing.

Mr. WIGGINS. Doctor, are you familiar with the drug Percodan?

Dr. EDISON. Yes.

Mr. WIGGINS. What is it?

Dr. EDISON. Percodan is used as an analgesic.

Mr. WIGGINS. Explain that to me. What do you mean?

Dr. EDISON. It is a pain-killing drug, a synthetic opiate or opiate-like drug to my knowledge.

Mr. WIGGINS. What's its chemical content, do you know?

Dr. EDISON. No.

Mr. WIGGINS. What is its effect other than pain killing? Does it have an addictive effect?

Dr. EDISON. It is suggested by the manufacturer that it should be regarded as habit forming or potentially habit forming.

Mr. Wiggins. What are some other examples of analgesic drugs?

Dr. Edison. The whole opiate group—morphine, codeine, the synthetic drug Demerol or meperidine. Aspirin is a mild analgesic.

Mr. Wiggins. It fits in that family of drugs?

Dr. Edison. Aspirin does not, of course, belong to the opiates.

Mr. Wiggins. Does Percodan?

Dr. Edison. Percodan is a nonopiate, I believe. But it has a strong potent analgesic effect, comparable, roughly, to codeine, comparable also to a drug called Darvon. One of the moderate strength analgesic drugs.

Mr. Pepper. Dr. Edison, you have been a very valuable witness and we appreciate your coming this long distance to give us this valuable testimony. You can see how much we are concerned about the problem and we know how much the medical profession is concerned about it.

Thank you very much.

This concludes these hearings intended for this day.

(Whereupon, at 12:30 p.m., the committee adjourned, to reconvene subject to the call of the Chair.)

15. Selection From "Interim Report of the Commission of Inquiry into the Non-Medical Use of Drugs"

Ottawa, Canada, 1970

AMPHETAMINES

(pp. 49–57)

87. Amphetamines are synthetic amines which are in many ways similar to the body's own adrenalin (epinephrine). These drugs generally evoke an arousal or activating response not unlike one's normal reaction to emergency or stress. Amphetamines were first synthesized in the early part of the century and entered medical use by the 1930's. Although a variety of related drugs and mixtures currently exist, the most common amphetamine substances are amphetamine (Benzedrine*), dextroamphetamine (Dexedrine*), and methamphetamine (Methedrine* or Desoxyn*), with Benzedrine* being the least potent. Generally, if the dose is adjusted, the psychological effects of these various drugs are similar and, consequently, they will be discussed as a group. Other drugs with somewhat similar pharmacological properties are phenmetrazine (Preludin*), methylphenidate (Ritalin*) and piradol (Meratran*). Common slang terms for amphetamines include: 'speed', 'crystal', 'meth', bennies', 'dexies', 'A', 'uppers', 'pep pills', 'diet pills', 'jolly beans', 'truck drivers', 'co-pilots', 'eye openers', 'wake-ups', 'hearts' and 'footballs'.

The stimulating effects of the amphetamines were widely used by soldiers during World War II to counteract fatigue. Since then, they have been commonly used both medically and non-medically by vehicle drivers on long trips, night-shift workers, fatigued housewives, students studying for exams and others who must meet deadlines, athletes for increasing performance, and others for general stimulation, pleasure or fun.

88. In the 1940's, much of the wartime stockpile was dumped on the world market and in many countries amphetamines were available on a non-prescription 'over the counter' basis. Widespread use followed in most industrialized areas with numerous unpleasant consequences. Use reached epidemic proportions, for example, in Japan in the 1950's—a country which had never had a previous serious drug problem,[24] Since this time amphetamines have been quite uniformly put under governmental control and in some countries (e.g., Sweden) are currently prohibited from medical and non-medical applications. Although the popularity of both medical and non-medical use of these drugs spread rapidly in all age groups and social classes in North America after the war, heavy use was apparently largely confined to delinquents and to members of the criminal-addict population of a few decades ago. The drug was usually taken orally, sometimes injected by heroin addicts, or sniffed. In many instances it was used interchangeably with cocaine (a short-acting but powerful stimulant). Frequent use was made of 'dismantled' Benzedrine inhalers, which were on the unrestricted legal market at that time.

More recently, major concern has developed in many circles for a relatively new amphetamine phenomenon—that of massive doses used intravenously by persons often referred to as 'speed freaks'. Although this practice has been most frequently noted among youthful multi-drug-taking individuals, considerable opposition to such use of amphetamines has developed within the 'hip' community. The 'speed trip' is in many respects the antithesis of the experience sought with the psychedelic drugs. Instead of the orientation towards the 'consciousness expansion', personal insight, and aesthetic and religious awareness often attributed to the psychedelic drug experience by users, the speed phenomenon is usually characterized by action, power, arrogance and physical pleasure ('kicks'), and regularly leads to suspicion, paranoia, hostility and often aggression. In addition to these undesirable personality changes, which render 'speed freaks' highly unpopular in the community, such individuals generally present a picture of chronic ill-health unparalleled among youthful drug users.

89. The message received by the Commission at public and private hearings, and in written communications with youthful drug users has been mostly negative towards 'speed'. Many experienced illicit drug users consider amphetamines extremely dangerous and undesirable, and have expressed surprisingly hostile attitudes towards these drugs in no uncertain terms. Recently, numerous persons well known to youth, who have had considerable influence on drug attitudes

during the past decade (e.g., John Lennon and the Beatles, Frank Zappa and the Mothers of Invention, Timothy Leary, and Donovan), have made public statements against the use of 'speed' and related drugs.

Many physicians have suggested that the supply of amphetamines legitimately imported and manufactured in Canada greatly exceeds medical need. As with other prescription drugs which are widely used, such as the barbiturates and tranquilizers, the distinction between medical and non-medical use is not always easily made.

MEDICAL USE

90. As early as 1935, amphetamines (in doses from 20-200 mg) were found to be a specific treatment for narcolepsy, an uncommon illness which is characterized by sudden attacks of sleep and weakness. Since the 1940's, amphetamines (in doses of 10-50 mg) have been used in the treatment of overactive children who showed disorders of attention and impairment of learning capacity. In the last few years, several investigators have again published results of clinical trials which revealed that amphetamines and methylphenidate were among the most effective treatments for these childhood disorders.

Psychiatrists have frequently used intravenous injections of methedrine (in doses of 15-30 mg) for diagnostic purposes. Administered in this fashion, the drug induces a state of excitation, elation and increased talkativeness, during which a previously inhibited patient might reveal information and symptoms which may be considered important for the understanding of his disorder. He might also express, more freely, previously suppressed emotions. It has been observed that some patients with a borderline psychosis show typical psychotic symptoms more clearly following an injection of amphetamines.

At one time, these drugs were used in the treatment of alcoholism and opiate narcotic dependency, but this practice was abandoned because amphetamines often produce dependency when taken for longer than two or three weeks. Since alcoholism is a chronic condition, some alcoholics who took this treatment for long periods of time became dependent on amphetamines and alcohol.

91. Early hopes that amphetamines would prove to be an effective general treatment for severe depression were soon disappointed. Although these drugs are powerful stimulants and increase a depressed person's activity, they may also make him more anxious and agitated, deprive him of sleep, and may fail to elevate his mood or to reverse the fundamental depressive process. In some individuals, these drugs have been effective in reliving mild depression and chronic fatigue, however.

Amphetamines, and some related drugs, have a strong suppressive effect on appetite. Most so-called 'diet pills' contain amphetamines or similar preparations. However, the appetite-suppressing action of amphetamines usually disappears after about two weeks, together with the pleasant stimulating effects, unless the dose is continuously increased.

Amphetamines have also been occasionally used to treat petit mal epilepsy, parkinsonism, pregnancy nausea, asthma, nasal congestion, and sedative poisoning. Many observers feel that because of the risk of dependency and undesirable personality change with amphetamines, even the medical use of these substances should be severely restricted.

ADMINISTRATION, ADSORPTION, DISTRIBUTION AND PHYSIOLOGICAL FATE

92. Amphetamines are available in a variety of tablets, capsules (both in immediate and delayed release forms), elixirs, injections and, until recently, inhalers. These drugs also appear in powder ('crystal') form on the black market. Amphetamines are available commercially combined with such drugs as barbiturates (e.g., Dexamyl*) and other sedatives, atropine, caffeine, vitamins and minerals, thydroid extract, and, on the illicit market, amphetamines are reportedly sometimes added to LSD. One of the most esoteric pharmaceutical combinations has been described as follows:[133] "This is a multi-coated tablet of pentobarbital on the outside to induce sleep rapidly, phenobarbital under a delayed dissolving coating to extend the sleep, and under another coating, an amphetamine to awaken the patient in the morning."

Amphetamines are usually administered orally and are readily absorbed from the gastrointestinal tract. Occasionally both intramuscular and intravenous injections are used medically. In the past, an amphetamine-base inhaler was also

available. Non-medical users may employ any of these administration routes, including sniffing 'crystal', although chronic 'speed freaks' prefer intravenous injections.

About half of the amphetamine which enters the body is excreted unchanged in the urine, the remainder being previously deactivated or chemically altered in the liver prior to elimination. Although excretion is generally rather rapid, traces of the drug can be found in the urine up to a week after withdrawal. Because of the considerable proportion excreted unchanged, certain individuals have been known to extract and re-use crystals obtained from the urine. (This general practice of 'reclaiming' excreted drugs is not new and such procedures have been recorded for centuries.)

EFFECTS

93. Both the psychological and physiological response to amphetamines vary profoundly with dose, and the effects of intravenous injections of massive quantities may differ greatly in character from, and bear little resemblance to, responses to low doses administered orally. These effects vary continuously over the full dosage range, but for clarification in the following discussions, the use of moderate quantities of amphetamines will be separated from the discussion of the practice of high-dose intravenous injection.

94. *Moderate-dose effects.* At typical therapeutic doses (e.g., 5-30 mg), amphetamines produce electrophysiological signs of central nervous system (CNS) activation along with a variety of adrenalin-like peripheral (sympathomimetic) effects such as increased blood pressure, pulse-rate and blood sugar, slight dilation of some blood vessels and constriction of others, widening of the pupils, increased respiration rate, depression of appetite and some relaxation of smooth muscle. Such effects might last 3–4 hours.

The psychological response varies considerably among individuals, but might typically include increased wakefulness, alertness, and vigilance, improvement in concentration and a feeling of clearer thinking, greater responsiveness to environmental stimuli, decreased fatigue and boredom, elevation of mood, mild euphoria, a feeling of sociability, increased initiative and energy, and increased verbal and other behavioural activity. There may be an improvement in some simple mental tasks, and athletic performance may be increased. In general, improved functioning is most likely to occur when prior performance was at a subnormal state due to drowsiness, fatigue or boredom.

On the other hand, a moderate dose of amphetamines in different individuals (or perhaps even in the same individual at different times) might produce irritation, restlessness, insomnia, blurred vision, tremor, nausea, headache, inability to concentrate, dizziness, heart palpitation, confusion, anxiety, chest pains, chilliness, diarrhea or constipation, and other adverse symptoms. In cases of higher dose or hypersensitivity, delirium, panic, aggression, psychosis, hallucinations and cardiovascular abnormalities may occur in some individuals. Although deaths are rare, some have been reported among athletes.[15]

95. After continued administration of moderate doses, recovery may be associated with fatigue, drowsiness and, not infrequently, emotional depression. The increased energy and alertness elicited by the drug merely postpones the need for rest and clearly provides no long-term substitute for it. Many regular users of stimulants rely on the drug for energy when fatigued and often do not get proper rest for long periods of time.

The amphetamine toxic psychosis may be indistinguishable from schizophrenia.[56] While this syndrome is generally associated with high-dose use, many of the symptoms have been observed with the use of more moderate amounts. There does not appear to be any irreversible physiological damage associated with long-term use of moderate doses of amphetamines although temporary disorders do occur.

96. *Tolerance and dependence with moderate doses.* Tolerance to the various drug effects develops at different rates and to different degrees—some responses 'drop out' in chronic use sooner than others. The tendency to increase dose depends upon which of the potential drug effects is rewarding or reinforcing drug use. Many individuals, for instance, who use amphetamines to control narcolepsy, may reach a stabilized dose and show very little need for increased quantity over a period of years. On the other hand, those using the drug to control appetite generally increase their dose. Many psychological effects such as the

mood-elevating response, may show a considerable sensitivity to tolerance, and individuals who either began using the drug to obtain these effects, or who acquired the taste for them after initially using amphetamines for other purposes, generally show a marked tendency to increase dose over time. Tolerance to some of the toxic properties occurs, and certain chronic users administer thousands of milligrams intravenously in a day, while even a fraction of that quantity would be extremely toxic in a non-tolerant user. As with other drugs, the rate of development of tolerance to the different pharmacological effects depends on the doses used, the frequency of administration and various individual factors. No suggestion of physiological dependence on amphetamines occurs with moderate doses; but psychological dependence on even low doses is frequently reported, and is considered a major hazard in both medical and non-medical amphetamine use.

97. *High-dose effects.* The chronic high-dose intravenous amphetamine syndrome has recently been described by several authors. [124], [71] The cycle or pattern of use usually begins with several days of repeated injections (usually of Methedrine*), gradually increasing in magnitude and frequency. Some users may 'shoot' or 'crank' up to several thousand milligrams in a single day. Initially the user may feel energetic, talkative, enthusiastic, happy, confident and powerful, and may initiate and complete highly ambitious tasks. He does not sleep and usually eats very little. After the first few days, however, toxic unpleasant symptoms become stronger, especially as the dose is increased. These toxic effects may be similar to those described earlier for lower doses, but appear in amplified form. Some symptoms commonly reported at this stage are: confused and disorganized patterns of thought and behaviour, compulsive repetition of meaningless acts, irritability, self-consciousness, suspiciousness, fear, and hallucinations and delusions which may take on the characteristics of a paranoid psychosis. Aggressive and anti-social behavior may occur at this time. Severe chest pains, abdominal pain mimicking appendicitis and fainting have also been reported.[207]

Towards the end of the 'run', (usually less than a week), the toxic symptoms dominate; the drug is discontinued, fatigue sets in, and prolonged sleep follows, sometimes lasting several days. Upon awakening, the user is usually lethargic, often emotionally depressed and ravenously hungry. The user may overcome these effects with another injection—thus initiating the cycle anew. Runs are often separated by days or weeks, however, at a time. In certain instances, 'down' drugs, such as barbiturates or tranquilizers, or even opiate narcotics may be used to 'crash' or terminate a run which has become intolerable or otherwise unpleasant.

98. The immediate effects of the intravenous injection of amphetamines are a sudden, overwhelming pleasurable 'rush' or 'flash' which has been described by users as 'an instant total body orgasm'. This effect is qualitatively different from the warm, drifting sensation associated with the opiate narcotics, but is reported to be initially similar to the 'splash' produced by intravenous cocaine.[124] Some users claim that the immediate pleasure of the injection is the prime motivation for the drug use and that other effects are secondary.

Some individuals report that sexual activity is prolonged, and may continue for hours. When orgasm finally comes it may be more pleasurable than normal, although, on the other hand, some describe an inability to reach a climax. While only a minority of users report increased sexual activity, some people give this reason as a primary one for taking the drug. [124], [23]

Some investigators have reported that many users claim that they take the drug for euphoria or 'kicks', or because it enables them to be more confident and active. In addition, there are reports of 'needle freaks', in whom the use of the hypodermic syringe has special rewarding connotations.

99. The clinical picture of the chronic 'speed freak' is a distressing one indeed. Continued use of massive doses of amphetamines often leads to considerable weight loss, sores and non-healing ulcers, brittle fingernails, tooth grinding, chronic chest infections, liver disease, a variety of hypertensive disorders, and in some cases, cerebral haemorrhage.[124] The extent to which these effects are the direct result of the drug or the secondary consequences of poor eating habits, over-exertion and improper rest is unclear. Further complications may be caused by unsterile injections, including hepatitis and a variety of other infections.[47] Although some users feel that certain of their mental abilities have

been impaired by amphetamine use, no clear picture of permanent brain damage has been demonstrated.

100. Heavy use of amphetamines frequently precipitates a psychosis which is indistinguishable from paranoid schizophrenia. In addition, several investigators contend that schizophrenics, and others with borderline psychotic conditions, are more likely to use the drug intravenously than are other individuals. In one study, 41% of those requiring hospital admission for treatment of amphetamine disorders were thought to be schizophrenic before taking the drugs.[100] However, there is still no reliable information on what proportion of users develop psychoses and what the predisposing factors actually are. The majority of acute psychotic reactions occur towards the end of a run, and such symptoms are usually dissipated by a few days rest.

'Speed freaks' are generally unpopular within the multi-drug-taking community and are often shunned. Consequently, these individuals may live together in 'flash houses' totally occupied by amphetamine users. Frequent 'hassles', aggression and violence have been reported in such dwellings. Heavy users are generally unable to hold a steady job because of the drug habit and often have a parasitic relationship with the rest of the illicit drug-using community. There are reports that many users support themselves through petty crime.[184 23]

101. *High-dose dependency.* The question of physical dependence on amphetamines depends on the definition of the withdrawal symptoms necessary to meet the criterion. While it is clear that withdrawing amphetamine from chronic users does not produce the dramatic, physically painful and often dangerous abstinence syndrome associated with alcohol, barbiturates, or opiate narcotics, many investigators feel that the fatigue, prolonged sleep, brain wave (EEG) changes, voracious appetite, cardiovascular abnormalities, occasional gastrointestinal cramps, lethargy and, often, severe emotional depression following the 'speed binge' constitute a physiological reaction analogous to the more dramatic withdrawal seen with depressant drugs.[56 207]

The tendency for tolerance-producing drugs to manifest a 'rebound' type of physiological and psychological pattern upon withdrawal has been given considerable attention; amphetamine abstinence in chronic users is generally characterized by a profound sedation, and depression of mood and physiological function, while drugs such as the sedatives and the opiate narcotics (all of which produce sleep in high doses) generally exhibit a withdrawal syndrome of severe and toxic overstimulation (in some instances to the point of convulsions).

The fact that amphetamines have, if any, a physically rather benign withdrawal syndrome, clearly indicates that a profound physical dependence is not a necessary component in an overall severe drug dependency situation. Subjective psychological factors seem to have considerably greater motivational importance in many instances—especially with chronic high-dose amphetamine use.

102. "*Speed Kills*". In recent years, the slogan 'Speed Kills' has received much attention, and the idea appears to play a significant role in the attitude that some users and non-users have towards the drug. One commonly hears the view that once you're 'on speed' you have only two to five years left to live. Some chronic 'speed freaks' incorporate this notion into the identity they present to others and the image they entertain of themselves. Many observers contend that the chronic use of intravenous amphetamines reflects a thinly disguised suicidal tendency, as well as an attention and sympathy gaining device. "Hello, I'm Philbert Desanex; I'm a speed freak and I'm going to be dead by fall", is only a slightly exaggerated caricature of the image purposefully projected by some of these individuals.

103. What is the evidence, in fact, that "Speed Kills" in the literal direct physical sense? Fatalities due to acute overdose are rarely reported. We have no reliable knowledge of the extent of intravenous amphetamine use, and although we hear many dire predictions, there is no good information on the long-term prognosis or outcome of such use. It would certainly appear, however, that chronic adherence to this practice is most detrimental to the individual and, often, to those with whom he interacts.

Although there is no clear evidence that the life expectancy of 'speed freaks' is lower than others living under similar circumstances, many investigators suspect this to be so. While there are few cases in the literature of death directly attributed to chronic amphetamine use, Clement, Solursh and Van Ast,[47] " . . .

have recently become aware of a number of cases of death on the streets (of Toronto) apparently related to high-dose amphetamine abuse. At autopsy, however, pathological evidence of death directly due to amphetamines is rare in such cases." After a thorough review of the literature, Cox and Smart of the Addiction Research Foundation reported: "Currently there is no evidence available on mortality rates among speed users and it is not certain that speed itself is a lethal drug. There is no evidence to support or deny that "Speed Kills".[60]

The slogan was originally borrowed from a highway traffic campaign of the last decade and it has been suggested that, originally, in adopting this phrase, drug users were referring to the 'death' of the personality, the 'spirit', or the freedom of the individual when he becomes dependent on amphetamines, rather than to physical mortality.

AMPHETAMINES AND OTHER DRUGS

104. As noted earlier, amphetamines are frequently used in conjunction, or in alternation, with a variety of depressant drugs such as barbiturates, alcohol and even heroin. The barbiturate and amphetamine up-down cycle has been described in both youthful and 'respectable' adult users at a variety of doses. Amphetamines intensify, prolong or otherwise alter the effects of LSD and it is reported that the two drugs are sometimes mixed. In addition, it would appear that the majority of youthful speed users have also had experience with a variety of psychedelic and other illicit drugs. Persons dependent on the opiate narcotics also frequently make use of stimulants such as cocaine and amphetamine—either as mixtures of drugs or used separately on different occasions It is interesting to note that STP (DOM) and the newer MDA, both extremely potent psychedelic-hallucinogenic drugs, are chemically closely related to amphetamine.

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287. The amphetamines are most commonly prescribed for appetite suppression and weight control, fatigue and the relief of mild depression and has certain other special therapeutic applications. Their nonmedical use has risen sharply in recent years, and witnesses appearing before the Commission expressed particular concern about the increased use of amphetamines in high dosages by the young.

Canada is not a pioneer in amphetamine use and abuse. A number of reviews have summarized the extensive use of these drugs since World War II in such countries as the United Kingdom, Germany, Japan, Ireland, Switzerland, Sweden, Australia, the United States and Yugoslavia. Indeed, the Swedish government recently responded to the abuse of amphetamines by prohibiting their possession for any purpose—medical or non-medical.

288. In Canada, the oral ingestion of amphetamines has been rising since the mid-forties. By 1964, approximately 60 million standard doses were produced for the Canadian market. This increased to more than 100 million doses in 1966 and dropped to 56 million in 1968, the last year for which statistics are presently available.[13] But these statistics refer only to the legal manufacture and importation of the drug. They tell us little about the degree of non-medical use of amphetamines and nothing about the volume produced and distributed illicitly in Canada. It has been put to the Commission, however, that the volume of legally manufactured and imported amphetamines greatly exceeds medical needs. As in the case of other drugs used widely for both medical and non-medical purposes—e.g., the barbiturates—it is believed that a significant proportion of the original supply of amphetamines probably finds its way to the user through unlawful channels. The relative frequency of illegal sales and thefts along the route between the manufacturer and the consumer is uncertain, and illegitimate distribution has been widely reported at all social levels of our society.

289. There is also evidence that some individuals make use of legitimate channels by obtaining numerous prescriptions from several physicians at the same time, or by using false identification or forged prescriptions. There has also been some carelessness in the extent to which they have been prescribed by physicians. While the tranquilizers do not appear to be manufactured illegally, there is evidence that amphetamines reach the streets from both legitimate and illegitimate manufacturing sources.

290. It is difficult to determine precisely when non-medical use of amphetamines began in Canada. In his appearance before the Commission, R.C.M. Police Assistant Commissioner Carriere testified:

> Prior to 1961, the extent of the abuse of amphetamines and methamphetamines was not known. Following the enactment of Part III of the Food and Drug Act, it was found that an extensive traffic in these drugs existed among long distance truck drivers. By 1963, through the co-operation of several trucking firms, publicity and investigation, the use among drivers was virtually non-existent. With the emergence of marijuana and LSD abuse, the amphetamine drugs, particularly methamphetamine, gained considerable popularity to the point where today a very active illicit traffic is in existence.

Low-dose oral amphetamine use and dependence are not uncommon in every age group. High school students swallow them for kicks, as a cheap, readily available and easily-taken drug; housewives can become habituated to the mood-elevating and energizing effect of amphetamine-type diet pills; tired professionals and executives use them; and even members of men's clubs meet to take these stimulants and strong coffee while their friends enjoy the more traditional pleasures of the afternoon cocktail.

The prevalence of stimulant use can not be determined with any degree of accuracy. Recent surveys, published in Appendix 'D', show that among high school students in the areas surveyed, use ranged from 3.6 percent to 9.7 percent. These surveys do not indicate the circumstances under which the stimulant was taken, nor the dosage.

THE "SPEED" PHENOMENON

291. In the last year or so there has been increasing reference to the use of "speed"—prolonged, high-dosage use of amphetamines, usually methamphetamine, and usually by intravenous injection. It should be pointed out, however, that the use of 10 to 15 milligrams, the normal prescribed daily dosage, is not considered an aspect of the 'speed' phenomenon. Rather, this phenomenon is characterized by high levels of dosage rising to 150 to 250 milligrams daily and, in some cases, as much as a gram or more a day.

'Speed' use appears to be on the increase in Canada, particularly in some of the larger urban centres. Distributors have given private testimony with respect to the quantities of amphetamines being used in certain areas.

The young people who have appeared before the Commission have stated that most 'speed freaks' are in their teens or very early twenties. This parallels the findings of studies in Japan which reveal that the 'speed' user is almost invariably young.

292. It is known that in addition to the regular commercial supplies, there exists a considerable amount of 'home-made' amphetamine on the illicit market, produced by clandestine 'speed factories'. Since these drugs are rather easy to synthesize, after even limited formal training in chemistry, and because the chemical ingredients are inexpensive, bootleg production and distribution by amateurs is therefore quite feasible.

Despite the relative ease with which some amphetamines can be produced, analyses of street samples in recent months indicate that alleged 'amphetamines' are by no means invariably free of impurities. Of 38 samples analysed by Dr. J. Marshman in Toronto, 45 percent contained traces of other drugs.[25]

The serious dangers of heavy amphetamine use have been well known to the 'hip' sub-culture for several years, as reflected in the 'Speed Kills' buttons sold at 'head shops'. Many experienced drug users have expressed their anxieties to the Commission in public and private hearings about this drug and its apparent growing use.

At many points the Commission was told that the use of amphetamines is feared by most young people and the 'speed freak' is looked down on by many of his peers.

In the ensuing year, the Commission intends to investigate further the prevalence and characteristics of this phenomenon.

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4. AMPHETAMINES

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405. *The problem of knowing what is being referred to.* The quality and potency of the drugs sold as amphetamines ('speed') on the illicit market, are apparently less variable than are those of cannabis or LSD. Amphetamines have been in wide medical use for more than 30 years and are legally produced in large quantities by the pharmaceutical industries. Thus, the problems of illegal production and quality control which beset cannabis and LSD are much less in evidence with the amphetamines. It appears that a large proportion of the amphetamines available on the illicit market has simply been diverted from authorized industrial production into illegal channels of importation and distribution.

Many of the orally administered tablets and capsules of prescription drugs such as dextroamphetamine (Dexedrine*)' and the great variety of amphetamines contained in 'diet pills' [e.g., phenmetrazine or (Preludin*)] which are prescribed for weight control are legally produced. This also applies to methylphenidate (Ritalin*), or pipradol (Meratran*) which are pharmacologically closely related to the amphetamines.

But there is some evidence that much of the amphetamine which is most frequently used by the 'speed freaks' for intravenous injection (e.g., methamphetamine or Methedrine*) is produced in small clandestine laboratories which may sometimes by run by amateur chemists. In these cases, there is little adequate quality control and the user can not be sure of the chemical nature of the drug alleged to be methamphetamine, or of its dose.

It is important to keep these different forms of amphetamines or 'speed' in mind:

1. Pure prescription amphetamines (e.g., Dexedrine*) or closely related drugs, (e.g., Ritalin*).
2. Prescription amphetamines in combination drugs (e.g., 'diet pills').
3. Illegally produced and distributed amphetamines (e.g., methamphetamine) in tablet or powdered form.

While there is a dependence problem with the prescription amphetamines and the 'diet pills', this is usually not the same as the newer 'speed problem'. 'Speed freaks' are almost without exception young, under 25 years of age, and 'shoot' (inject) amphetamines intravenously in very large doses (e.g. from several hundred to several thousand milligrams). Amphetamine-dependent persons who use prescription drugs, tend to be older, between 30 and 50 years of age, take the drug orally and use much smaller doses (e.g., from 10 to 100 milligrams).

406. *The proper classification of amphetamines.* Amphetamines and drugs with amphetamine-like effects are generally classified in the pharmacological category of *stimulants*, although one might find them occasionally included in the category of anti-depressants. It was assumed originally, when these drugs

were introduced into clinical medicine in the 1930's, that amphetamines would be useful in the treatment of morbid depression, because they frequently induced euphoria in normal subjects. But it was soon observed that in severely depressed persons these drugs would often not elevate the mood and thus did not serve as true anti-depressants, but simply increase tension, restlessness and insomnia. Today, amphetamines and amphetamine-like drugs are used only occasionally in the treatment of severe depression; drugs more frequently used for this therapeutic purpose are those generally classified as anti-depressants (see classification table in Chapter Two) and are used almost exclusively on a medical basis. Many stimulants, on the other hand, enjoy wide non-medical use. Amphetamines are controlled drugs under Schedule G of Part III of the *Food and Drugs Act.*

407. *Short-term physical effects.* More than 30 years of medical use have allowed for thorough investigation of the short-term physical effects of the amphetamines. Moderate doses produce EEG signs of electro-physiological arousal of the central nervous system and peripheral effects indicative of activation of the sympathetic (adrenalin-like) part of the autonomic nervous system, which manifest themselves as increased pulse rate, increased blood pressure, dilatation of the pupil and some relaxation of smooth muscle (e.g., in the gastro-intestinal tract). Another regular, immediate effect is suppression of appetite (anorexogenic effect), produced through some action on the appetite-regulating centers in the brain.

408. *Short-term psychological effects.* Typical short-term psychological effects are a feeling of increased energy, drive and initiative, often leading to an awareness of greater vitality and heightened self-confidence, and thus often resulting in a mood change in the direction of euphoria. Fatigue and boredom are diminished, pre-existing drowsiness is overcome and prolonged wakefulness is induced. In general, persons under the influence of amphetamines find it easier to tackle cognitive and emotional problems, work faster and often more efficiently—although they may be somewhat more easily distracted—and experience a facilitation of their interaction with other people.

It should be noted, however, that these effects occur by no means regularly in everyone exposed to the drug. Individuals who are chronically anxious or temporarily under stress, and therefore irritable and tense, frequently react to amphetamines with a further increase of anxiety, tension or irritability. Under these circumstances, they experience, of course, no euphoria, and their general functioning tends to be impaired rather than improved.

Test performance on simple mental tasks is frequently improved under the effects of amphetamines, particularly when rapidity of response, staying power and speed of sustained activity are being tested, and when the subject is fatigued or bored. General intelligence, however, is not improved by amphetamines when measured by the usual tests except perhaps very occasionally, and in a secondary way, through a temporary increase of motivation. A person's judgment is, as a rule, not affected by moderate doses of amphetamines, but when high doses are administered, as by the 'speed' user, judgment may be greatly impaired. Also, with higher doses, it becomes increasingly difficult for the subject to concentrate, and thus a marked deterioration of cognitive functioning might result.

Psychomotor abilities may be temporarily facilitated, and athletic performance might improve under the influence of moderate doses of amphetamines. This fact has recently made it necessary to enforce strict regulations against 'doping' with these drugs in those taking part in athletic competitions.

With extremely high doses of amphetamines, which the 'speed' user might employ (up to 1000 times the therapeutic dose) all mental activity loses its focus, concentration becomes impaired, all critical faculties are seriously reduced and the person's judgment becomes blurred. Psychomotor coordination suffers, as well, once this state has been reached, and emotional control is often lost. Nevertheless, the person under the influence of these extremely high doses of amphetamines, far from being aware of his mental limitations, experiences a 'rush' of pleasant feelings and becomes convinced that he is more capable and more powerful than ever. This sequence of drug-induced psychological events, creating unrealistically inflated feelings of self-confidence, self-righteousness and power, might lead to delinquent behavior, as the result of 'acting out' of latent aggression and hostility.

409. *Long-term effects.* If moderate doses of amphetamines, such as are prescribed for medical purposes, are taken over long periods of time, three different categories of outcome may be observed:

1. No adverse effects may occur, and the person for whom the drug was prescribed or who took it without medical authorization, but in moderate doses, may go on for months or even years, taking the same dose regularly and suffering no ill effects from it. Many mildly depressed or chronically fatigued people ('tired housewife syndrome') who obtain their amphetamine on prescription, fall into this category. Also, in this category are a sizable number of persons who feel the need for mild stimulation of the amphetamine type at regular intervals because of the special kind of stress their work is placing on them, e.g., journalists, commercial artists, public speakers or performers who are required to work to deadlines, or 'produce' original ideas on demand. There is considerable evidence—though little systematic documentation—of the existence of a large group of such people who regularly use amphetamines, often without a prescription.

2. More frequently, however, a person who has started taking an amphetamine, with or without medical prescription, becomes dependent, not only on the therapeutic effects for which the drug has been taken originally (e.g., a reduction of appetite, to facilitate weight loss), but even more so, on its 'fringe benefits' such as the feelings of euphoria and increased energy produced by the drug. Tolerance to these particular effects of the amphetamines develops rapidly in most people, with the result that they are inclined to increase their doses. Although this might enable them to extend the period of time during which they can experience the particular drug effect on which they have become dependent, they now also induce a number of highly undesirable effects which are the results of the prolonged ingestion of doses of amphetamines which are considerably higher than those with which they started.

These new undesirable effects consist primarily of insomnia, loss of appetite and general nervousness, which often make it necessary for the person thus affected to take gradually increasing doses of sedatives, setting up in this way, a vicious cycle of forced stimulation and sedation—of ups and downs—which greatly disrupts his normal rhythm of functioning. If continued for several months, this pattern often results in general debilitation and exhaustion and might finally lead to a psychotic breakdown. At this stage, the chronic amphetamine user has become irresponsible, expresses delusions of persecution and requires treatment and hospitalization for mental illness.

There is, unfortunately, no reliable way of predicting which persons will fall into the first category and be able to take amphetamines regularly without increasing their dose (and thus with relative impunity) and which persons will become dependent on the drug, develop tolerance, increase dose and then invariably suffer effects destructive to their physical and mental health. Since the risk that this might occur is high, amphetamines should not be taken without close medical supervision, nor should they ever be prescribed by physicians who are not thoroughly informed about the dependency potential of amphetamines.

3. The third category of amphetamine users is constituted of 'speed freaks' usually young persons who most often inject intravenously extremely large quantities of the drug. Users in categories 1 and 2 may start taking amphetamines for medical reasons and would continue obtaining amphetamines on prescription, which then might later be used for non-medical purposes; but, the 'speed freaks' rarely start the drug under medical supervision and rarely, if ever, begin use through legitimate prescription channels.

To this date there is little evidence that the slogan 'speed kills' has concrete applicability. The disastrous effects of massive doses of 'speed' on the user's physical and mental health, appearance and behaviour either cause him to quit using the drug on his own initiative, or to be hospitalized for physical or mental breakdown, or to be arrested for delinquent behavior, long before his drug habit has killed him. This interruption of his exposure to the toxic effects of 'speed' may save his life, and may help him to give up amphetamines, while his body can still repair the damage he has inflicted on it. There seems to be little doubt, however, that nobody could survive a long, interrupted exposure to the devastating effects of high 'speed' doses of amphetamines on

his cardiovascular system, his resistance to infection and his central nervous system.

The Commission intends to investigate further the allegations of relationship between drug use and other criminal activity.

C—EXTENT AND PATTERNS OF NON-MEDICAL DRUG USE

(Pp. 220–224)

413. At this time only general statements can be made about the extent of non-medical drug use in Canada. There can be no doubt that it is widespread. Clearly there has been growing interest in and use of the psychoactive drugs by the young and indeed by all ages.

The Commission has gathered epidemiological information from a number of sources: governmental records, police statistics and estimates, various surveys of drug use among students and the informed and sensitive opinions of experts, drug users and distributors. While this information, taken together, gives the Commission some sense of the extent of the phenomenon, it does not provide the basis for any detailed or specific epidemiological statements. *A major research project is being carried out on behalf of the Commission. It is expected that the results of this study will use a basis for more accurate estimates of the extent of drug use in Canada.*

Alcohol has been and remains the most popular psychoactive drug among Canadians of all ages and classes. Its use continues as our most serious drug problem. However, during the early 1960's, the acceptance and use of other psychoactive drugs such as cannabis and LSD began to be noteworthy. Marijuana had been used previously but its use had been confined to a small number of musicians and entertainers. The spread of the use of the drug appears to have begun among university students and among the mobile, alienated out-of-school young people of the cities. It did not take long for it to appear in the high schools and its use probably spread more rapidly there than in the universities. While the phenomenon began in the larger cities, it also appeared relatively quickly in smaller urban centers and in rural communities.

It seems reasonable to think that probably more than 8 or 10% of high school students have used cannabis. Some studies have found much higher proportions. For instance, a recently published British Columbia study estimates the level of cannabis use in the schools which were studied at 20%. In the hearings we have heard extreme estimates. Many parents and teachers provide low estimates and strongly contend that the extent of use has been grossly exaggerated. Students, notably those who use drugs, suggest that as many as 60 or 70% of their fellows have smoked cannabis. At the university level, the data we have seen suggest that more than 25% of students have at least experimented with it. There is not as great a tendency to deny widespread use among college students as there is to deny it at the secondary school level.

The use of LSD seems to have emanated from the 'hip' subculture of the cities. Its spread began somewhat later than that of cannabis, but today its use has probably reached virtually the same population, although involving fewer individuals. Initially, the acceptance of LSD use was inhibited by the statements of a probable medical and genetic risk. The persuasive force of these statements seem to have been greatly attenuated during the past year or 18 months. An increasing repertoire of other new hallucinogenic drugs has appeared, and has been accepted for use by the drug communities. It is more difficult than in the case of cannabis to estimate the extent of use of these drugs. In large part this is due to the fact that their use is much more recent and there have been virtually no current attempts at measurement by surveys. However, we have heard estimates that in some high schools as many students have now used LSD as have smoked cannabis and there seems to be an awareness in the public of an increased use of hallucinogenic drugs, notably LSD, by both high school and university students.

The non-medical use of stimulants, particularly the high dosage administration of the amphetamines, is a matter of serious concern. There are conflicting reports of the extent of the so-called 'speed' phenomenon but there can be little doubt of a rapid increase in the use of these dangerous drugs in recent years. This increase seems to have taken place after the spread of cannabis and LSD. The intravenous use of amphetamines does not appear to have a wide following among university students, but these drugs seem to have achieved their greatest popularity for oral use among high school students

and for intravenous use among out-of-school young people. The use of this drug has been deplored in virtually all quarters, including the cannabis and LSD communities. We have heard estimates that several thousand young people were making dangerously regular high dose use of amphetamines in Toronto. Such estimates have been accompanied by forecasts of anticipated high death and disease rates among the users.

It has come to the Commission's attention that an increasing number of young drug users are probably using or experimenting with a wide variety of drugs or drug combinations. Unfortunately, there is little survey data to indicate the extent or the pattern. We have considered the causes of multiple drug use above.

It is quite clear that many students at the high school and college levels have had drug experiences, notably with cannabis and LSD. There is no evidence that the number involved is diminishing, or that the frequency of use is lessening. Among high school and school drop-out users, there seems also to have been an increase in multiple-drug use.

The system of distribution of cannabis and LSD appears to differ significantly from that of heroin. There does not appear to be an organized crime involvement at this time, although hashish distribution might be attractive to organized crime in the future. In many cities there are large importers of marijuana, hashish, and LSD who supply a multi-levelled network of distributors. Most of the distributors at the street level can not properly be thought of as pushers in the sense of the traditional heroin pushers. There is also a large number of smaller importers. Much of the distribution of these drugs seems to be informal and even casual. They often seem to move among friends in a fashion similar to alcohol or tobacco in 'straight' society. It is probable that the most important factor in the rapid development of this phenomenon has been the influence of one individual upon another—the reporting of one's own drug experiences to friends and acquaintances.

The use of heroin and the other opiate narcotics has been a problem in Canada for a number of years. However, the last available government statistics indicate that the proportion of addicts in the total population has declined.[6] The Commission is concerned, however, by reports in Canada and the United States of the increasing use of heroin, particularly by young people.

It is important to realize that the non-medical use of psychotropic drugs has been increasing among adults as well as among the young. We have cited statistics to show the increase in the use of alcohol and such drugs as the barbiturates, stimulants and minor tranquilizers. We have also heard much about the purported increased use of cannabis by adults for recreational purposes.

D—CAUSES OF NON-MEDICAL DRUG USE

414. The Commission feels that one of its most important responsibilities is to provide some reasonable explanations of non-medical drug use and to give the Canadian people assistance in understanding at least some of the major causes and causal patterns. There are causal forces involved at the individual, the group and the society-wide levels. Our primary concern is with those pressures to drug use that have a wide applicability, although we do not ignore the idiosyncratic.

We feel that it is important to stress that there is no single or simple explanation available—nor is one likely to be found. Motives vary widely between users and groups of users. The motivation of the individual user may vary through time. Motivation is also a function of the real and expected effects of the various drugs.

There has been some tendency to think of the motives for drug use as pathological or as reflecting a pathological psychological condition. This is shown by the tendency to turn to the physician, and particularly to psychiatrists, for help in understanding the drug phenomenon. There is no doubt that some drug users are to some degree mentally ill. However we are convinced that the vast majority fall within the normal range of psychological functioning.

Probably the most important single factor that has encouraged an increase in the use of cannabis has been the description by one individual to another of the drug's effects as being pleasant, fun, interesting or exciting. The search for fun, pleasure and excitement is also probably the most important factor favoring the continued use of this drug. While newspapers, magazines and the popular music industry have played a role in creating an interest in drug

use and experimentation and have provided information about the effects of the drugs, it seems likely that their influence has been far less than that of individuals upon each other. There is also now a fad of drug-taking and experimentation.

The smoking of marijuana and hashish is primarily a group practice, although there are solitary smokers. While it is often said that smoking cannabis aids communication, lessens inhibitions, and causes laughter and gaiety, there is also much emphasis on its capacity to alter perception and enhance the enjoyment of music. LSD is much more an individual experience and there is a stress on new insights into the self and existence that are said to follow its use. We are told that both drugs provide the user with new perspectives of reality and new contexts in which to absorb experience. LSD is often spoken of almost as a sacrament. Its effects are said to be essentially indescribable and hence capable of being understood or fully appreciated only by those who have experienced the drug.

The introspection, the search for meaning within the self, the desire to explore what are said to be new frontiers of the mind seem to be related to a collapse of many traditional explanations of existence including religious expressions and syntheses of experience. In the past, when ideologies or religions lost their appropriateness, man has similarly turned inwards to find meaning and satisfaction within the self.

There also seems to be a relationship between drug use and the concern of the young for the future. Many appear to have lost faith not only in a traditional God but in the power and capacity of human reason. They fear that reason can not cope with the problems of nuclear arms, pollution, overpopulation, poverty and racial hostility. Their doubt of man's capacity to survive and their loss of faith in reason seem to have encouraged an emphasis on feeling and emotion and on life and pleasure in the here-and-now.

The general affluence of our society has also been a factor. This affluence has paradoxically become a source of boredom from which drugs provide an escape. It also permits the luxury of time for introspection to a large number. There is also a rejection of the life style characteristic of the affluent society with its emphasis on striving for material gain and competitive success and its perceived willingness to place material gain above the psychological and spiritual needs of the individual. Drugs are said to have the capacity to help liberate the user from these molds and structures.

Many have used the term alienation in trying to explain the sources of drug use to us. This is not an easy word to define. But as used in our hearings it has tended to refer to what some feel to be an estrangement from the institutions, processes and dominant values of the society, a sense of powerlessness to affect the future of the society or of themselves within it, and a lack of belief that a full and meaningful life is available for them in the society.

Some of the young seem fearful that they can not live up to the expectations that have been set for them or feel that to do so would demand too much sacrifice of their personalities.

The increased use of 'speed' has been interpreted as symptomatic of a widespread depression and sense of powerlessness.

We make no full attempt at this stage to present a statement of the causes of the spread of non-medical drug use. In Chapter Four, we point to some explanatory themes that we feel might help to illuminate the phenomenon.

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16. LETTER AND ATTACHMENTS FROM A. B. MORRISON, PH.D., ASSISTANT MINISTER, HEALTH PROTECTION BRANCH, OTTAWA, ONTARIO, MARCH 24, 1972; ATTACHMENTS ENTITLED, "SPECIAL REPORT, LEDAIN COMMISSION REPORT-TREATMENT," C.M.A. JOURNAL, MARCH 4, 1972, VOL. 106, PAGES 604A–604F; AND, "STATEMENT BY NATIONAL HEALTH AND WELFARE MINISTER JOHN MUNRO ON GOVERNMENT ACTION TO CONTROL ABUSE OF METHADONE AND AMPHETAMINES," FEBRUARY 24, 1972

MINISTER DE LA
SANTE NATIONALE ET DU BIEN-ETRE SOCIAL,
Ottawa, Ontario, K1A OL2, March 24, 1972.

MS. MARY JOLLY,
Senate Annex,
Washington, D.C.

DEAR MS. JOLLY: Further to our recent telephone conversation I attach herewith the statement on Methadone and Amphetamines made by my Minister on 24 February, 1972 in the House of Commons. Medical comment on this proposal from the Canadian Medical Association also is attached.

I hope this provides information of value to you.

Yours sincerely,

A. B. MORRISON,
Assistant Deputy Minister, Health Protection Branch.

[From the C.M.A. Journal, Mar. 4, 1972]

LEDAIN . . . MUNRO . . . METHADONE . . . AMPHETAMINES . . . AND THE CANADIAN MEDICAL ASSOCIATION

LE DIAN COMMISSION REPORT—TREATMENT

On January 26, some 32 months after its establishment, the Commission of Inquiry Into the Non-Medical Use of Drugs submitted the first of four volumes that will compose its final report. Among other things it was probably the strongest official attack ever made on the competence of the Canadian medical profession.

". . . *traditionally, doctors have been assuming to be experts in all matters concerning the effects of drugs on human beings. This was a reasonable assumption 30 or 40 years ago. Today, however, with the number of drugs used in the treatment of specific diseases increasing constantly, and with so many new drugs appearing, which are not used primarily for the treatment of diseases, no physician can reasonably claim to be an expert on all drug effects.*

Psychopharmacology, the rapidly growing science of drugs which influence consciousness, mood and behaviour, has been in existence for only two decades, but it has come to occupy an important controversial position in our lives and thinking, raising issues in a wide variety of fields, including foreign policy, law enforcement, public health and personal ethics. This may be the reason why the entire subject of psychotropic drugs has left the medical profession divided, indecisive, and poorly prepared to deal with it, or even understand it. It is, in fact, the first large scale public health problem in which medicine has not assumed a major leadership role and which few individual physicians have faced squarely. Medical education, both undergraduate and continuing, has utterly failed, in terms of its response to psychotropic medical and non-medical drug use, to keep up with the rate at which this problem of public health has grown in recent years.

Few physicians can bring themselves either to give or to accept advice on the handling of troubled young people today; a doctor's help in cases of non-medical drug use is often strongly questioned by his patients.

Drug education and even treatment are now being left largely in the hands of users and former users, detached streetworkers and other paramedical personnel who are often well-informed and able to provide constructive help, but who in such cases provide information and advice that are questionable and controversial. The very emergence of innovative services the major function of which is to act as mediators, moderators and translators between patient and therapist, is a dramatic indicator of how relatively inept and unresponsive the medical profession has been."

In the concluding notes of the Commission's Report:

"*Speakers at the Commission's public hearings mention the fear and dislike of young persons for hospitals; the sterility and structure of the hospital setting, where, in the midst of a bad drug trip, one may have to wait two hours to see a psychiatrist and then be asked his name, social insurance and hospital insurance number; the fear of young persons that the doctors might call the police; their fear that the doctors would contact their parents; and the inability or reticence on the part of many doctors to deal pleasantly, if at all, with drug cases.*"

The 125-page Report is divided into eight chapters or sections—Introduction, the Treatment of Opiate Dependents, the Treatment of High-dose Amphetamine (Speed) Dependents, the Treatment of Alcoholism, the Hallucinogens, Short Term Medical Management—or the physician's first-aid manual for the treatment of drug patients as it has been tabbed by the lay press—Therapeutic Communities, Organization and Coordination of Community Treatment Services.

The Report in its entirety will be distributed to all practicing physicians in Canada in the near future.

INTRODUCTION

Following the above-mentioned criticism of the medical profession, the Introduction engages in a philosophical discussion on the meaning of sickness—with an attempt to outline which types of sickness require therapeutic intervention. It then proceeds to a sociomedical philosophical discussion re the meaning of treatment and therapy, the goals and types of treatment, etc.

TREATMENT OF OPIATE DEPENDENTS

Following a general review, including specific reference to the narcotic treatment programs and facilities at Oakalla Prison Farm in Burnaby, B.C., the Alex G. Brown Memorial Clinic in Mimico, Ontario, the Vanier Centre for Women and the Matsqui B.C. Penal Institution Program, the Report looks at therapeutic communities, treatment with narcotic antagonists and total abstinence. It is in this section that the Commission suggests that heroin should be made available in special, very strictly regulated clinics to help a limited number of patients to withdraw from the drug—if this cannot be achieved in any other way. At the press conference, at which the Report was tabled, Mr. LeDain indicated that the Commission was split relative to this subject and, in fact, submitted it in the body of the Report not as one of the specific recommendations presented in the usual bold-face type at the conclusion of the chapter. He indicated that the Commission believed the physician should not be restricted relative to the pharmacological armamentarium available for the treatment of narcotic addicts—and warranted trial at least on a research basis.

A section dealing with methadone maintenance is in essence very similar to the report and recommendations of the Joint C.M.A.-F.D.D. Committee on Methadone published in the December 4 issue of C.M.A. Journal. The Commission went one step further and recommended that only specific physicians with the necessary expertise, and having access to the laboratory and ancillary services required be allowed to prescribe methadone.

The Commission recommended:

1. Methadone maintenance programs should continue to be developed as a method for the management of opiate dependence and should exist in all geographical areas.

2. Scrupulous care, including a period of residence in a clinic or hospital, should be taken in screening candidates for methadone programs to ensure that they are indeed physically dependent on an opiate.

3. Methadone maintenance programs should be developed only—and methadone be available only—in specialized clinics, preferably hospital-based, as part

of an overall maintenance program serving an area. The prescription of methadone by private physicians should be terminated except where there is a special arrangement with the clinic, and then under continuing close supervision by the clinic. This exception should be permitted only where auxiliary facilities, including counselling services, laboratory monitoring, and careful control including monitoring by the Food and Drug Directorate may be ensured.

4. In special cases where the patient cannot reasonably have regular access to a specialized clinic or authorized physicians because of geographical location, private physicians, pharmacists, public health nurses or other suitably qualified persons may be authorized to administer methadone. In such cases, however, the person specially authorized to administer methadone should perform the necessary counselling and monitoring services and should make regular reports to the specialized clinic which has assumed and retained overall responsibility for the patient's maintenance program. Alteration of the dose of methadone should be subject to prior approval by the specialized clinic. This exceptional procedure of administration should be authorized only after the patient's adaptation to methadone has been clearly established.

5. All persons who are offered methadone programs should first be clearly informed of the nature of this treatment and of other treatment options available to them.

6. All established programs should institute intensive evaluation to identify the characteristics of their patients, the types of patients, the types of patients who remain in the program, and the success rate as measured by the criteria indicated under Goals of Methadone Treatment. Data gathered should include age, sex, socio-economic background, education, duration of drug use, types and patterns of drugs used in the past, full family and occupational histories and personality profiles. Such data should be available to all the specialized clinics.

7. An opiate user should be considered for methadone maintenance only where it has been established that he is dependent on opiate use and where, in the opinion of a physician, it appears likely that other alternatives would not be successful.

8. Since the administration of methadone to young persons may be preferable to incurable dependence on heroin, we do not think that such administration should be precluded in principle but that it should be left to the discretion of physicians. When it is administered to persons under 18, such administration should be preceded or accompanied by intensive efforts to effect a cure by psychotherapy.

With respect to opiate dependents in general, the Commission recommended:

1. Because of the high cost of treatment programs and their relative lack of success, major efforts should be directed toward the prevention of opiate narcotic dependence, particularly among young people. These efforts should include early identification of high risk persons, particularly chronic amphetamine users.

2. Community treatment facilities for dependence on opiate narcotics should have built-in evaluative and research components.

3. Wherever feasible, such facilities should be equipped to provide the full range of treatment programs. Where this is not possible in a single complex, adequate provision should be made, by referral, for giving the patient access to the full range of treatment opportunities.

4. The recommended course of treatment in the usual case would be as follows:

(a) Treatment of acute effects in hospital with gradual withdrawal, using methadone.

(b) After this stage, and suitable evaluation, the patients should be offered either:

(i) Individual or group psychotherapy, vocational guidance, job placement and similar rehabilitation measures, or

(ii) Maintenance on a narcotic antagonist with close follow-up on an outpatient basis. Such maintenance should not serve only a "watch dog" function but should include active intervention in the life of the patient, such as the provision of occupational or educational opportunities and daily assistance in coping with problems. This can only be satisfactorily accomplished if counseling is available during the evening hours.

(c) In all cases, the physician should make regular, not less than weekly, urine tests to monitor the patient's drug use.

5. After a reasonable trial of this program, those who fail should be offered a choice of methadone maintenance or other opiate maintenance (subject to the conditions outlined above), or residence in a therapeutic community.

TREATMENT OF HIGH-DOSE AMPHETAMINE (SPEED) DEPENDENTS

The Commission recommended:

1. Because of the high cost and low return in the treatment of chronic speed users, our major effort should be aimed at prevention, including identification of high risk persons and situations, and attempts to avoid or remove conditions conducive to such use. Another important reason for prevention of the use of speed is the strong evidence of progression from amphetamines to heroin.

2. Catchment and continued care of speeders depend on close liaison between the street worker, innovative service, hospital, and rehabilitation services. Education of workers in these areas is needed to help them understand the unique problem of speed users.

3. Residential facilities for the post-detoxification period are needed for at least the first few crucial months to provide isolation from the outside drug scene and to begin the rehabilitation process.

4. Small therapeutic communities, restricted to speed users, offer the best hope for successful treatment and rehabilitation.

5. The Federal Government should support research on the development of an effective antagonist for amphetamines.

TREATMENT OF ALCOHOLISM

The presentation of this 11-page section came as a surprise to many individuals. The report made no reference to tobacco. The Commission recommended:

If we are to offer really effective treatment services for alcoholics, we will need to have:

1. Clearer formulation by individual researchers and by the medical-rehabilitative communities, of treatment goals based not on certain routine assumptions—for example, that only total abstinence must be aimed at under all circumstances—but on a careful and individualized assessment of each alcoholic's needs in the context of his history, environment, interpersonal relationship and personal assets and liabilities.

2. A universal catchment system which will be able to reach those who need help in all segments of society.

3. An integrated treatment program operating over the full span of time from identification of the alcoholic patient through a year or more of long term follow-up.

4. Replacement of present criminal-oriented drunk tanks by medically oriented detoxification centers.

5. A variety of treatment modalities available to meet the specific needs of individual patients.

6. Clinical research designed to evaluate the effectiveness of different programs and techniques in relation to the various patients using them.

HALLUCINOGENS

This extremely short 1 and 1/5th page report contained no specific recommendations. It did indicate that the hallucinogens: L.S.D., M.D.A., mescaline and S.T.P. do not lead to physical dependence and less frequently than other psychotropic drugs to strong psychological dependence. The closest that the Commission came to making a recommendation was the statement "any strong dependence on drugs, including even coffee, is a potential health hazard and as such calls for medical attention." The Commission also indicated that "there are no special therapeutic modalities for the treatment of dependence on cannabis or L.S.D." It was one of the few references in the Report to cannabis—which will be dealt with in detail in a 250-page Report to be tabled in March.

SHORT-TERM MEDICAL MANAGEMENT

This 23-page section of the Report attempts to outline the facilities and resources required for the treatment of "drug patients." It then goes on to outline the management of overdose patients—according to the type of substance utilized.

THERAPEUTIC COMMUNITIES

The Commission extended the traditional definition of a therapeutic community to include comment on such organizations and treatment approaches as Synanon, Day Top Village, X-Kalay, Gateway and the new therapeutic community sponsored by the Ontario Addiction Research Foundation in London, Ontario.

The Commission recommended:

1. Therapeutic communities should be one option available in any national multi-modal drug-dependence program.
2. An aim of the therapeutic community should be to equip those of its members who wish to return to the society to do so with success.
3. While the therapeutic community is built on the skills and self-confidence of the ex-addict, it should recognize that there may be a need, in some cases, to avail itself of the resources of professional staff or consultants.
4. All programs should have a research component, seeking criteria useful in selecting candidates, predicting success, and comparing various approaches to treatment.
5. The Department of National Health and Welfare of the Federal Government should encourage the development of additional therapeutic communities in Canada through financial and other assistance to those already in existence and organizations which appear to be effective in this field.

ORGANIZATION AND COORDINATION OF COMMUNITY SERVICES

This short but excellent chapter will obviously be utilized by the Federal Government's Department of National Health and Welfare Non-Medical Use of Drugs Directorate as the guide for its program.

C.M.A. RESPONSE

Following study of the Report by the Association's Council on Community Health Care and the Board of Directors, a C.M.A. response to the Report was issued at a press conference on February 14.

The press conference was also utilized to publicly table the final position of the C.M.A. re the non-medical use of drugs. This document contained the major views, positions and recommendations of the association as submitted in the Interim Brief to the LeDain Commission (November 1969), the second formal submission to the Commission in May of 1970, the Report of the Council of Community Health Care that was submitted to the Commission as a resource document and which provided the basis for the Association's second submission. The final position of the Association was tabled in accordance with the decisions of General Council in June of 1971, re the differences of opinion between the Council and the C.M.A. Board of Directors.

In response to the Commission's Treatment Report, Dr. H. D. Roberts, President, stated:

"*We wish to commend the Commission for a good start on a most difficult and complex task. We are particularly pleased to see that the Report is generally presented in a most practical form. While the Association cannot agree with all the contents, recommendations, or criticisms of the profession and hospital services in the Report, we would like to stress its positive aspects and encourage the governments of Canada to give the Report thorough consideration and to implement the recommendations that give promise of beneficial results as soon as possible.*"

The Association:

Endorsed the Report and recommendations of the Commission on methadone—which were comparable to the Joint C.M.A.-F.D.D. Report published in 1971. The Association also endorsed the more stringent controls re the prescribing of methadone as recommended by the Commission.

Supported the five recommendations re the treatment of high dose ampheta-

mine dependents but warned that efforts to discover effective antagonists have not been highly successful to date.

While not specifically referred to in the Commission's Report, the C.M.A. reiterated its concern regarding the rapidly declining but still significant medical misuse of amphetamines and similar substances. The Association cited the marked reduction in the prescribing and sales of amphetamines and amphetamine-like substances as evidence that the educational efforts within the medical and pharmacy professions, "is rapidly reducing the use of these substances to medically indicated purposes only." The Association repeated its opinion that amphetamines "should be utilized for the management of hyperkinesis in children, narcolepsy, and other specific, medically indicated conditions only. The use of amphetamines and amphetamine-like substances as anorexiants (for weight reduction) or for the treatment of depression is not in keeping with responsible medical practice."

The Association stated it saw no need for, indeed would oppose, the enactment of legislation that would designate specific physicians only being allowed to prescribe these drugs. It indicated there may be merit in restricting the number of pharmacy outlets to realize more effective monitoring so as to eliminate "physican shopping" to obtain several prescriptions for drug misuse. "It may even be desirable to establish a system to register patients for whom these drugs may be prescribed."

The Association voiced its pleasure with seeing the section dealing with alcoholism and reiterated its opinion that "alcohol and tobacco remain the drugs of major misuse in all age groups. In terms of morbidity—social and medical, alcohol misuse leads to untold miseries, illness and social complications and far overshadows all other drug misuse."

The Association questioned the validity of the Commission's statements that the life expectancy of an alcoholic is ten to twelve years less than the average or that alcoholics may be successfully treated so as to allow them to return to the category of social drinkers but commended the Report and its recommendations, in particular "that criminal oriented drunk tanks be replaced by medically-oriented detoxification centers and that a variety of treatment modalities be available to meet the specific needs of individual alcoholic patients."

The Association accepted with serious reservations the efforts of the Commission to produce a short term medical management manual. "A fair start towards the production of such a guide has been made. However, it is obvious that the manual was written some months ago—is a little out-of-date, there are omissions, and errors and a few of the recommendations of the Commission are not practical." The Association recommended that, "a revision of this chapter be distributed to all members of the medical profession, hospital emergency departments, street clinics and other facilities and health care personnel involved in the short term medical management of non-medical drug users. We would recommend that if distributed in its current form that the Federal Government consider attaching a letter to the Report to bring it up-to-date and to make the important corrections that are required." The Association had previously recommended the production of a practical detoxication guide.

The Association found no major disagreements with the chapter on therapeutic communities and encouraged the adoption of the organization and coordination of the community treatment services section as a guide for the Federal Government's program in this area.

The Association disagreed "in the strongest possible terms" with the suggestion that heroin be used in reduced dosages for the treatment of heroin addiction.

While agreeing that the profession is subject to some criticism on its dealing with the non-medical use of drugs problem, it objected to the unqualified, negative criticism of the profession, and hospital services, as outlined in the context of the Commission's Report. The Association said: "as we have stated on numerous occasions, the non-medical use of drugs is not a medical problem but a social problem with medical manifestations. To anticipate or expect medicine to provide the answers to the majority, let alone all the problems involved, is both inappropriate and unrealistic."

The Association cited evidence to indicate a marked improvement in the attitudes and abilities of the profession, and other health workers, to cope with the medical aspects of the non-medical use of drugs.

In concluding, Dr. Roberts assured the people of Canada that the Canadian medical profession will meet and fulfill its responsibilities regarding the medi-

cal aspects of the non-medical use of drugs. The Association also offered its services to the Federal Government—"in any way in which we may be helpful relative to this problem."

MUNRO MOVES

On February 24, the Honourable John Munro, Minister of National Health and Welfare, announced in the House of Commons that he would introduce regulations under the Food and Drug Act to restrict the availability of methadone, amphetamines, phenmetrazine and phendimetrazine.

The regulations relative to methadone will likely be invoked by Order in Council by the time this Journal is distributed.

"Physicians will be permitted to prescribe methadone only after they are authorized to do so by the Minister of National Health and Welfare. Those so authorized will be considered to be qualified by reason of expertise and having access to the necessary laboratory and ancillary services to effectively utilize methadone in the treatment of heroin abuse." In effect, the Minister has announced he will invoke controls according to the recommendations of the Joint C.M.A.-F.D.D. Committee and the LeDain Commission.

Physicians associated with approved clinics only will be allowed to prescribe methadone. It is expected that patients from smaller communities, and more remote parts of Canada, will have to travel to these relatively few clinics for confirmation that they are narcotic addicts and for the introduction of their methadone replacement therapy. Once stabilized, they will be able to return to their communities—and continue to receive their maintenance methadone dosage from local physicians, and other health personnel, associated with the clinic for that specific purpose. In general, private practitioners will no longer be allowed to initiate methadone treatment.

The use of amphetamines, and the related drugs phenmetrazine and phendimetrazine, will be limited to the treatment of those disorders for which there are proven medical bases. Use of these drugs for the treatment of obesity, as "diet pills," will no longer be permitted. Any physician wishing to prescribe amphetamines, phenmetrazine and phendimetrazine will be authorized by the Minister of National Health and Welfare to do so—provided he wishes to use the drugs for treatment of bona-fide narcoleptics and hyperkinetic children. A list of consulting physicians to verify such diagnoses is to be drawn up by the Department in co-operation with the Canadian Medical Association and L'association des Medecins de Langue Francaise du Canada.

The Minister expressed his pleasure with the cooperation being offered by the medical associations of Canada and indicated that the details relative to the new amphetamine control program would be worked out in co-operation with the medical profession during the next few months. He expressed the opinion that the program will be fully operational by September 1, 1972.

C.M.A. RESPONSE

The C.M.A. commended the Federal Government for its prompt action relative to the control of methadone, expressed the hope that the regulations would be enacted and enforced as soon as possible, and offered its support for the action, and the resultant changes in the treatment of narcotic addiction that would be created.

With respect to the announced controls on amphetamines, phenmetrazine and phendimetrazine, the Association expressed its qualified agreement. Earlier, following the Association's review of this subject, including the major physicians' prescribing habits survey conducted in December 1970, the Association recommended more stringent controls of both amphetamines and amphetamine-like substances (phenmetrazine, phendimetrazine, methylphenidate and diethylpropion).

The Association had indicated that it would oppose any move to restrict prescribing privileges to specific physicians or classes of physicians. There was some concern that the Federal Government would enact regulations whereby only neurologists, or other specifically designated classifications of physician would be allowed to prescribe them. The Association felt that this would be an impractical step, established relative to controls on physician's prescribing privileges.

The C.M.A. confirmed that it would help in any way possible to design the tighter controls necessary to eliminate misuse.

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Following consultation with the Canadian Pediatric Society and the Canadian Neurological Society, the Association stated:

"To draw up these controls without placing unnecessary or costly barriers between patients and the treatment that they require and benefit from, will take considerable effort and some time to implement. We completely agree that amphetamines should not be used as anorectics, i.e., for weight control, or the treatment of depression—the conditions for which they are most commonly misused; however, these drugs are effective in the treatment of narcolepsy and hyperkinetic conditions in children. As the Minister has outlined, narcolepsy is a relatively rare and obscure disorder but there are several thousand Canadian children spread all across the land suffering hyperkinesis."

The Association also warned:

"These controls will not eliminate or even substantially reduce the use of amphetamines and amphetamine-like substances by so called 'speed freaks.' For the most part, these individuals obtain their drugs from illicit sources.

"Tighter controls on amphetamines, phenmetrazine and phendimetrazine may not solve the so called 'diet pill problem.' It may simply shift the problem to the use of other amphetamine-like drugs—with potentially similar problems. We have already recommended more stringent controls for some and will maintain a very close watch on all drugs used as anorectics for weight control. It may prove necessary to recommend even more controls on these drugs."

Dr. J. D. Wallace, General Secretary of the C.M.A. has requested a continuing study of the situation including active participation by: The Canadian Paediatric Society, The Canadian Neurological Society, The College of Family Physicians of Canada, The Canadian Psychiatric Association, and the Medical Section of the Pharmaceutical Manufacturers Association of Canada. Dr. Wallace also directed that C.M.A. Journal advertising copy for anorexiants used for weight reduction purposes is to be accepted only if it is in keeping with C.M.A. policy. This will also apply to those drugs not covered under the new Food and Drug Act regulations, but having the same basic physiological effect and potentially capable of creating dependence. Dr. Wallace stated: "As has been indicated in the limited advertising for these drugs in C.M.A.J., they are for short term therapy use only.

In the opinion of the Canadian Medical Association, this means for a period not exceeding thirty days.

To date, there is no evidence that these drugs are creating a drug dependence problem—when used for short term adjunctive therapy.

We believe that weight reduction should be accomplished, wherever possible, without the utilization of drugs. However, there is no doubt that some patients are helped by the taking of an appetite suppressant or anorectic. We shall keep a very close watch on all drugs used as anorectics for weight control. Should they prove to create drug dependency problems, we shall no longer accept advertisements promoting their sale in our journals and will recommend to the Federal Government that they be subjected to more stringent control."

[News Release, February 24, 1972]

STATEMENT BY NATIONAL HEALTH AND WELFARE MINISTER JOHN MUNRO ON GOVERNMENT ACTION TO CONTROL ABUSE OF METHADONE AND AMPHETAMINES, DEPARTMENT OF NATIONAL HEALTH AND WELFARE, OTTAWA, CANADA

Mr. Speaker, honourable members, As Honourable Members are aware, the government is deeply concerned about the non-medical use of drugs, and the effects of such use on the individual and on our society. As part of our program to combat this hazard though a balanced comprehensive strategy, I wish to announce important action relating to two different types of drugs, the abuse of which has been a public health problem of major proportions in this country. I refer to action against the abuse of methadone and the amphetamines.

Methadone is an opiate-type synthetic drug which has become widely used in the treatment of heroin addiction. During the last year, staff of my Department have received many reports of misuse and abuse of methadone. As a result of concern over misuse of this drug, the former Food and Drug Directorate of my Department, and the Canadian Medical Association established

a joint committee in 1970 to investigate the proper place of methadone in the care of narcotic addicts. Concern about the abuse of methadone also was raised by the LeDain Commission in its final report on Treatment, which was submitted to the government a few weeks ago.

As a result of the recommendations of the joint FDD-CMA Committee and of the LeDain Commission, I have decided to restrict the availability of methadone in the following way: Physicians will be permitted to prescribe methadone only after they are authorized to do so by the Minister of National Health and Welfare. Those so authorized will be considered to be qualified by reason of expertise and the availability of necessary facilities and ancillary services to effectively utilize methadone in the treatment of heroin abuse.

In line with the recommendations of the LeDain Commission, authorized physicians will be required to be associated with a specialized clinic. Requests for authorization will be considered by an expert advisory committee to be appointed by me in cooperation with the medical profession. I expect necessary regulatory changes can be made and the methadone control program instituted within a few weeks time. The program should be fully operational by 1 June of this year. In the meantime I call upon the physicians of Canada to utilize restraint in the use of methadone.

Although smaller amounts of amphetamine now are being prescribed in Canada than a few years ago, considerable evidence has come to the attention of my Department indicating the over-prescribing of these drugs by some medical practitioners. Considerable evidence also exists that the related drugs phenmetrazine and phendimetrazine are misused in a manner similar to that of amphetamines.

Medical authorities are agreed that the legitimate medical use of amphetamines are extremely limited. They have at best only a minor role in rational drug therapy—primarily for the treatment of two relatively rare and obscure disorders, narcolepsy and hyperkinesis in children.

As a result of my grave concern about the serious public health implications of amphetamine abuse, I have decided that the use of amphetamines and the related drugs phenmetrazine and phendimetrazine will be limited to treatment of only those disorders for which they are indicated on medical grounds. Use of these drugs for treatment of obesity as so-called "diet pills" will not longer be permitted. Any physician wishing to prescribe amphetamines, phenmetrazine and phendimetrazine will be authorized by the Minister of National Health and Welfare to do so provided he wishes to use the drugs for treatment of *bona fide* narcoleptics and hyperkinetic children. In cooperation with the Canadian Medical Association and L'Association des Medecins de Langue Francaise du Canada, a list of consulting physicians will be drawn up to aid in verification of the diagnosis of these relatively rare disorders.

I am extremely pleased with the cooperation being offered to us by the medical associations of Canada in helping solve this important problem.

I am fully aware Honourable Members, that this action to control misuse of legally prescribed amphetamines does not directly affect use of these drugs by so-called "speed freaks" who obtain their drugs from illicit sources. Nevertheless, this action does indicate the serious light in which the Government views amphetamine abuse and should have marked effects on an important aspect of abuse of these drugs—that by adults who obtain their drugs on prescription.

It will take a few months to work out the details of the amphetamine control program in cooperation with the medical profession. I expect, however, that the program will be fully operational by September 1 of this year.

In closing, Mr. Speaker, may I make a brief mention of another aspect of our total program to control the misuse and abuse of drugs. In January of this year ,we invited parents and others receiving Federal social assistance cheques to send for a free information booklet entitled, "A Parent's Guide to Drug Abuse." Public response to this offer has been most gratifying and in fact almost overwhelming. To date, nearly 500,000 requests for the booklet have been received by the staff of our Non-Medical Use of Drugs Directorate. Because of the large volume of requests, it is taking my staff longer than they had first anticipated to provide copies of the booklet to all who have requested it. I ask the public to be patient. Everyone who requests a copy of this useful publication will be sent one. This booklet is but the first in a continuing series of factual presentations on various aspects of drug abuse, aimed at providing the facts on this serious problem to Canadians, as part of our drug education program.

Thank you, Mr. Speaker.

17.

INTERIM REPORT OF THE TEMPORARY STATE COMMISSION TO EVALUATE THE DRUG LAWS, NEW YORK STATE—LEGISLATIVE. DOCUMENT (1972) No. 23 pp 246–247

ILLICIT DRUGS PRICE CHART—NEW YORK CITY[1]

	Low	High	Usual
Heroin:			
1 grain	$2	$7	$5
⅛ ounce (54 grains)	50	300	200
¼ ounce	75	500	350
1 ounce	250	1,800	1,000
8 ounces	4,000	8,000	6,000
16 ounces	5,000	20,000	10,000
Marihuana:			
⅛ ounce	4	7	5
¼ ounce	8	12	10
1 ounce	20	40	30
8 ounces	80	175	125
16 ounces	100	300	150
Amphetamine:			
10 tablets (1 tablet=250–300 milligrams with 5–25 milligrams amphetamine)	8	12	10
100 tablets (approximately 1 ounce)	40	70	50
300 tablets (approximately 3 ounces)	120	210	150
600 tablets (approximately 6 ounces)	240	420	300
Hahish:			
1 gram	8	15	12
¼ ounce	20	40	30
1 ounce	80	120	100

[1] The above was compiled from information obtained from law enforcement officials and community workers through their testimony and their responses to questionnaires.

ILLICIT DRUGS PRICE CHART—OTHER NEW YORK COMMUNITIES[1]

	Low	Hjgh	Usual
Heroin:			
1 grain	$4.00	$11.00	$7.00
⅛ ounce (54 grains)	63.00	112.00	88.00
¼ ounce	92.00	158.00	124.00
1 ounce	485.00	820.00	652.00
8 ounces	3,676.00	7,280.00	5,152.00
16 ounces	7,400.00	15,840.00	11,400.00
Marihuana:			
⅛ ounce	3.00	5.00	4.00
¼ ounce	5.00	11.00	8.00
1 ounce	14.00	27.00	19.00
8 ounces	78.00	131.00	107.00
16 ounces	139.00	213.00	173.00
Amphetam ne:			
10 tablets (1 tablet =250 to 300 milligrams with 5 to 25 milligrams amphetamine)	2.90	4.75	3.93
100 tablets (approximately 1 ounce)	24.00	49.00	33.00
300 tablets (approximately 3 ounces)	46.00	134.00	93.00
600 tablets (approximately 6 ounces)	108.00	258.00	171.00
Hashish:			
1 gram	5.00	10.00	7.00
¼ ounce	30.00	50.00	39.00
1 ounce	82.00	137.00	108.00

[1] The above was compiled from information obtained from law enforcement officials and community workers through their testimony and their responses to questionnaires.

18. ILLICIT USE OF DANGEROUS DRUGS IN THE UNITED STATES:

A Compilation of Studies, Surveys, and Polls

Dorothy F. Berg, M.A.

September, 1970

Drug Sciences Division
Office of Science and Drug Abuse Prevention
Bureau of Narcotics and Dangerous Drugs
United States Department of Justice

PREFACE

This report is the fourth edition of a compilation of studies, surveys, and polls on the extent, frequency, and current illicit use of dangerous drugs and other "exotic" substances. Included in the compilation are drug usage statistics for students in colleges and universities, senior high schools, and junior high schools. Additional statistics are shown for high school dropouts, hippies, working youth, adults, and enlisted men who served in Viet Nam. Categories of dangerous drugs and substances included in this report are the hallucinogens, stimulants, depressants, opiates, and other "exotic" substances, such as glue, gasoline, nitrous oxide, and cough syrup. Of the surveys of college students reported here, 14 were conducted in the West, nine were in the Northeast, four were in the South, and one was in the North Central region. At the secondary school level, 12 surveys were conducted among high school students in the North Central region, eight were in the West, three were in the Northeast, and one was in the South. The only survey of high school dropouts was made in the West. Included in the compilation are three junior high school surveys. These were conducted in the Northeast, the South, and the West, respectively. Of the four nationwide surveys reported here, three were conducted among college students and one was conducted among the adult population, 21 years of age and over. Surveys of young adults as well as hippie youth were conducted in the Northeast and West; surveys of adult populations were conducted in the West and the North Central region; and one survey of enlisted men was conducted in Viet Nam. It should be noted that the majority of the universities and high schools included in the compilation are located in large metropolitan areas. The studies, surveys, and polls presented in this compilation vary in reliability and validity. These shortcomings make it difficult to generalize the results of the studies. In some instances, results cannot be generalized even to the school where the survey was made because appropriate sampling techniques were not employed.

LIST OF TABLES

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Hallucinogens			Stimulants		
						LSD	Marihuana	Other hallucinogens	Amphetamines	Other stimulants	
COLLEGE STUDENTS											
Sample of full-time undergraduate students at Harvard-Radcliffe, Boston College, University of Massachusetts at Boston, and Suffolk University. Source: The Boston Globe, March 1970, and the "Survey Plan" by Becker Associates..	1970	Northeast	390	Telephone or personal interview	Used during past year		48.0	11.0 1/			This survey was conducted for the Boston Globe by Becker Associates. The universe of youth between the ages of 16 and 23 included high school students, college students, and working youth. The survey instrument was designed to be self-administered or administered by interviewers on the telephone or by personal visit. Findings indicate that marihuana had been smoked in the past year by 21 percent of high school youth, 48 percent of college youth, and 26 percent of employed youth. No information on the response rate was made available.
					Men		53.0	12.0			
					Once		6.0				
					A few times		13.0				
					Occasionally		23.0				
					Frequently		10.0				
					Women		34.0	8.0			
					Once		7.0				
					A few times		11.0				
					Occasionally		9.0				
					Frequently		8.0				
Sample of the undergraduate and graduate students at the University of Michigan. Source: John Bruce Francis and David J. Patch, Student Attitudes Toward Drug Programs At The University of Michigan. Study Conducted under the Auspices of the University Committee on Drug Education, Sept. 1969.	1969	North Central	580 58 percent return	Self-administered questionnaire (mail)	Ever used		44.0 2/	12.2 1/	24.7		The sample was chosen randomly by computer. Since the questionnaire was mailed by students immediately prior to final examinations, the 58 percent response rate "would indicate a widespread and generally high level of interest on the part of students. It is not possible to assert that the final sample... was random and representative." The purpose of this study was two-fold: (1) discover the extent and level of drug use, and (2) determine "what kinds of information about drugs were needed and desired by students and through what types of formats students were most likely to accept such information."
					Once		7.3	4.7	8.5		
					Seldom		21.4	5.2	12.5		
					Often		9.9	1.6	2.8		
					Regularly		5.4	0.7	0.9		

1/ Includes all hallucinogens except marihuana
2/ Reported as marihuana or hashish

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
Students in nine colleges, universities, and professional schools in the Denver-Boulder metropolitan area. Source: James T. Barter, George L. Mizner, Paul H. Werme, Patterns of Drug Use Among College Students: An Epidemiological and Demographic Survey of Student Attitudes and Practices, Department of Psychiatry, University of Colorado Medical School, 1970.	1969	West	26,111 66 percent return	Self-administered questionnaire (mail)	Ever used	5.4	26.0	5.0 3/	14.0		A large scale census of nine institutions of higher learning in the Denver-Boulder metropolitan area. Data on the response rate for each institution is not yet available. Given "the present state of computer technology," the researchers "felt that it was very feasible to carry out such a large-scale survey..." One of the several objectives of the study was to investigate the relationship between drug usage and differing college environments. This section of the report is not yet available.
					1-2 times		9.0		6.0		
					3-9 times		6.0		4.0		
					10-29 times		4.0		2.0		
					30 or more times		7.0		2.0		
Students enrolled in undergraduate classes in psychology and business administration at the University of Maryland. Source: James D. McKenzie, Trends in Marijuana Use Among Undergraduate Students At The University of Maryland, Research Report #3-70, Counseling Center, University of Maryland, College Park, Md.	1969	South	595	Self-administered questionnaire (classroom)	Ever used		35.6				Students who were included in the survey were maioly from the Colleges of Arts and Sciences, Education, and Business and Public Administration. Comparison of the proportion of students who reported use of marihuana in the present survey with proportions of students reporting use in other years reveals that use of the drug has risen from 15 percent in 1967 to 28.9 percent in 1968 to 35.6 percent in 1969. One of the findings was that marihuana use "is more common among students living off-campus and not with their families than among dormitory residents or students living with their families."
					Men		43.6				
					Once		11.0				
					Several times		24.6				
					Regularly		8.0				
					Women		29.3				
					Once		6.6				
					Several times		15.4				
					Regularly		7.3				

3/ Peyote

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
A total population survey of coed undergraduate and graduate students at Sacramento State College, California. Source: Richard L. Morrison, Associate Dean of Students, "Preliminary Report on the Incidence of the Use of Drugs at Sacramento State College," May 15, 1969.	1969	West	10,364 82 percent return	Self-administered questionnaire	Ever used 1-3 times 4-10 times Over 10 times	4.8 2.5 1.0 1.3	23.3 8.2 4.1 11.0		6.8 2.3 1.7 2.7		Survey form was included in the registration packets which were distributed on January 9-11, 1969 to the 12,700 Fall semester students who were registering in advance for the Spring 1969 semester. The survey directions stated that return of the card was to be voluntary and anonymous. Report indicated that men in the Upper Division were more frequent drug users than men in either the Lower or Graduate Divisions. Men in the Upper Division were also more frequent drug users than women in any of the three divisions. Although statistics on current drug use were collected in the survey, they were not included in the preliminary report.
A sample of all college students in Florida. Source: News release from the office of the Attorney General of Florida, Earl Faircloth, of the preliminary results of a survey of students enrolled in Florida's private and public universities and junior colleges.	1969	South	2,000 40 percent return	Self-administered questionnaire (mail)	Ever used	6.8	26.9				"The survey...was conducted by experts at Florida Atlantic University and professionals in psychiatry and medicine associated with Drug Research Foundation, Inc., a non-profit corporation. Heading the research and survey team were Dr. David Georgoff, Dr. Raymond R. Killinger, Jr. and Dr. Barry J. Hersker." Since the response rate was low--only 40 percent of the students returned their questionnaires--the data may not be representative of the college population in Florida.

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
A survey of full-time college students on 57 campuses in the U.S. conducted by The Gallup Organization for Newsweek. Source: Newsweek, Dec. 29, 1969, pp. 42-45.	1969	Nationwide	1,092	Self-administered questionnaire	Ever used	8.2	31.9		13.5		Rates of use of LSD and marihuana among college students were considerably higher in this survey than in one conducted six months earlier by Gallup. This may have been due to "secret ballots" for responses to items on drugs, sex, and protest.
A nationwide survey of students in private institutions, state supported institutions, and denominational or church related universities and colleges. Source: The Gallup Poll, reported by George H. Gallup, Jr. and John O. Davies III in The Washington Post, May 20, 1969.	1969	Nationwide	Not reported	Interview	Ever used	4.0	22.0				Data on drug use were part of a larger survey probing student disorders. Students who reported participating in demonstrations were more likely to say they had used drugs than those who reported they had not participated in demonstrations.
A random sample of undergraduate males in a large state university in Southeastern United States. Source: John H. Ewing, et al, Why Students "Turn On," Marijuana and other Drug Use in an Undergraduate Male Population. Paper presented at Second International Congress of Social Psychiatry, London, August 4-9, 1969.	Late 1960's	South	138 77 percent response rate	Interview	Ever used		30.0				Sample drawn at random from the university register of undergraduate male students and stratified by residence: dormitory, fraternity, and private accommodations. Results indicate that there is no relatiooship between marihuana use and place of residence.
					Less than 10 times		18.0				
					10-100 times		7.0				
					Over 100 times		5.0				
					Current users		17.0				

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
Undergraduate students at the University of California, Davis and their parents Source: S. Coopersmith and L. Dick, "Attitudes Towards Alcohol and Other Drugs Expressed by College Students and Their Parents," paper delivered at Intntl. Congress on Alcohol and Alcoholism, Sept. 18, 1969, Wash., D. C.	Late 1960's	West	Undergraduate students: 303 Parents of undergraduate students 218	Self-administered questionnaire	Ever used Students Parents	6.0 0.9	31.4 2.8				The authors state, "As a generality we might propose that the use of drugs has not increased between generations and that marijuana and alcohol play similar roles of social facilitating and relaxing agents for students and parents. Alcohol is still the most widely used drug for both generations but students are more likely to have used marijuana. The level of drinking is far greater for parents than for their college age offspring."
Random sample of members (male) of the Wesleyan graduating class of 1969 who had been enrolled as full-time students in each of six successive semesters. Source: C. Hess Haagen, Social and Psychological Characteristics Associated with the use of Marijuana by College Men. Wesleyan University, Office of Psychological Services, Middletown, Conn.	1968	Northeast	70 82 percent return	Self-administered questionnaire	Ever used Infrequent users Frequent users		4/ 59.0 36.0 23.0				Drug use on the Wesleyan campus prior to 1965 was minimal. By 1968 use of psychoactive substances on the campus was well publicized. One reason for studying members of the class of 1969 was that the period of their enrollment paralleled the period of increased availability and use of drugs at Wesleyan. The findings indicate that students who did not use marihuana never used any other hallucinogenic drug. "Twenty-six percent of infrequent users and 62% of frequent users reported having used LSD."

4/ 13 percent reported they had tried hashish.

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
A survey of the entire student body at Carnegie-Mellon University. Source: Joel W. Goldstein, et al, The Social Psychology of Student Drug Usage: Report on Phase One, A Report of the Carnegie-Mellon University Drug Research Project, June 1970.	1968	North-east	3,010	Self-administered questionnaire	Ever used	3.4	23.8	2.0 5/	12.3	1.1 6/	"An attempt was made to survey 100% of the full-time student body. This procedure was followed rather than a sampling one in order to aid in the protection of the anonymity of respondents by making it more difficult to identify them through their personal characteristics." A technique to further guarantee anonymity while permitting follow-ups was also employed. This technique was first used by Dr. Kenneth Eells in a 1967 drug use survey at the California Institute of Technology. A resurvey of freshmen in the spring of 1969 showed a 10 percent increase in marihuana usage.
					Once	1.4	4.8	1.0	2.9	0.6	
					2-10 times	1.4	8.2	1.0	5.5	*	
					10-50 times	0.5	5.8	*	2.6	-	
					More than 50 times	*	5.0	*	1.3	*	
Survey of student body at Ithaca College during Spring registration. Survey not a formal part of registration. Additional returns obtained from students in five large classes. Source: Martin E. Rand, et al, "A Survey of Drug Use At Ithaca College," presented at the American College Health Association Annual Convention, May 1968.	1968	North-east	2,145 70 percent return	Self-administered questionnaire	Male Ever used		28.9	4.8 7/	14.0		Not a representative sample. The 200 questionnaires completed in five classes following registration were not significantly different than those completed during registration. Investigators state, "The fact that there were no differences increases the reliability of the combined samples."
					Female Ever used		17.5	1.5 7/	7.0		

5/ Mescaline
6/ Cocsine
7/ Includes all hallucinogens except marihuana
* Less than one-half of one percent

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Hallucinogens			Stimulants		
						LSD	Marihuana	Other hallucinogens	Amphetamines	Other stimulants	
COLLEGE STUDENTS--Con.											
Random sample of students at five institutions of higher learning in California. Source: Richard Blum and Associates, Students and Drugs, San Francisco: Jossey-Bass, Inc., 1969.	1967	West	School I Private university 300 100 percent return	Interview; structured questionnaire	Ever used		21.0	6.0 8/			A five-campus study of student use of illicit as well as socially approved drugs. Students guaranteed anonymity. The five institutions differ by organization, course offerings, reputation, and location. Social charcteristics of drug users and abstainers are compared.
		West	School II Catholic university 270 98 percent return	Interview; structured questionnaire	Ever used		11.0	2.0			
		West	School III Junior college 201 97 percent return	Interview; structured questionnaire	Ever used		21.0	7.0			
		West	School IV State college 192 64 percent return	Interview; structured questionnaire	Ever used		33.0	9.0			
		West	School V State university 293	Interview; structured questionnaire	Ever used		10.0	2.0			

8/ Includes all hallucinogens except marihuana

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Hallucinogens			Stimulants		
						LSD	Marihuana	Other hallucinogens	Amphetamines	Other stimulants	
COLLEGE STUDENTS--Con.											
Undergraduate, graduate, and professional students at the State University of New York at Buffalo who appeared at a University office in September 1967 to obtain an I. D. card. Source: Edward F. Marra, et al, Intoxicant Drugs: Survey of Student Use, Roles And Policies Of The University, State University of New York at Buffalo, University Committee on Drugs and the Campus.	1967	North-east	8,545 70 percent return	Self-administered questionnaire	Ever used Current users	2.6 1.1	13.0 6.7	0.7 9/ *	8.5 2.8		The response rate for graduate and professional students was 85.3 percent versus 64.5 percent for the undergraduates. Some of the findings were: (1) the rate of drug use was higher among undergraduates than among graduate students, (2) liberal arts students are more likely to use drugs than students in other study areas, (3) current use rates are highest for students who live in rented apartments.
Relatively random sample survey of undergraduate and graduate students at California State College at Long Beach. Source: George Demoa, et al, "Drug Use On The College Campus: A Pilot-Study Survey," mimeographed.	1967-1968	West	540	Questionnaire	Ever used	6.0					A pilot study in which anonymity was assured. One of objectives was to obtain some indication of educational approaches most likely to deter use of potentially dangerous drugs.

9/ Mescaline
* Less than one-half of one percent

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
June 1967 male graduates of Dartmouth College. Source: Francis W. King, "Marihuana and LSD Usage Among Male College Students: Prevalence Rate, Frequency, and Self-estimates of Future Use," Psychiatry, Vol. 32, No. 3, August 1959, pp. 265-276.	1967	Northeast	576 78.9 percent return	Self-administered questionnaire (mail)	Ever used 1-2 times 3-10 times 11 or more times	3.7 1.6 1.2 0.9	22.0 9.2 6.6 6.2				All students (N=730) who received the BA degree from Dartmouth College in June 1967 were surveyed by mail about one month after graduation on use of marihuana and LSD. Respondents whose initial use of a hallucinogenic drug occured subsequent to their commencement "were classified as non-users for that drug. This was done to keep a uniform cutoff date and to limit the study to the drug behavior of undergraduates."
Undergraduate and graduate students at U.C.L.A. Source: Student referendum sponsored by U.C.L.A. Student Legislative Council. Reported in the New York Post, Dec. 8, 1967.	1967	West	9,261 32 percent return	Student referendum	Ever used	6.9	34.9				The proportion of students who voted in the referendum was too small to give a reliable estimate of drug abuse at U.C.L.A. in 1967.
Nationwide survey of college students. Source: American Institute of Public Opinion for Reader's Digest.	1967	U. S.	520	Interview	Ever used	1.0	5.0				Sample random but very small. Problems of response (non-sampling) error.

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con. 10

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
Representative random sample survey of undergraduate and graduate students at a West Coast university. Source: Edward A. Suchman, "The Hang-Loose Ethic And The Spirit Of Drug Use," Journal of Health & Social Behavior, Vol. 9, No. 2, June 1968.	1967	West	497 81 percent return	Two part questionnaire. One-half personal interview and one-half self-administered questionnaire	Ever used	2.2	21.1				A good survey of a university. An sttempt to relate student drug use with repudiation, or at least questioning, of idess, values, and beliefs of American society.
Survey of all undergraduate and graduate students at the California Institute of Technology. Source: Kenneth Eells, "Marijuana and LSD: A Survey of One College Campus," Journal of Counseling Psychology, 1968, Vol. 15, No. 5.	1967	West	1,288 90 percent return	Self-administered questionnaire (mail)	Ever used 1-2 times 3 or more times	5.5 2.0 3.5	13.7 5.0 8.7	2.3 10/	11.1		Excellent return for a survey dealing with a sensitive issue. Unique technique employed to guarantee complete anonymity while permitting two follow-ups.
Random aample survey of undergraduate student body at Yale. Source: Lillian L. Imperi, et al, "Use of Hallucinogenic Drugs On Campus," The Journal of the American Medical Association, Vol. 204, No. 12, June 17, 1968.	1967	Northeast	327 80 percent return	Self-administered questionnaire (mail)	Ever used	2.0	18.0				A one-page anonymous questionnaire on the use of hallucinogens mailed to both Yale and Wesleyan students. Similsrity of overall drug use suggest reliability of the instrument, but validity needs to be confirmed.

10/ Morning-glory seeds

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
COLLEGE STUDENTS--Con.											
Random sample survey of undergraduate student body at Wesleyan. Source: Lillian L. Imperi, et al, "Use of Hallucinogenic Drugs On Campus," The Journal of the American Medical Association, Vol. 204, No. 12, June 17, 1968.	1967	North-east	251 66 percent return	Self-administered questionnaire (mail)	Ever used	7.0	20.0				A one-page anonymous questionnaire on the use of hallucioogens mailed to both Yale and Wesleyan students. Similarity of overall drug use suggests reliability of the instrument, but validity needs to be confirmed.
Students at Mary Washington College (college for women) of the U. of Virginia. Source: Poll conducted by the Bullet, student newspaper.	1967	South	Number of students reporting unknown (two-thirds of student body polled)	Student poll	Ever used		5.6				Poll cannot be considered reliable. Low response rate.
Survey of all seniors graduating in the Spring of 1965 from Brooklyn College of the City University of New York. Source: Samuel Pearlman, "Drug Use And Experience In An Urban College Population." Paper presented at the 44th Annual Meeting of the American Orthopsychiatric Association, Washington, D. C., March 1967.	1965	North-east	1,245 55 percent return	Self-administered questionnaire (mail)	Ever used		4.2				Dr. Pearlman stated that, "The...survey must be considered to be a trial epidemiological effort, and the use of a questionnaire method within an anonymous framework has obvious limitations." Another limiting factor is the low response rate.
					Male		2.0				
					Female		2.2				
					Used Frequently		2.5				
					Male		1.1				
					Female		1.4				

* Less than one-half of one percent

Table 1.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Hallucinogens			Stimulants		
						LSD	Marihuana	Other hallucinogens	Amphetamines	Other stimulants	
COLLEGE STUDENTS--Con.											
U. S. born male graduate students at a large urban university in Southern California who responded to an advertisement for paid experimental subjects. They had no prior knowledge of what the study involved. Source: William H. McGlothlin and Sidney Cohen, "The Use of Hallucinogenic Drugs Among College Students," American Journal of Psychiatry, 1965, 122: 572.	1965	West	121	Interview	Ever used		10.7				"...the students were self-selecting volunteers and not necessarily representative of the entire male group in the graduate division of this university." 11/
Students in a medical school located in the Northwest. Source: Stanley N. Smith and Paul H. Blachly "Amphetamine Usage By Medical Students," The Journal of Medical Education, Feb. 1966, Vol. 41, No. 2.	1964	West	208 70 percent return	Self-administered questionnaire (mail)	Ever used				26.9		The survey guaranteed anonymity of students. Design of the survey is not discussed in the published article.

11/ Samuel Pearlman, "Drug Use and Experience In An Urban College Population." Paper presented at the 44th Annual Meeting of the Amreican Orthopsychiatric Association, Washington, D.C., March, 1967, p. 7.

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens LSD	Hallucinogens Marihuana	Hallucinogens Other hallucinogens	Stimulants Amphetamines	Stimulants Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS											
Sample of high school students across the state of Massachusetts. Source: The Boston Globe, March 1970, and the "Survey Plan" by Becker Associates.	1970	North-east	400	Telephone interview	Ever used		21.0	6.0 1/			This survey was conducted for the Boston Globe by Becker Associates. The universe of youth between the ages of 16 and 23 included high school students, college students, and working youth. The survey instrument was designed to be self-administered or administered by interviewers on the telephone or by personal visit. Findings indicate that marihuana had been smoked in the past year by 21 percent of high school youth, 48 percent of college youth, and 26 percent of employed youth. No information on the response rate was made available.
					Men		23.0	8.0			
					Once		7.0				
					A few times		5.0				
					Occasionally		4.0				
					Frequently		7.0				
					Women		18.0	5.0			
					Once		4.0				
					A few times		4.0				
					Occasionally		6.0				
					Frequently		4.0				
Population consisted of a 5 percent sample of junior and senior high school students in Montgomery County, Md. Source: A Survey Of Secondary School Students' Perceptions Of And Attitudes Toward Use Of Drugs By Teenagers, Vol. II, Final Report, March 10, 1970, Joint Com. On Drug Abuse, Montgomery County, Md.	1969	South	Senior H.S. 1,348	Self-administered questionnaire	Ever used	5.9	18.7		7.8		A very complicated technique was employed to select the county-wide 5 percent sample. According to the report, reliability was established during the pilot test. Twenty-six percent of the boys and 20 percent of the girls in the senior class reported that they had used marihuana. As in other studies, use of alcohol far exceeded use of dangerous drugs.
					Tried but quit	2.2	7.3		4.5		
					Current users	3.7	11.4		3.3		
					About monthly	2.1	4.3		2.1		
					About weekly	1.2	4.3		0.8		
					About daily	*	2.8		*		
			Junior H.S. 1,429		Ever used	1.1	4.8		1.6		
					Tried but quit	0.7	2.7		1.1		
					Current users	*	2.1		0.5		
					About monthly	*	1.5				
					About weekly	*	0.6				
					About daily	*	-				

1/ Includes all hallucinogens except marihuana
* Less than one-half of one percent

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
All Utah public high school students enrolled in grades 10-12 in 36 school districts and 1,185 eighth and ninth grade students enrolled in five public junior high schools. Source: "Drug Use Among High School Students In The State Of Utah," in Advisory Committee Report On Drug Abuse, prepared by the Governor's Citizen Advisory Committee On Drugs, State of Utah, State Capitol Building, Sept. 1969.	1969	West	47,182	Self-administered questionnaire (mid-morning class period)	Ever used	4.9	12.2		10.0		All students enrolled in grades 10 through 12 and a selection of students enrolled in grades 8 and 9 were surveyed. No information is provided either on the proportion of all students in grades 10 through 12 who participated in the survey nor on how the sample was selected in grades 8 and 9. The final item on the questionnaire was an attempt to determine the accuracy of student responses on drug usage. One percent of the students said that their answers should be disregarded, 2.9 percent that most of their answers were accurate, 3 percent did not respond to the item, and the remainder said that their responses could be relied upon. One of the conclusions of the survey was that, "Drugs are being used by high school students in Utah but not extensively."
					Male	6.4	15.8		11.0		
					Once	2.2	4.5		3.6		
					2-5 times	1.5	4.1		3.3		
					6-10 times	0.8	1.7		1.3		
					More than 10 times	1.9	5.5		2.8		
					Female	3.4	8.6		8.9		
					Once	1.3	2.5		3.2		
					2-5 times	0.9	2.4		2.8		
					6-10 times	*	0.9		0.9		
					More than 10 times	0.8	2.8		2.0		
					Current users 2/						
					Male	4.4	8.5		5.1		
					Female	2.4	4.5		4.1		

2/ Respondents who reported use yesterday or today and a few weeks ago

* Less than one-half of one percent

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens LSD	Hallucinogens Marihuana	Hallucinogens Other hallucinogens	Stimulants Amphetamines	Stimulants Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
A random sample of high school dropouts in the 1967-68 and 1968-69 school years in 30 of 40 school districts in Utah. Source: "Drug Use Among High School Drop-outs In The State Of Utah," in Advisory Committee Report On Drug Abuse prepared by the Governor's Citizen Advisory Committee On Drugs, State of Utah, State Capitol Building, Sept. 1969.	1969	West	180 32 percent return	Self-administered questionnaire (mail)	Ever used	32.7	49.7		28.5		Response rate to the survey which had no follow-up was low. "Because of the methodology... responses may have come from those who are most cooperative. If this is so, it suggests that this study underestimates drug usage among high school drop-outs."
					Male	44.8	58.1		40.8		
					Rarely	10.6	11.6		12.3		
					Occasionally	15.3	5.8		19.8		
					Frequently	18.9	40.7		8.7		
					Female	20.5	35.6		15.6		
					Rarely	4.8	10.3		2.6		
					Occasionally	6.0	4.6		1.2		
					Frequently	9.7	20.7		11.8		
Stratified random sample of sophomore, junior, and senior students from five high schools in Madison, Wisconsin. Source: Jon G. Udell and Robert S. Smith, Attitudes, Usage, And Availability Of Drugs Among Madison High School Students, The University of Wisconsin, Bur. of Business Research and Service, Madison, Wisconsin, July 1969.	1969	North Central	781	Questionnaire	Ever used	5.8	22.6	13.9 3/	5.4 4/	5.6 5/	Information on the design of the survey and procedures in administering the questionnaire are not included in the report. The results indicate that alcohol is used more than any other drug.
					1-2 times	3.4	11.6	6.8	3.7	1.6	
					Infrequently	1.3	5.9	4.3	1.5	1.8	
					Frequently	1.1	5.1	2.8	*	2.2	

3/ Hashish
4/ Methamphetamine
5/ Cocaine
* Less than one-half of one percent

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens LSD	Hallucinogens Marihuana	Hallucinogens Other hallucinogens	Stimulants Amphetamines	Stimulants Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
All San Mateo County students in the homeroom at one point in time in 1969 in all the public high schools with the exception of one district, all the parochial high schools, and all the private high schools with the exception of one. Source: Five Mind-Altering Drugs, prepared by the Research and Statistics Section, Dept. of Public Health and Welfare, San Mateo, California.	1969	West	23,649	Self-administered questionnaire (homeroom)	Used during the last year	15.1	39.6		20.8		The questionnaire and procedures used in the 1968 and 1969 surveys were developed in a pilot study in 1967. The objective of the 1968 and 1969 surveys "was to make an assessment of the level of use of mind-altering drugs among San Mateo County high school students." Data for each of the two years indicate that the rate of use of marihuana among boys is greater for each succeeding class. Similarly the increased rate by class is noted for girls except that usage among girls tends to level off between the junior and senior year. However, the rate of marihuana use is greater for boys than girls. A comparison of rates for 1968 and 1969 indicates that the 1969 rates for both boys and girls have increased. In 1969, 50.1 percent of the Senior boys reported that they had used marihuana within the last 12 months. Data on LSD rates indicate that students reported a greater rate of use in 1969 than 1968. Rates of amphetamine use for boys and girls are very similar. For those respondents who did not specify their sex, the data reveal very large proportions of use for LSD, marihuana, and amphetamines.
					Boys	17.0	42.2		19.9		
					1-2 times	5.4	8.4		7.1		
					3-9 times	4.2	7.0		4.7		
					10 or more times	7.4	26.8		8.0		
					Girls	12.0	35.7		20.3		
					1-2 times	4.3	7.6		7.7		
					3-9 times	3.6	7.0		5.0		
					10 or more times	4.1	21.1		7.7		
					Sex not specified	24.6	49.9		30.4		
					1-2 times	8.3	9.2		9.7		
					3-9 times	5.5	7.1		6.8		
					10 or more times	10.8	33.6		13.9		
All San Mateo County students in the homeroom at one point in time in 1968 in all the public high schools with the exception of 2 districts. Source: Five Mind-Altering Drugs, prepared by the Research and Statistics Section, Dept. of Public Health and Welfare, San Mateo, California.	1968	West	18,774	Self-administered questionnaire (homeroom)	Used during the last year	10.7	32.0		16.3		
					Boys	12.3	34.6		16.3		
					1-2 times	4.3	8.3		6.3		
					3-9 times	3.3	6.6		3.9		
					10 or more times	4.7	19.7		6.1		
					Girls	8.4	28.4		15.5		
					1-2 times	3.3	8.3		6.2		
					3-9 times	2.3	5.4		3.6		
					10 or more times	2.8	14.7		5.7		
					Sex not specified	17.8	43.8		24.0		
					1-2 times	7.4	8.6		8.3		
					3-9 times	3.9	9.0		5.6		
					10 or more times	6.4	26.2		10.1		

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
A "sample" of San Mateo County 7th and 8th grade students in public, private, and parochial schools where permission was readily obtained to conduct the survey. Source: Five Mind-Altering Drugs, prepared by the Research and Statistics Section, Dept. of Public Health and Welfare, San Mateo, California.	1969	West	2,234	Self-administered questionnaire (homeroom)	Used during the last year 6/	2.4	11.1		5.6		The 7th and 8th grade survey was part of the larger San Mateo County high school survey of 1969 (See remarks on page 16).
					Boys	2.8	10.9		5.1		
					1-2 times	1.7	5.1		2.5		
					3-9 times	0.9	1.7		0.9		
					10 or more times	*	4.1		1.7		
					Girls	2.1	10.7		5.9		
					1-2 times	1.3	5.2		2.7		
					3-9 times	*	3.8		2.1		
					10 or more times	*	1.7		1.1		
Survey of all students in High School "A". Source: Juvenile Justice Commission, County of San Mateo	1967	West	878 (Male)	Questionnaire	Male						No information on design of survey or technique of questionnaire administration.
					Ever used	8.4	18.5				
					Once or twice	4.3	7.9				
					Three or more times	4.1	10.6				
			815 (Female)		Female						
					Ever used	4.3	8.6				
					Once or twice	2.3	4.4				
					Three or more times	2.0	4.2				

6/ Includes students who did not specify their sex

* Less than one-half of one percent

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
Samples of seniors in 11 high schools "which reflect the demographic, economic, and racial diversity" of Michigan. Source: Richard A. Bogg, et al, Drug Dependence In Michigan: A Study of Attitudes and Actions of The Young People of Michigan, Part III. Michigan Dept. of Public Health, 1968.	1968	North Central		Self-administered questionnaire	Type of School						An exploratory study. Samples of seniors cannot be said to be representative of all seniors in Michigan.
			89		Private Ever used	1.1	33.7	13.5 7/	1.1 8/		
			319		Suburban Ever used	2.8	10.3	3.4	5.3		
			148		Central City A Ever used	-	12.2	1.4	2.0		
			89		Central City B Ever used	1.0	12.4	3.4	2.2		
			113		Urban Community A Ever used	-	8.0	-	-		
			99		Urban Community B Ever used	-	11.1	2.0	1.0		
			104		Small Town Upper Peninsula Ever used	1.1	5.0	-	1.0		
			132		Small Town Lower Peninsula Ever used	2.3	7.6	0.8	0.8		
			64		Rural Community A Lower Peninsula Ever used	-	-	-	-		
			66		Rural Community B Lower Peninsula Ever used	-	-	-	-		
			156		Rural Community Upper Peninsula Ever used	1.3	5.7	1.3	2.2		

7/ Hashish
8/ Methamphetamine

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
Students in one upper middle class San Francisco Bay Area suburban high school. Source: Richard Blum and Associates, Students and Drugs, San Francisco: Jossey-Bass, Inc., 1969.	1967	West	1,614	Self-administered questionnaire	Male						Percentage of noo-response rate for item requesting whether respondents had tried marihuana was 31 percent, but non-response rate for item querying current use was 6 percent. Investigators hypothesize that high non-response rate may indicate that a much higher proportion of students may actually have tried the drug than actual response rate indicates.
					Ever used		16.0	10.0 9/			
					Currently using		5.0	7.0			
					Female						
					Ever used		10.0	5.0 9/			
					Currently using		3.0	1.5			
This survey was made in two schools. High School A Middle class students. High school in a suburban town located in the San Francisco Bay Area.	1967	West	839	Self-administered questionnaire	Male						Students guaranteed total anonymity. Survey administered and data collected by students from a local college. The questionnaire used in this study was a modification of the one used in the San Francisco Bay Area suburban middle class school.
					Ever used	14.0	31.0				
					Female						
					Ever used	13.0	28.0				
High School B Lower middle class and working class students. High school located in a Bay Area city. Source: Richard Blum and Associates, Students and Drugs, San Francisco: Jossey-Bass, Inc., 1969.			1,382		Male						
					Ever used	5.0	13.0				
					Female						
					Ever used	4.0	7.0				

9/ Includes all hallucinogens except marihuana

Table 2.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
Juniors and seniors of the three high schools in the Castro Valley Unified School District in Castro Valley, California. Source: Marvin E. Smith, District Superintendent, "Report To Parents of Students In Castro Valley Unified School District."	1967	West	1,272	Self-administered questionnaire completed in classroom	Male Ever used Female Ever used	15.4 8.7	35.0 22.3		21.5 17.7		Study guided and supervised by professors at the University of California at Berkeley. Questionnaire developed by a member of the School District to determine attitudes and behaviors of youth. Students guaranteed absolute anonymity.
All students attending classes at Mamaroneck Junior High School (grades 7-9) and Mamaroneck Senior High School (grades 10-12) on November 21, 1967. Source: Bernard F. Haake, Superintendent of Schools, Memorandum to the Board of Education, Mamaroneck, New York.	1967	North-east	Senior H.S. 1,225 Junior H.S. 1,294	Self-administered questionnaire completed in classroom	Ever used 1 time 2 or more times Ever used 1 time 2 or more times	2.9 1.0 1.9 0.6 * *	16.7 7.2 9.5 5.6 2.5 3.1		5.5 10/ 2.0 3.5 3.6 10/ 1.9 1.7		Some students who abuse drugs did not indicate usage while others who do not abuse drugs said they do. The school administration feels that these extremes tend to cancel each other out because of the large size of the sample.
All students attending classes on one day at Great Neck North Senior High School, Great Neck, New York. Source: M. Elliot Noyes, principal Great Neck North Senior High School, "Statement" for the Press Conference detailing some findings.	1967	North-east	2,587	Self-administered questionnaire completed in classroom	Ever used		8.0				This was a pilot study to test a questionnaire developed by Dr. Matt Chappell and Dr. Herman Goldberg. Data presented in this report are not "clean." According to Mr. Noyes, "...some students deliberately falsified the information and some misunderstood the questions and checked several responses in places where they were instructed to 'check only one.'"

10/ May include some amphetamines prescribed by physician
* Less than one-half of one percent

Table 3.--STUDIES, SURVEYS, AND POLLS OF OTHER POPULATION GROUPS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
OTHER POPULATION GROUPS											
Sample of young full-time employees of five major corporations in the Boston, Mass. vicinity. Source: The Boston Globe, March 1970 and the "Survey Plan" by Becker Associates.	1970	North-east	372	Self-administered questionnaire	Used during past year		26.0	7.0 1/			This survey was conducted for the Boston Globe by Becker Associates. The universe of youth between the ages of 16 and 23 included high school students, college students, and working youth. The survey instrument was designed to be self-administered or administered by interviewers on the telephone or by personal visit. Findings indicate that marihuana had been smoked in the past year by 21 percent of high school youth, 48 percent of college youth, and 26 percent of employed youth. No information on the response rate was made available.
					Men		45.0	18.0			
					Once		4.0				
					A few times		9.0				
					Occasionally		13.0				
					Frequently		19.0				
					Women		22.0	4.0			
					Once		4.0				
					A few times		7.0				
					Occasionally		6.0				
					Frequently		5.0				
A nationwide survey of adults, 21 years of age and over, conducted in more than 300 localities across the nation. Source: The Gallup Poll reported by George Gallup in The Washington Post, October 26, 1969.	1969	Nation-wide	1,539	Interview	Ever used		4.0				This survey shows that age and education are key factors in the use of marihuana. Use also varies by region of the country.
					21-29 years		12.0				
					30-49 years		3.0				
					50 years and over		1.0				
					Men		6.0				
					Women		2.0				
					College background		9.0				
					High school		3.0				
					Grade school		1.0				
					East		5.0				
					Midwest		2.0				
					South		2.0				
					West		9.0				

1/ Includes all hallucinogens except marihuana

Table 3.--STUDIES, SURVEYS, AND POLLS OF OTHER POPULATION GROUPS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
OTHER POPULATION GROUPS--Con.											
A representative cross-section of the population, 18 years of age or older, in San Francisco. Source: Dean I. Manheimer, Glen D. Melinger, and Mitchell B. Balter, "Marijuana Use Among Urban Adults," Science, Dec. 19, 1969, Vol. 166, No. 3912, pp. 1544-1545.	1967-1968	West	1,104	Interview	Ever used Men Women	3.0	13.0 18.0 9.0				"This research was part of a study designed primarily to examine the acquisition and use of psychotherapeutic drugs, including tranquilizers, stimulants, sedatives, and hypnotics." The researchers believe that most respondents were candid about their drug use. The researchers found that "A relatively high proportion of young adults in San Francisco have used marijuana one or more times. The propurtion in this age group who have used marijuana is as great among nonstudents as among students."
A 3.82 percent sample of all enlisted men in the lower and middle ranks (E-2 through E-6) who were being processed at a replacement center in Long Binh, South Vietnam for return to the United States. Data were collected between August 1 and November 1, 1967. Source: Roger A. Roffman and Capt. Ely Sapol, "Marijuana in Vietnam," The International Journal of the Addictions, 5(1), pp. 1-42, March 1970.	1967	South Vietnam	584 93 percent return	Self-administered questionnaire	Ever used Used in South Vietnam		31.7 28.9				The authors note certain reasons for caution in interpreting and generalizing from the data. "The representativeness of the current sample is restricted by the researchers' choice of rank distribution, i.e., enlisted men above the rank of E-6 and all officers were excluded from this study. Because the respondents were primarily assigned at the time of their rotation home to units in the two southern tactical corps areas, the data cannot be considered representative of Army enlisted men throughout Vietnam. It is possible that marijuana availability and use in the northern sectors is quite different."

Table 3.--STUDIES, SURVEYS, AND POLLS OF OTHER POPULATION GROUPS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Hallucinogens			Stimulants		
						LSD	Marihuana	Other hallucinogens	Amphetamines	Other stimulants	
OTHER POPULATION GROUPS--Con.											
An "opportunity" sample from the Haight-Ashbury Clinic "population and from other congregation areas and community agencies within the 20 square block Haight-Ashbury neighborhood." Source: J. Fred E. Shick, David E. Smith, and Frederick H. Meyers, "Use of Marijuana In The Haight-Ashbury Subculture" in David E. Smith (ed.), Journal Of Psychedelic Drugs, Vol. II, Issue I, (Fall) 1968 and J. Fred E. Shick, David E. Smith, and Frederick H. Meyers, "Use of Ampbetamine in the Haight-Ashbury Subculture" in David E. Smith (ed.), Journal Of Psychedelic Drugs, Vol. II, Issue II	1967	West	413	Interview	Ever used	87.0					Members of the Haight-Ashbury Community administered the instrument to the sample. At the time of the survey the hippie influence was still important but waning. The Haight-Ashbury "could be described as composed of sons and daughters of the white middle class, who often had some college experience and who frequently experimented with various drugs." Data indicates that marihuana served as a substitute for alcohol. Many in the community used marihuana and wine concurrently because they believed they became more stoned. Shick defines "the occasional /amphetamine/ oral user as one who indicated use up to 8 times in the month preceding the questionnaire, the oral regular user indicated use 9 to 30 times, and the oral abuser more than 30 times in the prior month." Intravenous experimental amphetamine users were divided into three categories by use in the previous month: (1) experimental-used one time; (2) periodic-used 2 to 8 times; (3) abuser-used 9 to more than 30 times.
					Male		94.6				
					Female		98.4				
					Current use		94.2				
					Men		92.3				
					Occasional		11.7				
					Regular		33.8				
					Habitual		46.8				
					Women		96.3				
					Occasional		13.1				
					Regular		45.0				
					Habitual		38.2				
					Oral						
					Occasional				60.5		
					Regular				4.6		
					Abuser				2.2		
					Intravenous						
					Experimental				17.7		
					Periodic				9.0		
					Abuser				7.3		

Table 3.--STUDIES, SURVEYS, AND POLLS OF OTHER POPULATION GROUPS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Hallucinogens: LSD	Hallucinogens: Marihuana	Hallucinogens: Other hallucinogens	Stimulants: Amphetamines	Stimulants: Other stimulants	Remarks
OTHER POPULATION GROUPS--Con.											
A pilot study of drug use among hippies in New York City. Most live in the East Village area. Source: Theo Solomon, A Pilot Study Among East Village "Hippies", Monograph #35. Associated YM-YWHA's of Greater New York, March 1968.	1967	North-east	51	Interview	Male						Sampling design not rigorous, therefore reaults cannot be generalized to all hippies. Interviewers who were drawn from the hippy population had at least a college education and were known within the hippy community.
					Ever used	97.0	100.0	94.0 2/	52.0 3/		
					Use now	58.0	97.0	81.0	29.0		
					Female						
					Ever used	80.0	100.0	90.0 2/	70.0 3/		
					Use now	65.0	100.0	85.0	35.0		
Negro men of normal IQ, born and reared in St. Louis, who attended a Negro elementary school. Source: Lee N. Robins and George E. Murphy, "Drug Use In A Normal Population of Young Negro Men," American Journal of Public Health, Vol. 57, No. 9, Sept. 1967.	1965-1966	North Central	221 94 percent of sample interviewed	Interview and record research	Ever used		47.0		17.0		A well-designed study with a carefully selected sample.

2/ Hashish
3/ Methamphetamine

Table 3.--STUDIES, SURVEYS, AND POLLS OF OTHER POPULATION GROUPS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF HALLUCINOGENS AND STIMULANTS--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Hallucinogens			Stimulants		
						LSD	Marihuana	Other hallucinogens	Amphetamines	Other stimulants	
OTHER POPULATION GROUPS--Con.											
Representative sample of peraons 21 years old and over in one city and one town in California. Source: Richard Blum, Institute for the Study of Human Problems, Stanford University. Hearings Before the Subcommittee of Executive Reorganization of the Com. on Government Operationa, U.S. Senate, May 24, 25, and 26, 1966, U.S. Govt. Printing Office, p. 123.	Early 1960's	West	200	Interview	Ever used Regular users	3.5 0.5	9.0 2.0				Sample is small. According to Dr. Blum, these "...results can be considered only suggestive rather than as genuine estimates."

Table 4.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants		Percent of use: Opiates		Percent of use: Glue & other substances	Remarks
						Barbiturates	Tranquilizers	Heroin	Other opiates		
COLLEGE STUDENTS											
Sample of the undergraduate and graduate students at the University of Michigan. Source: John Bruce Francis and David J. Patch, Student Attitudes Toward Drug Programs At The University Of Michigan. Study Conducted under the Auspices of the University Committee on Drug Education, Sept. 1969.	1969	North Central	580 58 percent return	Self-administered questionnaire (mail)	Ever used Once Seldom Often Regularly		12.1 3.1 7.8 1.2 -		16.9 1/ 6.3 9.9 0.5 *		The sample was chosen randomly by computer. Since the questionnaire was mailed by students immediately prior to final examinations, the 58 percent response rate "would indicate a widespread and generally high level of interest on the part of students. It is not possible to assert that the final sample... was random and representative." The purpose of this study was two-fold: (1) discover the extent and level of drug use, and (2) determine "what kinds of information about drugs were needed and desired by students and through what types of formats students were most likely to accept such information."
Students in nine colleges, universities, and professional schools in the Denver-Boulder metropolitan area. Source: James T. Barter, George L. Mizner, Paul H. Werme, Patterns of Drug Use Among College Students: An Epidemiological and Demographic Survey of Student Attitudes and Practices, Department of Psychiatry, University of Colorado Medical School, 1970.	1969	West	26,111 66 percent return	Self-administered questionnaire (mail)	Ever used	10.0	10.0		2.0 1/	2.0	A large scale census of nine institutions of higher learning in the Denver-Boulder metropolitan area. Data on the response rate for each institution is not yet available. Given "the present state of computer technology," the researchers "felt that it was very feasible to carry out such a large-scale survey..." One of the several objectives of the study was to investigate the relationship between drug usage and differing college environments. This section of the report is not yet available.

1/ Reported as narcotica
* Less than one-half of one percent

76-891 O - 72 - 30

Table 4.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquilizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
COLLEGE STUDENTS--Con.											
A total population survey of coed undergraduate and graduate students at Sacramento State College, California. Source: Richard L. Morrison, Associate Dean of Students, "Preliminary Report on the Incidence of the Use of Drugs at Sacramento State College," May 15, 1969.	1969	West	10,364 82 percent return	Self-administered questionnaire	Ever used 1-3 times 4-10 times Over 10 times				2/ 1.5 0.9 0.2 0.4		Survey form was included in the registration packets which were distributed on January 9-11, 1969 to the 12,700 fall semester students who were registering in advance for the Spring 1969 semester. The survey directions stated that return of the card was to be voluntary and anonymous. Report indicated that men in the Upper Division were more frequent drug users than men in either the Lower or Graduate Divisions. Men in the Upper Division were also more frequent drug users than women in any of the three divisions. Although statistics on current drug use were collected in the survey, they were not included in the preliminary report.
A nationwide survey of students in private institutions, state supported institutions and denominational or church related universities and colleges. Source: The Gallup Poll, reported by George H. Gallup, Jr. and John O. Davies III in The Washington Post, May 20, 1969.	1969	Nationwide	Not reported	Interview	Ever used	10.0					Data on drug use were part of a larger survey probing student disorders. Students who reported participating in demonstrations were more likely to say they had used drugs than those who reported they had not participated in demonstrations.

2/ Reported as hard narcotics

Table 4.--STUDIES, SURVEYS AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Depressants		Opiates		Glue & other substances	
						Barbiturates	Tranquilizers	Heroin	Other opiates		
COLLEGE STUDENTS--Con.											
A survey of full-time college students on 57 campuses in the U.S. conducted by The Gallup Organization for Newsweek. Source: Newsweek, Dec. 29, 1969, pp. 42-45.	1969	Nationwide	1,092	Self-administered questionnaire	Ever used	11.7					Rates of use of LSD and marihuana among college students were considerably higher in this survey than in one conducted six months earlier by Gallup. This may have been due to "secret ballots" for responses to items on drugs, sex, and protest.

Table 4.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquillizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
COLLEGE STUDENTS--Con.											
A survey of the entire student body at Carnegie-Mellon University. Source: Joel W. Goldstein, et al, The Social Psychology of Student Drug Usage: Report on Phase One, A Report of the Carnegie-Mellon University Drug Research Project, June 1970.	1968	Northeast	3,010	Self-administered questionnaire	Ever used	4.5	12.0	0.5	2.6 3/		"An attempt was made to survey 100% of the full-time student body. This procedure was followed rather than a sampling one in order to aid in the protection of the anonymity of respondents by making it more difficult to identify them through their personal characteristica." A technique to further guarantee anonymity while permitting follow-ups was also employed. This technique was first used by Dr. Kenneth Eells in a 1967 drug use survey at the California Institute of Technology. A resurvey of freshmen in the spring of 1969 shows a 10 percent increase in marihuana usage.
					Once	1.1	2.7	*	1.2		
					2-10 times	2.6	6.1	*	1.3		
					10-50 times	0.5	2.1	-	*		
					More than 50 times	*	1.1	*	*		
Survey of student body at Ithaca College during Spring registration. Survey not a formal part of registration. Additional returns obtained from students in five large classes. Source: Martin E. Rand, et al, "A Survey of Drug Use At Ithaca College," presented at the American College Health Association Annual Convention, May 1968.	1968	Northeast	2,145 70 percent return	Self-administered questionnaire	Male Ever used	3.3			3.8 4/		Not a representative sample. The 200 questionnaires completed in five classes following registration were not significantly different than those completed during registration. Investigators state, "The fact that there were no differences increases the reliability of the combined samples."
					Female Ever used	1.7			1.3		

3/ Opium
4/ Reported as opiates
* Less than one-half of one percent

Table 4.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquilizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
COLLEGE STUDENTS--Con.											
Random sample of students at five institutions of higher learning in California. Source: Richard Blum and Associates, Students and Drugs, San Francisco: Jossey-Bass, Inc., 1969.	1967	West	School I Private university 300 100 percent return	Interview; structured questionnaire	Ever used				1.0	6.0 5/	A five-campus study of student use of illicit as well as socially approved drugs. Students guaranteed anonymity. The five institutions differ by organization, course offerings, reputation, and location. Social characteristics of drug users and abstainers are compared.
		West	School II Catholic university 270 98 percent return	Interview; structured questionnaire	Ever used				1.0	4.0	
		West	School III Junior college 201 97 percent return	Interview; structured questionnaire	Ever used				2.0	11.0	
		West	School IV State college 192 64 percent return	Interview; structured questionnaire	Ever used				1.0	8.0	
		West	School V State university 293	Interview; structured questionnaire	Ever used				1.0	3.0	

5/ Includes glue, gasoline, nitrous oxide, cough syrup

Table 4.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquilizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
COLLEGE STUDENTS--Con.											
Undergraduate, graduate, and professional students at the State University of New York at Buffalo who appeared at a University office in September 1967 to obtain an ID card. Source: Edward F. Marra, et al, Intoxicant Drugs: Survey of Student Use, Roles and Policies Of The University, State University of New York at Buffalo, University Committee on Drugs and the Campus.	1967	North-east	8,545 70 percent return	Self-administered questionnaire	Ever used Current users	3.7 1.0		0.6 *			The response rate for graduate and professional students was 85.3 percent versus 64.5 percent for the undergraduates. Some of the findings were: (1) the rate of drug use was higher among undergraduates than among graduate students, (2) liberal arts students were more likely to use drugs than students in other study areas. (3) current use rates were highest for students who live in rented apartments.
Survey of all undergraduate and graduate students at the California Institute of Technology. Source: Kenneth Eells, "Marijuana and LSD: A Survey of One College Campus," Journal of Counseling Psychology, 1968, Vol. 15, No. 5.	1967	West	1,288 90 percent return	Self-administered questionnaire (mail)	Ever used	7.1 6/					Excellent return for a survey dealing with a sensitive issue. Unique technique employed to guarantee complete anonymity while permitting two follow-ups.

6/ Sleeping pills
* Less than one-half of one percent

Table 4.--STUDIES, SURVEYS, AND POLLS OF COLLEGE STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use					Remarks
						Depressants		Opiates		Glue & other substancea	
						Barbi-turates	Tranquil-izers	Heroin	Other opiates		
COLLEGE STUDENTS--Con.											
Survey of all seniors graduating in the Spring of 1965 from Brooklyn College of the City University of New York. Source: Samuel Pearlman, "Drug Use and Experience In An Urban College Population," paper preaented at the 44th Annual Meeting of the American Orthopsychiatric Association, Washington, D.C., March 1967.	1965	North-east	1,245 55 percent return	Self-administered questionnaire (mail)	Ever used	0.8					Dr. Pearlman stated that, "The ...survey must be considered to be a trial epidemiological effort, and its use of a queationnaire method within an anonymous framework has obvious limitations." Another limiting factor is the low response rate.

Table 5.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants		Percent of use: Opiates		Percent of use: Glue & other substances	Remarks
						Barbiturates	Tranquilizers	Heroin	Other opiates		
SECONDARY SCHOOL STUDENTS											
Population consisted of a 5 percent sample of junior and senior high school students in Montgomery County, Md. Source: A Survey Of Secondary School Students' Perceptions Of And Attitudes Toward Use Of Drugs By Teenagers, Vol. II, Final Report, March 10, 1970, Joint Com. On Drug Abuse, Montgomery County, Maryland.	1969	South	Senior H.S. 1,348	Self-administered questionnaire	Ever used	7.2		1.9		7.4 1/	A very complicated technique was employed to select the county-wide 5 percent sample. According to the report, reliability was established during the pilot test. Twenty-six percent of the boys and 20 percent of the girls in the senior class reported that they had used marihuana. As in other studies, use of alcohol far exceeded use of dangerous drugs.
					Tried but quit	4.8		1.2		6.4	
					Current users	2.4		0.7		1.0	
			Junior H.S. 1,429		Ever used	1.1		0.5		6.6	
Stratified random sample of sophomore, junior, and senior students from five high schools in Madison, Wisconsin. Source: Jon G. Udell and Robert S. Smith, Attitudes, Usage, And Availability Of Drugs Among Madison High School Students, The University of Wisconsin, Bur. of Business Research and Service, Madison, Wisconsin, July 1969.	1969	North Central	781	Questionnaire	Ever used			1.3		5.1 1/	Information on the design of the survey and procedures in administering the questionnaire are not included in the report. The results indicate that alcohol is used more than any other drug.
					1-2 times			0.6		3.3	
					Infrequently			*		1.0	
					Frequently			*		0.8	

1/ Glue

* Less than one-half of one percent

Table 5.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants		Percent of use: Opiates		Percent of use: Glue & other substsnces	Remarks
						Barbi-turates	Tranquil-izers	Heroin	Other opiates		
SECONDARY SCHOOL STUDENTS--Con.											
All Utah public high school studenta enrolled in grades 10-12 in 36 school districts and 1,185 eighth and ninth grade students enrolled in five public junior high schools. Source: "Drug Use Among High School Students In The State Of Utah," in Advisory Committee Report On Drug Abuse, prepared by the Governor's Citizen Advisory Committee On Drugs, State of Utah, State Capitol Building, Sept. 1969.	1969	West	47,182	Self-administered questionnaire (mid-morning class period)	Ever used					7.1	All students enrolled in grades 10 through 12 and a selection of students enrolled in gradea 8 and 9 were surveyed. No information is provided either on the proportion of all students in grades 10 through 12 who participated in the survey nor on how the sample was selected in grades 8 and 9. The final item on the questionnaire was an attempt to determine the accuracy of student responses on drug usage. One percent of the students said that their answers should be disregarded, 2.9 percent that most of their answers were accurate, 3 percent did not respond to the item, and the remainder said that their responses could be relied upon. One of the conclusions of the survey was that, "Drugs are being used by high school students in Utah but not extensively."
					Male						
					Once					9.5	
					2-5 times					3.5	
					6-10 times					2.3	
					More than 10 times					1.5	
					Female					2.2	
					Once					4.8	
					2-5 times					2.2	
					6-10 times					1.2	
					More than 10 times					0.8	
					Current users 3/					0.6	
					Male					1.8	
					Female					0.9	

2/ Glue
3/ Respondents who reported use yesterday or today and a few weeks ago.

Table 5.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants		Opiates		Glue & other substances	Remarks
						Barbiturates	Tranquilizers	Heroin	Other opiates		
SECONDARY SCHOOL STUDENTS--Con.											
Samples of seniors in 11 high schools "which reflect the demographic, economic, and racial diversity" of Michigan. Source: Richard A. Bogg, et al, Drug Dependence In Michigan: A Study of Attitudes and Action of The Young People of Michigan, Part III. Michigan Dept. of Public Health, 1968.	1968	North Central	89	Self-administered questionnaire	Type of School Private Ever used					2.2 4/	An exploratory study. Samples of seniors cannot be said to be representative of all seniors in Michigan.
			319		Suburban Ever used					4.7	
			148		Central City A Ever used					3.4	
			89		Central City B Ever used					4.5	
			113		Urban Community A Ever used					3.5	
			99		Urban Community B Ever used					8.1	
			104		Small Town Upper Peninsula Ever used					-	
			132		Small Town Lower Peninsula Ever used					3.0	
			64		Rural Community A Lower Peninsula Ever used					-	
			66		Rural Community B Lower Peninsula Ever used					3.0	
			156		Rural Community Upper Peninsula Ever uaed					7.0	

4/ Glue

Table 5.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquilizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
A random sample of high school dropouts for the 1967-68 and 1968-69 school years in 30 of 40 school districts in Utah. Source: "Drug Use Among High School Dropouts In The State Of Utah," in Advisory Committee Report On Drug Abuse prepared by the Governor's Citizen Advisory Com. on Drugs, State of Utah, State Capitol Building, Sept. 1969.	1969	West	180 32 percent return	Self-administered questionnaire (mail)	Ever used	31.2			21.8 5/		Response rate to the survey which had no follow-up was low. "Because of the methodology,.. responses may have come from those who are most cooperative. If this is so, it suggests that this study underestimates drug usage among high school dropouts."
					Male	42.9			27.2		
					Rarely	20.8			12.3		
					Occasionally	15.5			9.9		
					Frequently	6.6			5.0		
					Female	17.7			16.3		
					Rarely	2.5			10.0		
					Occasionally	5.1			3.8		
					Frequently	10.1			2.5		
Students in one upper middle class San Francisco Bay Area suburban high school. Source: Richard Blum and Associates, Students and Drugs, San Francisco: Jossey-Bass, Inc., 1969.	1967	West	1,614	Self-administered questionnaire	Male						This survey is the second of several surveys in which a questionnaire was being developed to determine illicit use of drugs by high school students. Only 16 percent of the students felt that they were under pressure to use drugs. Investigators found that "there was no feeling of the innocent seduced or of the naive being misled" in drug-using situations.
					Ever used	4.0				7.0	
					Female						
					Ever used	6.0				2.5	

5/ Reported as narcotics

Table 5.--STUDIES, SURVEYS, AND POLLS OF SECONDARY SCHOOL STUDENTS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES--Con.

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquilizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
SECONDARY SCHOOL STUDENTS--Con.											
Juniors and seniors of the three high schools in the Castro Valley Unified School District in Castro Valley, California. Source: Marvin E. Smith, District Superintendent, "Report To Parents of Students In Castro Valley Unified School District."	1967	West	1,272	Self-administered questionnaire completed in classroom	Male Ever used	15.7		4.7		10.0	Study guided and supervised by professors at the University of California at Berkeley. Questionnaire developed by a member of the School District to determine attitudes and behaviors of youth. Students guaranteed absolute anonymity.
					Female Ever used	12.5		3.4		3.8	
All students attending classes at Mamaroneck Junior High School (grades 7-9) and Mamaroneck Senior High School (grades 10-12) on November 21, 1967. Source: Bernard F. Haake, Superintendent of Schools, Memorandum to the Board of Education, Mamaroneck, New York.	1967	North-east	Senior H.S. 1,225	Self-administered questionnaire completed in classroom	Ever used	6/ 3.4				7/ 6.1	Some students who abuse drugs did not indicate usage while others who do not abuse drugs said they do. The school administration feels that these extremes tend to cancel each other out because of the large size of the sample.
					1 time	1.0				4.1	
					2 or more times	2.4				2.0	
			Junior H.S. 1,294		Ever used	6/ 1.4				7/ 8.3	
					1 time	0.8				6.9	
					2 or more times	0.6				1.4	

6/ May include some barbiturates prescribed by physician.
7/ Glue

Table 6.--STUDIES, SURVEYS, AND POLLS OF OTHER POPULATION GROUPS ON EXTENT AND/OR FREQUENCY OF ILLICIT USE OF DEPRESSANTS, OPIATES, GLUE, AND OTHER SUBSTANCES

Population and source of data	Year	Region	Number or percent reporting	Method of data collection	Have ever used and/or frequency of use	Percent of use: Depressants: Barbiturates	Depressants: Tranquilizers	Opiates: Heroin	Opiates: Other opiates	Glue & other substances	Remarks
OTHER POPULATION GROUPS											
A pilot study of drug use among hippies in New York City. Most live in the East Village area. Source: Theo Solomon, A Pilot Study Among East Village "Hippies", Monograph #35. Associated YM-YWHA's of Greater New York, March 1968.	1967	North-east	51	Interview	Male Ever used Current users Female Ever used Current users			13.0 - 20.0 5.0			Sampling design not rigorous, therefore results cannot be generalized to all hippies. Interviewers who were drawn from the hippy population had at least a college education and were known within the hippy community.
Negro men of normal IQ, born and reared in St. Louis, who attended a Negro elementary school. Source: Lee N. Robins and George E. Murphy, "Drug Use In A Normal Population of Young Negro Men," American Journal of Public Health, Vol. 57, No. 9, Sept. 1967.	1965-1966	North Central	221 94 percent of sample interviewed	Interview and record research	Ever used	14.0		13.0			A well-designed study with a carefully selected sample.

19. "Anorexiants," Drugs of Choice 1970–1971, Walter Modell, Ed., Chapter 20, Pages 284–293, 1970

INTRODUCTION

For cultural and social reasons, as well as for reasons of health, there is great pressure on both our male and female population to shrink its diet as well as its waistline. In a country with so much nutritious food so easily obtained, straightforward efforts in this direction have been notably unsuccessful. As a result, some easier way out has been sought, for example, a drug that would assist by depressing the appetite; hence the recent interest in anorectic agents, of which there are a number now on the commercial drug market and about whose actions and virtues there is little precise information.

In some instances, so heroic have the attempts been to induce weight loss, either by total starvation or by excessive doses of drugs or combinations of drugs, that serious reactions have been common and even deaths have been reported.

In practice the anorectic drugs are not used simply to depress the abnormal appetite, for even if there is severe bulimia or polyphagia, these drugs are not given unless there also is obesity. Thus the problem of the use of these drugs is inseparable from the problem of obesity and its causes as well as from overeating, and any attempt to consider the question of their choice on a strict pharmacologic basis simply as drugs that depress the appetite is unrealistic.

The designation "anorexiant" to a particular group of drugs in common use is perhaps unfortunate because it implies a precise pharmacologic action on the central nervous system that has never been demonstrated. As a matter of fact, direct depression of the central appetite-controlling mechanism is never even examined in the clinical studies on the anorectic effects of drugs, nor, for that matter, is there a report of the effect of these drugs on the eating habits of those with normal appetites. What these reports actually attempt to examine is a therapeutic accomplishment in the obese patient, loss in weight, without toxicity, which is, of course, also the result in which the practitioner is interested. Nevertheless, the group of drugs used in the treatment of obesity is now saddled with this inappropriate but highly suggestive term, and as a consequence of its unsubstantiated implications, studies of the mechanisms involved have been obscured by it, and in our opinion, the treatment of obesity is all the worse for it.

CLINICAL CONSIDERATIONS

As matters now stand, anorexiants are used exclusively in the relief of obesity, and to choose from among them as well as to apply the choice effectively there also must be an understanding of the probable basis of their effects in the obese patient.

This is, of course, no place to go deeply into the psychologic basis of obesity or the symbolic implications of overeating. It is sufficient to accept the uniformly stated opinion of experts that all cases of obesity not explainable on an organic or cultural basis are psychogenic and that the psychogenic cases comprise over 90% of the total. Beyond this there is the important fact that regardless of what measures are used to help the obese patient lose weight, unless something positive is done about the psychologic factors involved, when drug treatment stops, the painfully lost poundage will inevitably find its way back.

Stunkard states that most obese patients will not stay with dietary treatment for their obesity. Of those who stay with it, most will not lose weight and of those who lose weight, most ultimately will regain it. There is his discouraging experience that of twelve of 100 patients who lost more than 20 pounds under his care, after a year half had recouped their hard-won losses, and within the second year there remained only two who were not plump once more. This means that after 2 years of treatment only two patients out of 100 showed any benefit from treatment.

More than half of obese patients on strict reducing diets suffer some psychic reaction, and half of these are severe emotional disturbances. Stunkard noted that the "night-eating" syndrome often complicates otherwise successful treatment for obesity. This syndrome, which is a response to stress that appears in other situations as well, consists of insomnia, nocturnal pangs of hunger,

and morning anorexia. No part of this is a specific pharmacologic reaction to drugs that are used to depress appetite; rather it is all part of a psychologic reaction to a regimen that deprives patients of a form of support of deep psychic and symbolic significance, overeating. This speaks volumes for the importance of the psychologic background of the condition as well as the intensity of the psychologic resistance (despite all overt desire for weight loss) to measures that decrease food intake.

Lesses and Meyerson believe that the obese suffer from anhedonia; that is, although there appears to be a compulsive drive to eat, the act of eating, no matter how exessive, provides neither satiety nor satisfaction. Very often the obese are uncomfortably distended after eating. As a corollary, therefore, simple appetite depression would have little useful effect, for a physiologic appetite drive has nothing to do with their irresistible desire to eat. Nor does the gastric distress that follows serve as a deterrent. Although this may seem unusual, it is not really different from the plight of most alcoholics, many of whom often do not really enjoy the pharmacologic effects of alcohol, are mortified by its personal and social effects, and very much wish to stop drinking, but who, nevertheless, consume inordinate amounts of alcohol, often very rapidly, and even while inebriated appear to derive little or no gratification from what seems to be an irresistible desire to drink.

Mayer has suggested a metabolic or "glucostatic" mechanism that normally controls appetite and hunger; others have suggested a hormonal mechanism that controls intestinal activity related to the hunger drive, and still others have suggested a center in the nervous system for its control. We should like to press our view that, whatever the mechanism of the normal psychologic control of appetite may turn out to be, these are likely to have little to do with the problem of the obese, who do not eat in response to normal "appestat" reactivity to a physiologic drive but as the result of psychic compulsion.

The long-term results of anorexiant therapy are very poor at present. What is clearly missing in the effective treatment of obesity is useful understanding of the reasons why the obese continue to eat without reference to physiologic need or satiation. Failing this, an anorectic agent is likely to have as little effect on the overall problem of obesity as disulfiram (Antabuse) has had on the overall control of alcoholism. In the face of a compulsive desire to overeat none of the anorexiants are effective unless food intake is controlled as well; hence, it is obvious they really are not very effective against this force. It is clear that in most instances of resistive obesity, therefore, psychotherapy of some sort is the most logical therapy, and, as a matter of fact, the best (over 50% improvement) as well as the most durable results reported have been after psychotherapy of some type and not through the use of drugs unless combined with psychotherapy.

PHARMACOLOGIC CONSIDERATIONS

Anorexia is a common adverse effect of drugs. For example, sodium chloride tablets may induce nausea and thereby reduce the desire for food in even the most compulsive of eaters. The search for an effective anorectic drug, therefore, is not really for a drug that depresses appetite per se, but rather for one in which a loss of interest in food is not associated with distress and discomfort. This makes matters difficult, since even in the obese patient drug action inducing nausea can be counted upon to continue to depress appetite without the development of tolerance, whereas tolerance to the so-called anorexiants now in use is one of their outstanding limitations.

The search for a useful anorectic agent is further complicated by the fact that an effect is sought on a singularly human trait, the tendency to overeat. The abnormal drive for food in man with its symbolic overtones, its cultural implications, and its psychologic complications may not be satiated by amounts of food that satisfy the physiologically normal appestat demands, a psychopathologic situation not duplicated in the laboratory animal. Since the special communication necessary to indicate the pure anorectic state sought is not within the capacities of the laboratory animal (although we sometimes can distinguish nausea in the cat and dog), simple anorexia, without nausea or other distress that may distract the appetite, cannot be determined or explored in the laboratory animal. While it is a fact that by damaging the brain some laboratory animals have been made to overeat, this the obese patient who overeats with an undamaged and, so far as we know, a functionally normal brain.

The so-called anorexiants that seem to assist some obese patients in losing weight do not usually depress the growth curve in animals, although very large doses may depress appetite in adult animals. However, not only is it impossible to compare dosage in the animals with that which may be used without distress in man, but also it is impossible to compare the biologic effects induced or to say what minor distresses the animal might have suffered along with the anorexia. Since anorexia in the animal may well mean something other than that which is sought in the obese man, regardless of apparent desirable or meaningful effects in animals, only the experiment in man provides the final answer to the complex issues involved in the relief of obesity.

It is interesting in this connection that, if these drugs were specific anorexiants and if their supporters really believed so, it would not be necessary, as all of them seem to find, to put patients on restricted diets. If their appetites were, in fact, depressed by the drugs, what always happens when appetites are really depressed would also happen in this case; the obese patients would eat less regardless of how much was in sight; sometimes even less in the face of abundance, whereas the obese patients usually eat less only if less is available. It seems clear, therefore, that despite their stated nthusiasm, even the staunchest supporters of the anoretic drugs are basically insecure about their anorectic potency. We suggest an examination of the loss of appetite due to overdosage with digitalis or alcohol for a view of the phenomenon of a drug-depressed appetite—these victims will not and cannot eat.

Whereas many of the studies on anorectic drugs currently available have indicated by one means or another that their use is associated with weight loss, most of these studies have no useful controls whatever, resting their case entirely on the fact that patients lost weight after taking the new drugs and overlooking the common experience that a large proportion of obese persons tend to lose weight on entering any new treatment and with each association with a new therapeutist. In other studies that use a placebo a difference in the weight loss after the placebo, vis-à-vis the drug, is taken as evidence of the effectiveness of the drug in question. Only in a relatively few instances is a double-blind control used to remove bias.

Many studies have indicated that within 30 minutes of the taking of any of the modern anorectics, the subjects clearly experience a "lift," an improvement in the sense of well-being, stimulation, and a tendency to increased activity. This being the case, even when the double-blind technique is used to start, after 30 minutes some patients know which is medication and which is placebo, and only the physician remains blind. All the psychic impact of the knowledge that an effective drug is being taken is thus exerted in favor of the drug being tested. From this point of view, therefore, a difference between the effects of the placebo and the drug in these studies may well result from the *detection* of this difference by the patient as well as from the *action* of the drug itself.

While some designs undoubtedly make a sterner attempt than others to control the experiment, the fact remains that few are properly designed to eliminate or take into account the well-established influence of suggestion and the offer of a crutch to the obese patient about to embark on the trial of refraining from overeating. However, this is not the place for a thorough analysis of the many reasons which may invalidate the conclusion that the positive results after the taking of the anorectic drugs prove a specific anorectic action. The clinical fact remains that in the obese the use of many of the so-called anorexiants with proper dietary controls is followed by greater weight loss than when placebo is used under the same circumstances.

The fact that the sensations produced in the central nervous system by the modern anorectic drugs are very impressive is of importance to patients anxiously seeking a crutch to help them lose weight. That they appreciate some sensations after taking a drug proves to them that they are getting medical assistance. This crutch, therefore, means more to them than the mere taking of an inert placebo—in this case an "ert" placebo seems to have special ancillary pharmacodynamic actions worthy of further study

The effect of the so-called anorectic drugs on the psychic state of the obese patient has not been examined carefully in the case of the more recently introduced members, and whereas such an action is disclaimed or by implication denied, the high incidence of wakefulness and of other central nervous system stimulant actions strongly suggests that this may be a regular, if not the only

important, pharmacologic action. Should these drugs provide the sort of lift for which amphetamine has long been used, it may, indeed, distract the obese from the psychic reasons for their compulsion and provide a substitute for overeating by the obese who regularly overeat to chase their depressions.It may also explain the limited value of these drugs. In any event central stimulation surly should not be brushed aside as "side effects," for it is likely to be the central reason for whatever anorectic action these drugs exert. Recent extensive observations on a group of obese schizophrenic patients indicate that despite unusually large doses of dextroamphetamine, these patients experienced neither central stimulation nor appetite loss (or weight loss), strongly supporting the inseparable relationship between these two actions.

There are other interesting implications in one of the effects on the central nervous system that have been reported. There is clear evidence in animals as well as in man that, beyond a certain norm, decreased physical activity increases appetite and, vice versa, increased physical activity decreases appetite. This applies to the obese person as well as to the thin person. Increased activity is the common symptom, often termed a "side effect," of the anorectic drugs. Therefore, in addition to the calorigenic effect of increased physical activity because of these drugs, there may well be decreased intake as a concomitant, and if this is so, th anorexiants may be associated with a weight loss through still another central stimulant action. Stunkard has indicated that limited physical activity may be a more important feature of obesity than is generally appreciated. Central nervous system stimulation may be an important action of these drugs in some weight-loss studies; a primary effect on an appetite center, ascribed to anorexiants by so many, is of little importance.

In any case most of a large number of studies on the effects of regimens using anorexiants indicate clinical effectiveness, and only a few suggest that they are of no value at all. Those who do recommend the use of anorectic drugs all seem to agree that the drugs are merely a crutch and should be used only for a limited period of time.

THE SEVERAL DRUGS

Amphetamine-like drugs

There is an erroneous but widespread impression that amphetamine sulfate (Benzedrine) was the first of a series of anorectic drugs leading to the development of the current series of analogues As far back as 1889 tetrahydrobetanaphthylamine was synthesized and soon recognized to have both sympathomimetic and cephalotropic as well as calorigenic actions. Because of toxic effects, interest was lost in "tetra," and although some work with the drug continued into the first decade of the twentieth century, the similarity in actions and structure to the sympathomimetic amines was generally ignored.

The cephalotropic action of drugs closely related to epinephrine and ephedrine was early recognized. In the case of amphetamine this action was emphasized as both new and unique. It is now abundantly clear that this action is neither unique nor even new but, in the case of amphetamine, is perhaps not overshadowed by other dramatic pharmacologic actions and hence is more obvious. At present in the same group of drugs there are also dextroamphetamine (Dexedrine), methamphetamine (Desoxyn and about thirty other proprietary names), phenylpropanolamine (Propadrine), phenmetrazine (Preludin), phentermine resin (Ionamin), diethylpropion (Tenuate, Tepanil), benzphetamine (Didrex), phendimetrazine (Plegine), amphetamine succinate (Cydril), and chlorphentermine (Pre-Sate), which are promoted and used clinically as anorexiants, it is easy to demonstrate that all really belong to the same pharmacologic group of drugs as amphetamine and that their pharmacologic actions are also the same.

As explained previously, it is by no means definite that these drugs have any primary effect on appetite at all, and there is a strong suggestion that they may assist in the reduction of weight through other and entirely different pharmacologic actions on the central nervous system. There is reason to suppose that the anorectic effect is caused by an action on the higher centers rather than on any appetite control center situated elsewhere in the central nervous system.

In varying degree all the amphetamine-like drugs induce central stimulant effects, wakefulness, increased mental and physical activity, and in some instances, excitement and agitation. Recent evidence also indicates that large

doses of these drugs are hallucinogenic. With the usual clinical doses, many patients clearly experience a lift. The intensity of these effects is proportional to their anorectic potency. Nor can these be properly termed "side effects" if it is the cephalotropic action that is the basis of their effect in obesity and if it is because of a sense of well-being and elation that subjects with an emotional drive which makes them overeat are better able to accept dietary restrictions There has been described as well a loss of acuity of olfactory and gustatory sensibility, which may be an additional factor in the so-called appetite depression The amphetamine-like drugs are of no value for the night-eating syndrome, since their action to induce insomnia contraindicates their use late in the evening or before retiring.

Although there have been some deaths from these drugs, in general they are not very toxic and relatively few cases of acute poisoning or physical reactions have been reported as the result of their large-scale and continued use. Aside from the indirect consequence of prolonged insomnia, the most serious complication is dependence On the other hand, tolerance may develop, so that such effects as they may induce are likely to be relatively short lived, whereas in order to continue the effects doses must be increased—a procedure that tends to increase disagreeable effects, especially nervousness and insomnia. Finally, withdrawal reactions with transient psychosis have been described. This fact tends to identify the group as addictive. Indeed, addiction to amphetamine (Benzedrine), dextroamphetamine (Dexedrine), methamphetamine, phenmetrazine (Preludin), and diethylpropion (Tenuate, Tepanil) has been reported The drugs, therefore, should not be used for prolonged therapy, and they may be dangerous. Many drugs in this group recently have been placed in the restricted category by the F.D.A. because of proved abuse, and the other members are under careful scrutiny. It seems to us that the danger applies to the group as a whole. "Speed" and many other abused drugs belong to this group.

As epinephrine congeners, the effects on the cardiovascular system are important. A rise in blood pressure and the tendency to palpitations are often matters for serious consideration, especially since weight reduction is commonly prescribed for cardiac patients Aside from the probable higher incidence of such effects from amphetamine (Benzedrine), there is little to choose among the others, and in them a proper fitting of drug and patient often has to be made by trial.

The history of most of the drugs in the following discussions is remarkably similar—a wave of enthusiasm for it followed by a wave of enthusiasm for the next newcomer to the same series. Drugs of this series that are much the same clinically are not included only because they are little used.

Amphetamine

The cardiovascular effects of the racemic and levo forms of amphetamine (Amphate, Bar-Dex, Benzedrine, Dietamine, Monophos, Profetamine, Racephen, Raphetamine) are likely to be disturbing; therefore, amphetamine has limited value in obesity and is rarely used today.

dl-*Amphetamine resin complex*

The complexing of *dl*-amphetamine with resin (Biphetamine resin) may prolong its action, but even this may be questioned. Whether it also segregates the cardiovascular from the cephalotropic action is doubtful, and on this basis it would not appear to have any special pharmacodynamic advantage.

Phentermine resin

Through exchange with electrolyte, phentermine resin (Ionamin) releases phenylbutylamine, and amphetamine congener, in the gastrointestinal tract. All systemic effects, therefore, stem from an amphetamine-like action There is no good evidence that this is in any way a superior member of the group.

Dextroamphetamine

Dextroamphetamine (Dexedrine), which is the dextrorotatory form of amphetamine, differs from the racemic and levo forms in that, whereas the cephalotropic actions are well developed, the cardiovascular effects are much feebler. The relative segregation of effects makes the drug the more desirable when, as in obesity, cephalotropic actions alone are needed. This also serves to emphasize the importance of cephalotropic actions of drugs in obesity.

Methamphetamine

The only feature that greatly distinguishes this congener of amphetamine from amphetamine itself is the exceedingly large number of trade names under which this material is sold: to name some, Amphedroxyn, Apamine, Deofed, Desamine, Desoxedrine, Desoxo-5, Desoxyephedrine, Desoxyn, Desyphed, Detrex, Dexoval, Dexstim, D-O-E, Doxyfed Drinalfa, Efroxine, Lanazine, Methamphin, Methedrine, Methoxyn, Miller-Drine, Norodin, Oxyfed, Oxydess, Premodrin, Normadrine, Norodin, Semoxydrine, Stimdex, and Syndrox. There is no evidence that its action differs from that of amphetamine in any way except that the action on the cardiovascular system is somewhat less intense and the action on the central nervous system is somewhat more intense. This drug is probably abused more than any other of the group.

Phenylpropanolamine

The vasoconstrictant action of phenylpropanolamine (Propadrine) tends to elevate blood pressure and thereby limits its usefulness in the treatment of obesity. Nostrums containing this drugs have been removed from the market because of unsupportable and in some cases grossly illegal advertising claims as well as danger of abuse.

Phenmetrazine

Much has been written recently about phenmetrazine (Preludin), less because of real superiority than because of timing. The interval since the appearance of amphetamine and its introduction was just right to attract attention and cause the appearance of a flood of publications on the results of trials with a new drug. Like the reports for the others they indicate that phenmetrazine is an effective anorectic agent. Some publications indicate that soon (30 minutes) after administration many patients appreciate cephalotropic actions. Phenmetrazine appears to have relatively little effect on the cardiovascular apparatus Whether its apparent desirability is because of its relative impotence or because of a specific action remains after many years yet to be demonstrated. Despite statements to the contrary, this drug belongs to the amphetamine group of drugs. Cases of addiction have been reported.

Phendimetrazine

All that has been said of phenmetrazine, to which phenlimetrazine (Plegine) is closely related, applies equally to this parvenu.

Diethylpropion

There is no evidence that diethylpropion (Tenuate, Tepanil), an amphetamine congener, is at all superior to dextroamphetamine; it simply is newer and therefore less has been written against it.

Benzphetamine

Benzphetamine (Didrex), an amphetamine congener, has no established advantages over dextroamphetamine. On a strictly pharmacologic basis there is no reason to suppose that it should.

Chlorphentermine

Characteristically it is claimed that chlorphentermine (Pre-Sate) is a potent anorectic which causes neither nervousness nor insomnio. This contention has not been proved.

Summary

Largely because the problems involved have not been dissected and because the pharmacologic role of the sympathomimetic amines in the treatment of obesity has not been defined, there is no clear basis for indicating which of these drugs, for whatever it may contribute, is the best It is reasonable to suppose, however, that because elevation in blood pressure and cardiac acceleration are not useful in any case and may sometimes be harmful, since obesity in patient with heart disease is often treated with these drugs, amphetamine and phenylpropanolamine are clearly the least desirable Methamphetamine is apparently the most likely to lead to abuse. The history of these agents is that notions of superiority regularly disappear with accumulating experience. As matters now stand, from a pharmacologic point of view it may be taken that dextroamphetamine is probably the most desirable of the lot. It also has the advantage of being the least costly.

Calorigenic agents

About 35 years ago dinitrophenol, which increased metabolic rate without inducing the sensation of warmth commonly complicating the use of thyroid materials, had a brief period of trial. Weight was lost by many who used it, but because of the development of cataracts the use of the drug was discontinued. No drug with similar calorigenic effects is now in use.

Thyroid and related materials

It has long been recognized that increased thyroid activity causes loss of weight despite increased ingestion of food. This seems to provide an approach to the treatment of obesity that avoids the difficult problem of controlling food intake, and with this aim in view thyroid materials have been used in obesity. Unfortunately, unless deficiency in thyroid function is the basis for the obesity, the approach ultimately fails, and it fails just as frequently whether the old-fashioned desiccated thyroid or a more modern form, such as liothyronine (Cytomel), is used. Neither is recommended, nor is any intermediate between the two. In addition to their overall ineffectiveness the thyroid materials may lead to intense nervousness, insomnia, discomfort caused by the calorigenic effect, excessive perspiration, and palpitations. If drugs are to be used, dextroamphetamine seems clearly to be the one of preference.

Sedation

Inasmuch as obesity often is an expression of some emotional disturbance that may be aggravated by attempts to restrict the intake of food, it is not at all surprising that central sedation and tranquilization sometimes can assist in the weight-loss regimen. If sedation is intense enough to dull mental activity or induce a degree of sleepiness, the appetite drive will be depressed along with other centrally controlled functional activities. There is evidence of sorts in a study by Ressler that tranquilizing doses of chlorpromazine (Thorazine), and therefore presumably also of its congeners, may be effective in weight loss. Unfortunately the study is virtually uncontrolled. Sedation and tranquilization may be effective in the case of the night-eating syndrome.

Bulk producers

Methylcellulose, a nondigestible but otherwise harmless bulky material, has been suggested as an appetite satiator for the treatment of obesity. This has proved to be no more effective a device for the treatment of obesity than the high-residue, low-calorie diet itself. Apparently obese persons want to eat real food. The solution is not simply a matter of distending their stomachs with indigestible matter until they can tolerate it no longer.

The canned diet

Nutrient formulas such as Albacal, Cal-a-Day, and Metrecal, which reduce the feeding of the obese person to an infantile level, whatever their merit or disadvantage and however unappetizing or successful, do not apply to this discussion, which deals with drugs.

Special diets

Unusual diets that permit large amounts of fat and protein but restrict carbohydrate and recommend special items such as safflower oil are also outside the scope of this chapter. "A new concept" in dietary treatment involving a 48-hour fast (or even longer periods of starvation) followed by dietary reeducation may have special merits, which time will tell, but it also has dangers about which time has already told a sad tale.

Starvation

This unquestionably effective means of losing weight has been used with increasing frequency in recent years. In the last year, death and myocardial damage have been reported as results.

THE CHOICE OF AN ANOREXIANT

The decision more important than the choice of an anorexiant is whether or not to use such a drug at all. All investigators, even those who approve of the use of the anorectic drugs, agree on the psychologic basis for obesity in the patients for whom these drugs are designed That being so, drugs clearly

provide no cure for obesity, and at the very best only a crutch to be used during a brief initial period of dietary restriction. Any assistance the medication provides during this period is to be weighed against the "letdown" the patient suffers when his crutch is removed and he has to face the rigors of dietary restriction while suffering from his abnormal desire to eat.

Under these circumstances the drug of choice is the one that causes the fewest undesirable effects. Of the drugs in common use, all of them presently belonging to the amphetamine group, dextroamphetamine seems to be the least likely to induce cardiovascular effects. Claims for superiority resulting from prolonged action apply equally to duration of side effects. Unfortunately, despite regular claims to the contrary, it does not seem likely that the cephalotropic actions, especially insomnia and nervousness, can be divorced from any effect these drugs may exert on obesity and for this reason it seems unlikely that the "ideal" anorexiants will be a derivative of our current crop. It is interesting to note that when these drugs are abused by "teenagers and hippies" (who call them bennies, "speed," etc.) they are not particularly slimming.

REGIMEN FOR THE USE OF ANOREXIANTS

There is evidence that the use of certain anorexiants, all congeners of amphetamine, is associated with weight loss for a longer or a shorter period of time. It is agreed by specialists who recommend them that however they are used and however they may work, they should not be taken for a prolonged period but rather as an adjuvant to a restricted diet in the early stages of the weight-losing regimen. There are others who take the view that the assistance these drugs provide may make it even more difficult for obese persons to keep to the proper diet after the drug is discontinued. The best compromise between these two views is to use the drugs in effective doses for a short period (i.e., in doses that induce the cephalotropic effects that probably account for any action that they may exert indirectly on the appetite) and having accomplished some weight loss with such a program, to discontinue the drug and continue with a maintenance diet. At the same time the basic psychologic trouble must be treated.

It is well to remember that the anorectic drugs in current use do not exert the kind of depressant effect on the appetite which will keep the obese from overeating if good food is in sight. It is necessary, therefore, also to prevent patients who are taking these drugs from overeating by some other mechanism, usually a rigidly enforced low-calorie diet. For most obese people these drugs make sticking to a diet somewhat less difficult for a limited period of time.

It must also be remembered that all of these drugs are potentially addictive and now have come under special regulation by the F.D.A.

Salt and water regulation for the obese patient is a problem currently being studied on a controlled basis and may turn out to be deserving of attention. Its significance is not now known.

WHAT IS NEEDED IN A NEW ANOREXIANT

What is needed in anorexiants is not another version of a drug that distracts the appetite of the obese person indirectly by means of a stimulant action on the central nervous system but one that depresses the appetite control mechanism directly, that is, a truly specific pharmacologic anorexiant. Investigations of such a drug action would probably be better carried out in subjects with normal appetites than in those with the abnormal, complicated, and poorly understood appetite drives of the obese person.

What is needed is a drug that will keep the patient from eating too much when too much is available, not one that must be used in conjunction with food restriction. This, too, is where the current supply of available drugs fail, because the overabundance and easy availability of attractive and tasty foods is one of the features of our society that makes normal eating habits so difficult for the obese in the first place.

What is wanted is a drug that, when it does depress the appetite, does not make the obese patient ill, deprive him of the emotional comfort he needs, make him nervous, or keep him awake at night so that he is tempted to embark on a midnight refrigerator raid. Unless there is a substitute comfort, there is certain to be a high incidence of emotional reaction to the regimen itself and a high incidence of backsliding.

What is needed, therefore, is a regimen rather than a drug that, with considerable specificity, corrects the psychic disturbance in the obese person that upsets his appestat. As matters stand, no drug is available on which to base such a therapy, and in its absence it seems clear that, regardless of its expense and relative difficulty, for most patients the best approach to obesity is some form of psychotherapy. The best results (about 50% improvement) have come with such methods. Since there are many symptoms they suffer in common, it would seem that group therapy through organizations similar to Alcoholics Anonymous and TOPS (Take Off Pounds Sensibly) might provide the best hope for the obese person.

There is, however, a drug to avoid: *alcohol*. No amount of French cooking in sight or smelling distance is as likely to overcompensate with calories as the alcoholic beverage.

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Chapter 33

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Anorexiants

The amphetamines and amphetamine-like drugs are commonly used as adjuncts in the management of obesity. Whether they *should* be used for this purpose has been challenged. Their untoward effects, their tendency to produce psychic dependence, and their evanescent effectiveness in reasonable dosage leave much to be desired.

These anorexiants are used temporarily to suppress the appetite of patients who overeat to gratify inappropriate hunger or who have difficulty in adhering

to a prescribed diet because of hunger. The effect of anorexiants appears to be related principally to stimulation of the central nervous system; they produce varying degrees of alertness, mood elevation, decreased sense of fatigue, increased initiative, and increased motor activity. Such effects can lessen the distress arising from strict adherence to a program of decreased caloric intake and, in so doing, contribute to the success of a weight reduction program. However, effective weight reduction and maintenance require an understanding of good nutrition and successful alteration of the underlying psychologic or pathologic factors producing excessive caloric intake.

Anorexiants can be used as short-term adjuncts in an overall program of weight loss, but their use is appropriate only as long as fat loss continues without undesirable effects, psychic dependence, or need for an increase in dosage. Prolonged use of therapeutic doses or short-term use of large doses of these drugs is almost always followed by fatigue and mental depression.

The amphetamines (eg, amphetamine [Benzedrine], dextroamphetamine [Dexedrine]) were the first drugs used widely to suppress the appetite and are still the standard to which newer drugs are compared. Dextroamphetamine is regarded as the prototype of drugs used for anorexia. It has been demonstrated to be more active as a central nervous system stimulant than amphetamine and, relatively, has less effect on the cardiovascular system. Therefore, dextroamphetamine is more useful as an anorexiant since appetite suppression is related to central nervous system activity and less pronounced cardiovascular actions are preferable. Methamphetamine [Desoxyn, Drinalfa] also has more effect on the central nervous system than on the cardiovascular system, although there is less difference with these effects than with dextroamphetamine.

A number of other adrenergic agents with actions similar to the amphetamines are used in weight control. These agents (benzphetamine [Didrex], chlorphentermine [Pre-Sate], diethylpropion [Tenuate, Tepanil], phendimetrazine [Plegine], phenmetrazine [Preludin], phentermine hydrochloride [Wilpo], and phentermine resin [Ionamin]) were developed in the hope that they would produce a greater anorexiant effect with fewer untoward reactions. Although the amphetamines also have been used as stimulants in some unrelated conditions to be discussed later, these amphetamine-like agents ordinarily have been recommended only for use as anorexiants. In spite of minor differences in their actions and untoward effects, none of the amphetamine-like agents has been found to be superior in effectiveness to dextroamphetamine.

Phenylpropanolamine, another adrenergic agent with some central stimulant properties, is available without prescription in various proprietary products for weight reduction. This agent is probably ineffective in the dose provided (25 mg).

It is unfortunate that other drugs not technically classed an anorexiants have been misused in the treatment of overweight patients. These agents include digitalis, diuretics, laxatives, antispasmodies, and thyroid. Digitalis is absolutely contraindicated in uncomplicated obesity, for its use is irrational and dangerous. In "effective" dosage, its only apparent action in a weight-reduction program would be to cause anorexia, a symptom of digitalis poisoning. Diuretics produce impressive temporary decreases in total body weight by increasing the excretion of water, but they do not affect body fat. Their use only aggravates the often exaggerated body water changes in obese patients and further contributes to their lack of understanding of the treatment of obesity. Laxatives, when used in large doses to produce diarrhea, can induce both water and nutrient losses. Antispasmodies exert no effect on body fat or caloric balance.

Thyroid preparations are specific in treating hypothyroid patients; their use to promote weight loss in euthyroid patients by increasing metabolism is irrational and should be discouraged. Hypothetically, the initial dosage of exogenous hormone might increase metabolism briefly, but only until the thyroid gland adjusts with a compensatory decrease in secretion of endogenous hormone. Thus, increasing the dosage again might cause another brief increase in metabolism until the gland is depressed further or even completely. If this does occur, the increased metabolism might stimulate the appetite, making the program of weight reduction more difficult and perhaps preventing even limited success. If the dosage reaches a level significantly greater than the amount that the gland normally would secrete, thyrotoxicosis results. Furthermore, when

the medication eventually is stopped, the depressed gland must again adjust its secretion to return to normal function. During the interval of this readjustment, the patient may experience manifestations of hypothyroidism and may gain weight.

It has been claimed that daily injections of chorionic gonadotropin have caused weight loss and redistribution of body fat. However, results of studies have shown that the weight loss results from the concomitant hypocaloric diet and the placebo effect of frequent office visits and injections.

The amphetamines are of unequivocal usefulness only in a few conditions. These include narcolepsy and cataplexy; hypersomnia (eg, in Kleine-Levin syndrome); adjunctive use in certain highly selected patients with aggressive psychiatric or neurologic disorders (eg, childhood behavioral problems, psychomotor epilepsy, psychopathic personality), all beyond the scope of this discussion; and incapacitating drowsiness occurring in some patients who must take sedating anticonvulsants. Their value in psychiatric depression is limited at best and somewhat controversial; they often may aggravate the condition instead of help it. The use of amphetamines for fatigue is unjustifiable except under the most extraordinary circumstances; they are dangerous for drivers and those engaged in comparable activities, and they have no legitimate role in athletics. Their use for conditions such as dysmenorrhea, premenstrual tension, and migraine principally involves the partial masking of symptoms by substituting a drug-induced euphoria, and other methods are preferable. Nocturnal enuresis similarly should be treated by methods other than inducing light sleep with amphetamines. Their value in drug-induced depression is insignificant. For discussion on the use of certain amphetamines as vasopressor agents and adjunctively in motion sickness, see Chapter 5, Agents Used in Hypotension and Shock, and Chapter 84, Antiemetics.

ADVERSE REACTIONS AND PRECAUTIONS

The untoward effects produced by the amphetamines are related to their spectrum of pharmacologic actions; thus, these agents may cause nervousness, restlessness, insomnia, and cardiovascular and gastrointestinal disturbances. Chills, collapse, and syncope may occur with overdosage. If signs of toxicity appear, these drugs should be discontinued. Because the amphetamine-like adrenergics have a relatively weak peripheral activity, usual oral doses of these agents seldom produce such undesirable effects as hypertension, tremors, tachycardia, and mydriasis.

The physician should be aware that susceptible patients may develop psychic dependence. Further, since harmful self-medication may be fostered in patients' relatives or neighbors, supervision should remain strict. The usual safeguards are to prescribe small quantities of the drug and to limit the number of times the prescription may be refilled. Prescriptions become void if not filled within six months. The Drug Abuse Control Amendment to the Federal Food, Drug and Cosmetic Act prohibits the refill of individual prescriptions for amphetamines and certain other agents more than five times in the six-month period after they are written.

Although tolerance to the appetite-suppressant effect has never been demonstrated in the laboratory, it does occur clinically, usually within several weeks. In such instances the anorexiants should no longer be regarded as acceptable adjuncts in the treatment program and should be discontinued. It is emphasized that the dosage should not be increased because this may produce marked restlessness, irritability, and combativeness, in addition to the anorexia and insomnia observed with smaller doses. Toxic psychoses, characterized by auditory and visual hallucinations and by paranoid delusions, also may develop. If these symptoms occur, the drug should be discontinued, sedatives used, and custodial care and psychotherapy employed when needed.

Acute overdosage results in accentuation of the usual pharmacologic effects: excitement, agitation, tachycardia, mydriasis, slurred speech, ataxia, tremor, hyperreflexia, and rapid respiration. In severe cases this may cause peripheral vascular collapse and death.

Amphetamine, dextroamphetamine, and methamphetamine ("Speed") are available in sterile solutions for intravenous use. This dosage form is not indicated for use as an anorexiant; individuals who abuse these drugs frequently take four to six intravenous injections daily with total daily doses as large as several grams.

Withdrawal of these agents from abusers may unmask symptoms of chronic fatigue (general depression, weakness, tremors, and gastrointestinal disturbances) and, in some individuals, may be followed by drowsiness and prolonged sleep. Generally, these drugs should not be used in patients with hypertension, cardiovascular disease, and hyperthyroidism because their sympathomimetic effect may aggravate these conditions. They are contraindicated in those receiving monoamine oxidase inhibitors. They also are contraindicated in emotionally unstable individuals who are known to be susceptible to drug abuse. They should be used with caution in patients who are overly sensitive to the adrenergic agents.

Evidence of deleterious effects on the fetus has not been observed during pregnancy; however, routine precautions should be followed if they are used in women of childbearing age (see the statement in the Introduction on Use of Drugs in Pregnancy).

AMPHETAMINES

Dextroamphetamine sulfate (Dexedrine), *dextroamphetamine phosphate*

Most effective anorexiant in amphetamine group of drugs and as effective as any of the amphetamine-like agents. Useful as adjunct in treatment restriction. Has relatively more of the desired central stimulatory and anorexiant effects and less of the undesired cardiovascular effects than other amphetamines. Because tolerance develops, drug generally should not be used longer than 6 to 10 weeks at a time. New dietary habits should be developed so that decreased caloric intake continues after the drug is discontinued. Data insufficent to evaluate timed-release preparations, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

Untoward effects on the central nervous system include insomnia, restlessness, nervousness, dizziness, and tremor. Dystonic movements of the head, neck, and extremities have been reported. If insomnia occurs, last dose should be given in midafternoon. Cardiovascular stimulation may cause increased pulse rate and blood pressure, headache, and palpitation. Drug should be discontinued promptly if anginal pain or cardiac arrhythmias occur. Dryness of mouth, mydriasis, nausea, diarrhea, and constipation also have been reported. Stimulant action may cause undesirable effects, including psychic dependence, in emotionally unstable individuals known to be susceptible to drug abuse.

Withdrawal in abusers may unmask symptoms of chronic fatigue (general depression, weakness, tremors, and gastrointestinal disturbances) and, in some individuals, may be followed by drowsiness and prolonged sleep. Serious and sometimes psychotic depressive reactions may follow intensive use of dextroamphetamine in a program of strenuous dieting in some individuals. Generally dextroamphetamine should not be used in patients with hypertension, cardiovascular disease, and hyperthyroidism because its sympathomimetic effect may aggravate these conditions. Contraindicated in those receiving monoamine oxidase inhibitors. Should be used with caution in patients who are overly sensitive to adrenergic agents.

Evidence of deleterious effects on the fetus has not been observed during pregnancy however, routine precaution should be followed if used in women of childbearing age (see statement in the Introduction on Use of Drugs in Pregnancy). See Introductory Statement for additional information on adverse reactions and precautions.

For other uses, see Chapter 32, Antidepressants, and Chapter 34, Analeptics.

Usual dosage—

Oral: adults, 5 to 10 mg three times daily taken 30 to 60 minutes before each meal alternatively, timed-release capsule in appropriate size is taken once daily in the morning.

Intravenous: Not recommended for use as anorexiant.

Preparations—

Dextroamphetamine phosphate: Oral, Tablets 5 mg.

Dextroamphetamine sulfate: Dexedrine (Smith Kline & French). *Oral,* Capsules (timed-release) 5, 10, and 15 mg; elixir 5 mg/5 ml; tablets 5 mg.

Additional trademarks—

Dextroamphetamine Phosphate: Dextro-Profetamine Phosphate (Clark & Clark). *Dextroamphetamine Sulfate:* Carrtime (Century), Cendex (Central),

Dextrosule (Arnar-Stone), Perke One (Ascher). Drug also marketed by many manufacturers under generic name.

Amphetamine sulfate, amphetamine phosphate

Racemic form of amphetamine. Actions and uses similar to those of dextroamphetamine, but not recommended for use as anorexiant because it has more pronounced effect on cardiovascular system and less effect on central nervous system than dextroamphetamine or methamphetamine (see Chapter 32, Antidepressants). Data insufficient to evaluate timed-release preparation, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for additional information on adverse reactions and precautions. For other uses, see Chapter 32, Antidepressants, and Chapter 34, Analeptics.

Usual Dosage—Not recommended for use as anorexiant.

Available Trademarks—

Amphetamine Sulfate: Benzedrine (Smith Kline & French). *Amphetamine Phosphate Leptamine:* (Bowman). Monophos (Durst). Drug also marketed by other manufacteurers under generic name.

Methamphetamine hydrochloride (Desoxyn, Drinalfa)

Similar to dextroamphetamine but its effects on cardiovascular system are more pronounced. It is not the anorexant of choice. Methamphetamine ("Speed") is the amphetamine preparation most commonly abused. Large doses can produce a moderate degree of physical dependence and classic withdrawal reactions lasting two or four days. Data insufficient to evaluate timed-release preparation, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for information on adverse reactions and precautions. For other uses, see Chapters 5, Agents Used in Hypotension and Shock; 32, Antidepressants; and 34, Analeptics.

Usual dosage—

Oral: Adults, 2.5 to 5 mg three times daily taken 30 to 60 minutes before each meal; alternatively, timed-release capsule in appropriate size taken once daily in the morning.

Intravenous: Not recommended for use as anorexiant.

Preperations—

Desoxyn (Abbott). *Oral:* Tablets 2.5 and 5 mg; tablets (timed-release) 5, 10, and 15 mg.

Drinalfa (Squibb). *Oral:* Tablets 5 mg.

Additional trademarks—Des-Oxa-D (Walker), Desoxo-5 (Sutliff & Case), Detrex (Mallard), Dexstim (Central), D-O-E (Durst), Efroxine Hydrochloride (Strasenburgh), Norodin Hydrochloride (Endo), Oxydess (North American), Semoxydrine Hydrochloride (Semed), Stimdex (Ulmer), Syndrox (McNeil). Drug also marketed by many manufacturers under generic name and under name, Desoxyephedrine Hydrochloride.

OTHER ADRENERGIC AGENTS

Benzphetamine hydrochloride (Didrex)

Same degree of usefulness in treatment of obesity as other amphetamine-like agents.

Minimal number of untoward effects have been associated with drug's use. Long-term use, especially of larger than usual therapeutic doses, may result in psychic dependence. See monograph in New Drugs section and Introductory Statement for additional information on adverse reactions and precautions.

Usual dosage—*Oral: Adults,* 25 to 50 mg one to three times daily.

Preparations—Didrex (Upjohn). *Oral:* Tablets 25 and 50 mg.

Chlorphentermine hydrochloride (Pre-State)

Comparable to other amyphetamine-like agents in suppressing appetite of obese individual.

Produces fewer reactions attribuable to central nervous system stimulation (eg, nervousness, palpitation, dizziness, insomnia) than emphetamine and

phenmetrazine. Long-term use, especially of larger than usual therapeutic doses, may result in psychic dependence. See monograph in New Drugs section and Introductory Statement for additional information on adverse reactions and precautions.

Usual dosage—*Oral: Adults*, 65 mg once daily after morning meal.

Preparation—Pre-State (Warner-Chilcott). *Oral: Tablets* 65 mg.

Diethylpropion hydrochloride (Tenuate, Tepanil)

Although drug produces less cerebral stimulation than other amphetamine-like agents, weight loss is less than that obtained with use of those agents that cause greater central nervous system stimulation. Data insufficient to evaluate timed-release preparations, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

Long-term use, especially of larger than usual therapeutic doses, may result in psychic dependence. See Introductory Statement for additional information on adverse reactions and precautions.

Usual dosage—*Oral: Adults*, 25 mg three times daily one hour before meals. An additional dose may be taken in the evening for nighttime control of hunger. Alternatively, timed-release preparation may be taken once daily.

Preparations—Tenuate (Merrell), Tepanil (National). *Oral:* Tablets 25 mg; tablets (timed-release) 75 mg.

Phendimetrazine tartrate (Plegine)

Similar of other amphetamine-like compounds in usefulness as an anorexiant and incidence of untoward effects.

Long-term use, especially of larger than usual therapeutic doses, may result in psychic dependence. See monograph in New Drugs section and Introductory Statement for additional information on adverse reactions and precautions.

Usual dosage—*Oral: Adults*, 25 to 50 mg one to threee times daily.
before meals.

Preparations—Plegine (Ayerst). *Oral:* Tablets 35 mg.

Phenmetrazine hydrochloride (Preludin)

Comparable to dextroamphetamine in suppressing the appetite in obese indidividuals. Degree of effects on central nervous system may be much less than with amphetamine compounds. Data insufficient to evaluate timed-release preparations, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

Long-term use may result in psychic dependence. See Introductory Statement for additional information on adverse reactions and precautions.

Usual dosage—*Oral:* Adults, 25 mg two or three times daily one hour before meals. Alternatively, timed-release preparation may be taken once daily.

Preparations—Preludin (Geigy). *Oral:* Tablets 25 mg; tablets (timed-release) 75 mg.

Phentermine hydrochloride (Wilpo), *Phentermine resin* (Ionamin)

Usefulness of phentermine hydrochloride is comparable to that of other amphetamine-like agents. Also, phentermine is available as a complex of the base with an ion-exchange resin. In vitro the studies purport to show that agent is released from the resin into the gastrointestinal tract over a period of several hours, thus producing a sustained effort. However, available clinical data are insufficient to evaluate comparative effectiveness of the resin with the hydrochloride.

Long-term use, especially of larger than usual therapeutic doses, may result in psychic dependence. See Introductory Statement for additional information on adverse reactions and precautions.

Usual dosage—*Oral: Adults.* (hydrochloride) 8 mg 30 minutes before meals; (resin) 15 to 30 mg before breakfast or 10 to 14 hours before bedtime.

Preparations—

Phentermine Hydrochloride: Wilpo (Dorsey). *Oral:* Tablets 8 mg.

Prentermine Resin: Ionamin (Strasenburgh). *Oral:* Capsules 15 and 30 mg.

MIXTURES

A number of mixtures are available for use in weight control. These include combinations of amphetamine and dextroamphetamine, combinations of am-

phetamines and barbiturates or antianxiety agents, and preparations containing vitamins, bulk laxatives, or various other ingredients in addition to amphetamines. These preparations are generally irrational.

A sedative is often added to an anorexiant to counteract some of the stimulant effects of the latter. These preparations have the well-recognized disadvantage of a fixed-dosage ratio that makes individualization of doses of the constituents in the combination impossible However, the sedative is usually present in a sufficiently small dose to avoid a predominating sedative action.

Anorexiant mixtures designed to provide a vitamin supplement to a dieting patient are often appropriate; if such a combination product is chosen, however, the physician should note the precise formulation in determining the patient's needs.

Some combination products contain a bulk laxative such as methylcellulose which, when taken with adequate fluid, absorbs water, thus increasing the bulk in the large intestines and inducing a sense of satiety. In spite of this, these preparations do not serve a useful purpose in most patients being treated for obesity. Harsher laxatives are even more irrational.

Other mixtures that are available include the multicolored so called "rainbow pills" that may contain, in addition to an amphetamine, a barbiturate, digitalis, a diuretic, a thyroid preparation, a laxative, and an antispasmodic. There is great potential danger in the use of such combinations and deaths have occurred after their use (see the Introductory Statement to this chapter). Thus, there is no rational basis for their use in the treatment of obesity and their use is condemned.

ANOREXIANTS WITH SEDATIVES

Ambar

Phenobarbital is combined with methamphetamine to partially counteract stimulant effects of the latter. Data insufficient to evaluate timed-release preparations, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Methamphetamine Hydrochloride for information on adverse reactions and precautions.

Usual dosage—*Oral: Adults*, one tablet three times daily; alternatively, one timed-release tablet of appropriate strength may be taken once daily in the morning.

Preparations—Ambar (Robins). *Oral:* Each tablet contains methamphetamine hydrochloride 3 mg and phenobarbital 22 mg; each tablet (timed-release) contains methamphetamine hydrochloride 10 or 15 mg and phenobarbital 65 mg.

Appetrol, Bamadex

The antianxiety agent meprobamate may partially counteract stimulant effect of dextroamphetamine sulfate present in the mixture (see Chapter 28, Antianxiety Agents). Other claims for the combination are fanciful. Data insufficient to evaluate timed-release preparation, but preparation has inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for information on adverse reactions and precautions.

Usual dosage—*Oral: Adults*, one or two tablets three times daily, one-half to one hour before meals; alternatively, one timed-release capsule daily may be taken one-half hour before breakfast.

Preparations—Appetrol (Wallace), Bamadex (Lederle). *Oral:* Each capsule (timed-release) contains dextroamphetamine sulfate 15 mg and meprobamate 300 mg; each tablet contains dextroamphetamine sulfate 5 mg and meprobamate 400 mg.

Biphetamine, Biphetamine-T

Biphetamine contains equal amounts of racemic amphetamine and dextroamphetamine in a resin complex; Biphetamine-T also contains the sedative and hypnotic, methaqualone. No rationale for inclusion of amphetamine in the formulation is discernible. Data insufficient to evaluate these timed-release preparations, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for information on adverse reactions and precautions.

Usual dosage—

Biphetamine. *Oral: Adults,* one capsule of the appropriate strength daily, taken 10 to 14 hours before retiring.

Biphetamine-T. *Oral: Adults,* one capsule of the appropriate strength daily, taken upon rising.

Preparations—

Biphetamine (Strasenburgh). *Oral:* Each capsule contains 3.75, 6.25, or 10 mg each of dextroamphetamine and amphetamine.

Biphetamine-T (Strasenburgh). *Oral:* Each capsule contains 6.25 or 10 mg each of dextroamphetamine and amphetamine and 40 mg of methaqualone.

Desbutal

Pentobarbital sodium is combined with methamphetamine to partially counteract stimulant effects of the latter. Data insufficient to evaluate timed-release preparation, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for information on adverse reactions and precautions.

Usual dosage—*Oral: Adults,* one capsule two or three times daily; alternatively, one timed-release tablet of appropriate strength may be taken once daily in the morning.

Preparations—Desbutal (Abbott). *Oral:* Each capsule contains methamphetamine hydrochloride 5 mg and pentobarbital sodium 30 mg; each tablet (timed-release) contains methamphetamine hydrochloride 10 or 15 mg and pentobarbital sodium 60 or 90 mg.

Dexamyl

Amobarbital is combined with dextroamphetamine to counteract stimulant effects of the latter. Data insufficient to evaluate timed-release preparation, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for information on adverse reactions and precautions.

Usual dosage—*Oral: Adults,* one tablet or one teaspoonful of elixir two or three times daily, 30 to 60 minutes before meals; alternatively, one timed-release capsule daily may be taken in the morning.

Preparations—Dexamyl (Smith Kline & French). *Oral:* Each capsule (timed-release) contains dextroamphetamine sulfate 10 or 15 mg and amobarbital 15 or 65 mg; each 5 ml of elixir or each tablet contains dextroamphetamine sulfate 5 mg and amobarbital 32 mg.

Eskatrol

Prochlorperazine, an antipsychotic agent, is combined with dextroamphetamine to provide relief from emotional stress felt by the overweight patient attempting to lose weight. However, use of either a barbiturate or an antianxiety agent is preferred because risks may outweigh the benefits of using the phenothiazine derivative, prochlorperazine. Antipsychotic agents are not indicated for routine use solely for their sedative effect. Data insufficient to evaluate this timed-release preparation, but such preparations have inherent disadvantage of introducing at least one more factor to influence physiologic availability of the drug.

See Introductory Statement, individual evaluation on Dextroamphetamine, and Chapter 29, Antipsychotic Agents, for information on adverse reactions and precautions.

Usual dosage—*Oral: Adults,* one capsule daily, taken in the morning.

Preparations—Eskatrol (Smith Kline & French). *Oral:* Each capsule (timed-release) contains dextroamphetamine sulfate 15 mg and prochlorperazine maleate 7.5 mg.

Similar mixtures—

Amodex (Fellows-Testagar): dextroamphetamine hydrochloride, amobarbital.

Amo-Dextrosule (Arnar-Stone): dextroamphetamine sulfate, amobarbital.

Cendexal (Central): dextroamphetamine sulfate, amobarbital.

Du-Oria (Ascher): methamphetamine hydrochloride, reserpine.

Mepho-d (Walker) : metamphetamine hydrochloride, pentobarbital, mephobarbital.

Perke Two (Ascher) : dextroamphetamine sulfate, amobarbital.

Phedoxe 4B (Elder) : dl-methamphetamine hydrochloride, amobarbital, butabarbital, pentobarbital, phenobarbital.

Q-Caps (Fellows-Testagar) : dextroamphetamine hydrochloride, amobarbital.

Seco-Synatan (Mallinckrodt/Neisler) : dextroamphetamine tannate, secobarbital.

Tobie Timed Caps (Fellows-Testagar) : dextroamphetamine hydrochloride, aloin, phenobarbital.

15–90 (Elder) : dextroamphetamine sulfate, amobarbital.

ANOREXIANTS WITH SEDATIVES AND/OR BULK-PRODUCING AGENTS AND VITAMINS

Obedrin

Contains methamphetamine, pentobarbital, ascorbic acid, thiamine, riboflavin, and niacin. It seems unlikely that a dieting patient requires vitamin supplementation precisely with these ingredients and none other. This mixture is singled out for comment only because it is popularly prescribed. Data insufficient to evaluate timed-release preparation, but such preparations have inherent disadvantage of introducing one more factor to influence physiologic availability of the drug.

See Introductory Statement and individual evaluation on Dextroamphetamine for information on adverse reactions and precautions.

Usual dosage—*Oral: Adults*, one tablet or capsule at 10 a.m. and at 3 p.m. A third dose may be needed in the evening to discourage snacks during the night; alternatively, one timed-release tablet may be taken at 10 a.m.

Preparations—Obedrin (Semed). *Oral:* Each capsule or tablet contains methamphetamine hydrochloride 5 mg, pentobarbital 20 mg, ascorbic acid 100 mg, thiamine mononitrate 0.5 mg, riboflavin 1 mg, and niacin 5 mg, each tablet (timed-release) contains methamphetamine hydrochloride 12.5 mg, pentobarbital 50 mg, ascorbic acid 200 mg, thiamine mononitrate 1 mg, riboflavin 2 mg, and niacin 10 mg.

Similar mixtures—

Adjudets (Ives) : dextroamphetamine phosphate, vitamins A and D-2, thiamine hydrochloride, riboflavin, pyridoxine, ascorbic acid, niacin-amide.

Amphedase (Parke, Davis) : dextroamphetamine sulfate, thiamine mononitrate, ascorbic acid, nicotinamide, Aspergillus oryzae enzymes.

Arda (Fellows-Testagar) : dextroamphetamine sulfate, amobarbital, ascorbic acid, vitamins A and D, thiamine hydrochloride, riboflavin, niacinamide, ferrous sulfate, copper sulfate, potassium iodide.

Bamite (First Texas) : dextroamphetamine sulfate, phenobarbital sodium, ferrous gluconate, methylcellulose.

Biphetacel (Strasenburgh) : amphetamine phosphate, dextroamphetamine phosphate, methylatropine nitrate, carboxymethylcellulose sodium.

Cello-Dex (Fellows-Testagar) : dextroamphetamine hydrochloride, methylcellulose, dicalcium phosphate.

Nexorin (Dorsey) : dextroamphetamine sulfate, amobarbital, methylcellulose, magnesium trisilicate, thiamine hydrochloride, riboflavin, niacinamide.

Obocell (Mallinckrodt/Neisler) : dextroamphetamine phosphate, methylcellulose.

Obocell Complex (Mallinckrodt/Neisler) : dextroamphetamine phosphate dibasic, methylcellulose, choline bitartrate, inositol, thiamine mononitrate, riboflavin, niacinamide.

Obocell TF (Mallinckrodt/Neisler) : dextroamphetamine phosphate dibasic, methapyrilene hydrochloride, methylcellulose.

Obolip (Lakeside) : dextroamphetamine sulfate, phenobarbital, methylcellulose, choline bitartrate, methionine, cyanocobalamin.

Opidice (Boyle) : methamphetamine hydrochloride, methylcellulose, choline bitartrate, ascorbic acid, vitamins A and D, thiamine mononitrate, riboflavin, niacinamide, ferrous fumarate.

Quadamine (Tutag) : dextroamphetamine sulfate, amobarbital, vitamins A and D, thiamine hydrochloride, riboflavin, ascorbic acid, niacinamide, ferrous sulfate, copper sulfate, sodium molybdate, zinc sulfate, potassium iodide.

Revicaps (Lederle): dextroamphetamine sulfate, methylcellulose, vitamins A and D, thiamine mononitrate, riboflavin, pyridoxine hydrochloride, cyanocobalamin, ascorbic acid, niacinamide, pantothenate calcium, ferrous fumarate, calcium, phosphorus, iodine, copper, potassium, manganese, zinc, magnesium.

Vi-Dexemin (Smith Kline & French): dextroamphetamine sulfate, vitamins A and D, thiamine mononitrate, niacinamide, riboflavin, pyridoxine hydrochloride, cyanocobalamin, ascorbic acid, pantothenic acid, folic acid, ferrous sulfate, potassium iodide, calcium phosphate.

Vio-Dex (Rowell): dextroamphetamine sulfate, phenobarbital, thiamine mononitrate, pyridoxine hydrochloride, ascorbic acid, vitamin A acetate, niacinamide, pantothenate calcium, riboflavin, ergocalciferol.

ANOREXIANTS WITH THYROID PREPRATIONS AND SEDATIVES

The use of anorexiant mixtures containing thyroid is irrational. (See the Introductory Statement.)

AVAILABLE MIXTURES

Cydril with Tuloidin (Tutag): levamphetamine succinate, thyroid.

Methaloid (Tutag): methamphetamine hydrochloride, amobarbital, defatted pork thyroid.

Nobese (Durst): amphetamine sulfate, phenobarbital, thyroid, atropine sulfate, aloin.

Obestat (Lemmon): methamphetamine hydrochloride, amobarbital, thyroid.

Perke Three (Ascher): amphetamine sulfate, thyroid, atropine sulfate, aloin, phenobarbital.

MISCELLANEOUS ANOREXIANT MIXTURES

Adipex (Lemmon): methamphetamine hydrochloride, amobarbital, homatropine methylbromide.

Bifran (Strasenburgh): methamphetamine hydrochloride, pentobarbital, dehydrocholic acid.

Ridupois (Elder): levamphetamine tartrate, glyceryl guaiacolate.

Tempotriad (Smith, Miller & Patch): dextroamphetamine sulfate, pentylenetetrazol, caffeine.

[From Psychosomatics, Volume 6, pages 217–219, July–August 1965]

21. The Hazard of Amphetamine Medication*

(By Carl Breitner, M.D.)

In its November-December 1963 issue, Psychosomatics published a paper on "Appetite Suppressing Drugs as an Etiologic Factor in Mental Illness."[1] The paper attracted an unexpected degree of attention, which indicates that others have observed or at least felt, that administration of amphetamines can precipitate, if not cause, a certain type of mental disorder. This article attempts to present additional evidence and some new thoughts on the subject. The literature in this and other countries is replete with reports regarding the hazards of high doses of amphetamine administration with regard to mental health as well as to addiction. This material has been reviewed in the original paper and references will be found at the end of this article.

CHEMISTRY AND PHARMACOLOGY

The name "Amphetamine" is a generic name derived from Alpha-methylphenethylamine. The chemical derivation stems from epinephrine which is a catecholamine with two methyl groups. A related compound is ephedrine, the name of which stems from the Chinese herb, Ephedra vulgaris. These amines are sympathomimetic. In the brain they inhibit synaptic transmission as has been determined by Marazzi.[15] This reduces cortical inhibition with an alerting effect on the midbrain.

Toxic symptoms on shortlasting administration are due to the effect on the brain and include restlessness, dizziness, tremors, tenseness and irritability.

*Presented at the 11th Annual Meeting, Academy of Psychosomatic Medicine, New York, October, 1964.

There may be confusion, delirium, anxiety and hallucinations. A period of depression may follow stimulation. Headache, cardiac arrhythmia and anginal pain may also be noted. Chronic poisoning from amphetamines exhibits the same symptoms as are found in poisoning from single large doses. In addition, there may be marked weight loss and a harmful effect on mental health.

Amphetamines are prescribed by physicians for various and different purposes: (1) for the control of appetite and weight reduction, (2) for the euphoriant effect in emotional depressions, (3) for the control of allergies, (4) for the control of nasal stuffiness. Ephedrine is a favorite drug for the suppression of asthma attacks. The drugs serve their purpose well for a short period, but only to leave serious and adverse side effects with prolonged use.

By far the most widespread but also the most dangerous application is in the field of appetite suppression in those who are emotionally ill.

CLINICAL OBSERVATION

This article will not present case histories. Such histories have been presented earlier and are known to all who have prescribed amphetamines, except that the administration of amphetamines seems often unrelated to mental conditions or has not been correlated by some. The clinical effects of amphetamines, particularly in relation to mental conditions, may be described as follows: To begin with, there is an alerting and euphoriant effect. In small doses a feeling of well-being is produced and as the effects increase patients may become talkative, more alert and eventually sleepless. Appetite is markedly diminished. Prolonged administration produces increased irritability, nervousness with the appearance of typical neurotic symptoms. The drugs have a definitely addicting and habituating property inasmuch as the avoidance of amphetamine intake in habituated individuals will produce a marked letdown. In some individuals, somnolence occurs, which is undesirable and annoying. The patient may increase the dosage and as time goes on become more irritable and emotionally unstable. Some have crying spells without any psychogenic reasons; some develop rage reactions and in some patients definite paranoid symptoms occur. Episodes of marked depression with frequent suicidal thoughts may be seen, in a number of patients repeated suicidal attempts have been observed. The entire picture resembles schizophrenic disorganization of the personality. The similarity to schizophrenic reactions is so striking that numerous patients in institutions have been diagnosed by experienced psychiatrists as suffering from true schizophrenic reactions and only upon questioning is a history of amphetamine intake obtained.

One particularly interesting factor, namely, the compounding of amphetamine with sedatives, has contributed to the even more widespread use of the amphetamines. Quite frequently the patient who begins taking, for instance, Dexedrine or Preludin, will report that he notices such increased nervous irritability that he is reluctant to continue the intake of these drugs even when it is prescribed by physicians. The drug industry has quickly seized on this "shortcoming" of their product and various drug firms have combined amphetamines with some tranquilizing or soporific agent under various trade names. One outstanding example of such combinations is Dexamyl, a combination of Dexedrine and Amobarbital. Another one is Ambar, a combination of methamphetamine hydrochloride and phenobarbital. There are innumerable such combinations on the market and the purpose of this combination is obviously to hide or mask the alerting and nerve irritating properties of the medication, thereby inducing patients to abandon their natural healthy caution against a toxic substance by adding another toxic and habit forming substance such as a barbiturate. Combinations with meprobamate and phenothiazines are also on the market.

One further tragic "progress" has been made in the field of amphetamine administration under the pretext of making a medication more appealing. This is by introduction of the prolonged action compound. In this category we find "spansules," "extentabs" and numerous compounds under different trade names which produce prolonged and gradual action. One example of these is "Biphetamine" which incorporates the amphetamine in a resin which slowly disintegrates and releases the active substance. It is felt that these slow release medications are particularly dangerous for the following reason: We know from animal experimentation that lasting adverse drug reactions, such as

addiction in experimental animals, are hard to produce if we feed or administer the medication to the animal only once a day. (Personal communication—Albert Picchione.) To really show the ill effects of the drug, one has to feed it several times a day. The one-a-day administration allows the briefly intoxicated organism to recover between administrations. The individual or animal shows the immediate neurotoxic effect for one to several hours and then develops a compensating lethargy and recuperating rest. On the other hand the insidious and prolonged everlasting intoxication exerts an influence from which the organism cannot recover. It is a typically chronic intoxication which compares unfavorably with the interrupted administration of short acting drugs and in the author's opinion it is this insidious prolonged action of the medication which has the most harmful effects on the mental status of the patient.

A discussion of pharmacological effects is incomplete without the inclusion of laboratory findings. Lately an attempt has been made to gather evidence of disturbed function such as disturbances in glucose or steroid metabolism. Some observations have been made but they are so far not conclusive and not ready for publication.

TREATMENT

The "amphetamine illness" usually does not show spontaneous remission after discontinuation of the drug. On the contrary, once initiated, the disease progresses in geometric proportion. The clinical picture of the amphetamine reaction responds in a limited way to tranquilizing medication. However, the physician will encounter more difficulty than in the treatment of "spontaneous" or natural disturbances, e.g. while nervous instability will usually improve with phenothiazines such drugs will frequently produce a lethargy hard to tolerate by the patient. One must not forget that the discontinuation of the toxic amphetamine often produces this lethargy, yet it is associated with an increased emotional instability. Among the phenothiazines, Stelazine 5 mgs. b.i.d. has been used to advantage. In milder cases, Librium 25 mgs. b.i.d. is well tolerated. When severe somnolence occurs after drug withdrawal, Ritalin 10 to 20 mgs. t.i.d. may be helpful as a temporary substitute for the alerting effect of the amphetamines. Practical experience shows that daily use of insulin subcomas (10 to 25 units per treatment) often produces good effects after one to eight weeks. Nonconvulsive electric stimulation of the diencephalon as described in 1956 [18] is of great value in cases of severe agitation. In some cases the withdrawal lethargy reaches catatonic dimensions. In such instances ordinary electric convulsive therapy (ECT) may be of value.

Generally speaking the treatment of severe amphetamine psychoses is just as difficult or more so than the treatment of spontaneously occurring schizophrenic reactions. However, the prognosis is somewhat more favorable if the patient is prevented from committing suicide which is a great hazard in the disorder in question.

SUMMARY

Amphetamine medication may produce ill effects upon the patient's mental condition. Particularly the drugs which are employed for reduction of appetite in obesity may produce psychoneuroses and as a further consequence truly psychotic conditions of a schizophrenic reaction pattern.

Amphetamines are prescribed in many therapeutic areas often disguised under various trade names in all three states of matters, solids, liquids and gases. Some are sold without prescriptions in patented medicines. They are being used not only for dietary purposes but also for mental depressions, to increase alertness, for the control of allergies, asthma, hay fever, etc.

In recent years the hazards of amphetamine administration have been increased because of the compounding of these drugs with sedatives such as barbiturates or tranquilizers. This and the introduction of time-released medication has increased the hazard of chronic toxicity.

The clinical effects of chronic intoxication with amphetamines is discussed and treatment modalities are recommended.

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Article From Psychosomatics, Volume IV, November–December 1963, pp. 327–333

22. Appetite Suppressing Drugs as an Etiologic Factor in Mental Illness

Carl Breitner, M.D.

■ This study originated five years ago when a hospitalized college student, diagnosed as suffering from Paranoid Schizophrenia, disclosed that he liked Dexedrine and Dexamyl. He had started the use of these drugs sometime before in order to stay awake for his studies. He had been hospitalized for years. He had passes on weekends and whenever he left the hospital would secretly get a supply of these drugs. Once alerted by this experience, literally hundreds of cases of hospitalized and nonhospitalized mental patients admitted upon questioning that they had been taking various amphetamines for different periods of time and for various reasons. During the last few years it became quite evident that these drugs can cause or precipitate mental disorders.

In reviewing the domestic and particularly the English literature, it would appear that this report might be superfluous; however, amphetamines, in various forms, are still dispensed through samples and prescriptions in amounts measurable in tons annually.

Literature

Reports regarding the hazards of amphetamines with respect to mental health appear in the literature as far back as 1942. Some of the earlier reports deal with the toxicity of Benzedrine to experimental animals. A comprehensive list of these publications will be found at the end of this paper. However, in 1949 Brown[1] reported on Benzedrine habituation, Gunderson[2] on acute poisoning and a number of publications deal with a possible therapeutic effect of amphetamines in psychiatry. In 1945 Norman N. Shea[3] in an article entitled "Acute Hallucinosis as a Complication to Addiction to Amphetamine Sulfate" reported "A case of acute hallucinosis" in a patient who was addicted to amphetamines (Benzedrine sulfate). In 1954, Chapman[4] reported in the American Journal of Psychiatry on "Paranoid Psychosis Associated with Amphetamine Usage." This author felt that the causation of paranoid psychosis might depend on a previous disposition to paranoid thinking, which is, of course, quite possible. However, in 1958, Grahn[5] in an article entitled "Amphetamine Addiction and Habituation" expresses the thought that amphetamines can be used over a long period of time without causing habituation. This article is a refutation to the apparently, even then, publicly expressed opinion that amphetamines are habit-forming drugs. Morris Herman and Simon Nagler[6] reported in 1954 the development of "Psychosis Due to Amphetamines" and substantiate this title by eight cases. These authors felt that there is a predominance of psychotic reactions due to amphetamines in the male and that other drugs like alcohol might be contributory. However, the typical reaction is described as "essentially one of a paranoid psychosis with auditory and visual hallucinations in a setting of agitation and excitement." Beamish and Kiloh[7] reported in 1960, in an article entitled "Psychosis Due to Amphetamine Consumption," seven cases of development of psychosis and they feel that "in the majority of cases the picture resembles more closely that of paranoid schizophrenia."

McCormick[8] reported in 1961 on three cases of paranoid psychoses which developed in patients with narcolepsy. Recently Richman, Williams and Brown[9] published an article on "Acute Toxic Psychiatric Reactions Related to Amphetamine Medication." This article described 18 cases and concluded that "regardless of the disorder for which theso drugs are taken, there is always the ever present danger, if they are used consistently and persistently, of the patient developing a psychotic disorder of characteristic nature."

An article by Beale H. Ong[10] published in 1962 in the New England Journal of Medicine, cast some light on the prevalence of amphetamine consumption. This author stated that in 1959, 75,000 pounds were produced

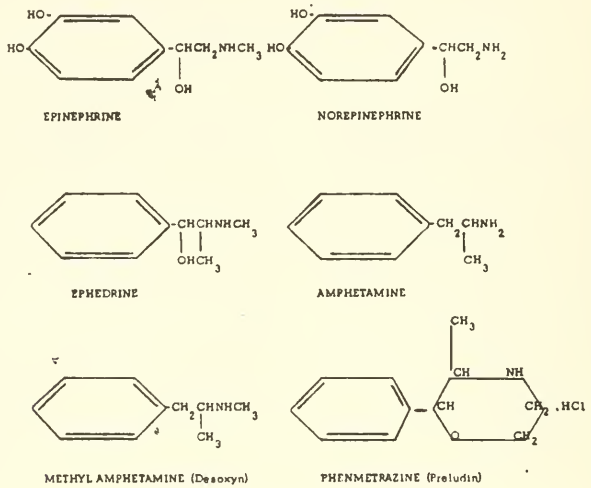

Fig. 1.

"or enough to provide 20 tablets for each man, woman and child in the United States." As recently as January 1963, Bell and Trethowan[11] in Australia, published an article on amphetamine addiction. They state "an incorrect diagnosis of schizophrenia has been made based upon false accounts" and the characteristic symptoms of the disorder are described in an article by Kiloh and Brandon[12] "Habituation and Addiction to Amphetamines." To quote, "The most striking complication of excessive consumption of these drugs is the occurrence of an amphetamine psychosis which usually takes the form of a schizophrenic-like illness" and furthermore, "the frequency is still not readily seen by psychiatrists and they (the patients) are often misdiagnosed."

One might assume that so many publications on this subject would alert the medical profession, and particularly psychiatrists, to the dangers of the amphetamines but daily clinical experience teaches us that this is not so and this fact serves as justification for this report. Further justification, however, might be found in the fact that only recently a study in book form has been published by Chauncey D. Leake,[13] in the American Lecture series, entitled "The Amphetamines, Their Actions and Uses." This book lauds the usefulness and benefit which amphetamines may provide, without sufficient warning of their dangers.

CHEMISTRY AND PHARMACOLOGY

In order to define and identify the various drugs involved, a brief review of chemistry and pharmacology seems in order.

Chemistry.—The name amphetamine is a generic name derived from alpha-methyl-phenethyl-amine. The chemical derivation stems from epinephrine which is a catecholamine with two methyl groups (Fig. 1). A similar compound is ephedrine which is longer lasting and extensively used in allergies such as asthma (this stems from the Chinese herb, Ephedra vulgaris) and the volatile base, Benzedrine, which is the trademark of Smith, Kline and French. All of these amines are sympathomimetic; however, the dextroisomer is supposed to have less side effects. There

are, at present, more than 25 different compounds and additional combinations on the market (Table I). They can be subdivided into three types. (1) The amphetamines which

TABLE I. TRADE NAMES

Epheurine	Tepanil
Benzedrine	Tenuate
Desoxyn	Preludin
Dexedrine	Desbutal
Dexamyl	Tyzine
Appetrol	Otrivin
Didrex	

Recommended Uses

Decongestant	Stimulant
Anorexiant	Anti-allergics

suppress appetite, (2) the volatile forms which are used as vasoconstrictors, and (3) the ephedrine-like compounds which are largely used in allergic conditions such as bronchial asthma. The amphetamines include Amphetamine sulfate and its volatile base, Benzedrine, usually dispensed as dextroamphetamine sulfate under the trade-name of Dexedrine, and methamphetamine hydrochloride (Desoxyephedrine) dispensed under the trade-names of Desoxyn or Pervitin. Some compounds and their actions are listed in Table II.

Physiology.—The compounds in question are slowly metabolized. They are not oxidized by amino-oxidase but possibly by another enzyme, phenoloxidase, which can activate deamination. Such an enzyme is found in the liver, kidney and in the brain. The physiologic action of amphetamines in the brain is to inhibit synaptic transmission, as has been determined by Marazzi.[14] This reduces cortical inhibition with an alerting effect on the mid-brain.

Pharmacology.—The pharmacological action of amphetamines is one of producing alertness and wakefulness. The effects can be subdivided in:

(a) *General*—Concerning reaction on the reticular activating system in the brainstem and it should be mentioned that continued administration increased susceptibility to subsequent doses. Among the most significant compounds, Benzedrine acts mostly sympathomimetic. Dexedrine is most alerting and the action of Desoxyn lies somewhat between.

(b) *Local*—The amphetamines produce blanching of mucous membranes. The autonomic nervous system is effected in an adrenergic fashion. Peripheral effects are mild but long-lasting. Vasoconstriction is characteristic.

(c) *Effect on muscle*—Muscle tone is increased and contractility is increased. Fatigue is reduced.

TABLE II. COMPOUNDS AND THEIR ACTIONS

Name	Chief Sympathomimetic Action
Amphetamine Sulfate USP Benzedrine	central nervous system stimulation; fatigue reduction; mild vasoconstriction
Biphetamine	appetite depression
Bralitate	
Dextro-amphetamine Sulfate USP Dexedrine	central nervous system stimulation† fatigue reduction; appetite depression
Epinephrine Hydrochloride USP Adrenalin	general sympathomimetic action
Ephedrine Sulfate USP	long-acting sympathomimetic action, especially bronchodilation, vasoconstriction and vasopression
Isonroterenol Hydrochloride USP Aludrine Isuprel	bronchodilation; cardio-acceleration
Levarterenol Bitartrate USP Levophed	vasopression; coronary vasodilation
Mephentermine Sulfate USP Wyamine	vasoconstriction central nervous system stimulation
Methamphetamine Hydrochloride USP Desoxyn Pervitin	central nervous system stimulation; vasoconstriction; appetite depression
Methoxyphenamine Hydrochloride Orthoxine	bronchodilation; intestinal relaxation
Nanhazoline Hydrochloride Privine	vasoconstriction
Phenmetrazine Hydrochloride Preludin	appetite depression
Propylhexedrine USP Benzedrex	vasoconstriction
Tetrahydrozoline Hydrochloride Tyzin	local vasoconstriction

(d) *Effect on CNS*—Increased activity in the brainstem with attentiveness and awareness and reduced fatigue results. Cerebral blood flow has been observed to be decreased in animals. The amphetamines inactivate amino-oxidase. They have an analeptic effect counteracting the effect of barbiturates. They increase visual and auditory acuity and facilitate synaptic transmission which can be proven by increased peripheral reflexes. The amphetamines also have a mild analgesic action.

(e) *Cardiovascular effects*—Blood pressure is slightly increased and the pressure effect is markedly increased by atropine. (This would contraindicate the administration of atropine for any purpose in patients who are suffering from amphetamine effects.)

(f) Amphetamines have been observed to create an increase in blood sugar. This may contribute to the reduction of appetite as well as the known central action on the appetite regulating center. Lesions in the ventral medial hypothalmic nucleus are followed by increased appetite and food intake with consequent obesity. It is assumed that amphetamines act by stimulating the ventral medial hypothalmic inhibiting center and this assumption is based on a presumed "stimulating" effect of amphetamine on brainstem functions. Chauncey D. Leake[13] writes: "However, since Marazzi and Hart[14] have clearly shown that the amphetamines inhibit synaptic transmission in the brain it would seem more likely that the appetite reducing effects of the amphetamines are due to blocking the activity of the lateral food intake centers." It is also interesting that Williams and his associates[15] found that a tolerance to Dexedrine with respect to reduction in appetite may develop after a few weeks of administration. However, if the drug is stopped for a short time the appetite effect returns on readministration. Kidney function is not altered by amphetamines. There is no good evidence that the amphetamines significantly alter endocrine secretion.

The pharmacologic action is well summarized in Leake's book.[13] "In summary, it may be stated that the outstanding action of amphetamines is upon the central nervous system from the cerebral cortex to the spinal cord." According to Mann and Quastel,[16] this may result from inhibition of the action of the enzyme, amino oxidase. "This enzyme acts on amines to form aldehydes. Since the amphetamines inhibit amino oxidases, they might thus reduce the amount of aldehyde formed and thus allow for increased brain respiration and in this way give increased central nervous system activity. On the other hand, the increased tone of the muscle and joints under the action of the amphetamines must result in increase of peripheral proprioceptive feed-back to the central nervous system with resulting increased alertness and attentiveness. An important aspect of the increased activity of the central nervous system under the influence of the amphetamines is reduction in appetite and food intake."

Further, with regard to the anti-appetite action of the amphetamines, it is the consensus of opinion that it is due in some way to the central action of these agents. On the other hand, there is some evidence to indicate that the amphetamines may relax stomach musculature and reduce stomach secretions. This effect might reduce hunger sensations and thus be a part of the anti-appetite action. However, the specific mechanism is inhibition of the lateral food intake center of the hypothalmus.

Toxic Symptoms.—"The common toxic symptoms in humans are those which are due to the effect on the brain and include restlessness, dizziness, tremors, tenseness and irritability. There may be confusion, delirium, anxiety and hallucinations. A period of depression may follow stimulation. Headache, cardiac arrhythmia and anginal pain may also be noted. Chronic poisoning from amphetamines exhibits the same symptoms as are found in poisoning from single large doses. In addition, there may be marked weight loss."

CASE HISTORIES

A few case histories will exemplify various degrees of anxiety followed by depression or other neurotic symptoms leading to some—as the condition becomes worse—into schizophrenic-like reactions and sometimes frank schizophrenic pictures.

Case 1.—This is the case of the college student mentioned in the introduction and exact history is no longer available because the patient was seen in New York State, but from memory I recall that he was about 23 or 24 years old; that he was suffering from paranoid delusions. He felt that people were against him and that his family wanted to keep him in the hospital. He was also tremulous and nervous and had to take barbiturates to sleep at night. He had several series of ECT which helped him only over short periods of time. It was elicited that he had been addicted to Dexamyl, which he obtained in an illegal manner. This addiction started when he wanted to study for examinations and took "energy pills" to stay awake. The outcome of this case is not known to me since I lost track of the patient due to my de-

parture from New York. At that time, following up this case did not appear as important as it would now, but it is mentioned here because it was the first case which drew my attention to amphetamine reactions.

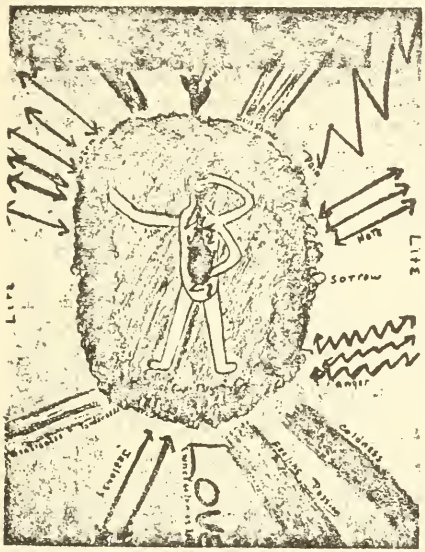

Fig. 2.

Case 2. (H.P.).—This is the history of a school teacher in her early forties, the mother of three children, who had some marital difficulty and had been nervous and depressed. To improve her mood she was placed on Dexedrine by a local psychiatrist. After initial improvement she became more agitated and, at the same time, despondent and depressed. After a suicidal attempt with barbiturates, she was placed in a private mental hospital under the care of another psychiatrist who spent much time with her in a psychotherapeutic effort and also administered some ECT when the patient did not seem to recover from her depression. At that time the patient produced a drawing which I believe is a classic picture of schizophrenic art (Fig. 2.) She finally improved with drug therapy at the hospital, but in the year following her discharge she made at least six or seven suicidal attempts, some of which appeared to be quite serious. All this time she was given amphetamines to lift her spirits. When her bill for private care exceeded what her husband wanted to pay for her recovery, she consulted me at the out-patient clinic at the Arizona State Hospital. At that time all amphetamines were discontinued and the patient was placed on antidepressive and tranquilizing medication (Marplan and Librium). After several months, she was able to resume her occupation as a teacher, and one year later was able to successfully finish a course in counselling. She is now active in this capacity at a local high school. She does well while taking moderate amounts of tension relieving medication such as Librium, but becomes still agitated when she attempts to discontinue it. However, there have been no more suicidal attempts during the last 18 months.

Case 3. (F.B.).—This was a married woman in the early fifties who had been hospitalized several times because of abuse of all sorts of drugs, including barbiturates. She was a college graduate; her husband was a professor at the State University. She had to be hospitalized in the State Hospital twice because she had episodes of withdrawal alternating with excitement, destroying records, books and appliances belonging to her husband. She was unable to dress herself. She was disorganized when first seen, could not complete sentences, displayed severe disturbance of memory, and in a fragmentary conversation believed that she hated herself, that she did not want to live and that she hated her husband. She admitted that she had been taking excessive amounts of sleeping pills and Dexedrine. The picture was such that she was diagnosed as a psychotic reaction due to drug addiction and was hospitalized in a private hospital, where she continued a somewhat stilted behavior and remained silly and superficial for approximately 2 weeks. During this time she had been on Librium, and after the third week of hospitalization she improved sufficiently to be discharged. She remained on the same medication for approximately 18 months and improved continuously. A year ago, she was able to secure a teaching position and reports to me occasionally from Tacoma, Washington, where she is now living and employed. There have been no more psychotic episodes.

Case 4. (Z.J.).—This is a well-developed, athletic appearing, married man who was 31 years old when he was first seen. He had a history of moderate alcoholism and was referred to me by a physician who treated him for overweight and hypertension. He had reduced his weight from 263 to 198 pounds by taking Preludin and Diuril and dieting. He was extremely excited, spoke of blowing his brains out and had grabbed a knife with the intent to kill himself. His condition is well documented by some shorthand notes that his wife took during one of his rages. He spoke of hating himself enough to kill because "they" are trying to hurt him. He spoke of hot flashes and "then I start leaving my body." He thought that "they are plotting against me to see how crazy I am." He said: "All I want to do is to destroy," et cetera. The patient improved after a few ECT and was kept on Librium for a period of time. It is more than a year now since the patient left the hospital and he is doing well.

Case 5.—This is a 31-year-old woman, the wife of a physician. This patient had been suffering from Multiple Sclerosis for a number of years. However, at the time I saw her she had no symptoms of this

disorder. She was unhappy, dissatisfied, nervous, sleepless and had crying spells. She related that she was concerned about being overweight and had been taking Dexedrine in one form or another for the last 18 years for weight control (with interruptions). She described herself as "tied in knots." At times she was worried, self-abating, felt unworthy and in emotional turmoil. She also had feelings of depersonalization and of distortion of perception, but no paranoid symptoms. She was treated with non-convulsive electric stimulation and tranquilizing medication, and a determined psychotherapeutic effort was made. All amphetamines were definitely discontinued. She improved considerably and is, at the present time, undergoing analytic treatment by another physician.

Case 6. (D.M.).—The patient was a 19-year-old girl referred by her physician after she had made a suicidal attempt. She also felt that people were talking about her and she disclosed that she felt disgusted with herself. She cried profusely, reported repetitive dreams in which she felt like killing someone; that she was running and that people were running after her. She could not say whom she wanted to kill. She had been on reducing pills which were originally prescribed by her physician but, when the patient found that they gave her a lift, she took more to keep awake. Now, one year later, the patient is improved considerably after a period of time during which she took Librium and a short course of ECT when she was first seen. She is now employed and planning to return to her studies at the university.

Case 7. (J.R.).—This is the case of an 18-year-old boy who had a long history of delinquent behavior, starting at the age of 13. He had abused alcohol and also had taken Dristan and various other inhalants, using them by tearing them down and getting a big dose of the stimulant so that sometimes he could not sleep for 30 hours. At times he was depressed and cried and at other times he was aggressive. At all times he was confused and disorganized. In getting better acquainted with this boy, it was felt that we were not dealing with a delinquent individual but that his disorganization and symptomatology resembled rather closely a schizophrenic reaction. However, the drug intoxication was never left out of sight. He received a number of insulin comas, some ECT, some non-convulsive stimulation, and a year later now the boy is working regularly and has had no more trouble with the law. It is believed that various stimulants, including amphetamines, were at least contributory to this boy's condition.

DISCUSSION

The few case histories quoted above, as well as evidence given in numerous articles in the literature, make it appear more than likely that amphetamines can lead to a state of tension and anxiety with aggravation to the point where psychotic symptoms, mostly depressive and paranoid in nature, appear. It is, of course, true that not every person who takes stimulating or appetite-controlling drugs may suffer ill effects from it. And it is further questionable whether the lack of sleep induced by the stimulant is responsible for the development of the anxiety reaction and the possibly subsequent psychosis. However, in questioning patients who are restless, tense, agitated and sometimes disorganized, one finds an incidence of use or abuse of amphetamines which is certainly remarkable. The clinical picture in these patients shows close resemblance between cases. By the time the patient consults a psychiatrist with regard to his nervous condition, he often has reached a fairly advanced state. He is usually tense and tremulous, complains of insomnia and anorexia, and frequently has a history of suicidal attempts. Many cases show a sharp resemblance with the agitated depression which occurs in the involutional period, and some show classical schizophrenic pictures such as loose associations, inappropriate affect, confusion, depersonalization and vague expression of hallucinations and delusions.

It cannot be unequivocally stated that amphetamines lead to mental disorders because there may be some patients who are able to tolerate these drugs even over prolonged periods of time. However, the evidence is certainly sufficient to advocate extreme care in dispensing these drugs. It is felt that the potentially dangerous drugs include the amphetamines as well as epinephrine, if it is used over a period of years, such as is the case in some asthmatic patients who, incidentally, also use the volatile stimulants such as are contained in various inhalants for the purpose of shrinking nasal membranes or for the purpose of dilating bronchial tubes (Isuprel, etc.).

One might expect that the reports so far published in the literature would already have alerted most physicians to the hazards of amphetamine administration. However, obviously, this is not the case as tons of these drugs dispensed yearly prove. Furthermore, it is understandable that physicians, as well as patients, are fond of amphetamines because initially they exert a very pleasant spirit-lifting effect and the serious adverse consequences appear often only after various lengths or periods of time. One might anticipate quick recovery upon the discontinua-

tion of the drug. This is unfortunately not the general experience. In fact, improvement is slow and energetic treatment must be instituted in addition to the drug withdrawal. It seems that the illness once started has a tendency to perpetuate itself as is commonly the case in mental disorders.

The attention of the profession is again directed to the hazards of amphetamine administration.

SUMMARY

In spite of numerous warnings in the American and English literature, amphetamines are still distributed by the tons for stimulation of depressed patients and even more for dietary reasons. In this report a brief identifying description of the drugs in question is given. Their chemistry, physiology and pharmacology is briefly discussed. A few cases of psychotic reaction due to amphetamine intake are described and the profession is once more alerted to the hazards and possible delayed adverse reactions to amphetamine administration.

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23. FAT-MOBILIZING ACTION OF AMPHETAMINE

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(Pps. 653–672)

INTRODUCTION

Numerous synthetic analogues of the naturally occurring sympathomimetic amines were shown to have a capacity for mobilizing fat; however, little information was available on amphetamine. We showed first in 1964 that amphetamine induced fat mobilization in man (Pinter and Pattee, 1965).

The study to be reported here was initiated in order to characterize and quantitate some metabolic changes induced by such an extensively used compound as amphetamine. Fat mobilization and the role of the adrenergic nervous system in the hyperadipokinesis of starvation in the lean and the obese were also studied in an attempt to provide a physiologic point of view of the therapeutic use of the sympathomimetic amphetamine drugs.

In this study evidence was obtained that amphetamine causes an increase in plasma free fatty acid (FFA) levels. The assumption that increments in plasma FFA levels after amphetamine administration were due to increased FFA production was corroborated with kinetic studies of FFA. It was also shown, based on studies with catecholamine depletion, that the adipokinetic effect of amphetamine was predominantly dependent on the presence of endogenous catecholamines.

It was also demonstrated in the starvation studies that neither the humoral regulation underlying increased fat mobilization of fasting in general nor the adipokinetic defect in the starving obese is primarily explainable by the contribution or inappropriate function of the adrenergic nervous system.

MATERIAL AND METHODS

A group of 88 volunteers of both sexes (41 lean and 47 obese) were studied. The obese subjects were kept on a moderately restricted diet whereas the food intake of the lean subjects was not controlled.

All procedures were conducted within an 8–14 hr post-absorptive period at complete physical rest, in a darkened room. Venous blood was obtained without obstruction of blood flow through an indwelling needle kept patent by 0.9% saline infused at a rate of approximately 60 ml/hr.

In order to measure the adipokinetic action of the different substances used, we adopted the following standardized procedure: venous blood was collected at intervals of 20 min, in the resting state on three occasions (usually between 8 A.M. and 9 A.M.) into heparinized tubes, and kept on crushed ice. The adipokinetic compound, dissolved in 50 ml of 0.9% saline, was then infused into the antecubital vein at a steady rate during a period of 15 min. Blood samples were obtained at the 10th min of infusion and at 0, 10, 20, 30, 45, 60, and 90 min after the infusion.

Other agents which were expected to modify the adipokinetic action of epinephrine or amphetamine (with the exception of reserpine—see below) were administered as intravenous saline infusions preceding the adipokinetic agent. There was some variation in the time intervals between infusions, depending on the compound used for pretreatment, but the basic protocols for amphetamine or epinephrine were identical.

A detailed description of the various procedures used is given below, under Results, grouped according to the aims of this study.

In the kinetic studies rapid intravenous injections of albumin-bound palmitic acid-^{14}C were given before and after the infusion of the adipokinetic agents. Five or six blood samples were obtained at 2-min intervals after each injection of the tracer.

Compounds

Adipokinetic. (a) Epinephrine hydrochloride (Parke Davis, Detroit, Mich.) total dose, 0.500 μg/kg i.v. for 15 min (0.416 μg/kg epinephrine base). (b) Amphetamine sulfate (Benzedrine, Smith, Kline & French Laboratories, Philadelphia, Pa.), total dose, 0.22 mg/kg i.v. for 15 min (0.146 mg/kg amphetamine base). (c) Methamphetamine hydrochloride (Methedrine, Burroughs Wellcome & Co., Tuckahoe, N.Y.), total dose, 0.200 mg/kg i.v. for 15 min (0.160 mg/kg methamphetamine base).

Adrenergic inhibitors. (a) Dihydroergotamine methanesulfonate (DHE 45, Sandoz Inc., New York, N.Y.), total dose, 2 mg i.v. for 30 min preceding the adipokinetic infusion by 60 min. (b) Reserpine (Ciba Pharmaceutical Company, Summit, N.J.); a 48-hr pretreatment period with 8 hourly i.m. injections of 5 mg reserpine followed by the usual adipokinetic procedures. (c) Propranolol (Ayerst Laboratories, Montreal, Canada), 0.3 mg/kg i.v. for 15 min. (d) Phenoxybenzamine hydrochloride (Dibenzyline, Smith Kline and French, Montreal, Canada), 1 mg/kg i.v.

Tracer. Albumin-bound palmitic acid-1-^{14}C (New England Nuclear Corp., Boston, Mass.). Each tracer injection contained 2 or 5 μc of ^{14}C in 6–10 ml of 25% salt-poor human serum albumin. The tracer was prepared by exposing unsaponified palmitic acid-^{14}C to albumin solution on a sterile surface, a procedure based on the principles of a method described previously (Kessler, Demeny and Sobotka, 1967; Adlersberg, Bossak, Sher and Sobotka, 1955).

The isotope studies were based on the method of successive measured injection of tracer substance (Hetenyi, Rappaport and Wrenshall, 1961; Wrenshall and Hetenyi, 1963). The actual procedure employed was a technical modification of the method described by Wrenshall and Hetenyi (1959) for the study of rates of transfer and pool sizes of glucose. Radioactivity was measured in a liquid scintillation spectrometer (Ansitron).

The calculations of the rate of transfer of FFA and of the FFA pool size were based on the quantity dilution principle. An IBM 7094 digital computer was programmed to carry out all calculations in the kinetic studies.

Total fat was determined by a gravimetric method (Bragdon, 1960), triglyceride according to the method of Van Handel and Zilversmit (Van Handel, 1961), FFA by the Dole procedure (1956),[1] and blood sugar in an Auto Analyzer with the method of Hoffman (1937). Plasma corticoids were measured by the method of Murphy (1968). FFA were prepared for isotope counting by a saponification extraction (Friedberg, Harlan, Trout and Estes, 1960). This involved an initial extraction, as in the Dole procedure, followed by the addition of 0.1 N NaOH in order to convert the fatty acids to the sodium salt and to extract them into an aqueous phase. Finally, after acidification, the fatty acids were reextracted with heptane. The above procedure eliminated all other lipid elements in the final extract which was used for FFA titration and isotope counting.

RESULTS

A. Adipokinetic action of amphetamine

In all subjects the FFA levels rose and reached a peak 30 min after amphetamine infusion. The average rise, expressed as ΔFFA in relation to

[1] We previously determined FFA using simultaneously the Dole procedure and the Trout modification (Trout, Estes and Friedberg, 1960) before, during and after different agents that influence fat mobilization (epinephrine, nicotinic acid, and propranolol) on 10 occasions. As expected, the FFA concentrations obtained by the unmodified Dole method were consistently higher (6–18%). We found, however, that the changes vs. the resting values of FFA (ΔFFA) were reflected within a $\pm$ 12% range of error by the Dole procedure.

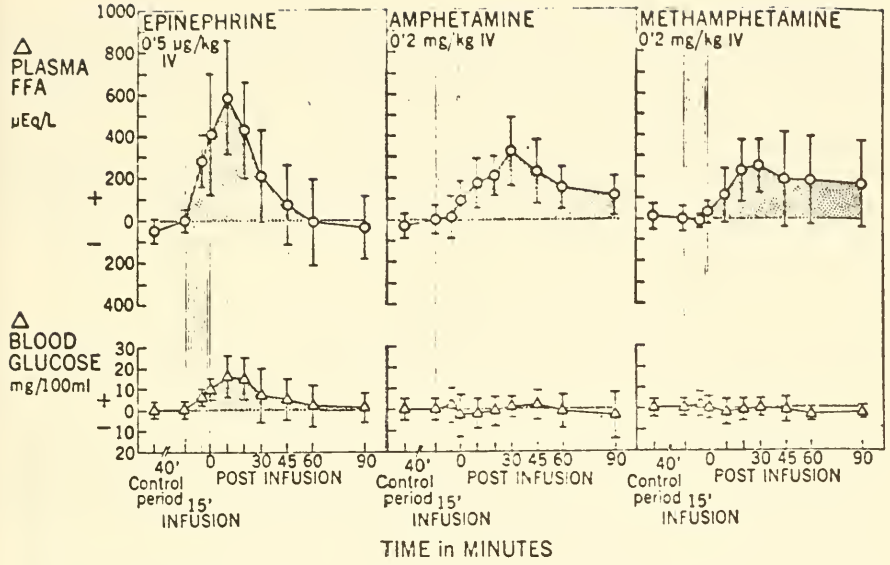

FIG. 1. The effect of intravenous epinephrine, amphetamine, and methamphetamine infusions on plasma FFA and blood glucose levels (in 14, 15, and 6 subjects, respectively). The individual curves show the mean changes (Δ) ± S.D. in relation to the baseline levels obtained in the control periods. The shaded areas represent the + ΔFFA and + Δ blood glucose areas; bounded by the temporal plot of ΔFFA and Δ blood glucose from the beginning of the infusions up to 90 min and by a horizontal line drawn at the level of baseline concentrations.

the FFA value obtained at the end of a 40 min period of rest in bed, was 326 ± 163 μEq/L above the preinfusion concentration.[2] Plasma FFA levels were still above the resting range at 90 min after the infusion of the compound (Fig. 1).

In order to compare the blood FFA rise after injecting amphetamine with that after epinephrine, we infused epinephrine in 14 subjects (9 of these were also included in the amphetamine series). The mean peak FFA concentration amounting to 589 ± 265 μEq/L of FFA above the preinfusion level occurred 10 min after epinephrine administration. Epinephrine produced an increase in blood sugar in contrast to amphetamine.

[2] The absolute variation of the plasma FFA concentrations from the beginning to the end of the control period was + 11 ± 63 μEq/L. In 40 randomly selected patients under identical conditions of bed rest and saline administration the following mean plasma FFA values were obtained: 0 min 774 ± 261 μEq/L; 20 min, 810 ± 281 μEq/L; 40 min, 776 ± 227 μEq/L.

The mean slopes[3] of rising FFA concentrations for amphetamine and epinephrine were found to be +7.17 and +23.55, respectively. A similar difference was found in the early returning slopes (amphetamine, −5.70; epinephrine, −15.35).

The basal concentrations of total fat and triglyceride were 568 ± 181 and 92 ± 21 mg/100 ml in the amphetamine group and 587 ± 82 and 96 ± 34 mg/100 ml in the epinephrine group, respectively. These showed no significant changes up to 90 min after the administration of amphetamine and epinephrine.

B. Measurement of amphetamine induced adipokinesis with ^{14}C-labeled, albumin-bound palmitic acid

In four individuals (obese and lean), rapid intravenous injections of albumin-bound palmitate-^{14}C were made before and 12 min after amphetamine infusion (Table I). Both the rate of appearance of FFA and FFA pool size increased. The increment in FFA pool size was due to increased fat mobilization since the rate of disappearance of FFA showed no simultaneous decrease. Actually an increment was seen in the FFA disappearance

TABLE I

Kinetic data of plasma FFA at rest (control period) and following a 15 minute intravenous infusion of amphetamine (0.2 mg/kg)

Subjects	Control period				12 min post i.v. amphetamine			
	N	*Ra*	*Rd*	λ	*N*	*Ra*	*Rd*	λ
1	4330	1000	1035	0.231	6960	1488	1463	0.213
2	3900	945	985	0.242	5425	1234	1150	0.227
3	4000	870	895	0.217	5600	1495	1362	0.267
4	2210	663	665	0.300	3390	745	774	0.220
Mean	3730	870	895	0.248	5405	1240	1187	0.232
					post i.v. methamphetamine			
5[a]	4210	1032	1040	0.246	5650	1372	1345	0.243

[a] One subject, given a 15 minute intravenous infusion of methamphetamine (0.2 mg/kg).
N : plasma FFA pool (μEq)
Ra : plasma FFA production (rate of appearance; μEq/min)
Rd : plasma FFA utilization (rate of disappearance; μEq/min)
λ : fractional turnover rate: $\frac{(0.693147)}{t_{1/2}}$

[3] The slope is expressed as the tangent of the angle of inclination per unit of time of the mean FFA curve ($\tan \alpha = \Delta y / \Delta x = \Delta FFA / \Delta t$).

rates, presumably due to a mass action effect of the increased amount of circulating FFA. Methamphetamine was also followed by an increase in the rate of FFA production and of FFA pool (one patient).

In order to compare the magnitude of these changes with those after epinephrine, we gave tracer injections before and at 0 min after epinephrine infusion in five patients (obese and lean) (Table II). The increments in FFA pool again were due to a primary rise of FFA appearance rates.

C. Adipokinetic action of methamphetamine

In the six patients studied there was an average rise of FFA levels of 244 ± 125 μEq/L above resting levels, 30 min after infusion (Table 1; Fig. 1).

D. Comparison of the adipokinetic effectiveness of amphetamine and methamphetamine with the fat-mobilizing potency of epinephrine

The following indexes were used to quantitate the adipokinetic response: (a) peak plasma FFA, (b) +ΔFFA area[1] (see Fig. 1), (c) the

TABLE II

Kinetic data of plasma FFA at rest (control period) and following a 15 minute intravenous infusion of epinephrine (0.5 μg/kg)

Subjects	Control period				0 min post i.v. epinephrine			
	N	*Ra*	*Rd*	λ	*N*	*Ra*	*Rd*	λ
1	4050	915	1040	0.226	10170	2280	1842	0.224
2	3420	1028	955	0.300	7600	2210	1780	0.290
3	2485	910	910	0.365	10710	1700	1670	0.158
4	6450	1825	1620	0.283	12610	2430	2185	0.193
5	4570	1038	923	0.227	9260	1865	1680	0.201
Mean	4400	1142	1090	0.280	10060	2100	1832	0.215

N : plasma FFA pool (μEq)
Ra : plasma FFA production (rate of appearance: μEq/min)
Rd : plasma FFA utilization (rate of disappearance: μEq/min)
λ : fractional turnover rate: $\frac{0.693147}{t_{1/2}}$

[1] Figure 1 illustrates that the mean ΔFFA values become negative 45 min after epinephrine administration whereas +ΔFFA still persist at 90 min postamphetamine. As the comparisons were made in relation to a standard 90 min epinephrine procedure, the mean +ΔFFA area for amphetamine expresses the adipokinetic potency per an arbitrarily chosen unit of time (90 min).

absolute and percentage increment of plasma FFA production rate, and (d) of plasma FFA pool size, measured after the administration of the compounds (Table III). The more pronounced changes in +ΔFFA area reflect the longer duration of action of amphetamine and methamphetamine in comparison with epinephrine. We believe that the latter data are more pertinent, from a physiological point of view, than the isolated consideration of peak effects.

E. Mechanism of adipokinetic action of amphetamine

The mode of action of amphetamine in mobilizing fat could be explained either by a direct action due to its aromatic amine structure or by an indirect effect via the release of endogenous catecholamines. Two agents were used in an attempt to suppress epinephrine induced adipokinesis, dihydroergotamine (2 mg/30 min i.v.) and glucose (250 mg/kg per 60 min, i.v.). These substances were administered on separate occasions preceding amphetamine and epinephrine infusions, respectively. Glucose administration suppressed both epinephrine and amphetamine induced adipokinesis. Intravenous dihydroergotamine led to a significant elevation of base line FFA (Fig. 2). The fat-mobilizing effect of both epinephrine and amphetamine were, however, suppressed to some extent (45 and 38%, respectively, expressed as peak ΔFFA) by the earlier administration of dihydroergotamine. These findings made the possibility of an adipokinetic action of amphetamine independent of its aromatic amine structure unlikely, as they indicated that a sympathomimetic amine was responsible for increased fat mobilization after amphetamine. The findings, however, did not indicate whether the responsible amine was amphetamine (direct action) or endogenous catecholamine released by the former compound (indirect action), since dihydroergotamine suppressed the effects of both epinephrine and amphetamine to nearly an equal degree.

In order to clarify the role of endogenous catecholamine release by amphetamine, we pretreated six subjects with large doses of parenteral reserpine (Fig. 3). When amphetamine was infused after 48 hr of reserpine pretreatment there was a marked inhibition of the amphetamine induced adipokinesis (80%, as suppression of peak FFA). Epinephrine given after reserpine pretreatment, on the other hand, was followed by an enhanced response (149%, as peak FFA response). This part of the study was interpreted as evidence for the dependence of the amphetamine induced fat mobilization on endogenous catecholamine release.

The residual fat mobilization in the reserpinized state could be due

TABLE III

Comparative representation of the different indices of adipokinetic effectiveness of epinephrine

GROUPS	ΔFFA data					
	Rising slope	Early returning slope	Late returning slope	Peak rise	Percent vs. epineph-rine	+ΔFFA area[a]
amphetamine (15 subjects)	+ 7.17	− 5.70	− 1.17	+ 326	55.3	17,205
methamphetamine (6 subjects)	+ 5.42	− 4.13	− 0.22	+ 244	41.5	15,925
epinephrine (14 subjects)	+ 23.55	− 15.35	− 1.04	+ 589	100.0	20,581

[a] in arbitrary units.
+ΔFFA area is bounded by the temporal plot of the plasma FFA concentrations and a horizontal line drawn at the level of plasma FFA concentration obtained

[b] one subject.
N : plasma FFA pool
Ra : plasma FFA production rate

to a direct action of amphetamine or to another adipokinetic hormone stimulated by amphetamine.

Our current studies of 4 subjects showed that the concentrations of circulating corticosteroids increase significantly following i.v. methamphetamine (Fig. 4). As the change in corticosteroids is elicited by increased ACTH output, pituitary and adrenal hormonal influences conceivably contribute to the indirect adipokinetic action of amphetamine compounds.

F. Fat mobilization in starvation

Finally, studies were made of fat mobilization and of its inhibition by alpha and beta blocking agents during starvation in lean and obese subjects in order to elucidate the possible contribution of some aspects of anomalous adipokinesis to obesity and to assess the role of the adrenergic system in nutritional situations of fat mobilization. This latter study was hoped to provide a physiological point of view in connection with the therapeutic use of amphetamines.

It was shown that 76% of the obese had a marked lag in the magnitude of FFA response to fasting, as compared with the lean group (at 48 hr of

amphetamine and methamphetamine infusions in relation to effects of the standard infusion

FFA kinetic data						
Percent vs. epineph-rine	ΔN (μEq)	Percent vs. epineph-rine	N percent change	ΔRa (μEq/min)	Percent vs. epineph-rine	Ra percent change
83.7	+ 1675	29.6	+ 45.0	+ 370	38.6	+ 42.6
77.5	+ 1440[b]	25.4[b]	+ 34.3[b]	+ 340[b]	35.5[b]	+ 32.9[b]
100.0	+ 5660	100.0	+ 128.5	+ 958	100.0	+ 83.9

(from the beginning up to 90 min following the infusion of the compounds indicated) at the beginning of the infusion.

starvation, ΔFFA = +282 ± 200 μEq/L above the prefasting level vs. ΔFFA = +991 ± 323, obtained in the lean group) (Fig. 5).

G. Tracer studies of FFA production, utilization and pool sizes

Twelve lean and 11 obese subjects were studied (a) at rest, (b) during epinephrine administration, and (c) during starvation (Fig. 6).

(a) At rest the production rates (Ra) and pool sizes (N) of circulating FFA were found to be significantly higher in the obese than in the lean ($p < 0.005$).

(b) Kinetic measurements following epinephrine infusion showed a markedly greater FFA response of the obese in comparison with the lean group both in absolute and percentage increments of pool sizes and production rates.

(c) During starvation, the absolute amounts of FFA pool and FFA production rates in the obese exceeded those found in the lean. There is however an important difference between the lean and obese groups in both the absolute and relative increments of pool size and production rate, as starvation proceeds beyond 30 hours. These increments are significant in the lean ($p < 0.02$), whereas the rises of both pool and production rate are at no time significant up to 100 hours of starvation in the obese. Likewise, the absolute amounts of increments in pool and production rate (over the

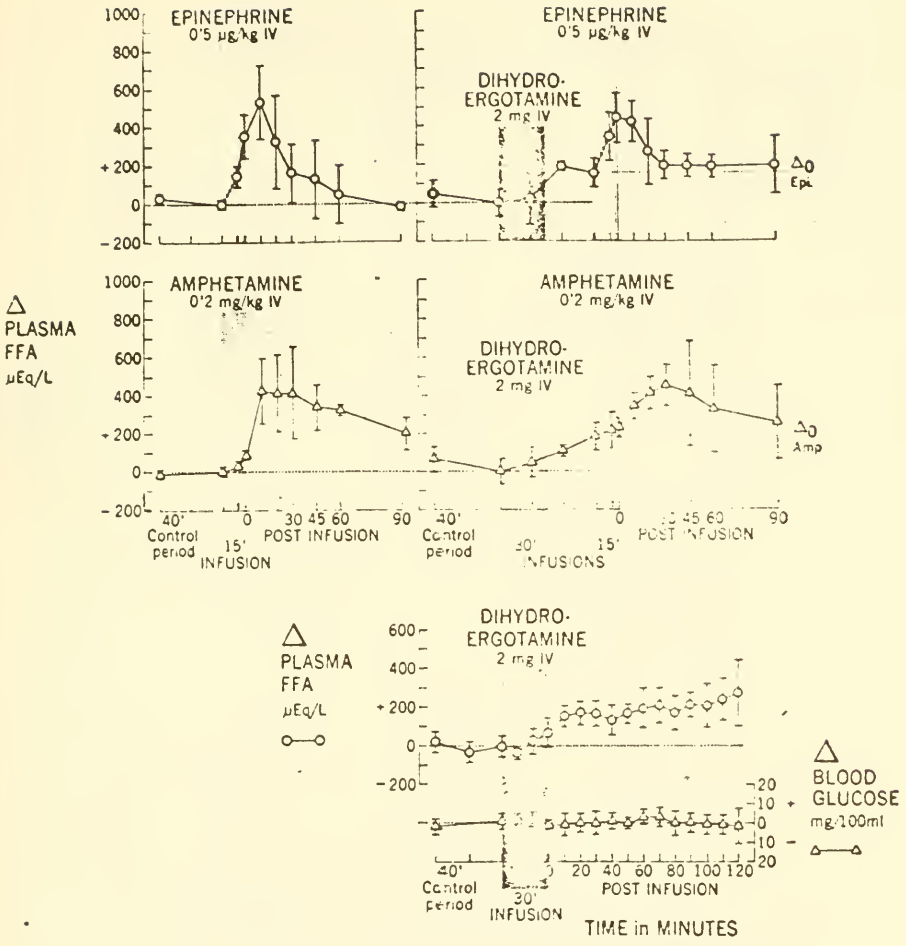

FIG. 2. The effect of dihydroergotamine pretreatment on the fat-mobilizing action of intravenous epinephrine and amphetamine infusions (5 subjects in each group) and the influence of intravenous dihydroergotamine alone on plasma FFA and blood glucose levels (in 4 subjects). The effects without pretreatment are included for comparison. Plasma FFA increased after dihydroergotamine (shown as Δ Epi and Δ Amp). The subsequent changes were estimated in relation to these higher baselines, as dihydroergotamine alone caused a significant increase in plasma FFA concentration, reaching a slightly rising plateau at 20 min post infusion.

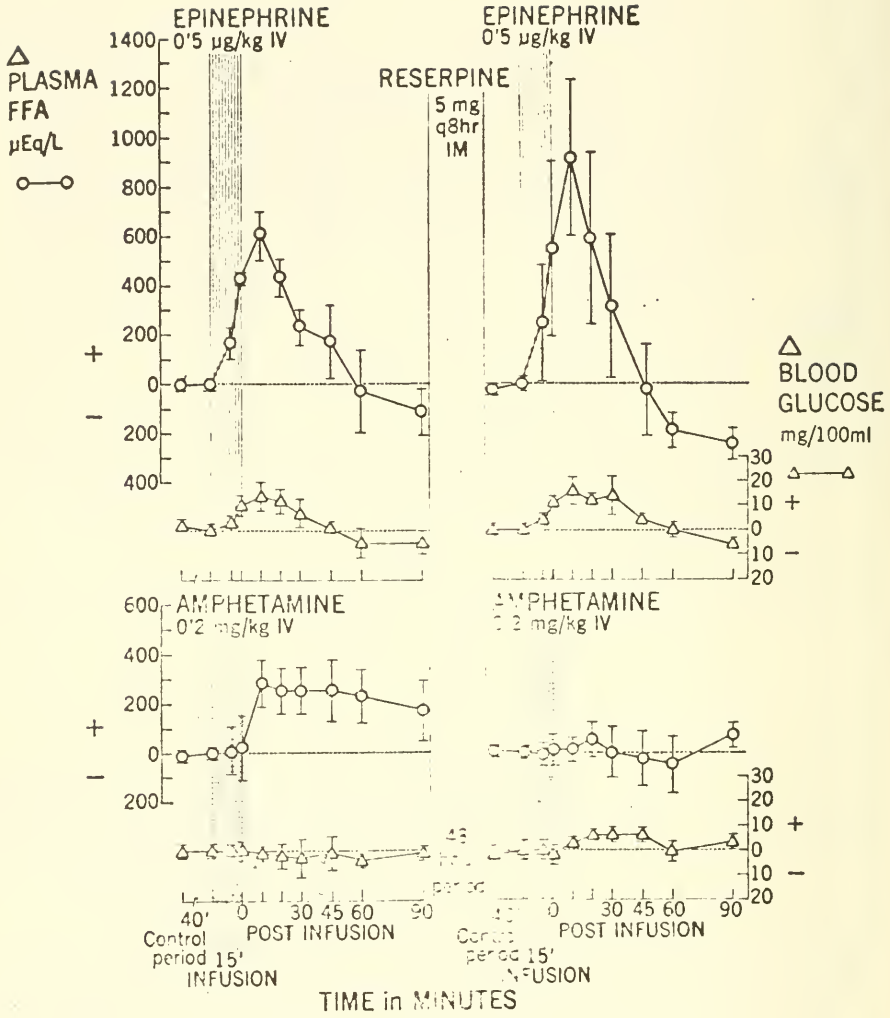

FIG. 3. Modification of the effects of intravenous epinephrine and amphetamine infusions by prolonged reserpine administration (6 subjects in each group). The changes (Δ) ± S.D. in plasma FFA and blood glucose levels are shown before and after a 48 hr period of parenteral reserpine treatment.

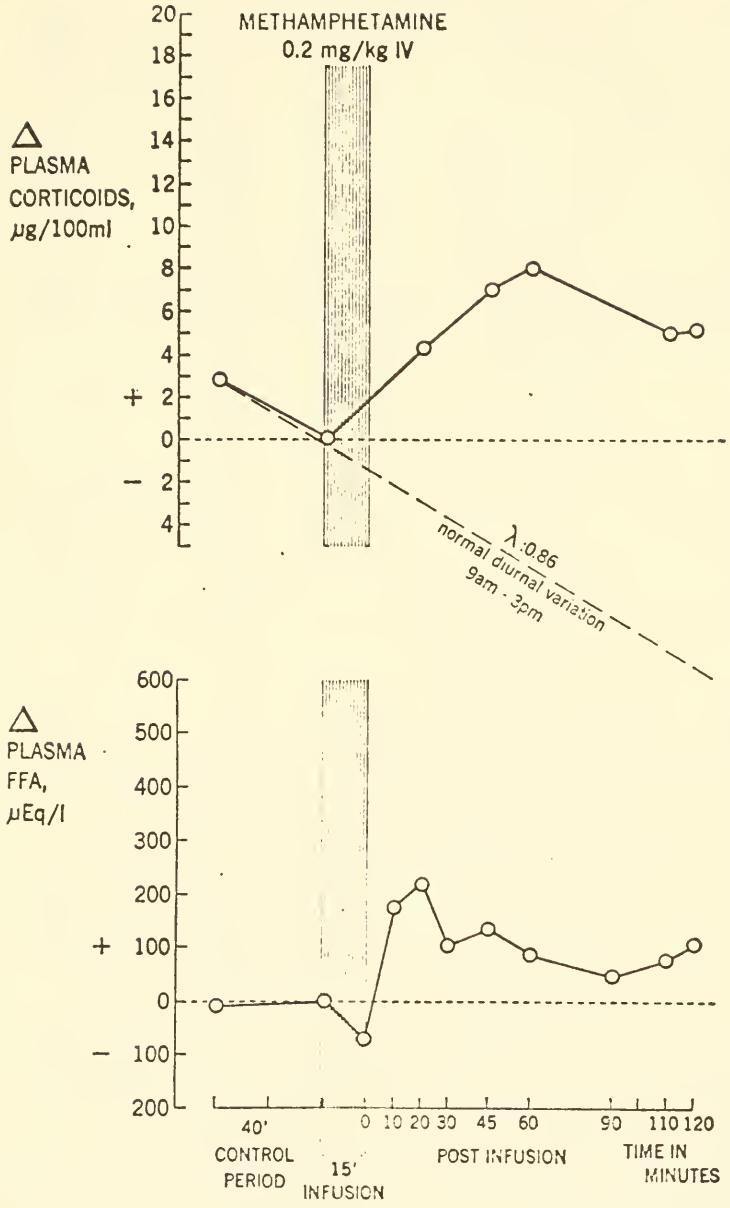

FIG. 4. The effect of intravenous methamphetamine on plasma corticoids and on plasma FFA (4 subjects). The individual curves show the mean changes (Δ) in relation to the baseline levels. As the diurnal variation should be taken into consideration in the assessment of plasma corticoid changes, the mean diurnal decrease (obtained in 20 subjects) is superimposed on the upper diagram (dotted line).

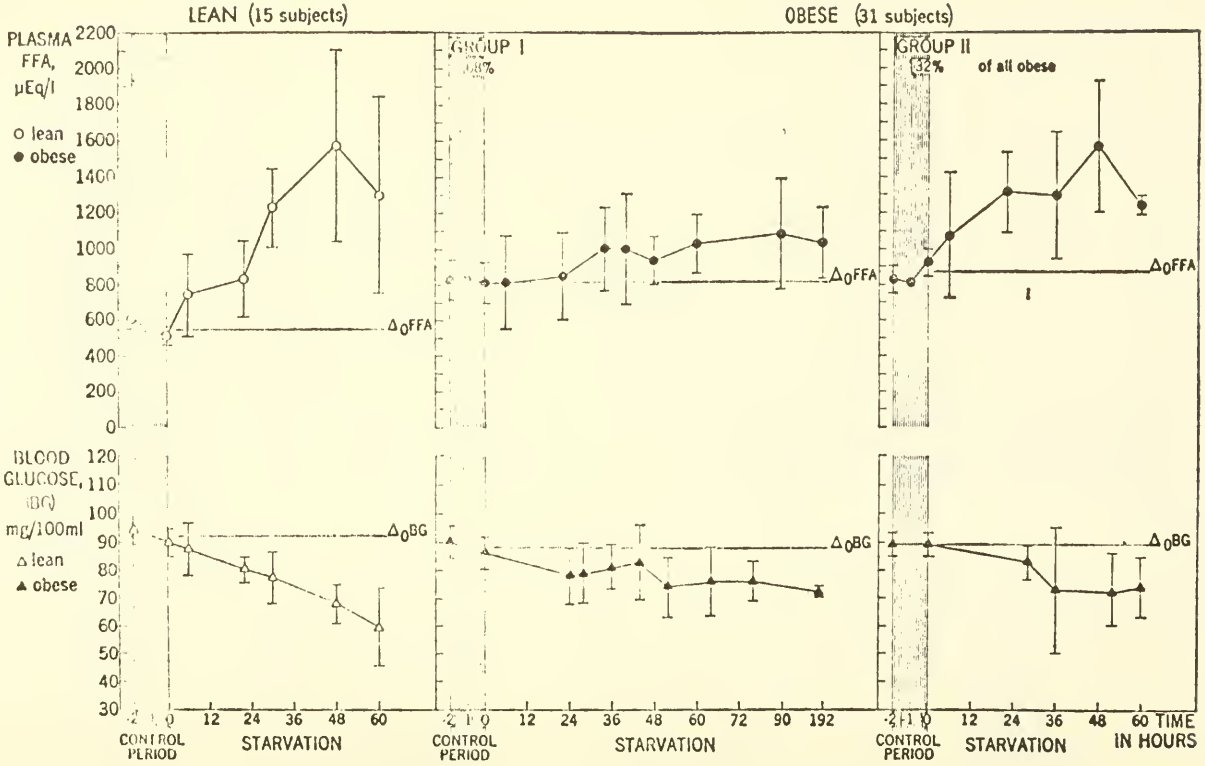

FIG. 5. The temporal sequence of plasma FFA and blood glucose changes in lean and obese subjects during starvation. The mean concentrations and the S.D. of the changes in relation to the basal values (Δ_0) are shown. The obese subjects were subdivided into groups I and II according to their peak FFA response.

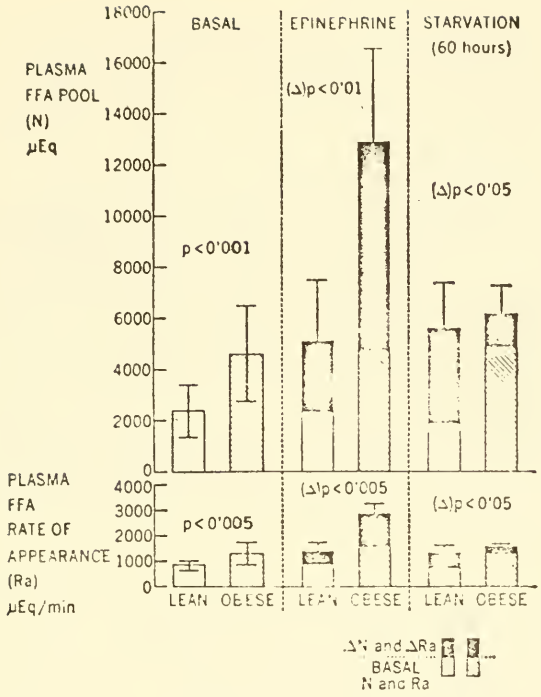

FIG. 6. Kinetic data of plasma FFA (pool sizes *N*, and appearance rates *Ra*) in lean and obese subjects at rest, during i.v. epinephrine stimulation and in starvation. The increments above the resting values (ΔN, ΔRa) are visualized as black bars. The absolute amounts of FFA appearance rate and pool in the obese exceed those of the normal both at rest and during progressive fasting. The increments associated with starvation (ΔN, ΔRa) are greater, however, in the lean subjects, than those in the obese. Fat mobilization induced by a non-nutritional stimulus (epinephrine) in the obese, on the other hand, is unimpaired and exceeds significantly that found in the lean.

baseline values) are significantly less in the obese than in the lean ($p < 0.05$). Thus it appears that there is a marked lag in the capacity of the obese to increase the rate of FFA mobilization, both in relative and absolute terms during progressive starvation. This defect is in sharp contrast to the findings obtained in exogenous (epinephrine) stimulation in which the obese showed a supranormal response.

A conversion of kinetic data to values per square meter of body surface tends to lessen the differences between the obese and lean at rest. The differences in the supranormal response to epinephrine and in the infranormal reaction to starvation still obtained, however, when the groups of obese and lean subjects were compared.

As to the role of the adrenergic nervous system in the meditation of starvation hyperadipokinesis in the normal and in the defect of fat mobilization in the starving obese, the following data were collected:

(a) There was a lack of positive correlation in the obese group between their responsiveness to starvation (expressed as plasma FFA increment) and the standard adrenergic stimulation by epinephrine (Fig. 7).

(b) Urinary excretion of the metabolite vanilomandelic acid (VMA) was measured in 24 obese and in 7 lean subjects at rest and during starvation up to 27 days. We were unable to find a correlation between the duration of fasting and the amount of VMA excreted daily in either group. It was also impossible to detect a meaningful difference in VMA excretion between the

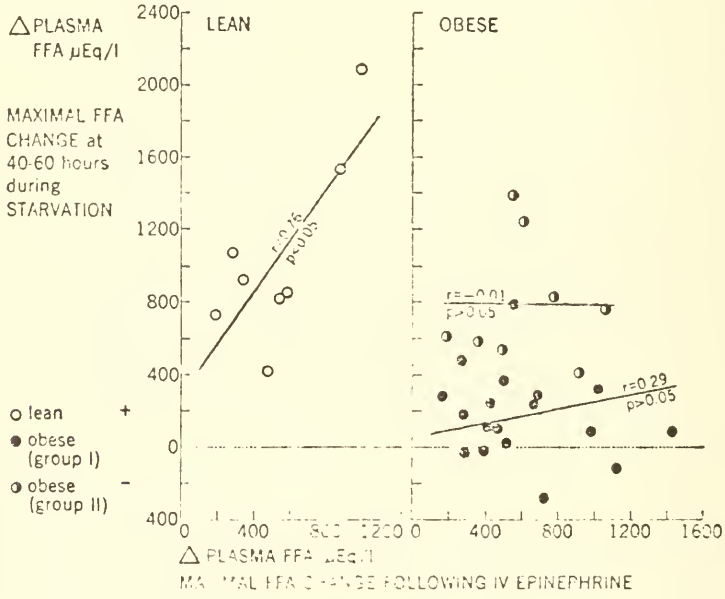

FIG. 7. In contrast to the obese group, the correlation between the responsiveness to an exogenous (epinephrine) and an endogenous (starvation) stimulus of fat mobilization is significantly positive among the lean subjects.

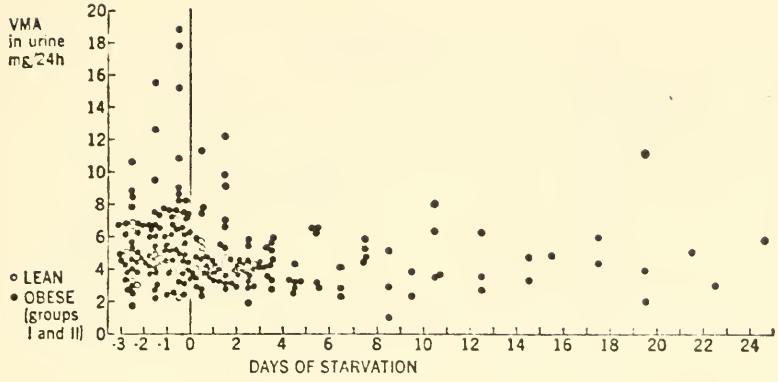

FIG. 8. Data of urinary excretion of vanilomandelic acid (VMA) in lean and obese subjects on regular feeding and during fasting. No meaningful changes could be demonstrated in starvation; some grossly obese subjects showed abnormally high VMA excretion.

obese and the lean group at metabolic rest, *i.e.*, on regular feeding, with the exception of abnormally high values in some obese subjects (Fig. 8).

(c) An intravenous infusion of a beta adrenergic receptor blocking agent (propranolol; 0.3 mg/kg/15 min) was given to 4 subjects at the 58th and 62nd hour of fasting. The beta adrenergic blockade failed to alter significantly and/or uniformly the stimulated state of fat mobilization, as shown by kinetic studies of FFA (Fig. 9).

Finally, alpha adrenergic receptor blockade was induced by I.V. phenoxybenzamine (1 mg/kg) in 4 subjects during prolonged starvation. This failed to reduce fat mobilization; in fact a significant stimulation of prevailing adipokinesis was shown (Fig. 10).

DISCUSSION AND CONCLUSIONS

Estimated from a dose ratio (amphetamine:epinephrine) of 352:1, the relative adipokinetic potency of amphetamine, expressed as peak ΔFFA rise, +ΔFFA area, and ΔFFA production rate, respectively, was found to be 55%, 84%, and 39% in comparison with the same effects of epinephrine. The more pronounced changes in +ΔFFA area reflect the longer duration of action of amphetamine as compared with epinephrine.

This study demonstrates that amphetamine is an adipokinetic agent causing an increase in the plasma FFA pool of a lesser extent but of longer

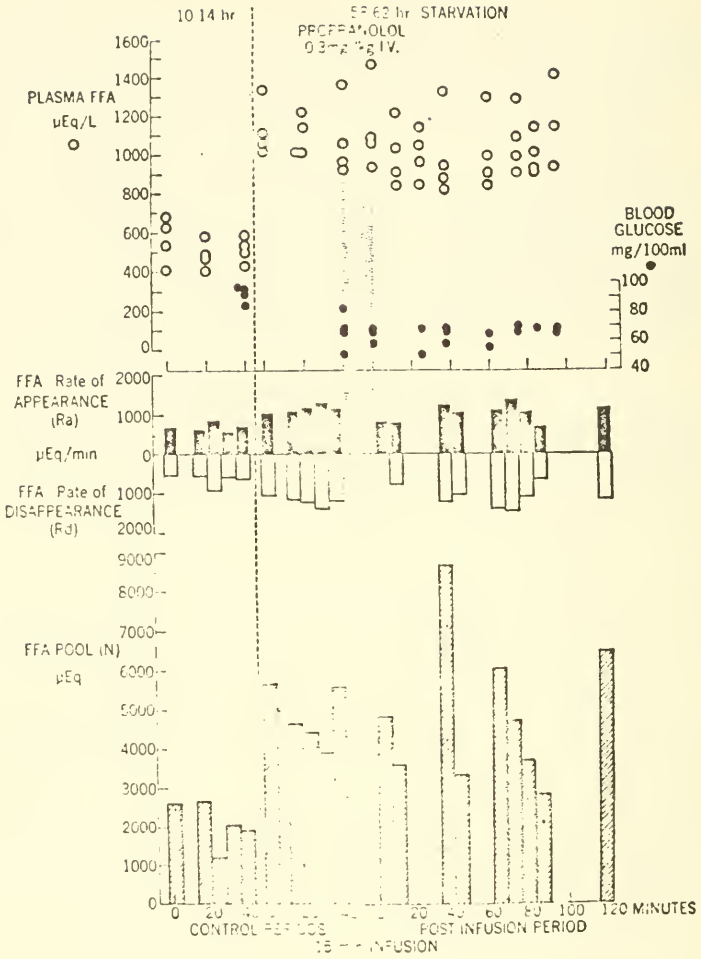

FIG. 9. Effects of beta adrenergic receptor blockade (propranolol, 0.3 mg/kg/15 min i.v.) on plasma FFA (kinetic data of FFA) and blood glucose concentrations during starvation (3 lean and 1 obese subjects). Prolonged starvation (58–62 hr) leads to an increase of FFA (least marked in the obese) and to a drop of blood glucose concentrations, as compared to the initial values (10–15 hr p.c.). Although there was a slight decrease in the plasma FFA in some subjects, beta adrenergic blockade failed to alter uniformly and/or significantly the hyperketonemia associated with starvation. The blood glucose concentrations remained essentially stable.

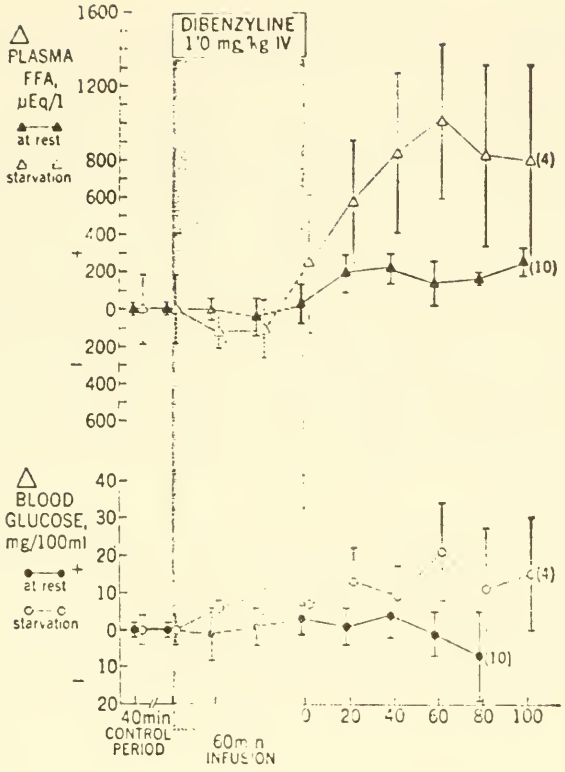

FIG. 10. The effect of i.v. dibenzyline on fat mobilization stimulated by starvation $\geq$ 60 hours, and on blood glucose concentrations in 4 subjects. For comparison, the effects of i.v. dibenzyline in 10 subjects at metabolic rest are also shown. The prevailing FFA concentrations rose markedly in the starving group following alpha adrenergic blockade exceeding the response seen at metabolic rest. Blood glucose increased following dibenzyline in starvation.

duration than equipressor doses of epinephrine. The mechanism of fat-mobilizing action of amphetamine is indirect, *i.e.*, dependent on endogenous catecholamine release.

Kinetic studies of FFA were also made in some of the subjects receiving amphetamine, methamphetamine, and epinephrine. It was shown that amphetamine and methamphetamine lead to an augmentation of plasma FFA pool due to a primary increase of FFA production rate.

Methamphetamine was shown to induce increments of circulating

corticoids. It is speculated that changes in pituitary-adrenal hormone secretions may contribute to the indirect adipokinetic action of amphetamine compounds.

It was felt that the demonstration of adipokinetic action of amphetamine has some significance in that repeated periods of needless hypermobilization of fat caused by the abuse of this compound or of any other adipokinetic agent, theoretically, may lead to adverse consequences, such as acceleration of thrombogenesis, increased endogenous triglyceride formation and hyperlipidemia with fatty infiltration of the liver, and decreased carbohydrate tolerance. On the other hand, the possibility exists of decreasing the mass of adipose tissue by a metabolic action (fat mobilization) independent of appetite regulation. An analogy for such action is provided by chronic administration of adipokinetic agents in the animal and by clinical reports on patients with pheochromocytoma (Kekwick and Pawan, 1963; Gifford, Kvale, Maher, Roth and Priestley, 1964). In both instances substantial weight losses were observed.

We have shown however that neither the humoral regulation of fat mobilization at rest and during starvation, in general, nor the adipokinetic defect in the starving obese are primarily dependent on the contribution and/or inappropriate function of the adrenergic nervous system (Pinter and Pattee, 1968*a; b*). Thus a sympathomimetic compound cannot be expected to correct the metabolic anomalies demonstrated in the obese.

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24. Studies on the Lack of Correlation Between Hyperthermia, Hyperactivity and Anorexia Induced by Amphetamine[1]

(pages 559–575)

(By P. Mantegazza, E. E. Müller, M. K. Naimzada and M. Riva, Department of Pharmacology, School of Pharmacy, University of Pavia, Pavia, Italy)

Although amphetamine has found a number of clinical applications, its present greatest use is as a food-intake depressant in the treatment of obesity. Concomitant with this action are, however, some undesirable side effects which result mainly from central nervous system stimulation. Some consider this central stimulation as the general mechanism by which amphetamine and its congeners depress appetite (Modell, 1960).

In the last years, however, experimental evidence has been accumulated which would suggest that anorexia may be separated from the other activities of amphetamine. This evidence is mainly derived from the observation that some amphetamine-like drugs, while showing a clear anorexic effect, are, however, devoid of a central stimulating activity (Le Douarec and Schmitt, 1964; Holland *et al.*, 1963).

This paper will report on two different types of experimental conditions which demonstrate that the anorexigenic activity of amphetamine can be divorced from some of the most typical properties of the drug.

Effect of propranolol on some activities of amphetamine

Mennear and Rudzik (1965) and Leszovsky and Tardos (1965) have shown that two β-adrenergic blocking agents, M.J.1999 and propranolol, are able to reduce the lethality of amphetamine in aggregated mice. Similar results were obtained by Moore (1965) studying the toxicity of amphetamine in hyperthyroid mice.

On the other hand, Grana and Sossi (1967) noticed that among many β-adrenergic blocking agents propranolol reduced the spontaneous activity increased by amphetamine. Since it appeared that propranolol might interfere with some other actions of amphetamine besides lethality, we thought it would be interesting to investigate the effect of this β-blocking agent on hyperthermia, anorexia, and increased spontaneous motility.

A. Methods

Animals. Swiss mice weighing 18–20 g were used. Females were employed in the study of locomotor activity, hyperthermia, and anorexia; males were used for toxicity studies. The animals were housed in a semidark and quiet room, the temperature of which was 20° C. These conditions were maintained throughout the experiments.

Toxicity. Mice were placed in groups of 10, in cages measuring 15 × 40 cm. Comparative studies were made with animals isolated in individual cages. Amphetamine was injected subcutaneously and deaths were recorded 24 hr later. At least 10 animals were used at each dose level. The calculation of the LD_{50} was made according to the method of Litchfield and Wilcoxon (1949).

Hyperthermia. Groups of six mice were fasted for 12 hr and were placed in cages measuring 45 ×40 cm. Rectal temperatures were measured hourly for six successive hours by means of an Electrical Universal Thermometer of TE_2 Ellab type.

Amphetamine was injected after the basal temperature had been taken twice. Animals that had a basal temperature below 36.8° C were discarded.

Spontaneous activity. The method used was similar to that described by Dews (1953) for the study of spontaneous coordinated activity in mice. Five mice were used at the same time in each experiment.

The cages measured 20 × 30 cm. To avoid disturbing effects, infrared photocells were used and the recording counters were installed in an adjacent room. Amphetamine was injected subcutaneously 30 min before placing the animals in the activity cages and activity was recorded for a 15 min period. Control experiments were made at random during the series of tests. At least 20 animals were used at each dose level.

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[1] Amphetamines and Related Compounds; Proceedings of the Mario Negri Institute for Pharmacological Research, Milan, Italy, Edited by E. Costa and S. Garattini. Raven Press, New York, © 1970.

Anorexia. Mice were trained to take food during 6 out of 24 hr. They were kept in groups of six in cages measuring 15 × 40 cm and generally developed a consistent habit of food intake within one week. On the day of the experiment a weighed meal was given immediately after amphetamine injection and the amount of food intake was registered after two hours.

Drugs. d-Amphetamine sulfate (Recordati) and 1-isopropylamine-3-(1-naphthyloxy)-2-propranolol hydrochloride (Inderal, I.C.I.) were used. These drugs were always administered subcutaneously over a range of doses to allow accurate representation of the activity pattern and according to schedules which are described with the results. An isotonic solution of sodium chloride was used for control injections.

B. Results

Toxicity in aggregated mice. The protective action of propranolol on amphetamine lethality was confirmed on our strain of Swiss mice. Figure 1 shows that propranolol (10 mg/kg. s.c.) given 30 min before amphetamine increased the LD_{50} from 15.5 to 140 mg/kg. In isolated mice, however, propranolol was unable to modify significantly the LD_{50} of amphetamine.

By pretreating aggregated mice with different doses of propranolol and injecting a constant dose of amphetamine (31 mg/kg s.c. = 2 LD_{50}) it could be seen (Fig. 2) that the β-blocking agent at the doses of 20 or 10 mg/kg gave almost complete protection. The action of propranolol was still evident at the very low dose of 0.31 mg/kg.

Hyperthermia. Results concerning hyperthermia are summarized in Figs. 3 and 4. Figure 3 shows that amphetamine at 10 or 20 mg/kg caused a sharp increase in body temperature within one hour. This increase was later followed by a decline in the temperature below the normal level. At lower doses (2.5 and 5.0 mg/kg) this drug did not significantly modify body temperature.

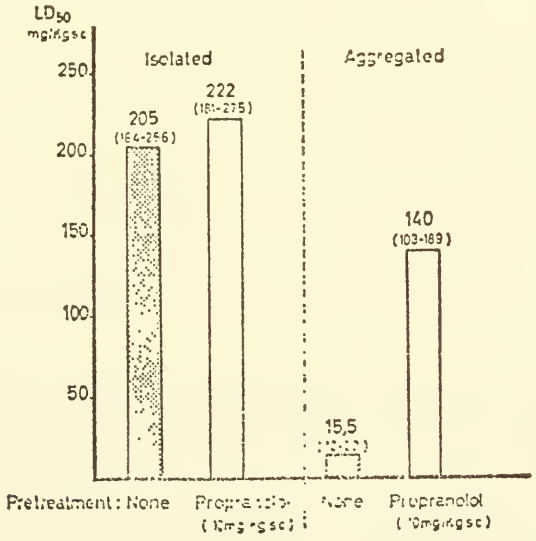


FIG. 1. Toxicity of amphetamine in normal or propranolol-pretreated mice.

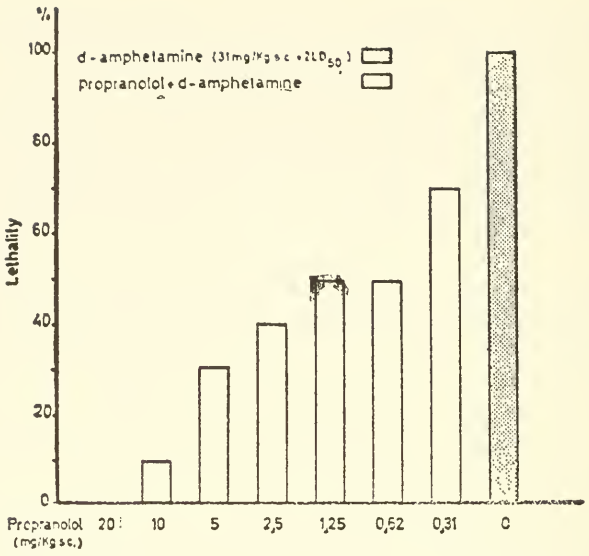


FIG. 2. Toxicity of amphetamine in aggregated mice, pretreated with different doses of propranolol. Ten animals were used at each dose level.

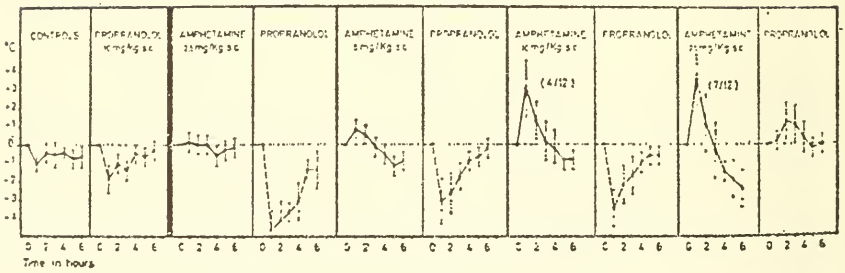


FIG. 3. Hyperthermia induced by amphetamine in aggregated mice pretreated or not pretreated with propranolol. Each point on the curve represents the mean temperature of 12 mice. Vertical lines indicate the standard error. Number of dead mice in each group is given in brackets. *Ordinate:* temperature changes in °C; *abscissa:* time in hours. Propranolol (10 mg/kg) was given subcutaneously 30 min before amphetamine.

Propranol by itself showed, at a dose of 10 mg/kg, a slight hypothermic effect. When mice were pretreated with propranolol (10 mg/kg), the hyperthermia due to the highest doses of amphetamine appeared to be reduced or reversed, while in mice treated with amphetamine at lower doses, a hypothermic effect was observed. The effect of different doses of propranolol on the hyperthermia induced by a constant dose of amphetamine (10 mg/kg) is shown in Fig. 4. It can be seen that even as small a dose as 1.25 mg of propranolol was able to reverse the effect of amphetamine.

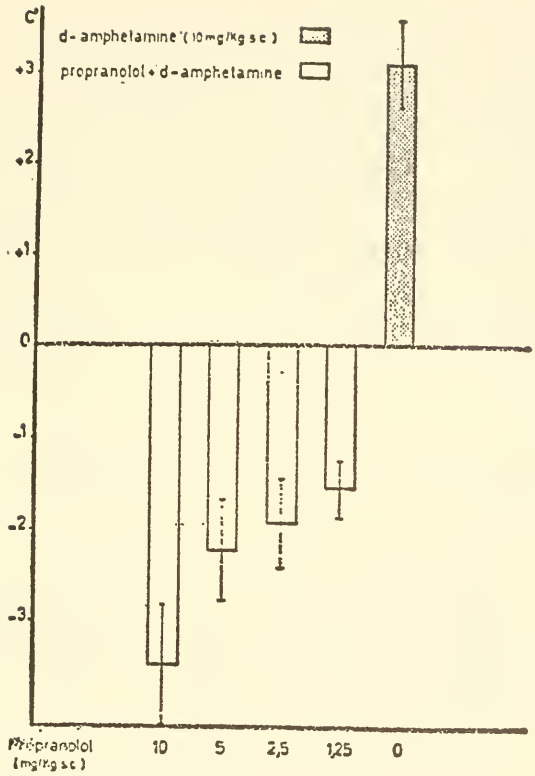


FIG. 4. Temperature changes induced by amphetamine (10 mg/kg s.c.) in mice pretreated with different doses of propranolol. *Ordinate:* temperature changes in C°. *Abscissa:* doses of propranolol. Vertical lines indicate the standard error. Propranolol was given 30 min before amphetamine. Temperature was recorded 1 hour after amphetamine. Ten animals were used at each dose level.

Increased locomotor activity. Amphetamine in doses ranging from 2.5 to 10 mg/kg increased spontaneous motility, and a straight log-dose effect relationship could be otbained (Fig. 5). In mice pretreated with propranolol (10 mg/kg) this effect was reduced and the dose-response curve was displaced and flattened. From this figure it is also evident that the dose of amphetamine which increased motility to 1.5 corresponded to about 4 mg in untreated mice and to 9 mg in animals pretreated with propranolol.

Results obtained by giving a constant dose of amphetamine (10 mg/kg) to animals pretreated with different doses of propranolol are summarized in Fig. 6. In this case, even a dose of 20 mg/kg of propranolol did not completely antagonize the effect of amphetamine. It must be pointed out that propranolol at the same dose did not modify either the normal spontaneous activity or the behavior of the animals.

The effect of propranolol on increased locomotor activity is at variance with the above-mentioned data on hyperthermia, since in that distance, a dose of propranolol as low as 1.25 mg/kg was able not only to block, but also to reverse the action of the amphetamine (Fig. 4).

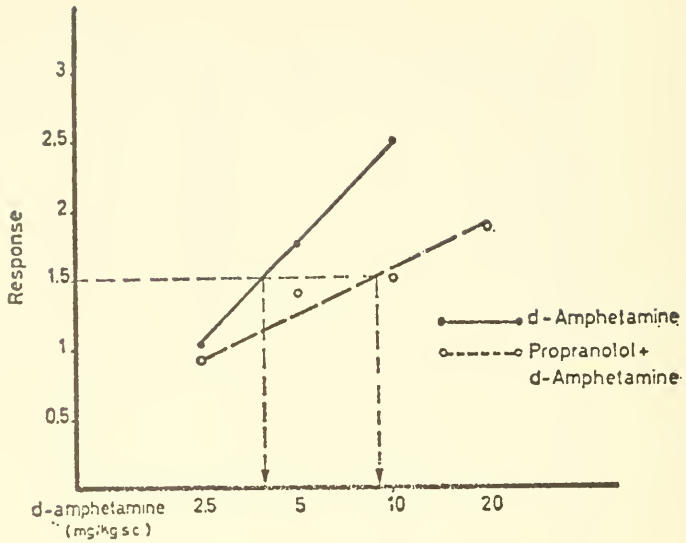


FIG. 5. Effect of amphetamine on the coordinated spontaneous activity of normal or propranolol-pretreated mice. Propranolol (10 mg/kg s.c.) was given 30 min before amphetamine. *Ordinate:* response expressed as ratio of the counts after drug administration to the counts of the controls on the same day; *abscissa:* doses of *d*-amphetamine.

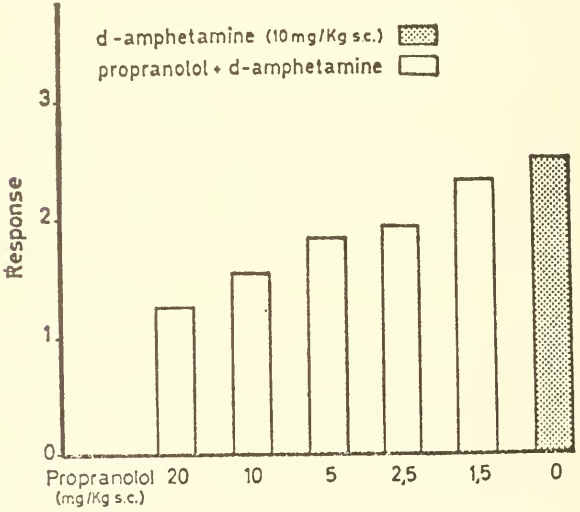
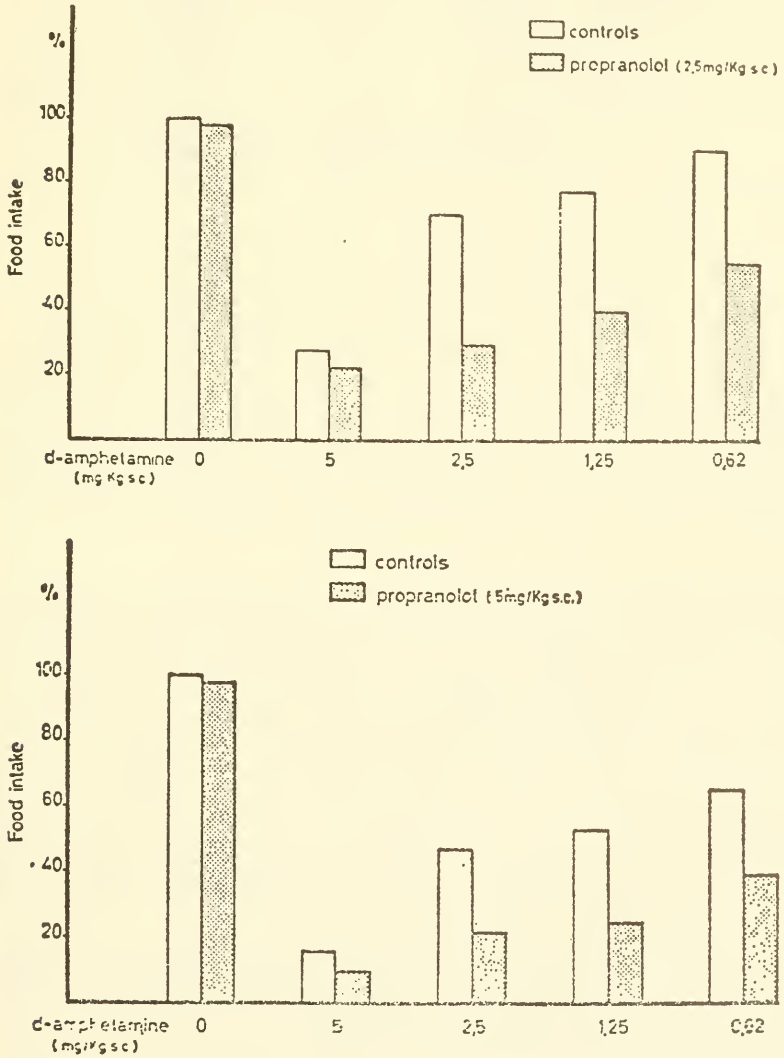


FIG. 6. Effect of amphetamine on the coordinated spontaneous activity of normal or propranolol-pretreated mice. *Ordinate:* response expressed as ratio of experimental values to basal values (basal = 1); *abscissa:* dose of propranolol. Amphetamine was given 30 min after propranolol.

Anorexia. A still more favorable opportunity to discriminate between the various activities of amphetamine was offered by studying the action of propranolol on anorexia. In this case, the action of amphetamine, far from being reversed or reduced, was clearly potentiated. Results obtained are shown in Figs. 7 and 8. Each series of results represents the mean of data from two experiments. Propranolol, at doses which by themselves do not modify food intake (2.5 and 5 mg/kg s.c.), potentiated the action of amphetamine at each dose level used. The effect of propranolol was still present using *l*-amphetamine instead of *d*-amphetamine (Fig. 9).

From these first series of data it appears that of the various activities of amphetamine we examined, hyperthermia and lethality were much more sensitive than increased spontaneous motility to the antagonistic effect of propranolol; while anorexia, instead of being antagonized, was clearly potentiated.



FIGS. 7, 8. Anorexigenic activity of amphetamine in mice pretreated with different doses of propranolol. Propranolol was given 30 min before amphetamine.

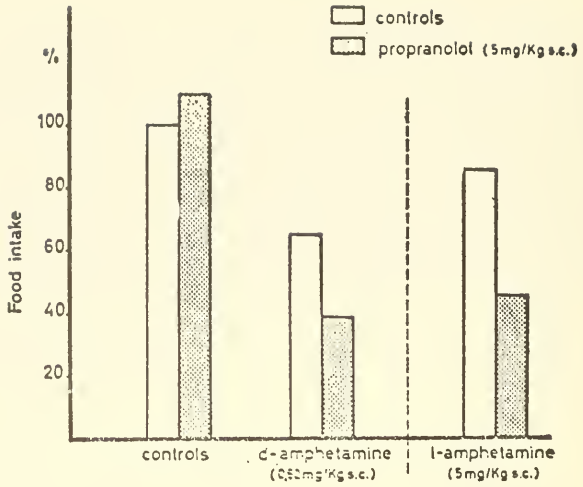


FIG. 9. Effect of propranolol on the anorexia induced by *d*-amphetamine or *l*-amphetamine in mice.

III. COMPARATIVE ACTIVITIES OF *dl*-AMPHETAMINE, *dl*-4-CHLOROAMPHETAMINE AND *dl*-4-METHAMPHETAMINE

As was mentioned before, one of the arguments in favor of the concept that the anorexic effect of amphetamine may be an independent activity was derived from the observation that some amphetamine-like drugs, while devoid of central stimulating properties, could be anorexic (Le Douarec and Schmitt, 1964; Holland *et al.*, 1963). Here, by contrast, we have considered the opposite condition: *i.e.*, two drugs, 4-chloroamphetamine and 4-methamphetamine which are more hyperthermic or motor exciting than amphetamine, but less anorexigenic.

A. Methods

Animals. Wistar rats weighing 150 g were used. Toxicity and anorexia were studied in male rats; female rats were used in the study of hyperthermia and locomotor activity. During the experiments the animals were kept in a semidark and quiet room, the temperature of which was maintained at 20–22° C.

Toxicity. Rats were aggregated in groups of 10 in cages measuring 25 × 40 cm. Drugs were injected subcutaneously and mortality was recorded 24 hr later. At least 10 animals were used at each dose level. The calculations were made according to the method of Litchfield and Wilcoxon (1949).

Hyperthermia. Groups of six rats were fasted for 12 hr and were placed in cages measuring 45 × 40 cm. Rectal temperature was measured hourly for five successive hr. by means of an Electrical Universal Thermometer of the TE_2 Ellab type.

Increased locomotor activity. The method used was similar to that described by Dews (1953) for the study of spontaneous coordinated motility in mice. Four rats were used at the same time in each experiment. The cages measured 45 × 30 cm. (For further details see Methods.)

Anorexigenic activity. Animals were trained to take food during 8 out of 24 hr. They were kept in individual cages and generally developed a consistent habit of food intake within two weeks. On the day of the experiment a weighed meal was given to each animal immediately after treatment, and the amount of food intake was registered hourly for 4 hr.

Drugs. dl-Amphetamine sulfate (Recordati), *dl*-4-chloroamphetamine and *dl*-4-methamphetamine hydrochloride (Vister) were used. The drugs were always given subcutaneously.

B. Results

Lethality. The toxicity of the drugs under examination is reported in Table I. It appears that 4-chloroamphetamine was more toxic than both amphetamine and 4-methamphetamine.

Hyperthermia. On comparing the hyperthermic effect of these drugs, it may be observed that 4-chloroamphetamine was the most active, its effect already being present at the dose of 2.5 mg/kg (Fig. 10). For eliciting a comparable degree of hyperthermia, amphetamine must be administered at a dose of 10 mg/kg. Methamphetamine-induced hyperthermia was similar to that of amphetamine.

TABLE I.—TOXICITY OF DL-AMPHETAMINE, DL-4-CHLOROAMPHETAMINE AND DL-4-METHAMPHETAMINE IN RATS

Drugs	I.D., (mg/kg s.c.)	Slope
dl-amphetamine	20. 5(17. 6–23. 7)	1. 27(0. 99–1. 62)
dl-4-chloroamphetamine	15. 0(11. 5–19. 5)	2. 00(1. 37–2. 90)
dl-4-methamphetamine	62. 0(44. 2–86. 8)	1. 70(1. 21–2. 37)

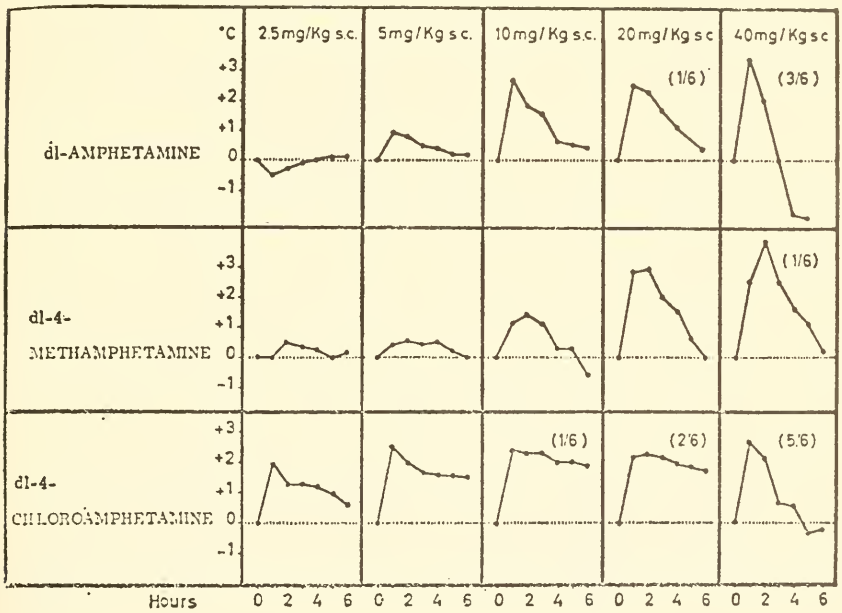


FIG. 10. Hyperthermia induced by *dl*-amphetamine, *dl*-4-chloroamphetamine and *dl*-4-methamphetamine in aggregated rats. Each point on the curve represents the mean temperature of 6 rats. Number of dead rats in each group is given in brackets. Ordinate shows the temperature changes in °C and abscissa the time in hours.

Spontaneous locomotor activity. In this test 4-methamphetamine elicited the most striking effect since it doubled the locomotor activity at the dose of 1.5 mg/kg; amphetamine and 4-chloroamphetamine induced the same effect at doses of 3.5 and 2.5 mg/kg, respectively (Fig. 11).

Anorexia. One hour after administration (the peak of activity) amphetamine proved to be more effective than both 4-chloroamphetamine and 4-methamphetamine, the ED_{50} of the drugs being 1.25, 1.90 and 5.00 mg/kg, respectively (Fig. 12). At the subsequent time intervals, however, 4-chloroamphetamine, which is the most slowly metabolized of the three drugs (Kaergaard Nielsen

et al., 1967), exhibited the most pronounced effect. This last series of results is summarized in Table II in which the active doses of the compounds are expressed in μmoles.

In order to give a more evident profile of the pharmacological properties of the three drugs, a comparison is made in Fig. 13 on the basis of the results reported in Table II between the potency of 4-chloroamphetamine and 4-methamphetamine. It is apparent that hyperthermia is the most characteristic property of 4-chloroamphetamine, while 4-methamphetamine is mainly characterized by a marked motor exciting activity. However, on considering the anorexigenic effect, both these drugs, but particularly 4-methamphetamine, are less active than amphetamine.

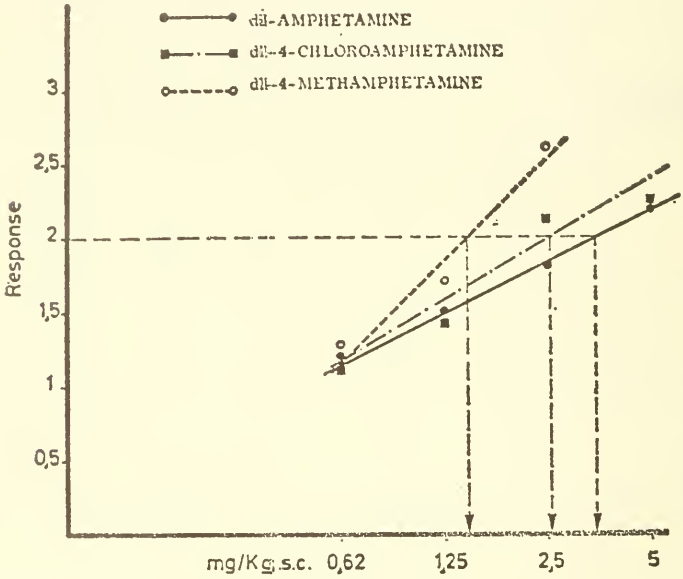


FIG. 11. Effect of *dl*-amphetamine, *dl*-4-chloroamphetamine and *dl*-4-methamphetamine on the coordinated spontaneous activity in rats. *Ordinate:* response expressed as ratio of the counts after drug administration to the counts of the controls on the same day; *abscissa:* drug dosage, mg/Kg.

IV. DISCUSSION

Our results show that propranolol can affect some of the actions of amphetamine differently. This β-blocking agent is quite effective in counteracting lethality and hyperthermia, slightly active in antagonizing the increased locomotor activity, but surprisingly potentiates the anorexia induced by amphetamine. The high sensitivity of hyperthermia and lethality to the antagonistic effect of propranolol suggests that these two properties of amphetamine may be closely related. By contrast, the observation that increased spontaneous activity appears to be slightly sensitive to the antagonistic action of propranolol coupled with the fact that anorexia, instead of being antagonized, is clearly potentiated by this drug, would suggest that these two last activities of amphetamine are quite independent from hyperthermia and lethality.

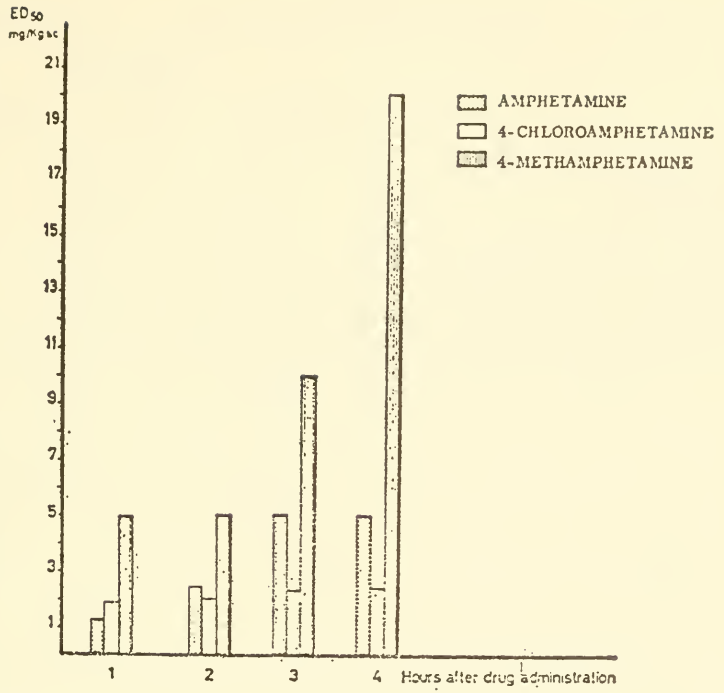


FIG. 12. Anorexigenic activity of *dl*-amphetamine, *dl*-4-chloroamphetamine and *dl*-4-methamphetamine in rats.

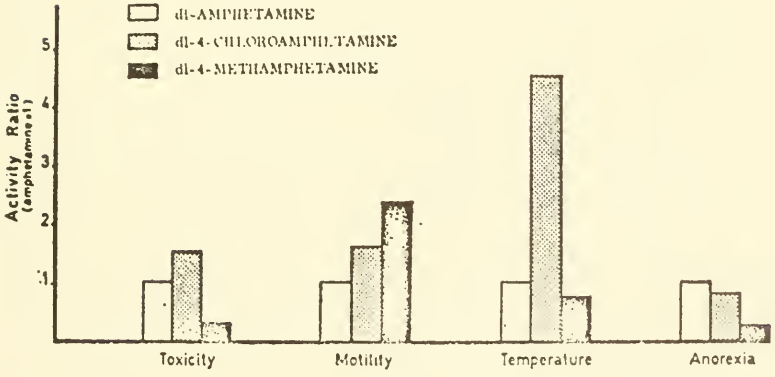


FIG. 13. Comparison between the pharmacological activities of *dl*-amphetamine, *dl*-4-chloroamphetamine and *dl*-4-methamphetamine.

TABLE II.—COMPARISON BETWEEN THE PHARMACOLOGICAL ACTIVITIES OF DL-AMPHETAMINE, DL-4-CHLORO-AMPHETAMINE AND DL-4-METHAMPHETAMINE

Drugs	Toxicity, LD_{50} (μmoles/kg s.c.)	Motility, dose doubling activity (μmoles/kg s.c.)	Temperature, dose increasing temperature of 2° C (μmoles/kg s.c.)	Anorexia ED_{50} (μmoles/kg s.c.)
dl-amphetamine	110.0	18.9	54.2	6.7
dl-4-chloroamphetamine	72.7	12.0	12.0	8.6
dl-4-methamphetamine	333.3	8.0	80.6	26.8

Several hypotheses could be formulated to explain the mode of action of propranolol in affecting amphetamine activity. The antihyperthermic effect might result from a blockade of the energetic processes responsible for the increased body temperature evoked by amphetamine. In keeping with this view are the data of Strubelt and Lubenau (1966) and Strubelt (1966) who reported that propranolol inhibits the enhanced oxygen consumption due to cold exposure or catecholamine administration. Exposure to cold stimulates the release of catecholamines, resulting in an enhancement of the metabolic and, consequently, of the thermogenic functions. These effects are impaired by propranolol. The antagonistic effect of this drug against amphetamine-induced hyperthermia might be operating through a similar mechanism since amphetamine releases catecholamines from peripheral stores (Moore, 1963).

Brodie, Cho, Stefano and Gessa (1969) and Gessa, Clay and Brodie (1969) conclude that the hyperthermia produced by amphetamine is a peripheral effect, resulting from oxidation of the free fatty acids which are mobilized when norepinephrine is released by the drug from sympathetic nerve endings in adipose tissue.

The antihyperthermic effect of propranolol could also explain the effect of this drug in antagonizing toxicity, recalling that hyperthermia has been repeatedly suggested as responsible for the lethal action of amphetamine (Askew, 1962). On the other hand, judging also from the present results obtained with propranolol, these two aspects of amphetamine action seem to be closerly related. However, as an alternative explanation, a protective action of this β-blocking agent on the effect of amphetamine at the cardiac level could be advanced (Halpern *et al.*, 1962). In addition, it must be recalled that propranolol exerts some depressant effects on the central nervous system (Leszkovsky and Tardos, 1965; Murmann *et al.*, 1966), so that some of the results obtained might be partially referred to an action at this level. Hyperthermia and lethality, however, were affected by propranolol at doses which were definitely lower than those exerting a central depressant effect (Murmann *et al.*, 1966). By considering only the action of propranolol on increased spontaneous activity, a central effect of propranolol cannot be excluded. In this instance, the doses that antagonized the action of amphetamine were much greater than those able to reduce lethality and hyperthermia.

On the basis of our present knowledge, the potentiating effect of propranolol on anorexia is difficult to explain satisfactorily. If the metabolic theories which have been put forward to explain anorexia are recalled (Fassina, 1966), an antagonistic instead of a synergistic effect could be anticipated. In fact, the increased levels of free fatty acids induced by amphetamine, which have been considered responsible for its anorexigenic effect, are reduced by propranolol (Zsoter *et al.*, 1966).

A more plausible explanation is to admit that propranolol, acting at a central level, may in some way potentiate the anorexia caused by amphetamine.

Whatever the interpretation of the results, it seems worth emphasizing that by using this pharmacological tool amphetamine-induced anorexia can be dissociated from the other effects of this drug.

Similar conclusions were obtained by studying this problem from a quite different approach, *i.e.*, by comparing the pharmacological properties of 4-chloroamphetamine and 4-methamphetamine with those of amphetamine. In fact, the examination of the pharmacological profile of these amphetamine derivatives allow us to state that apparently no correlation exists between anorexia and the other actions of amphetamine.

Thus, 4-chloroamphetamine and 4-methamphetamine have been found more hyperthermic or more motor exciting, respectively, than amphetamine; however, as far as their anorexigenic effect, both drugs are, at the peak of their activity, less effective than amphetamine.

To conclude, the bulk of our data, obtained by using two different experimental approaches, does favor the view that central nervous system stimulation, hyperthermia and anorexia are independent activities of amphetamine.

SUMMARY

The possibility that the anorexigenic effect of amphetamine may be completely independent from the other activities of this drug is currently the subject of considerable debate and uncertainty. In the present study, two different types of experiments are reported, which favor the concept that anorexia induced by amphetamine can be divorced from the other activities of the drug. In mice, propranolol, a β-adrenergic blocking agent, strongly antagonized lethality and hyperthermia, slightly counteracted increased locomotor activity, but clearly potentiated the anorexigenic effect of amphetamine. In rats, two compounds closely related to amphetamine (4-chloroamphetamine and 4-methamphetamine), while being more active than amphetamine in increasing body temperature and spontaneous activity, respectively, were less potent than this drug in inducing anorexia.

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[From The Lancet, pages 437–441, Aug. 29, 1970]

25. Comparison of Fenfluramine and Metformin in Treatment of Obesity

(By A. A. H. Lawson, J. A. Strong, P. Roscoe, Anna Gibson, and Patricia Peattie, University Department of Medicine, and Metabolic Unit, Western General Hospital, Edinburgh)

SUMMARY

A double-blind trial was undertaken to compare the efficacy of fenfluramine and metformin in promoting weight reduction in thirty-four obese women. Metformin proved to be less effective than fenfluramine and a total daily dose of 3·0 g. produced unacceptable side-effects. The effect of fenfluramine in a total daily dose of 80 mg. was still evident up to 32 weeks on a reducing regimen, and was free of serious side-effects. A further double-blind trial was conducted on eighteen of these obese women after 48 weeks of continuous dietary treatment, to study the effect of fenfluramine in a total daily dosage of 160 mg. and its suitability for long-term maintenance treatment. Fenfluramine in this dosage was found to be effective and safe.

INTRODUCTION

Obesity remains a major problem in any community where food is plentiful. A reduction in calorie intake is always followed by a loss of weight, and in treating obesity, the main object is to provide an acceptable method of restricting the intake of food. One common method, which is expensive and has other disadvantages, is to give an appetite-depressing drug, so reducing the personal effort which the patient must make if weight is to be lost. Extensive use of such drugs over prolonged periods has proved of limited value.

In contrast to numerous amphetamine-like drugs, fenfluramine has been reported to produce greater loss of weight [1] and fewer side-effects.[2 3] Dannenburg and Kardian [4] have demonstrated lipolytic activity with this drug in isolated fat cells and depressed synthesis of triglycerides. Butterfield and Whichelow [5] reported that fenfluramine increases glucose uptake in forearm muscles in a similar way to mild exercise.

Obese diabetic patients tend to lose weight during biguanide therapy.[6 7] Patel and Stowers [8] postulated that the biguanides had an anoretic effect, but Schless [9] suggested that they reduced lipogenesis, and Dettwyler and Butterfield [10] demonstrated that they increased glucose uptake in forearm muscles. Pedersen [11] reported that metformin promoted rapid loss of weight in seven obese non-diabetic patients.

Loss of weight has been observed both with fenfluramine [12] and biguanides [13] without the need for special steps to control the diet. In view of the postulated metabolic effects of these drugs, we decided to compare the clinical effects of fenfluramine and metformin in the treatment of obesity in non-diabetic patients, and to assess the efficacy of fenfluramine for long-term maintenance therapy at higher dose levels than are normally used.

PATIENTS AND METHODS

Stage 1

Thirty-four female patients were treated. Their ages ranged from 22 to 59 years (mean 36·2). The patients had all been obese for many years and all had attempted dieting under medical supervision on previous occasions without

success. The range of weight of these patients at the beginning of the study was 74·5–125·5 kg. with a mean of 96·7 kg., and the percentage of ideal weight[14] varied from 130 to 212 (mean 158). Each patient was examined clinically to exclude disabilities which might interfere with her capacity to participate in the trial. To exclude diabetes mellitus, an oral glucose-tolerance test using 50 g. glucose was undertaken in every patient, and plasma-protein-bound-iodine levels and a 4-hour uptake of ^{131}I were also checked before patients were accepted for the trial.

The double-blind trial was spread over four consecutive periods of 8 weeks. Throughout, patients were instructed to adhere to a diet providing 1000 C. daily. Tablets of identical appearance containing a starch lactose base, metformin 0·25 g., metformin 0·5 g., or fenfluramine 13·3 mg. were given to each patient for 8 weeks, in a dose of two tablets thrice daily with meals. The order of administration of these drugs was randomised, except that the period of treatment with metformin 3:0 g. daily followed immediately on the period of treatment with the smaller dose. The patients were seen at intervals of 2 weeks for medical and dietetic review. At these visits they were weighed under comparable conditions using the same machine. They were asked about any possible side-effects or difficulties with the diet. At each attendance ninety tablets (i.e., six in excess of requirements) were given to each patient. The numbers of tablets returned were counted as a check on the probable amount of the drug taken. The data were analyzed by the correlated Student's *t* test.

Stage 2

Eighteen of the thirty-four patients continued to attend the clinic at fortnightly intervals. Their ages ranged from 22 to 59 years (mean 38), and the percentage of ideal weight[14] varied from 114 to 204 (mean 143). For 16 weeks (period A) they were treated simply with 1000 C. diet and no drugs. Then a further double-blind trial was done over two consecutive periods of 11 weeks (periods B and C). As in stage 1 the patients were instructed to adhere to the diet providing 1000 C. daily. On this occasion identical tablets containing inert material and fenfluramine 20 mg. were given to every patient for 11 weeks, in a dose of two tablets twice daily with meals for the first week of each period, then two tablets thrice daily with meals for 1 week and finally two tablets four times daily for the remaining 9 weeks of each period of study. The order of administration was again randomised and during each period the patients were seen at weekly intervals for the first 3 weeks and thereafter every fortnight. The patients were subjected to the same type of assessment as in stage 1.

RESULTS

Stage 1

Thirty-one patients completed the trial. Of the other three patients, one aged 59, visited the clinic only twice and then said she was unable to attend further. She had lost no weight. A second patient, aged 29, defaulted after 12 weeks as she had obtained a new job and did not wish to continue attending the clinic. She had lost 3·0 kg. The third patient, aged 59, completed 8 weeks of the trial but throughout this time freely admitted that she was not adhering to the diet recommended. Her weight fell by only 1·5 kg. The remaining thirty-one patients all lost weight, the range of weight reduction being 2·27–35·0 kg. (mean 8·6 kg.).

TABLE I.—WEIGHT CHANGES DURING 2 STAGES OF THE STUDY IRRESPECTIVE OF DRUG USED

Mean (±S.E.M.) change in weight (kilogram) during period						
Stage 1 [1]				Stage 2		
1	2	3	4	A	B	C
−6·6 (±0·7)	−2·7 (±0·5)	−2·2 (±0·6)	−1·8 (±0·7)	+2·8 (±1·2)	−0·8 (±0·8)	−2·4 (±0·7)

[1] Patients were randomized among the 6-treatment orders compatible with the conditions of the trial as follows: 6 were on P/M1/M2/F, 5 were on P/F/M1/M2, 4 were on M1/M2/P/F, 6 were on M1/M2/FP, 6 were on F/M1/M2/P, and 4 were on F/P/M1/M2, where P=placebo, M1=metformin 1·5 g., M2=metformin 3 g., and F=fenfluramine.

The loss of weight, irrespective of treatment, during the successive periods is shown in table I. Much the greatest loss was in the first period. There was no

significant correlation between the degree of obesity at the start of the trial and the subsequent weight-loss; indeed the three heavist patients lost very little weight (fig. 1).

The results for the different drug regimens are shown in table II. Fenfluramine proved most effective in promoting loss of weight, followed by metformin in a dose of 1·5 g. The larger dose of metformin was associated with a loss of weight rather less than that achieved on the placebo tablets. The differences between the weight-loss on fenfluramine and losses achieved with placebos and with metformin 3 g. were highly significant. There was a significant difference between the two doses of metformin, 1·5 g. being more effective than 3 g. There was no significant difference between placebo and either dose of metformin. Almost as much weight reduction occurred in 8 weeks on fenfluramine as in 16 weeks on two dose levels of metformin (fig. 2, table III).

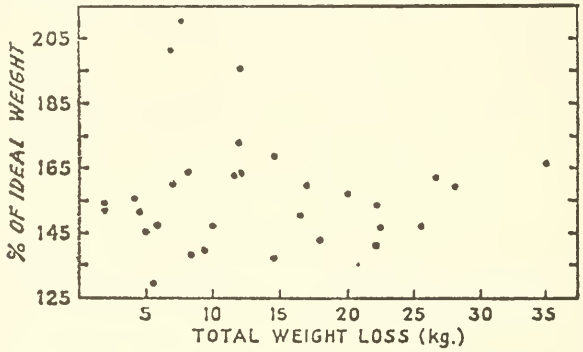

Fig. 1—Relation between initial body-weight (% of ideal weight) and loss of weight on treatment during stage 1.

r = 0·032; not significant.

TABLE II.—LOSS OF WEIGHT ON DIFFERENT DRUGS IRRESPECTIVE OF ORDER OF ADMINISTRATION (STAGE 1

Mean (±S.E.M.) weight-loss (kilogram) on			
Placebo	Metformin 1·5 g.	Metformin 3·0 g.	Fenfluramine
2·22 (±0·62)	3·60 (±0·54)	2·01 (±0·55)	[2] 5·20 (±0·63)

[1] Significantly greater than for metformin 3 g. ($P<0.02$).
[2] Significantly greater weight-loss than for placebo ($P<0.001$), metformin 1·5 g. ($P<0.05$), and metformin 3 g.) ($P<0.001$).

TABLE III.—RELATION BETWEEN PERCENT OF PRESCRIBED DOSE APPARENTLY CONSUMED AND WEIGHT-LOSS OBTAINED WITH EACH REGIMEN (STAGE 1)

Regimen	Mean percent of prescribed dose returned	Mean (±S.E.M.) weight-loss (kg.)
Control	11·18	2·22 (±0·62)
Metformin 1·5 g. daily	11·31	3·60 (±0·54)
Metformin 3·0 g. daily	18·53	2·01 (±0·55)
Fenfluramine	11·46	5·20 (±0·63)

The relation between the quantity of each series of tablets taken by the patients (as judged by the number of tablets returned) and the mean weight reduction is shown in table III. The amount of metformin taken in the larger dose was reduced, but not significantly so compared with the other tablets. Variation in the amounts of each preparation taken did not, therefore, seem to be an important cause of the differences in weight reduction. It is possible, however, that the patients disposed of tablets in order to seem cooperative.

When account is taken of the relative order of treatment there seemed to be a progressive loss of efficacy with the control tablets and with both dose levels

of metformin in successive periods, but with fenfluramine, apart from a reduction in weight-loss between period 1 and period 2, loss of weight was maintained and indeed increased in the final period (fig. 3, table IV).

During the first period of 8 weeks, three forms of treatment were used—placebo, fenfluramine, and metformin 1·5 g. A considerable weight-loss was achieved with each but there was no statistical difference between them. In period 2 there was no significant difference between the weight reductions achieved with each of the four regimens. In period 3, however, when the four treatments were also used, there was no weight-loss on placebo whereas with the other three preparations some weight reduction was maintained. There was a significant difference between placebo and both dose levels of metformin (in each case $P<0·02$) but the difference between placebo and fenfluramine in this period was not significant. In period 4, when placebo, fenfluramine, and metformin 3 g. were used, the patients treated with the placebo tablets on average gained weight slightly; fenfluramine had an advantage over metformin 3 g. ($P<0·01$), and especially over the placebo ($P<0·001$).

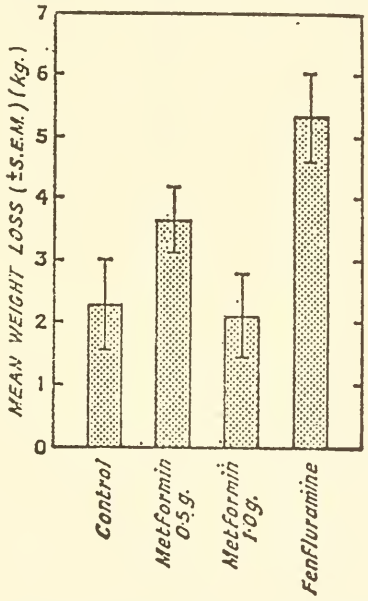

Fig. 2.—Mean loss of weight (± S.E.) on the four drug regimens in stage 1 irrespective of order of administration.

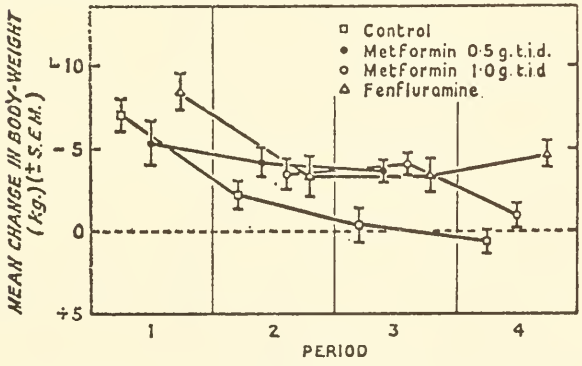

Fig. 3—Changes in body-weight during each period of 8 weeks of stage 1.

TABLE IV.—CHANGES IN BODY-WEIGHT, RELATIVE TO THE DIFFERENT DRUGS USED IN EACH PERIOD OF 8 WEEKS (STAGE 1)

	Period 1				Period 2				Period 3				Period 4			
	P	M1	M2	F	P	M1	M2	F	P	M1	M2	F	P	M1	M2	F
Number of patients	11	10	0	10	4	12	10	5	4	9	12	6	12	0	9	10
Average weight change:																
(kg.)	−5·99	−5·20		−7·73	−1·70	−3·20	−2·80	−2·50	−0·10	−2·90	−3·10	−2·60	+0·63		−0·71	−3·80
(±s.e.m.)	(±0·89)	(±1·06)		(±1·02)	(±0·80)	(±0·87)	(±0·89)	(±1·12)	(±0·87)	(±0·53)	(±0·58)	(±0·82)	(±0·40)		(±0·70)	(±0·76)

Note.—P = Placebo. M1 = Metformin 1·5 g. M2 = Metformin 3 g. F = Fenfluramine.

TABLE V.—SIDE-EFFECTS NOTED DURING THE 4 REGIMENS OF TREATMENT (STAGE 1)

Side-effect	Drug therapy			
	Control	Metformin 1·5 g.	Metformin 3·0 g.	Fenfluramine
Dryness of mouth	0	0	1	1
Hunger	4	2	1	0
Nausea	4	7	10	3
Vomiting	1	0	6	0
Abdominal pain	0	1	2	0
Diarrhea	0	5	6	2
Constipation	3	3	1	1
Skin reactions	0	0	1	1
Curtailment of treatment as a result of symptoms	0	4	5	0

The side-effects noted on the different drugs are shown in table v. The only serious symptoms were those related to the gastrointestinal tract, and included nausea, vomiting, abdominal pain, diarrhoea, and constipation. These were more severe and more frequent with metformin than with fenfluramine. Then patients on metformin complained of nausea; six of them vomited and had diarrhoea. As a result, five of these patients had to curtail treatment, as did four other patients on the smaller dose of metformin, two because of nausea and two because of diarrhoea. All these patients, however, were able to resume therapy after a few days rest from treatment. Abdominal pain was colicky in type and although troublesome was not severe. Two patients developed skin reactions during treatment with metformin 3 g., one a localised eczema and the other a mild lichen planus. These eruptions may not have been related to the drug therapy, but no special steps were taken to confirm or refute the suggested connection.

Stage 2

All eighteen patients completed stage 2. During the 16 weeks of period A (diet only) weight changes varied widely, ranging from a loss of 10·7 kg. to a gain of 15·9 kg. (mean weight gain 2·8 kg.). This period covered the summer holiday season, and this, together with the fact that these patients had just completed the rather prolonged and intensive dietary supervision of stage 1, no doubt resulted in a number of the patients exceeding their dietary recommendations.

During the second controlled drug trial, however, irrespective of treatment (table I) there was a mean weight loss of 1·6 kg. During treatment with fenfluramine irrespective of the order of administration of the tablets there was a mean weight-loss of 2·5 kg. (S.E.M. ± 0·6), whereas on the inert control tablets there was a mean weight gain of 1·2 kg. (S.E.M. ±0·5). This difference was highly significant ($P<0·001$). As judged by the numbers of tablets returned (95% of the prescribed dose of fenfluramine and 97% of the placebo tablets were taken during this trial) variation in the amounts of drug taken did not seem to be an important factor in the results obtained.

TABLE VI.—WEIGHT CHANGES WITH RESPECT TO TYPE OF TABLET AND ORDER OF ADMINISTRATION (STAGE 2)

A (control)	Mean (±S.E.M.) weight change (kg.) during period: B		C	
	F	P	F	P
+2·8 (±1·2)	[1] 1·9 (±0·8)	+1·1 (±0·9)	−[2] 3·1 (±0·8)	−0·9 (±0·6)

Note: F=Fenfluramine; P=Placebo.

[1] Significantly greater than for placebo ($P<0·05$).
[2] Significantly greater than for placebo ($P<0.001$).

The weight changes found with respect to the type of preparation and the order of administration are shown in table VI and fig. 4. In both periods there

was a progressive weight-loss with fenfluramine, especially when it was taken in a dose of 40 mg. four time daily. By contrast, with control tablets the patients gained weight despite maintenance of the same dietary regimen. In each period there was a significant difference between fenfluramine and control tablets.

The side-effects encountered with fenfluramine during this trial were mild, and in no case was it found necessary to curtail treatment. Four patients complained of mild drowsiness whilst taking the largest dose; two experienced some dryness of the mouth and slight nausea and three others had mild diarrhoea. None of the patients complained of hunger during treatment with fenfluramine whereas this was a marked feature in eight patients taking control tablets.

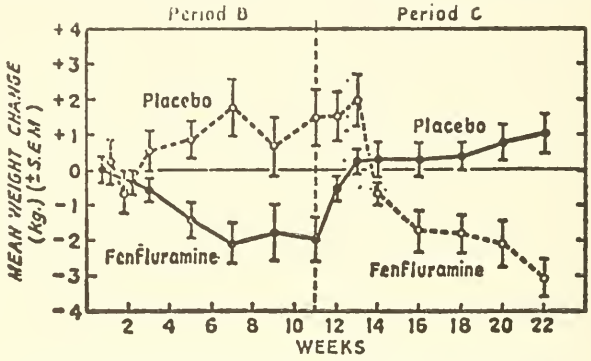

Fig. 4—Changes in body-weight during periods B and C of stage 2.

DISCUSSION

This study confirmed that fenfluramine was effective in reducing the weight of obese patients, and showed that metformin in a dose of 1·5 g. daily was also effective, but considerably less so than fenfluramine. The larger dose of metformin used, however, was ineffective. Despite a higher incidence of troublesome side-effects with the full dose of metformin, there was no significant difference between the proportions consumed of the different preparations prescribed. As metformin 3 g. daily always followed the use of the smaller dose of metformin, it is possible that there was a declining effect of the drug with continuing use, irrespective of dose.

The side-effects of these drugs were predominantly on the gastrointestinal tract, as previously noted.[1 12 15 16] Nausea, diarrhoea, vomiting, and abdominal pain were common with both dose levels of metformin, but with fenfluramine these effects were rare. With temporary withdrawal of treatment and subsequent graduated increments, metformin therapy could be resumed. Since metformin was less effective than fenfluramine, it is not a suitable preparation for the treatment of simple obesity, although valuable in the management of obese diabetic patients.[7 8]

Since the patients tended to gain weight during stage 2, especially in period A when being treated by diet alone, and also later when on diet and placebo, we assume that the dietary advice was not being followed consistently. This was unquestionably the case in a number of patients who increased weight rapidly during period A. Despite this, treatment with fenfluramine during the second stage was associated with rapid loss of weight in all patients, and this was sustained as long as the drug was given. These observations support the views of Lambusier,[12] who reported substantial and continued weight-loss in patients on prolonged treatment with fenfluramine but without strict dietary control. This effect is due no doubt in part to the anorexigenic effects of the drug, but might also be due to a lipolytic action.[5 17]

The results of these studies confirm that fenfluramine is an effective and safe preparation for the treatment of polyphagic obesity.[3 18] It is suitable for prolonged administration and provides an effective alternative to the stimulant

anorexigenic drugs which, because of their addictive effects, should no longer be prescribed for obesity.[19]

We are grateful to Dr. J. D. E. Knox, Dr. A. G. Donald, Dr. J. E. Simpson, Dr. I. H. Stokoe, Dr. H. P. Dinwoodie, and Dr. A. H. D. Large for their permission to study patients under their care; Dr. Cyril Boroda, Rona Laboratories Ltd., and Mr. N. Santer, Selpharm Laboratories Ltd., for preparing the test tablets; and Miss S. G. Gardner for dispensing the drugs for each clinic.

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[From the British Medical Journal, pages 178–179, Apr. 18, 1970]

26. Unusual Effect of Fenfluramine

Sir.—I wish to draw attention to possible side-reactions of the drug fenfluramine (Ponderax).

Recently I saw a 38-year-old married woman with no previous psychiatric referrals. She had a stable previous personality and her social situation was satisfactory. Because of increasing weight she was prescribed fenfluramine 20 mg. t.d.s. After three weeks on the drug her husband and friends remarked that she was depressed and slowed down. She was aware of being low in spirits, attributed this to the drug and stopped it. Her mood then improved and after an interval of several weeks she decided to restart fenfluramine because her weight was again increasing. Five days after restarting she set out on her weekly shopping expedition to the local supermarket. She was again feeling low in spirits and unusually agitated. In the supermarket she began to place goods in the wire carrier, but became increasingly confused, unable to find her purse, and feeling that she was late and must rush home. She then developed a state of depersonalization in which she was aware in a dream-like way of cramming goods which she did not need from the shelves into her own shopping basket with no attempt to conceal them. Having done this she rushed to the cash desk, paid for the goods in the wire carrier, but carrying out the other goods exposed in her own shopping bag. As soon as she had passed through the cash barrier she was stopped and subsequently charged with shoplifting. After she arrived home her husband concluded that her state of mind was due to the drug and she stopped taking it for the second time. As a result of the charge she was referred for psychiatric opinion, and when seen two weeks later her mental state was normal. It was concluded that her depression and confusional state had been due to the effects of fenfluramine.

Similar cases have been reported previously [1 2] and are presumably due to the psycho-active nature of the drug. Fenfluramine seems to possess a complex mixture of activities related to its amphetamine-like structure. It is known to interact with monoamine oxidase inhibitors,[2] and cause facial dyskinesia [2-4] as do other amphetamine derivatives. In therapeutic doses fenfluramine may cause sedation [5] or, in some cases, confusion as above, but in elevated doses the drug seems to show stimulant properties as reflected by recent animal work,[6] temporary mood depression on stopping the drug therapy,[7] anxiety, agitation, and convulsions noted on overdose,[4] and the inhibition and rebound of R.E.M. sleep. Oswald [8] states that the last is an indication of a dependence liability of the amphetamine type. The sedative action on the other hand could give rise to abuse commonly seen with this category of drug.

Fenfluramine exhibits in one molecule a wide spectrum of psycho-mimetic activity ranging from sedation to stimulation, which is reminiscent of the barbiturate/amphetamine mixtures. It should, therefore, be given with care so that its dependence-producing potential can be properly evaluated.—I am, etc.,

NORMAN W. IMLAH.

All Saint's Hospital, Birmingham 18.

[From the British Medical Journal, pages 265–266, Jan. 30, 1971]

27. DRUG-INDUCED PULMONARY HYPERTENSION?

(By F. Follath, F. Burkhart, W. Schweizer)[9]

SUMMARY

Of 40 patients with obstructive pulmonary hypertension studied in Basle, Switzerland, during the period 1966–68, 32 had been taking an anorectic drug, aminorex fumarate. Rapidly progressing exertional dyspnoea, central chest pain, and syncope on effort were characteristic features. The absence of the usual causes of pulmonary vascular disease seems to suggest the possibility of drug-induced pulmonary hypertension. Further studies are necessary, however, to clarify the role of aminorex fumarate in this condition.

INTRODUCTION

Obstructive pulmonary hypertension occurs most commonly after recurrent pulmonary thromboembolism (Goodwin *et al.*, 1963). When major embolic episodes or pulmonary infarction cannot be shown the aetiology of the vascular obstruction usually remains unknown and, especially in young women, "primary" pulmonary hypertension is considered. Recently a sudden increase in the incidence of rapidly developing pulmonary vascular disease was reported from several European countries (Gurtner *et al.*, 1968, Harmjanz *et al.*, 1968, Schwingshackl *et al.*, 1969). A common finding in these series was the prolonged use of an anorectic drug in most patients, which has therefore been suspected of playing some aetiological part (Schweizer, 1969).

This paper describes studies of a group of 40 patients obseerved during a three-year period in Basle.

PATIENTS AND METHODS

Forty patients (37 women and 3 men) with obstructive pulmonary hypertension were studied from January 1966 to December 1968. Their ages ranged

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ogy Division.

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[9] Medical Department, University Hospital, Basle, Switzerland, F. Follath, M.D., Clinical Assistant; F. Burkart, M.D., Cardiologist; W. Schweizer, M.D., Professor, Head of Cardiol-

from 31 to 72 (average 50) years. All cases were evaluated by physical examination, electrocardiography, chest *x*-ray examination, right heart catheterization, and pulmonary function studies. Lung scan was done in 25, pulmonary angiography in 8, and bilateral ascending phlebography in 14 cases. Detailed information was obtained from each patient and the referring physician on previous drug treatment, operations, periods of prolonged bed rest, pregnancies, and venous disorders of the lower extremities.

RESULTS

Rapidly progressing exertional dyspnoea was the first dominating symptom in all cases. Central chest pain (16 patients) and syncope on effort (nine patients) were other characteristic features. Only seven patients had previously had recognized pulmonary emboli (three postoperatively, two postpartum, one during acute thrombophlebitis, and one of unknown cause). All others had been perfectly well until their present illness. A feature common to most patients was the prolonged intake of the anorectic drug aminorex fumarate (2-amino-5-phenyl-2-oxazoline-fumarate), which has been widely used in Switzerland since 1965 to treat obesity (Table I). The treatment (14–42 mg/day) lasted more than one year in 11, 6–12 months in five, and 3–6 months in seven patients. In most the dyspnoa began during or shortly after the intake of aminorex fumarate. Only one of the patients used oral contraceptives.

A large "a" wave in the jugular venous pulse, abnormal right ventricular impulse, accentuation of the pulmonary closure sound, and atrial sound were the most frequent physical findings (Table II). Electrocardiographic and radiological signs of pulmonary hypertension were nearly always present. Cardiac catheterization (Talbe III) showed a pronounced rise in pulmonary arterly pressure (mean 44·4 mm Hg), a high pulmonary arteriolar resistance (mean 6·4 units) and an abnormal right ventricular end-diastolic pressure (mean 10·3 mm Hg). During exercise a further definite increase of the pulmonary artery pressure (mean 66.9 mm Hg) was noted.

Pulmonary function studies showed decreased arterial Po_2 and Pco_2 and mild restrictive ventilatory changes as the common pattern. No obstructive bronchitis or other lung disease was found. Detailed results will be published elsewhere. With the exception of two cases with known pulmonary embolism, the large and medium branches of the pulmonary artery appeared patent on lung scan and/or pulmonary angiography.

TABLE I.—HISTORY OF DRUG TREATMENT. AMINOREX FUMARATE USED IN 32 OUT OF 40 PATIENTS

Duration of treatment	Number of patients	Onset of dyspnoea	Number of patients
>1 year	11	During treatment	18
6 to 12 months	5	Within 3 months after treatment	4
3 to 6 months	7	3–6 months after treatment	2
1 month	3	>1 year after treatment	1
3 weeks	1	Exact time relation unknown	5
Unknown	5		

TABLE II.—PHYSICAL SIGNS

	Number	Percent
Large "a" wave in the jugular venous pulse	32	80
Right ventricular heave	25	62
Accentuatinn of oulmonary closure sound	39	98
Wide snlitting of S_2	32	80
Right atrial sound	30	75
Right 3rd sound	12	30
Pulmonary eiection click	15	37
Pulmonary eiection murmur	22	55
Early diastolic murmur (pulmonary)	3	7
Tricusnid svstolic murmur	7	17
Varicnse veins	25	62
Obesity	24	60

TABLE III.—HAEMODYNAMIC DATA (MEAN VALUES±S.D.)

	Rest	Exercise (30 watts)
Right atrial mean pressure (mm Hg)	7·0 ± 4·3	14·0 ± 5·0
Right ventricular systolic pressure (mm Hg)	73·5 ± 18·8	107·6 ± 13·5
Right ventricular diastolic pressure (mm Hg)	10·3 ± 4·5	19·0 ± 7·7
Pulmonary artery mean pressure (mm Hg)	44·4 ± 10·0	66·9 ± 8·7
Pulmonary wedge pressure (mm Hg)	6·6 ± 3·1	11·0 ± 6·3
Cardiac index (l·/min/ m²)	3·38 ± 1·14	4·42 ± 1·25
Pulmonary arteriolar resistance (units)	6·4 ± 3·1	6·8 ± 3·3
Arterial oxygen saturation (percent)	94·5 ± 2·5	91·0 ±

Twenty-five patients had varicose veins (Table IV). Phlebography (14 cases) showed deep-vein occlusion in all nine cases with varicose veins so tested and in two additional cases without clinical evidence of abnormal leg veins. Normal venous circulation was shown in only three instances.

In 18 patients a second haemodynamic study was performed after a mean interval of 10 months. For this group the pulmonary arteriolar resistance was unchanged, while the cardiac output and the right atrial pressure had slightly decreased. The detailed data have been given elsewhere (Burkart *et al.*, 1970).

DISCUSSION

In 1967 the incidence of obstructive pulmonary hypertension began to increase suddenly in Switzerland. In 1968 a tenfold to twentyfold rise was noted in three of the five cardiac centres of the country (Table V). This seems to be a true increase which could not be explained by improved clinical or haemodynamic methods of investigation or by an increased number of cases referred to cardiovascular units. A similar increase of the disease was noted in Germany and in Austria but not in other European countries.

This dramatic increase of a previously rare disease within a short period of time and a well-defined geographic area points to a common aetiology. Oral contraceptives which may promote the development of pulmonary vascular disease (Oakley and Somerville, 1968) were not considered as only one of our patients had used these drugs. The only common denominator, as in other Swiss series, was the fact that 32 of the 40 patients were treated with aminorex fumarate. A successful or attempted weight reduction by administration of this anorectic drug for several months emerged as a characteristic feature in most patients. The symptoms usually began during or shortly after treatment, and some patients spontaneously reported a further rapid increase of dyspnoea during a second course of aminorex fumarate. It seems highly relevant that the drug had been on sale only in Switzerland, Germany, and Austria, where the increase of the disease had been noted. Furthermore, the drug was introduced in 1966 and heavily sold in 1967–8 until it was withdrawn in November 1968, and the sales curve closely followed the incidence of the disease.

TABLE IV.—VENOUS DISORDERS OF LOWER EXTREMITIES

	Number of patients
"Chronic post-thrombotic state" (varicosis, oedema, atrophic skin, ulcer discoloration)	5
Varicosis of saphenous system	20
History of thrombophlebitis	9
Acute thrombophlebitis on admission	2
No thrombophlebitis	9
Total (62 percent)	25

TABLE V.—INCIDENCE OF PATIENTS WITH PULMONARY HYPERTENSION OF UNKNOWN ORIGIN IN THREE SWISS CENTRES (RIVIER, 1970)

	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969
I	2	2	0	1	0	0	0	1	0	12	25	10
II	0	0	0	1	0	1	1	1	2	11	28	9
III	1	1	1	0	1	0	0	1	2	9	34	6
Total	3	3	1	2	1	1	1	3	4	32	87	25
		9				6				148		

While on the above evidence a relation between aminorex fumarate and the disease appears probable, the pathogenetic mechanism remains unknown. Despite rapidly progressing physical disability neither acute pulmonary embolism nor infarction was ever clinically recognized in most patients. Absence of the "typical" symptoms and signs does certainly not exclude this cause. Recurrent small pulmonary emboli remain silent until severe pulmonary hypertension is established (Owen *et al.*, 1953), and even major emboli are discovered only at necropsy (Gorham, 1961; Smith *et al.*, 1964). The high proportion of patients with a history of previous thrombophlebitis, signs of chronic venous insufficiency, varicose veins, and phlebographic evidence of deep-vein thrombosis in our series would favour repeated emboli. However, in addition to negative clinical findings no occlusion of the pulmonary arteries could be shown by lung scan and/or pulmonary angiography. Emboli were also absent in the few similar cases studied at necropsy (Lang *et al.*, 1969; Jornod *et al.*, 1970). It therefore seems that the pulmonary hypertension is due to some form of small-vessel disease and not to thromboembolism. Thus the high incidence of venous disorders of the lower limbs in our patients could be just a complication of obesity, which has no direct relation to the pulmonary disease.

No specific vasculitis was found on lung biopsy or at necropsy (Gurtner *et al.*, 1968; Lang *et al.*, 1969; Jornod *et al.*, 1970). With one exception—mother and daughter affected, both taking the anorectic drug—no family history was elicited.

Aminorex fumarate has no adverse effect of platelet adhesiveness or coagulation factors (Gurtner *et al.*, 1968). Acute haemodynamic effects of the drug in man have not been reported, but pulmonary and systemic hypertension were found in dogs during infusion of small doses (Kraupp, 1969). Systemic hypertension was not present in our patients, therefore a generalized vasoconstriction is unlikely. An isolated action of aminorex fumarate or some of its metabolites on the pulmonary vascular system would be a theoretical possibility. The experiments of Kay *et al.*, (1967), who produced isolated pulmonary hypertension in rats by feeding *Crotalaria spectabilis* seed, are relevant here. There is, however, at present no definite indication that a similar reaction could occur by any substance in man. To clarify the exact role of aminorex fumarate in pulmonary vascular disease further studies are necessary. Possibly these studies will give a clue to the better understanding of the mechanism in the hitherto rare primary pulmonary hypertension (Dresdale *et al.*, 1951; Heath *et al.*, 1957; Schweizer *et al.*, 1959; Fowler *et al.*, 1966).

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[From the British Medical Journal, pages 67–70, July 10, 1971]

28. Chronic Fenfluramine Administration: Some Cerebral Effects

(By S. A. Lewis, Ian Oswald, D. L. F. Dunleavy)[1]

SUMMARY

Human cerebral function was monitored electrophysiologically during sleep over a period of months before, during, and after the intake of fenfluramine, 40–120 mg/day. Effects included dose-related reduction of paradoxical sleep, increase of intra-sleep restlessness, and changes in E.E.G. slow-wave sleep. It is hypothesized that weight loss may be associated with increase of the last. Grinding of teeth (bruxism) also was noted.

Long-term studies make it possible to demonstrate changing central effects with time, including tolerance phenomena. Withdrawal abnormalities are related to the time taken for the drug to be eliminated—in the present case reaching a maximum four days after withdrawal.

INTRODUCTION

Obesity is a major health problem, in the treatment of which most drugs have been amphetamine derivatives. The B.M.A. Working Party (1968) noted central nervous system effects of these drugs and considered fenfluramine the least undesirable. In previous reports we suggested that fenfluramine was qualitatively different in its action on the human brain, for we did not find the selective suppressing effect on paradoxical (R.E.M. or "rapid eye movement") sleep that is possessed by dexamphetamine, phenmetrazine, diethylpropion, or chlorphentermine (Oswald *et al.*, 1968; Lewis, 1970). However, like Gagnon *et al.* (1969), we did find a sleep-disturbing effect—fenfluramine caused greater intra-sleep restlessness—namely, more frequent shifts to stage 1 sleep (drowsiness).

These were acute studies. We now describe the effects of chronic administration and of withdrawal on a number of human brain functions. Parallel observations of subjective experience are described by Oswald *et al.* (1971).

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METHODS

Six patients aged 21–35 were studied. Four (Cases 1–4) were young men in good general health who volunteered for the study and who were considered only slightly overweight, whereas two others had an extreme degree of obesity, refractory to past treatments, and entered the study weighing 127 kg (Case 5) and 111.4 kg (Case 6). All were to refrain from alcohol and keep regular hours throughout the study.

The study was designed so that there should be a sequence of baseline, drug, and withdrawal periods. The same number of apparently identical tablets were taken daily by the patients for several months. The first four men at first received two blank (placebo) tablets at 8 a.m. and again at 6 p.m. Subsequently fenfluramine 40 mg was substituted for the afternoon dose and later for the morning dose also. Finally blank tablets were substituted during the withdrawal period. The Table shows the duration of each phase. Tablets were issued in separate packs for morning and evening, and in small, irregular batches in order to conceal the date of any change of content. The two grossly obese patients received tablets additionally at midday. Their packs contained either one fenfluramine 20-mg and one blank tablet, two fenfluramine 20-mg tablets, or two blank tablets. One patient (Case 5) was dropped from the study after 25 days on fenfluramine 60 mg/day because of drinking bouts. Case 6, unlike the others, was not subjected to abrupt withdrawal. After 101 days on the drug his evening pack of tablets was changed to blanks for 11 days, then his midday tablets also for seven days, and finally he received only blanks for the last eight days.

Cerebral function during sleep was monitored by continuous recording of electroencephalogram (E.E.G.), eye movements, and submental muscle tone, as described by Haider and Oswald (1970). The patients slept in quiet, ventilated rooms. The first two nights under full laboratory conditions were discarded as adaptation nights, after which came the first baseline nights. The number of nights under each condition is shown in the Table for the first four patients. The different type of regimen for Case 6 is shown in Fig.7.

The recorded data were analyzed in terms of standard criteria (Rechtschaffen and Kales, 1968) for each 20 sec. period. The total duration of sleep and the durations of orthodox (N.R.E.M.) and of paradoxical R.E.M.) sleep were obtained. Orthodox sleep was divided into stage 1 (drowsiness); stage 2, characterized by E.E.G. sleep spindles; and stages 3 and 4, with increase of high-voltage E.E.G. slow waves. The hour-by-hour distribution of all these stages of sleep and of transitions between them or into wakefulness was obtained.

RESULTS

The convenience of patients had to be considered and it was not possible to obtain laboratory data on the same drug-day for each person, though we started, changed, or stopped drug dosage just before times when more frequent recordings were possible. Consequently we present some results as illustrative graphs for individuals over the months of study.

Paradoxical sleep

Fenfluramine 40 mg had little effect on the proportion of sleep spent as paradoxical sleep, but on 80 mg/day the means of three of the first five *recorded* nights fell to more than 2 standard deviations (S.D.) below the baseline mean in respect of paradoxical sleep duration in the first three hours of sleep and rose to 2 S.D. above baseline after withdrawal (Fig. 1). Tolerance is suggested by the fact that the last recordings on the 80-mg dose approached baseline again. Withdrawal abnormalities in Case 2 are shown in Fig. 2. There was also a rebound in the mean whole-night paradoxical sleep, in excess of 2 S.D. above the baseline on the second and third recordings after withdrawal. Fig. 3 shows a curve fitted to the available withdrawal data for consecutive nights for the patients who stopped fenfluramine abruptly. The peak of rebound abnormality occurs at the fourth withdrawal night.

Intra-sleep restlessness

Spontaneous shifts to stage 1 sleep (drowsiness) or to wakefulness were more frequent during fenfluramine administration, as Fig. 4 shows for Case 1.

He had sub-baseline values during the early withdrawal period. The combined data for the second three hours of sleep of Cases 1–4 indicated a rise in intra-sleep restlessness after starting the larger dose, with tolerance for this action by the time the drug was withdrawn. Spontaneous tooth-grinding in sleep (bruxism), shown as rhythmic muscle potentials in the record, were noted on the larger dose of the drug, especially in Case 2, in whom it was not observed during baseline recordings (Fig. 5).

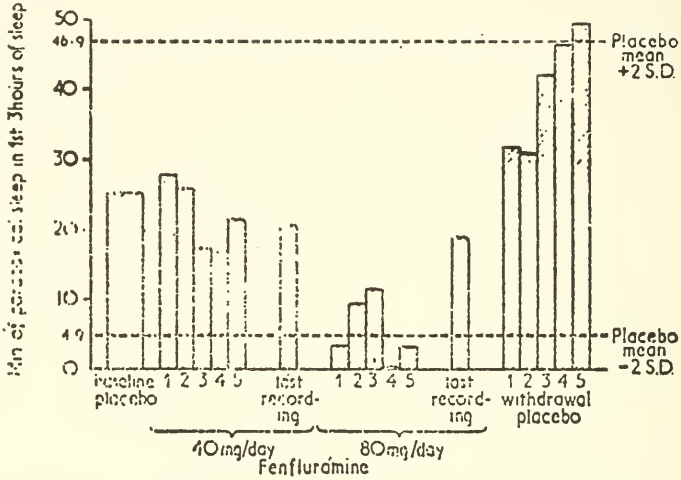

FIG. 1—Effect of chronic administration and withdrawal of fenfluramine on time spent as paradoxical sleep in the first three hours of total sleep (after falling asleep and excluding any awakenings) in Cases 1–4. The weighted mean of the patients' baseline means is shown, together with the 2 S.D. limit. The mean of the values of the first drug night, and the mean for the second night on drug that could be recorded from each man, and so on, are shown, together with the last drug night that was recorded on the low dose of 40 mg/day. Similarly the first five recorded nights and the last recorded night on 80 mg are shown, and the first five recorded withdrawal nights. On the 80-mg dose there is a suppression of paradoxical sleep at first, with three of the first five means falling over 2 S.D. from the baseline. A rebound excess occurs after withdrawal, rising to 2 S.D. above baseline on the fourth and fifth recorded withdrawal nights.

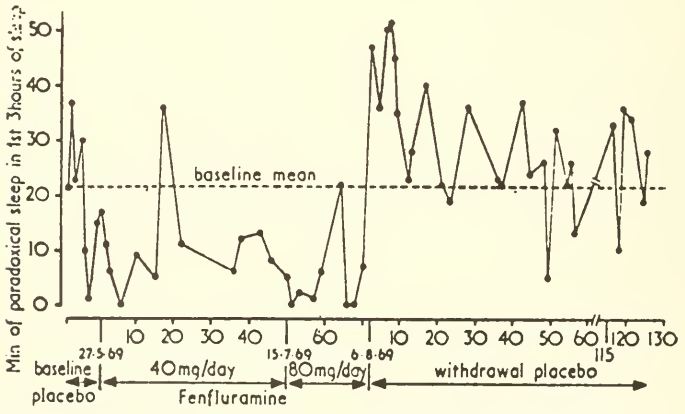

FIG. 2—In Case 2 a rebound abnormality occurred after fenfluramine withdrawal, shown by minutes of paradoxical sleep in the first three hours of sleep. A sustained peak occurred in the first 10 days after withdrawal.

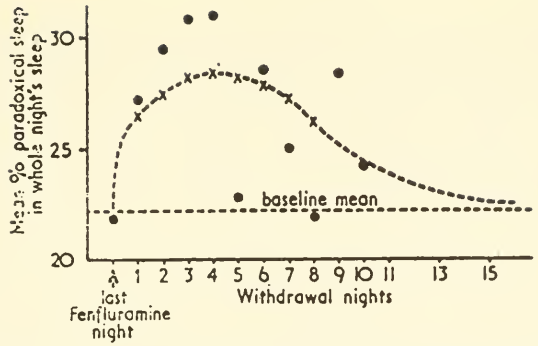

FIG. 3—Time-course of whole-night paradoxical sleep abnormality after fenfluramine withdrawal. The last fenfluramine night is the last one recorded, the withdrawal nights are all consecutive nights. The individual values are means for as many of the four patients as were recorded on the night concerned. All four patients contribute to the last fenfluramine night, and all four to the first and third withdrawal nights. The solid part of the curve is applied to calculated best-fit values (Elderton, 1938) and the broken-line parts of the curve are hand-fitted. The curve reaches a peak at the fourth withdrawal night.

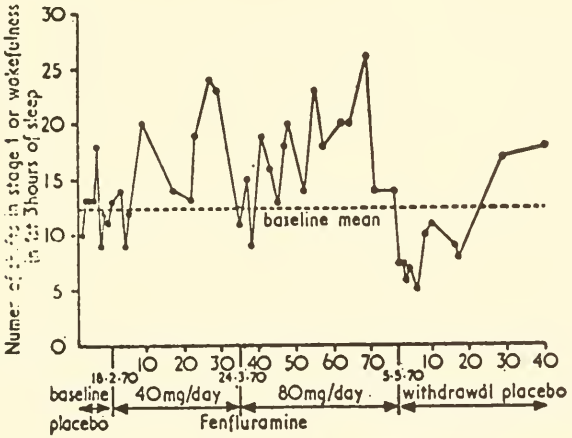

FIG. 4—Case 1. Increase of intra-sleep restlessness above the baseline mean during fenfluramine intake and a fall below baseline in the week after withdrawal of the drug.

Slow-wave sleep

Sleep stages 3 and 4 were at first dramatically increased by fenfluramine in Cases 2 (see Fig. 6) and 1. Stages 3 and 4 were not consistently affected in Cases 3 and 4, and appeared initially reduced in Case 6 (Fig. 7). The time of weight losses in relation to amounts of stages 3 and 4 sleep leave us with the impression that times of losing weight were associated with increased stages 3 and 4 sleep. It was also our qualitative observation that where the durations of stages 3 and 4 were increased during fenfluramine intake, the slow waves themselves appeared enhanced in voltage.

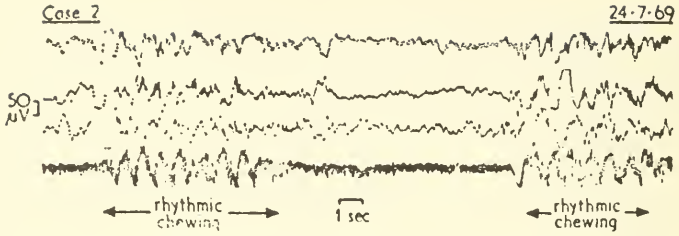

FIG. 5—Tooth-grinding during sleep (bruxism) of Case 2 on 80 mg of fenfluramine per day. Two episodes of rhythmic movement are visible in the bottom, submental electromyogram trace. The top two traces are from the outer canthi electrodes and the third trace, from the scalp, shows slow E.E.G. waves of stage 3 sleep just before the first of the two chewing episodes. E.E.G. signs of sleep persist throughout. These were 2 out of 53 such episodes, of 2-30 seconds' duration, occurring between 2.30 and 3 a.m., and among 184 such episodes during the whole of that night's sleep.

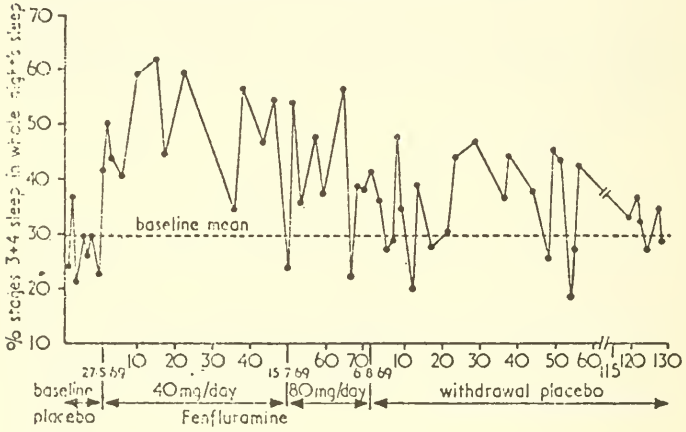

FIG. 6—Case 2. Dramatic and sustained rise above both personal baseline and normal values occurred in combined stages 3 and 4 (slow-wave) sleep as a result of chronic fenfluramine administration to this patient (who lost 3·4 kg). It appears maximal after about two weeks and seems to decline during the 71 days of administration.

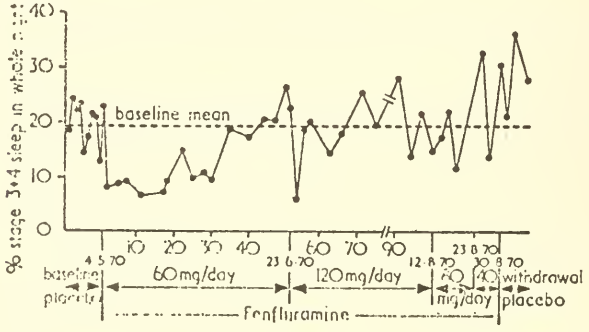

FIG. 7—In Case 6 (111 kg initial weight), who did not lose weight, fenfluramine 60 mg/day appears to cause a sustained fall in combined stages 3 and 4 sleep for the first month, with subsequent recovery to normal. His three highest values occur in the withdrawal phase, suggesting a degree of rebound.

DETAILS OF FOUR CASES

Case number	Initial weight (kg)	Weight at withdrawal (kg)	Weight change (kg)	Baseline days	40 mg/day	80 mg/day	Withdrawal days
1	82·12	76·67	−5·45	9 (9)	34 (10)	42 (15)	40 (11)
2	71·45	68·05	−3·40	10 (10)	49 (12)	22 (9)	56 (22)
3	77·93	73·94	−3·99	6 (6)	81 (16)	14 (5)	35 (12)
4	90·05	91·17	+1·12	10 (10)	49 (12)	28 (9)	50 (18)

Note: Numbers in parentheses indicate the number of nights of all-night sleep recording. Baseline numbers include predrug and late (about 4 months) postdrug baseline nights.

DISCUSSION

Our earlier single-dose studies had failed to show the effects of the drug on paradoxical sleep. Increase of intra-sleep restlessness, seen after single doses, is confirmed. The sub-baseline degree of restlessness, or frank inertia, after withdrawal seen in Fig. 4 has been noted after withdrawal of a drug resembling fenfluramine (Oswald, 1970). Reduction of stages 3 and 4 sleep was earlier described (Oswald *et al.*, 1968) whereas Fig. 6 now shows a striking increase to values that are, in our experience, and that of Williams *et al.* (1964), above the normal range.

Slow-wave sleep (stages 3 and 4), often considered "worth more" than stages 1 and 2 (Dement and Greenberg, 1966), is now thought to be an obligatory condition for the large nocturnal secretion of growth hormone (Sassin *et al.*, 1969a, 1969b). Growth hormone is a lipolytic agent (Fain *et al.*, 1965; Hunter, 1968), and the possibility arises that fenfluramine might partly reduce weight by an action on the brain that leads both to slow-wave sleep increase and to growth hormone secretion increase. Besser *et al.* (1969) reported that amphetamine provoked a rise of growth hormone secretion. First results of some current experiments strengthen our expectation that serial blood samples during sleep contain higher growth hormone levels during fenfluramine intake with weight loss.

Bruxism seemed to be provoked by fenfluramine. Brandon (1969) described daytime involuntary teeth-grinding and Riley *et al.* (1969) teeth-chattering after excess of fenfluramine, while Ashcroft *et al.* (1965) reported tooth-grinding as a feature of amphetamine abuse.

Time-course of events

Withdrawal of amphetamine is followed by rebound abnormalities of cerebral function persisting many weeks (Oswald and Thacore, 1963). In the case of such drugs as tricyclic antidepressants, heroin, or phenobarbitone, the number of days between withdrawal and the peak of paradoxical sleep rebound is about equal to the time required to eliminate the drug from the brain (Lewis and Oswald, 1969; Haider and Oswald, 1970; Lewis *et al.*, 1970). In Fig. 3 above the peak of the rebound is at about four days after drug withdrawal, and in a companion paper (Oswald *et al.*, 1971) we report mood depression maximal four days after fenfluramine withdrawal. The time-course may be understood in the light of fenfluramine's long half-life and the fact that three to four days are needed to establish equilibrium blood levels on continued dosage or, conversely, to allow the blood levels to fall to zero (Campbell, 1971).

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29. Drugs of Dependence Though Not of Abuse: Fenfluramine and Imipramine [1]

(By Ian Oswald, S. A. Lewis, D. L. F. Dunleavy, Vlasta Brezinova, and Marion Briggs)

SUMMARY

Measures of subjective feeling used by five patients indicated that depression of mood occurred about four days after fenfluramine withdrawal. An experiment in which another 11 patients took fenfluramine 80 mg for 28 days confirmed the depression, maximal on the fourth withdrawal day. It also indicated that in the first week of administration there was some mood elevation, but with feelings of impaired ability to concentrate. The drug reduced appetite and weight. A comparison is drawn with imipramine, which was found to induce initial and withdrawal changes of subjective experience (of dreaming) in six volunteers. It is suggested that certain mood-influencing drugs may not be drugs of abuse because of some unpleasant initial effects, though they can be drugs of dependence.

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INTRODUCTION

A few years ago amphetamine was not accepted as a drug of addiction because "physical" withdrawal features were supposedly absent. Nevertheless, clinicians encountered amphetamine addicts and observed inertia, sleepiness, and depression of mood following withdrawal. The brain is a "physical" organ and governs psychological function, and as techniques become more sophisticated withdrawal signs after more drugs must be discovered. They may be traditionally physical or, since brain physiology dictates mental life, of a psychological nature. Today we have drug "abuse" and drug "dependence" (W.H.O., 1969). The former implies use of a drug contrary to law or medical opinion. Dependence implies that the drug influences behaviour and that through repeated experience the organism is in some way changed, so that if the drug is stopped it is then missed and withdrawal features appear. Like other brain responses dependence could be expected to be a graded and not an absolute phenomenon.

We have found that regular intake of fenfluramine, an amphetamine derivative, leads to dependence on the drug for the maintenance of normal mood, and, for comparison, we show a minor form of dependence on imipramine.

MEASURING INSTRUMENTS

A drug may influence how a man feels. Observers can make inferences about how he feels and attempt measurement, but a man's inner, subjective experience is his alone, and he alone can truly describe it. Words are often inadequate, so we used a simple thermometer-like measure, a line, 10 cm long, on which the patient could make a mark to indicate where, along a continuum of feeling, he would place himself that day. The number of mm along the line was eventually measured. Visual-analogue self-rating scales of this type have been discussed by Aitken (1969).

The principal measuring device was a sheet of paper with space for name and date and a 10-cm line running across it with, at the left-hand end, the words, "Most depressed ever," and at the right-hand end, "most cheerful ever." The instructions were: "Please indicate by a mark on the line how you felt in your spirits today. If you have felt more lively and cheery than usual you should make your mark to the right of center, if more listless and gloomy than usual your mark should be to the left. An average day should mean a mark in the center." It was completed at night and the measures from it are taken as measures of *mood*.

Similar 10-cm lines were used to measure appetite. They were marked "no appetite at all" at one end, and at the other end "greatest ever relish for food." Patients were reminded that there is a difference between relish for food and amount eaten. Another sheet of paper gave a self-estimate of how well the patient had been able to concentrate mentally and ran from "extremely difficult to concentrate" to "wonderfully alert and penetrating mind." A morning sheet gave a self-estimate of dreaming and ran from "absolutely dreamless in retrospect" to "seemed to be vivid dreaming all the time."

FENFLURAMINE: FIRST EXPERIMENT

Five men of varying degrees of obesity participated in a laboratory study of the effect of fenfluramine on their sleep (Lewis *et al.*, 1971) and completed the mood self-rating each time they attended the laboratory. Periods of blank tablets (placebos), then of fenfluramine tablets, and of blank tablets again, followed one another over the course of months. Four men who had received fenfluramine 80 mg/day had mood scores that all fell in withdrawal. In one man (Case 1) this fall, to far below his previous other scores, was for only one day, the fourth since the last fenfluramine. In the others self-reported depression lasted longer, as Fig. 1 shows, but was worst three to five days after withdrawal.

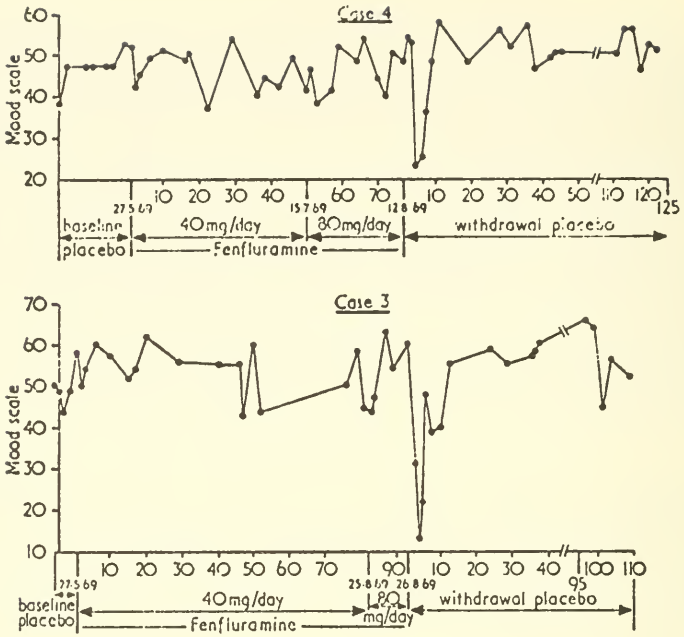

FIG. 1—After taking fenfluramine for 78 and 94 days respectively these two patients, when marking their self-rating mood scales, indicated that they felt depressed in the week after fenfluramine withdrawal.

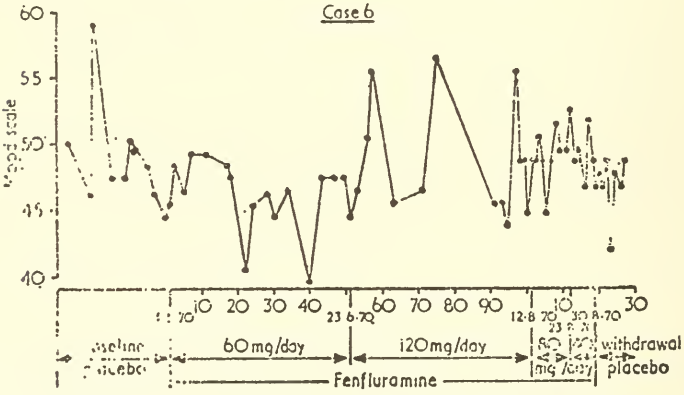

FIG. 2—When this patient was asked to make a *daily* self-rating of his mood the range of his scores appeared to narrow (right-hand side of graph). His fenfluramine was withdrawn in steps, but despite this he indicated a sharp drop on the fourth day after finally stopping the drug, when his absolute score was the lowest for three months.

Patients create their own scale and range of measures, and these can shift as time passes. Fig. 2 refers to a 111-kg man who received up to 120 mg of fenfluramine per day. Late in the study we asked him to complete his rating scale, not just on laboratory nights but on every evening, and it can be seen that his range narrowed. Dosage was reduced in steps, but even so, four days after withdrawal he marked his mood scale to indicate a greater degree of depression than he had done for the preceding three months.

FENFLURAMINE: SECOND EXPERIMENT

The first experiment led us to conduct a similar study with 11 patients who took fenfluramine for 28 days, *and to predict that they would reveal depression of mood, maximal on the fourth withdrawal day.*

Six women and five men aged 20–53 who wished to lose weight were asked to participate. None were grossly obese, and a different era of fashions possibly none of the women would have wished to slim. They received individual day packs of four tablets. The length of the initial blank-tablet period was deliberately varied from 7 to 13 days, and the final blank-tablet period between 9 and 13 days. They started on different week-days so that in the case of the women their expected menses should fall about the middle of the 28 days on fenfluramine 80 mg/day. Two tablets were taken before breakfast and two before the evening meal. Each evening they rated their mood, appetite, and concentration for the day. All had first been screened for a clear bill of mental health, personal and family. They were able to consult us if they wished, but we saw them for general inquiries only just before starting blank tablets, in the middle of the fenfluramine month, after 10 post-withdrawal days, and at the end.

RESULTS

We first examined the data in a way that took account of the patients' personal scales and ranges of subjective-feeling scores, examining ratios between a patient's own score for one day and that for his other days. All had at least seven baseline scores. The mean of these seven was found for the individual and then the deviation of each day's score from this personal baseline mean was determined. This was done for all 11 patients. The 11 personal deviations for each day were summed and divided by 11 to give a mean deviation for each baseline day. The standard deviation (S.D. or σ) of the baseline scores was obtained for each patient and the group S.D. for the same scores according to the formula, where N = number of observations, j = subscript denoting

$$\text{group S.D.} = \sqrt{\frac{\Sigma N j \sigma j^2}{\Sigma(Nj) - J}}$$

which patient, and J = number of patients. The mean deviations were similarly found for each fenfluramine day and for each withdrawal day, by again using individual deviations from personal baseline means.

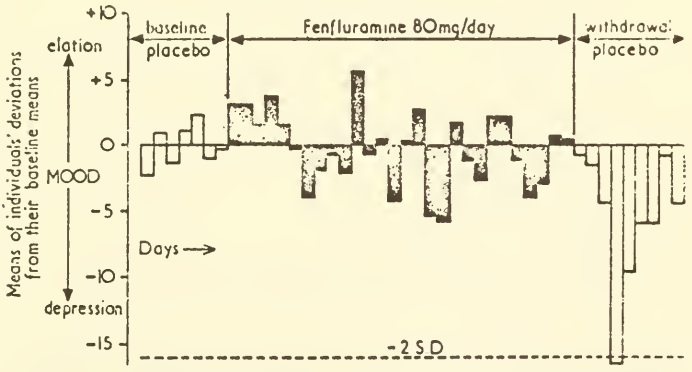

FIG. 3—Fenfluramine withdrawal causes depression of mood. The depression of these 11 patients is maximal, as predicted, on the fourth withdrawal day, and on that day is more than 2 S.D. below baseline. They had become dependent on the drug for maintenance of normal mood.

Mood scores fell after drug withdrawal and the patients indicated their most severe depression on the fourth day of withdrawal (Fig. 3). Since the most extreme deviation from the mean was on the predicted day among the 44, and in the predicted direction, the probability of the result arising by chance could be 1 in 88, but since that deviation exceeded 2 S.D. from the baseline mean, the likelihood that chance could be responsible is even more remote.

In the first experiment mood scores were started in case elevation might

occur with fenfluramine. No obvious elevation was observed, but in the second experiment higher mood scores clustered just after the start of fenfluramine. To smooth out transients, five-point moving means of raw scores, averaged across patients for each day, have been used to prepare Fig. 4 (thus days 1–5 were averaged to give the mean for day three, days 2–6 gave the mean for day 4, and so on). In Fig. 4 the highest point of mood elevation among the 40 possible occurs at the third day of drug administration and the low point at days 5 and 6 after withdrawal (Fig. 3 shows skew during withdrawal).

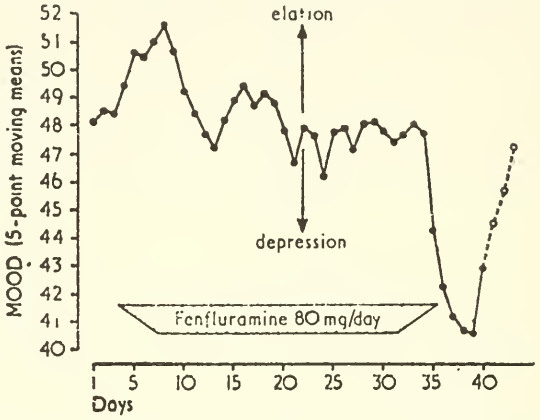

FIG. 4—When fenfluramine is first started patients tend to rate themselves as slightly elevated in mood, as well as depressed after withdrawal. The last three values are based on only 10, 9, and 8 patients respectively, owing to the staggered end of the study. The moving-mean technique causes both drug and drug-free days to contribute to certain points on the graph, as indicated by the trapezium.

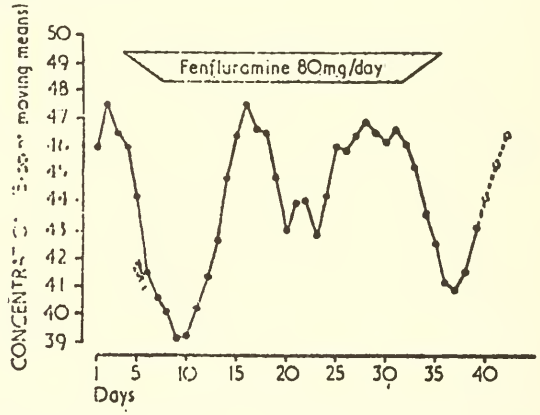

FIG. 5—Fenfluramine causes feelings of impaired mental powers when first given, and again during the eventual withdrawal period of mood depression. The last three values are based on 10, 9, and 8 patients only.

Patients were not requested to write comments on their rating sheets but did so, especially during the withdrawal period when phrases included, "feeling depressed," "extremely light-headed, drowsy, and depressed (for no reason) today," "a feeling of uneasiness," "unwell," "anxious," "tense," "a tightness which I felt throughout my body," "very tired and out of sorts," "very upsetting dreams," "headache," "palpitations," "irritable," "narky," and "may be starting a cold."

A 40-year-old man scored himself lower on the fourth withdrawal day than any previous day but went lower still until the ninth. When seen on the

tenth day he spoke of having "been weeping all week-end," to the alarm of his family. He recovered in the next few days.

The self-rating scores for concentration and for appetite on no day reached 2 S.D. from the baseline after the manner of Fig. 3, but five-point moving means show subjectively impaired concentration in the first week on the drug and in the withdrawal period (Fig. 5). There was a self-rated decrease of appetite while on the drug (Fig. 6), with lowest score on the tenth day and, interestingly, an upward acceleration from a week after drug withdrawal—as one man then wrote, "very hungry, eating sweets, most unusual for me." Mean weight loss over the whole period was 3.0 kg ($P < 0.02$).

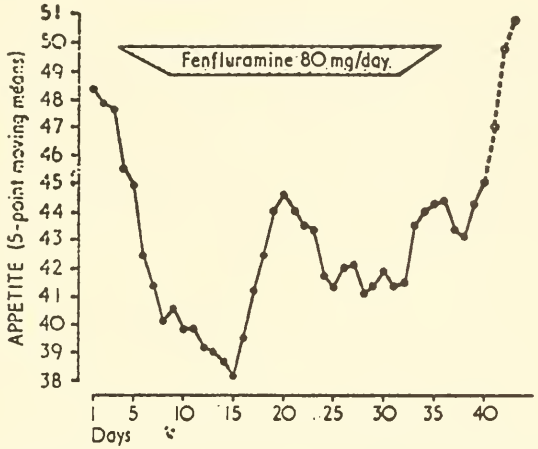

FIG. 6—Fenfluramine diminishes appetite, but a delayed increase of appetite seems to follow withdrawal. The last three values are based on only 10, 9, and 8 patients, however.

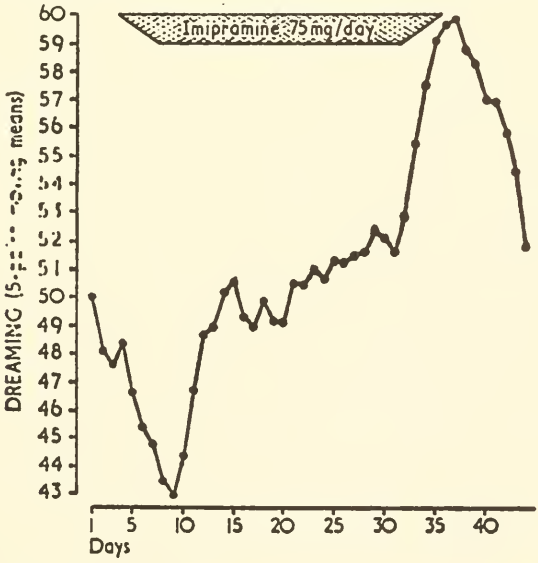

FIG. 7—Imipramine at first causes a subjective impression of reduced dreaming, but eventual withdrawal of the drug is followed by a subjectively great increase of dreaming. They had become dependent on the drug for maintenance of normal dreaming.

IMIPRAMINE EXPERIMENT

Six healthy male volunteers undertook dream self-rating for 48 successive mornings. They had taken 3 tablets at 9 p.m. each previous day, receiving 7 days of blanks, 28 days of imipramine 75 mg, and then 13 days of blanks. The five-point moving means are shown in Fig. 7 and indicate subjective diminution of dreaming when first on the drug, and an increase to a peak after the fourth withdrawal night. Examination of the data by the method used for Fig. 3 showed a rise to more than 2 S.D. above the baseline mean on withdrawal nights 1, 2, 3, 4, 6, and 8.

DISCUSSION

Fenfluramine is a drug that alters the brain concentrations of noradrenaline and dopamine (Ziance and Kinnard, 1964) and of serotonin (Duhault and Vordavainne, 1967) and might be expected to influence mood. It is an amphetamine derivative widely prescribed in Britain yet it has not shown abuse potential. Young drug-takers in London seem not to choose fenfluramine, according to Hawks (1970), of the Addiction Research Unit, Institute of Psychiatry (confirmed by personal communication, Hawks, 1971). Amphetamine addicts do not credit fenfluramine with effects qualitatively similar to those of amphetamine (Götestam and Gunne, 1971). Isolated reports of young persons who have experimented with fenfluramine above the recommended dose indicate that their experiences were unplasant (Brandon, 1969; Riley *et al.*, 1969).

Imipramine is used as a mood-altering drug, but there is nothing to suggest that it is a drug of abuse. Yet electrophysiological techniques can demonstrate withdrawal abnormalities after imipramine, maximal after about four days and lasting a month (Dunleavy, Brezinova, Oswald, MacLean, and Tinker, to be published) and Fig. 7 suggests withdrawal abnormalities of subjective experience that most people would think of as unpleasant.

Fenfluramine, though also not taken for pep at parties, caused withdrawal abnormalities of subjective experience (Figs. 1, 2, 3, and 4) that were certainly unpleasant, with a severity of depression sufficient to cause us concern in the case of one man. The nadir was reached after four days without the drug, and we suspect that this delay accounts for there being only one other report that recognizes depression as a consequence of fenfluramine withdrawal (Golding, 1970). The four-day delay parallels the delay to a peak of withdrawal abnormality in cerebral electrophysiology (Lewis *et al.*, 1971) and may be attributed to the slow elimination of the drug, for which three to four days are needed (Campbell, 1971). Gradual reduction of dose of fenfluramine would seem clinically important, though may not wholly prevent depression (Fig. 2).

In the measures of subjective experience, and in electrophysiological measures (Lewis *et al.*, 1971), some initial effects of fenfluramine decreased with time. When tolerance occurs and a drug "loses its effect" it is not the drug that is changed but the brain, and sometimes the liver. We would suppose that internal monitoring devices detect departures from normal brain physiology and lead to the cretion of neuronal modifications that counteract the drug. If the drug is stopped the modifications, now unrestrained by the drug, cause the withdrawal abnormalities, opposite in kind to the drug's actions, and do so until such time as the turnover of neuronal components, and perhaps shorter-term adjusting mechanisms, lead to restoration of normality. Obviously subjective powers of concentration can be impaired either directly by a drug or by withdrawal depression and anxiety (Fig. 5).

We believe that drugs such as imipramine and fenfluramine cause a number of differing initial subjective effects, some of which are unpleasant. The feeling of impaired mental powers after fenfluramine contrasts with feelings of enhanced mental powers often described with amphetamine. If unpleasant initial effects of a drug outweigh initial pleasant effects, and if elimination is slow and so prevents a rapid "let-down," the drug's abuse potential might be expected to be low.

Finally, we would emphasize that the techniques we have used could probably show unwanted subjective effects, both of administration and withdrawal, with many other drugs, including other slimming pills.

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30. Side Effects of Anti-Obesity Drugs

(By Ashton L. Welsh, M.S., M.D.)

(Pps. 115–134)

Not long ago, when phenylpropanolamine hydrochloride was available without prescription, the drug found its way into many across-the-counter remedies, such as Regimen, Di-Dol, Rx-121, Unitrol, and the like. Today, phenylpropanolamine hydrochloride is available only when prescribed. In spite of the evidence that if the drug is given in large enough dosages, it will induce some anorexia, the study by Fazekas and his associates, indicates that, in the usual dosages contained in these remedies (25.0 mg., or less), the drug is no more effective than a placebo. In any event, if dosages of sufficient size to induce anorexia were administered, most probably, difficulties would be encountered due to elevation of blood pressure (191).

SIDE REACTIONS AND TOXIC EFFECTS

Central nervous system effects

Dryness of the mouth has been mentioned, following therapy with phenylpropanolamine hydrochloride. Paradoxically, appetite, and weight may increase.

Cardiovascular system disturbances

There may be hypertension, headache, and tachycardia.

Phenmetrazine

Phenmetrazine is dl2-phenyl-3-methyl-tetrahydro-1, 4-oxazine hydrochloride, which may be represented by the following structural formula.

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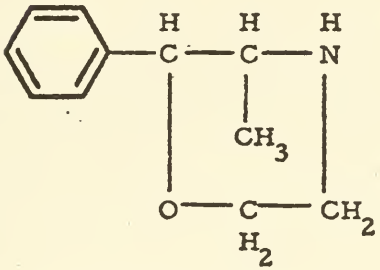
*Among others, severe environmental disorders during childhood, lack of purpose in life, dissatisfaction with the task of life, and disorders in sex life.

PHENMETRAZINE HYDROCHLORIDE



The compound was developed in Europe by C. H. Boehringer und Sohn of Ingelheim a. Rh., Germany.

In the United States, a salt of the racemic compound may be identified as Phenmetrazine Hydrochloride N.N.D. (204), for which the trademarked name and pharmaceutical supplier are shown, following:

Trademarked Name

Preludin
(Tablets, each tablet containing phenmetrazine hydrochloride 25.0 mg.)
Preludin Endurets
(Sustained-release tablets, each tablet containing phenmetrazine hydrochloride 75.0 mg.)

Pharmaceutical Supplier

Geigy Pharmaceuticals, Div. of Geigy Pharmaceuticals Corp.

MIXTURE CONTAINING PHENMETRAZINE HYDROCHLORIDE

A drug-mixture containing phenmetrazine hydrochloride is:

Trademarked Name

Prelu-Vite
(Capsules, each capsule containing phenmetrazine hydrochloride 25.0 mg., "with vitamins A, B, C and D and five minerals")

Pharmaceutical Supplier

Geigy Pharmaceuticals, Div. of Geigy Pharmaceuticals Corp.

PHARMACOLOGICAL ACTIONS

Phenmetrazine causes central nervous system stimulation and excitation which is one-seventh to one-tenth that of racemic amphetamine sulfate: and pressor effect which is 1/1,000 to 1/1,500 that of epinephrine (280). Phenmetrazine produces tachyphylaxis: and exerts no effect on the nictiating membrane after denervation or cocaine (280). (Phenmetrazine does not produce cotachyphylaxis for amphetamine.)

In distinction from racemic amphetamine sulfate, phenmetrazine increases the blood pressure effect of noradrenaline.

Phenmetrazine does not break down with amine oxidase and inhibit the activity of that enzyme.

In animal experiments carried out by Thomä and Wick (280), signs of acute toxicity of phenmetrazine were qualitatively identical with those of amphetamine, namely, vigorous motor movements, restlessness, incessant walking about, rising of the hair, exophthalmos, and, convulsions. In white mice, the LD_{50} of phenmetrazine, by the oral route, was 475.0 mg./kg., compared to 95.0 mg./kg., for racemic amphetamine sulfate. Unanesthetized dogs receiving phenmetrazine, 15.0 mg./kg., subcutaneously, showed a degree of excitement similar to the effect of 2.5 mg./kg. amphetamine.

In recent laboratory studies conducted by other investigators (260), orally-administered doses of phenmetrazine, 25.0 to 30.0 mg./kg., in dogs, produced almost complete anorexia. Excitement lasted for several hours after treatment. Continuous administration was not accompanied by any rebound of appetite by the eleventh or twelfth week, by which time, approximately one-third of initial body weight had been lost. When sacrificed, autopsy revealed cachexia, but no other pathologic change attributable to medication.

Intravenous administration of phenmetrazine in dosages of 1.0 to 4.0 mg./kg., caused a marked and lasting increase in the average blood pressure. Higher dosages, 8.0 to 16.0 mg./kg., caused a fall in blood pressure, the amplitude and duration of which increased as the dosage level increased (to 32.0 mg./kg.). Dosages of 2.0 to 16.0 mg./kg., caused a marked increase in average heart rate, which lasted more than 1 hour; dosages ranging from 1.0 to 32.0 mg./kg., increased respiratory rate, the tachypnea so produced often lasting longer than 2 hours. Sometimes, amplitude of respiration was reduced, and breathing became irregular, a finding reported, also, by Rumke and his co-workers (241) following administration of the drug to anesthetized rabbits. Pathologic changes in the electrocardiogram were observed.

Side effects of intravenously-administered phenmetrazine in dogs, have been observed, also, in cats (260).

Chronic oral administration of phenmetrazine to dogs, in dosages of 15.0 mg./kg., increased blood pressure, and produced pathologic changes in the electrocardiogram.

Generally speaking, oral administration, even in rather high dosages, resulted in substantially fewer circulatory side effects than did intravenous administration.

Effects of phenmetrazine on the circulation, in man, has been described in this way (259):

"In 25.0 mg. doses, the drug increases peripheral resistance and diminishes the stroke volume. In 75.0 mg.–150.0 mg. doses, it decreases peripheral resistance and increases the stroke volume."

CONTRAINDICATIONS

In this country, according to statements issued by the Council on Drugs of The American Medical Association (204), phenmetrazine hydrochloride,

". . . on theoretical grounds, should not be administered to patients with severe hypertension, thyrotoxicosis or acute coronary disease. It may be used with caution in patients with moderate hypertension and cardiac decompensation."

Phenmetrazine hydrochloride has not been in use, in the United States, for the same length of time, as it has been used in Europe.

GENERAL CLINICAL ACTIONS AND USES

Clinical use of phenmetrazine was originated in Germany, where Berneike (28, 29) gave to 50 patients one 25.0 mg. tablet, twice daily for 10 weeks, and found that all patients lost weight at an average rate of 1.9 lb. (0.9 kg.) per week.

In the United States, according to statements issued by the Council on Drugs of The American Medical Association (204):

"Like amphetamine, phenmetrazine exerts an appetite depressant effect: it is therefore useful as an anorexigenic agent in the management of simple obesity caused by excessive caloric intake. The mechanism of its effect upon appetite has not been explained. It should be used only as an adjuvant to a weight-reducing program and not as a substitute for conventional measures."

DOSAGE SCHEDULES: FOR WEIGHT REDUCTION

According to the same authoritative statements (204),

"Phenmetrazine hydrochloride is administered orally. The usual dose for adults is 25.0 mg., two or three times daily, one hour before meals. Because of variations in eating habits and appetite peak patterns, it is often advisable to adjust this dosage to the requirements of the individual patient."

Sustained-release tablet-form of the drug is recommended for administration once daily, in the morning, to adults, in place of the ordinary medications, in divided amounts.

Mixture containing phenmetrazine, vitamins and minerals, in capsule form, is claimed, with administration twice or thrice daily, not only to exert anorexigenic effect, but also, to help fortify the patient's nutritional status.

RESULTS OF ANTI-OBESITY THERAPY IN GENERAL PRACTICE

There have been a number of favorable reports, both here and abroad, concerning the anorexigenic action of phenmetrazine in the management of obese patients (5, 33, 92, 108, 131, 153, 160, 201, 226). Following is a brief summary of one favorable report (108), which appeared in our own medical literature:

The double-blind technic was utilized in a clinical evaluation of phenmetrazine in the management of 53 overweight patients. Average age of these patients was 47 years, and average pretreatment weight was 202 pounds.

Half of the patients were given three tablets, phenmetrazine hydrochloride 25.0 mg. each, to be taken 20 minutes before each meal, for a course of 6 weeks. Alternate patients received placebos for the same period, after which, the groups were switched, each patient thus serving as his own control. A diet of 1,000 calories daily was also prescribed.

"The rate of loss of weight while taking phenmetrazine was more than twice that observed when a placebo was used. Those patients receiving phenmetrazine showed an average weekly weight loss of 0.9 lb.; those on placebo, 0.5 lb."

Patients were re-examined biweekly, when weight, blood pressure, pulse rate and possible side effects were checked. Determination of basal metabolic rate, blood counts, hemoglobin and urine analyses were performed on a representative number of each group during therapy. No significant difference was noted in any of these findings which could be attributed to either the medication or the placebo.

No insomnia was reported, in spite of the fact that the last daily dose of the drug was administered 20 minutes before the evening meal.

Mild subjective side effects were reported by individuals receiving both active drug and placebo. These included a combination of faintness and dizziness in eight patients receiving the drug, and four on placebo: gastrointestinal complaints (gas, indigestion and nausea) in four, and three, respectively; and headache, in one, on the drug.

"This would indicate that side effects directly attributable to Preludin are not very frequent, and in no case did they necessitate discontinuance of the drug."

It was concluded, that this medication: ". . . permitted a stricter adherence to the prescribed dietary regime either by depressing the appetite mechanism, directly, or by stimulating a sense of well-being in the patient, so that symptoms of hunger were not so obvious or distressing."

There have been a number of unfavorable reports, both here and abroad. In this country, for example, Patterson (214) reported an incidence of side effects of 40 per cent produced by phenmetrazine hydrochloride, as compared with an incidence of 17 per cent, produced by dextro-rotatory amphetamine sulfate.

In England, for example, Randell (224) observed that single doses of phenmetrazine (25.0 and 50.0 mg.), administered to ten normal student-volunteers, produced palpitations, insomnia, irritability, perspiration, and difficulty of concentration. (The recommended dosage is 25.0 mg., twice or thrice daily.)

Another group of investigators (81), using a controlled double-blind trial of phenmetrazine hydrochloride and methylcellulose, as adjuncts in the treatment of 85 obese outpatients, whose obesity had proved refractory to routine dietetic advice, found that phenmetrazine, given for periods of 2 months, produced weight loss which, though statistically significant, was disappointingly small. They said:

"There is still no acceptable evidence of the efficacy of phenmetrazine given for longer periods. Prolonged studies have, however, shown that in the long run obese patients treated with amphetamine or dexamphetamine and diet, lost no more weight than those treated with diet alone. There is no reason to expect long-term management with phenmetrazine to be any better."

They pointed out that seven patients had "since asked for a renewed supply of the drug," which raised the serious question of addiction. (For discussion of addiction, see pages 124–133.) They concluded:

"Because of its cost, its small influence on appetite and the dangers of addiction, we do not regard phenmetrazine as a good drug for the routine treatment of obese patients."

The foregoing, reported by investigators from the Department of Therapeutics and Medicine, University of Edinburgh, and the Dietetic Outpatient Department of the Royal Infirmary of Edinburgh, Scotland, was published in June, 1960 (81). The following, appeared in the United States, April, 1960 (178).

Good, controlled clinical studies on phenmetrazine are lacking, and there is no basis or choosing between phenmetrazine hydrochloride and dextro-rotatory amphetamine sulfate, on either appetite-depressing effects or side effects.

Attention is called to the big difference in cost to the two compounds. Phenmetrazine hydrochloride costs the patient about eight cents per tablet, compared with five or six cents for one 5.0 mg. tablet of dextro-rotatory amphetamine sulfate, U.S.P., and about three cents for one 5.0 mg. tablet of lower-priced brands of the same compound sold under its generic name.

Both drugs have euphoriant effect which is, sometimes, desirable in helping patients through the difficult period of adjustment to low-calorie diets, but tolerance develops to both drugs, and overdosage and addiction can be a problem.

The sustained-release form of phenmetrazine hydrochloride has the same limitations arising from the unpredictability of absorption, as mentioned (177) on the long-acting dextro-rotatory amphetamine preparations.

RESULTS OF ANTI-OBESITY THERAPY IN DERMATOLOGICAL PRACTICE

Usefulness of phenmetrazine has been reported (213) in the treatment of obesities which have an adverse effect on certain forms of dermatosis; in the treatment of those diseases of the skin which are associated with internal insecurity, inhibitions and difficulties in the relationship of the patient with his environment, and psychogenic sexual dysfunctions.

In our own practice, we have observed response to phenmetrazine, administreed for anorexigenic effect, by a series of only 25 patients. In our evaluation of response, incidence of side effects was high (38 per cent). During our study, we encountered some patient-resistance to medication.

We have observed many patients, who consulted us for dermatological care, and who, when questioned about medications which they might be taking, said that they were taking Preludin. We have learned, when we contacted referring physicians (engaged in other fields of medical practice) that they were supervising anti-obesity therapy with Preludin for patients, who were receiving from us, concomitantly, treatment for dermatoses. We have encouraged two patients, who presented generalizde eruptions, who were undergoing Preludin therapy prescribed elsewhere, whose dermatitis medicamentosa cleared when Preludin was withdrawn.

Psychoses and addiction have, reportedly, followed therapy with phenmetrazine (see pages 124–133).

In this connection, we relate, from our own experience, the facts of one case:

We first observed an overweight young lady (accompanied by her mother), when we were consulted about lesions involving the girl's face, over her cheeks and forehead, and about the jawline. These lesions were erythematous, maculopapular, and, at first glance, appeared acneiform. We were puzzled to note that bright red "new" lesions involved areas which were pigmented, tannish-grey, which had, obviously been sites of "old" lesions.

The patient was five feet tall; she weighed 145 pounds; she was 14 years of age. Her history included previous (but now discontinued) therapy from a family doctor, who had tried, unsuccessfully, to correlate exacerbations of the eruption with foods, such as tomatoes and citrus fruits; irregularities of the menses (the patient had stated that "flares" of the eruption preceded the menstrual periods); and constipation.

When we questioned her, the patient said that she was not taking medication, of any kind.

We prescribed appropriate topical therapy; outlined a daily diet (omitting chocolate, seafoods, nuts and raw-milk products), providing 1,000 calories; and recommended internal therapy, consisting of a saline laxative, a multivitamin mixture, and an estrogen, the latter to be taken during the second half of the menstrual cycle.

We observed the patient (always accompanied by her mother), each week during an interval of five weeks. Improvement seemed very slow. Just as she was leaving from her fifth observation visit, her mother asked for permission to speak to us, privately.

The mother said that the girl was "taking too many of her pink pills, which the family doctor had prescribed." She said the prescription had been refilled, regularly, during an interval of more than two years. Re-fills were becoming more and more frequent. The parents had remonstrated with the girl, had even refused to obtain more medication, but the girl had become so irritable, unreasonable, hysterical, that more pills were procured and everything "would be fine, for a few days."

We reminded the mother that the patient had denied taking any medication. The mother admitted that this was so, but added that there had been so many "rows," about the "pink pills" that she had not contradicted the girl in our presence, because she did not want to precipitate another episode of unpleasantness. We promised to talk with the girl, the following week.

We ascertained by telephone conversation with the family doctor, that a prescription had been ordered for our patient, some two years previously, "to help her lose weight." So far as he knew, the patient had never lost any weight, and had "probably forgotten all about the prescription."

We never saw the girl again. We contacted her parents, repeatedly, by mail; finally, we talked with the mother and the father, by telephone. We were told that the girl refused to continue treatment: she was "wild and unmanageable." The parents were worried.

We relate the facts in this case to illustrate the danger of prescribing phenmetrazine without limiting or supervising therapy. Phenmetrazine is a potentially-dangerous drug. We regret that we were unable to determine whether or not Preludin was the sole causative agent of the acneiform eruption; and just what transpired when medication was withdrawn.

SIDE REACTIONS AND TOXIC EFFECTS

Prominent among the side reactions and toxic effects, which have followed administration of phenmetrazine hydrochloride, are manifestations due to the cerebral actions of the drug.

Central nervous system effects

Restlessness, increased nervous tension (19, 90, 94, 95, 220, 224, 244), inability to concentrate (224), and excitement (81, 108), increased reflexes, talkativeness (86), irritability (56, 224), euphoria (84), increased confidence, elation (86), aggressiveness and combativeness have been observed.

Patients, introduced to phenmetrazine because they wish to lose weight, become acquainted with the drug's stimulant action, and may take medication to "pep them up," combat depression, and restore energy (86). To maintain such effects, increasing doses are required. Increased energy and activity (19, 29, 56, 90, 94, 95, 201) are followed by after-effects of let-down and fatigue (86, 220).

There may be transient blurring of the vision (201); dryness of the mouth (19, 56), or metallic taste in the mouth (19, 56, 201, 229); insomnia; vertigo and dizziness (19, 56, 90, 94, 95, 220, 244); perspiration (224) and thirst (33); headaches (81, 90, 108, 201), sensations of cranial pressure (108), and depersonalization (86). Paradoxical increases in appetite (and weight) have been described: and paradoxical drowsiness (56) has been observed.

Overdosage is frequently followed by psychoses, consisting of delusions of a paranoid, nihilistic and depressive type; disorientation and hallucinations, both visual and auditory; as well as behavior disturbances (31, 37, 61, 71, 84, 86, 87, 110, 143), suicidal tendencies and definite schizophrenic thought-disorder, including vagueness, overinclusiveness and bizarre associations.

Addiction has been reported (31, 37, 61, 71, 84, 86, 87, 143, 224, 226, 238, 246, 299), as have withdrawal symptoms, consisting of marked depression, lethargy and liability of mood. Subacute delirium (253) has been described.

A few cases, illustrative of central nervous system manifestations of reaction to phenmetrazine, are abstracted, following.

Paranoid delusions were observed in a patient, who had taken phenmetrazine to "forget everything," and to be "able to enjoy herself." She talked constantly: displayed no confusion: no clouding of consciousness. She was very irritable, however: thought her jewelry had become electrified: that the floor was magnetized. She was fearsome of burglars, and so began to sprinkle talcum on her window sill, in order to get finger prints of intruders.

This patient had previously taken dextro-rotatory amphetamine sulfate. She found that she needed more phenmetrazine hydrochloride, in order to get the same effect (31).

A woman became agitated, depressed and restless. She started to take phenmetrazine, in order to slim. The drug gave her increased confidence, as well as decreased appetite, so she took as many as 60 tablets, daily. She described interesting parties in Soho and Chelsea, where guests regaled themselves from bowls of dextro-rotatory amphetamine sulfate, racemic amphetamine sulfate and phenmetrazine and "had orgies."

This patient had been an alcoholic, before developing a psychosis on phenmetrazine (61).

A young woman, a professional nurse of stable personality, had been, 2 years previously, the object of assault which had no physical sequelae. Her doctor had prescribed phenmetrazine, in therapeutic doses, for 2 weeks.

Three weeks before admission to the hospital, a niece, whose operation for congenital heart disease she had advocated, died under anesthetic. Our patient became mildly depressed, and for a week, before admission, started to take phenmetrazine, in doses of 30 tablets (or 750.0 mg.) daily.

She was admitted in a state of apprehension and agitation, with both auditory and visual hallucinations. The provisional diagnosis was an acute schizophrenic episode. Symptoms cleared within 48 hours.

When she appeared to be normal, a history of drug ingestion was admitted. During the period of medication, no drug other than phenmetrazine had been taken. Symptoms did not recur, and she was discharged from this hospital as normal.

This case exemplifies intoxication, representing a schigophrenic episode induced by phenmetrazine. It was submitted . . . "as further evidence towards a more stringent control of availability of such drugs" (71).

An alcoholic, who had taken racemic amphetamine sulfate and dextro-rotatory amphetamine sulfate, plus pentobarbitone, stopped drinking, decided to slim, and started to take phenmetrazine. He found that the "kick" from the newer drug was similar to that given him by alcohol; and that three or four Preludin tablets had the effect of one tablet of racemic or dextro-rotatory amphetamine sulfate. Phenmetrazine, however, "took a worse grip" on him than alcohol had taken. After three to five tablets of Preludin, and feeling just fine, there followed a period of depression, irritation, headache, difficulty in concentrating and insomnia. He started to take butobarbitone, at night, to get a little rest.

After taking 50 Preludin tablets, he became very garrulous. He discovered that Preludin, taken with cider, was wonderful. He began to take the drug, with gin. Then he became ataxic and developed difficulties in gait.

He stopped all drugs, and went into convulsions (110).

(Obviously, phenmetrazine is not the only factor implicated in this case.)

Evans (86) said, when cases of psychosis and addiction to phenmetrazine appeared in the literature:

"I supposed the condition to be rare, but within six months I saw no fewer than sixteen patients who had taken Preludin and had become ill. Twelve of these had a psychotic disturbance."

Case history of only one of the psychotic patients observed by Evans, is quoted, in its entirety:

"Case 8.—Woman, aged 24 single. In July 1957 she was introduced to Preludin by a friend who recommended it for slimming. She took the tablets in increasing doses so that at the time of admission (in November, 1957), she was consuming 15–20 tablets a day, although she said they had no effect on her, and she did not know why she took them. About fifteen months before admission the patient had become interested in religion. This interest dominated her conversation for three months before admission. At the same time the mild feelings of depression lifted. She declared that she had given herself to God and until he gave her back she was the vehicle of other people, and a living sacrifice for God. She became so restless and excited that she was admitted to an observation ward. On examination, she was cheerful and elated, talking at length in a rambling fashion. Two weeks later her condition was satisfactory but she remained elated and still dwelt on religious topics. Her second, third and fourth admissions were preceded again by intermittent consumption of large doses of Preludin—usually 20 at a time.

"On her fourth admission she had become deluded and halucinated again. Mood was elated. There was marked disorder of sequence in thinking—e.g., 'God has to obey the Queen. Dreadful for us, but the whole world would know. For

England is the mother country and they all come out of her.' This type of thinking did not appear in other patients. Her disturbance persisted for six weeks."

Other parts of Evans' report are quoted, following.

"DISCUSSION

"The twelve patients with a psychosis may be considered in two groups.

"The first group consists of patients 1, 3–7 and 12 whose symptoms were indistinguishable from those of an amphetamine psychosis. They had an illness in which delusions of a paranoid, nihilistic, and depressive type occurred, together with hallucinations and disturbance of affect. Behavior was altered; some were restless and agitated. No thought disorder typical of schizophrenia was elicited. Disorientation was found in two cases only. All recovered within a week. Patients 1, 4, 5 and 8 relapsed as a result of taking Preludin again. Similar cases have been reported by Bethell (1957), Brandau (1958), Lubenthal (1957), and others. The history of excessive intake of Preludin, a frank psychosis and its rapid resolution on stopping the drug, justifies the term psychosis due to Preludin.

"The second group, patients 2 and 8–11, had a delayed recovery. All (except case 10) had taken Preludin for months—10–20 or more tablets a day for several weeks. The symptoms differed slightly from the first group in so far as cases 2 and 8 were elated and more active. Cases 8 and 9 had definite schizophrenic thought disorder with vagueness, over-inclusiveness, and bizarre associations.

"It is possible that the psychosis coincided by chance with taking Preludin. It is also possible that the patients were taking Preludin to alleviate early symptoms of psychosis—though it is improbable that these symptoms could be suppressed for such a long time.

Despite close supervision patients may have continued to take the drug while in an observation ward, thereby prolonging the psychosis, but this is unlikely. This could not be excluded, however, because a biochemical test for Preludin has not been developed. There remains the likelihood that large doses of Preludin can cause a psychotic schizophrenic type of illness lasting weeks or months. As with amphetamine psychosis, in cases of delayed recovery the clinical picture was of a schizophrenic psychosis.

"BACKGROUND AND PERSONALITY

"Excluding patient No. 7 (a woman of 51) the patients were aged between 19 and 33. Eleven out of the sixteen were women. All but one were single or divorced. Their work record was unstable as thirteen had changed jobs frequently. Thirteen had taken drugs, alcohol, or amphetamine derivatives in the past. Five had had a severely disturbed upbringing. None had paranoid traits when well. Four were extroverts. Thus the impression emerges that this group resembles other drug addicts.

"DRUG DATA

"Drug addicts are well known for their capacity to lie about the amount of drugs taken. Some of my patients denied taking Preludin when first questioned and many admitted later that they had taken more than they had said at first. A number had taken Preludin for slimming and had then noticed its stimulant effect. This may account for the preponderance of females. Others had taken it as a 'pep' pill. All had found that the number of tablets taken had to be increased in order to obtain the same effects. Excluding the subacute intoxication, all the patients except one had taken over 10 tablets a day for many weeks. The amount taken did not appear to have a close relation to the severity of the illness. Withdrawal symptoms were not common, but patients 3 and 8–10 had depression and marked lethargy for some days where patient 1 had lability of mood; only two asked for further Preludin. At home, however, they had difficulty in refraining from taking Preludin. The after-effects of let-down, depression, or fatigue made them take more.

"In 1957 the Pharamaceutical Society advised pharmacists not to dispense Preludin except on doctors' prescriptions. However, none of our patients had had much difficulty in getting the tablets.

"DIAGNOSIS

"The diagnosis of any illness depends on awareness of its existence, and Connell (1958) pointed out that many amphetamine psychoses were missed for this reason. This applies equally in the diagnosis of addiction and psychosis due to Preludin. As amphetamine-like drugs are now listed as Schedule IV Poisons, they are more difficult to obtain and it is likely that many people who have used amphetamine derivatives in the past will turn to other drugs, and Preludin psychosis will increase.

"At present a history of taking Preludin is necessary for diagnosis, for no satisfactory biochemical test exists. The initial story from the patient should not be accepted as reliable; for some will deny taking tablets at first and admit it later. In all cases mood is disturbed. The majority are anxious, depressed, or frightened. There is no flattening or incongruity of affect.

"Two patients who had a delayed recovery were elated. Delusions and hallucinations, sometimes visual, are common. Pressure of talk is frequent but not invariable. Schizophrenic type of thought disorder is uncommon. Disorientation may occur. Clouding of consciousness is difficult to assess, but I found no obvious signs. However, these patients were usually not examined late at night—the time when many complained of an exacerbation of their symptoms. Fatigue on withdrawal of the drug may be present. Any physical signs of sympathetic activity present due to Preludin cannot be distinguished from those due to anxiety. A final important feature in the diagnosis is the rapid recovery after the drug has been withdrawn.

"If consumption of Preludin is concealed, psychosis due to Preludin cannot be differentiated from other psychoses. As with amphetamine, some cases of psychosis associated with Preludin intake have been eventually labelled schizophrenia. Whether abuse of the drug caused schizophrenia or was merely a symptom of the illness remains undecided.

"CONTROL OF PRELUDIN

"Apart from the cases of psychosis already described, I have seen four others of excessive consumption. All had disturbed behaviour resulting in admission to a mental ward.

"Preludin was taken by the patients to 'pep' them up, combat depression, or restore energy. To maintain this effect, increasing doses were taken, sometimes resulting in a psychotic episode. In one case seen by me and in two cases reported by Seager and Foster (1958), work and social capacity had become disturbed even to the point of stealing money to obtain Preludin. Three patients stated that in certain coffee bars and clubs in London, Preludin is used frequently as a pep tablet. On stopping Preludin in hospital, four showed marked fatigue and tiredness—two demanding more Preludin.

"The prospect of increasing abuse of Preludin raises the question of how much control of this drug there should be.

"The World Health Organization (1950) and the Drug-Addiction Committee of the American National Research Council have defined addiction as 'a state of periodic or chronic intoxication detrimental to the individual and to society, produced by the repeated consumption of the drug (natural or synthetic). Its characteristics include: (1) an overwhelming desire to continue taking the drug and to obtain it by any means; (2) a tendency to increase the dose; (3) a psychological and physical dependence on the effects of the drug.' Isbell and Fraser (1950), in an extensive review of addiction, disagree with the inclusion of the term 'dependence' as an essential part of addiction. Satisfactory as the definition is to the pharmacologist, the clinician is concerned with possible harm to an individual or society from a drug. Dependence is important mainly because it causes addiction to be continuous rather than periodic. Rigid adherence to the term 'dependence' prevents the inclusion of cocaine and marihuana as addiction-producing drugs. Because of its social consequences, Preludin should be defined as a drug of addiction for the same reasons as are cocaine and marihuana and should be placed on the list of Schedule IV Poisons of the Pharmacy and Poisons Act, 1933."

Ellison writes (84):

"For almost a decade 'Preludin' (phenmetrazine), has been used to lose weight and to relieve the misery that the fat endure. Weight loss has certainly been effected, but the consequences of addiction have been grave.

"I have been making inquiries, and the situation has been the same in Europe and America. The consequences of the unrestricted sale of this drug are not widely known. The cycle of elevation of mood followed by depression, hallucinations, and paranoic phenomena are very common, and when restrictions upon the purchase of this disastrous drug occur the addicts' problem will remain. Will they turn to alcohol? The sales throughout the world of Preludin must have been enormous."

Addiction to phenmetrazine hydrochloride has been reported in the United States. For example (238):

"A 23-year-old white woman, who worked as an usherette in a movie theatre, presented herself in the office with a chief complaint of 'tiredness, dizzy spells, and nervousness.' She stated that she slept well, but arose tired in the morning and had always been nervous. The remainder of the history and physical examination at that time was non-contributory.

"The initial diagnostic impression was that the patient had a psychoneurosis with mild depression. She was tried on various combinations of drugs, including methylphenidate hydrochloride (Ritalin), hydroxyzine hydrochloride (Atarax), synthetic L-triiodothyronine (Cytomel), and meprobamate (Equanil), none of which brought about any noticeable change.

"In October, 1956, the patient was given dextro-rotatory amphetamine sulfate, 10.0 mg. spansules, which brought about immediate improvement. She was seen irregularly until December, 1957, and had continued to take dextro-rotatory amphetamine sulfate the entire time, having obtained the drug from numerous other physicians and pharmacists. At this time she admitted to taking two to three capsules a day and stated, 'I can't do without them every morning.' Her weight had remained stable, and at this time she seemed in good physical condition.

"It was felt that the patient, if not already addicted to amphetamine, was well on the way to addiction. In seeking a replacement for it the patient was given phenmetrazine. We had used phenmetrazine in many patients for weight reduction, and it seemed to give many of them a mental 'lift.' Up until this time we were unaware of any possible addicting qualities of the drug. It also seemed ideal for this patient because it was a mild drug for the relief of minor depression. She was given 25.0 mg. of phenmetrazine twice daily. Between December, 1957 and September, 1958 she was seen sporadically; she was in apparent good health and even gained four pounds. At the latter date the patient revealed that she had been taking as many as fifteen tablets of phenmetrazine daily.

"The patient was tried on various so-called psychic energizers, none of which seemed to replace the phenmetrazine adequately. In December, 1958 the patient finally admitted taking at least twenty to thirty phenmetrazine tablets (500.0 to 750.0 mg.) daily for the past year. The family informed us that the patient had even forged several prescriptions in order to get the drug when pharmacists and other physicians refused to supply her. At this time it was suggested that she see a psychiatrist, to which the patient readily acquiesced, mainly because of fear that the large amounts of the drug might be harmful to her. She said that occasionally she would try to do without the drug and would feel 'shaky,' but that while taking it she seemed to have confidence and 'pep.'"

A second case is quoted, following (238):

"A 26-year-old married woman was referred by her physician for psychotherapy because of an apparent addiction to phenmetrazine hydrochloride. She was seen for a total of forty-five therapeutic hours over a period of eight months.

"Her case history revealed that she had taken medication to lose weight at the age of 17 under the direction of a physician, and while taking this medication she experienced 'unusual energy.' After a reasonable period, having lost the desired amount of weight, the medication was discontinued. Several years later, at about age 23, she began taking medication not for the purpose of losing weight, but for the express purpose of 'getting pep.' This medication had been prescribed by her physician and was apparently amphetamine or an amphetamine compound. After approximately two years of this medication, her physician gave her phenmetrazine hydrochloride. Of her own volition, she increased the dosage to as high as thirty tablets a day (600.0 mg.).

"Without the drug, the patient was frequently unable to perform even the simplest of daily chores. She had no desire to do anything productive. She felt tired and irritable, and would stay in bed, read, or sleep, and feel blue and stuporous. On occasion she could rouse herself and with great effort could muster

sufficient energy to accomplish the barest and most inescapable household tasks, but always with mounting irritability, anger and resentment. At times her depression would reach such depth that she would contemplate suicide but she never made any overt attempts on her life. She had made several unsuccessful attempts to conquer her addiction, but a characteristic lack of resistance or impulsive need for the drug would inevitably prevail.

"When she was able to avail herself of the drug she became energetic to the point of sleeplessness and seeming absence of all fatigue. She could perform prodigious amounts of work, was friendly, affable, and outgoing almost to the point of euphoria. As her need for the drug increased and the supply diminished as a result of her physician's efforts to curtail her mounting addiction, the patient sought out other physicians who were unsuspecting of her problem. She would 'gobble up' their supply in a few days rather than spread it out over as long a period as possible. Her behavior in this regard is reminiscent of the more familiar addiction to alcohol and narcotics."

. . . "In appearance the patient was of slight, though solid build, attractive and quite feminine. . . . During the course of therapy it was readily observable when she was taking the drug and when she was not. In the former instance she would appear dainty, prim, and starched and in the latter would appear disheveled and dowdy, wearing slacks or skirt and blouse."

Finally, the patient voluntarily asked for hospitalization so that she could not obtain the drug. Her request was granted.

"In the protected, cared-for atmosphere of the hospital, the patient emerged and fluorished and experienced the not-uncommon flight into health. This lasted for about one week after discharge, at which time she became depressed and shortly thereafter once again found need to resort to the use of the drug."

CARDIOVASCULAR SYSTEM DISTURBANCES

Cardiovascular reactions to phenmetrazine include palpitations (81, 108, 160, 224, 244); arrhythmias; anginal pain (19), accentuation of anginal symptoms, although the E.K.G. remained unchanged, or "a return of previous angina pectoris" (81); faintness and generalized weakness (108); and, increases, as well as decreases in systolic and diastolic blood pressures (131).

It is interesting to note that blood glucose and cholesterol levels (81) have, reportedly, "changed considerably in some patients during therapy with phenmetrazine hydrochloride. There could be detected, however, no consistent trend, either up or down, nor any apparent relation to losses or gains in weight." Also, "Cholesterol determinations showed no significant change in patients with normal values; those having low pre-treatment levels, however, evidenced some increase." (131).

Ressler (229) reported that while one patient made no complaints, the electrocardiogram, during phenmetrazine therapy, showed occasional premature ventricular contractions, although . . . "this presumably was not due to toxicity." The patient was taken off the drug for a few days, and was able to resume therapy without incident.

Dermal reactions

In Clien's patient (61) (see page 125), who, daily, took as many as 60 tablets of phenmetrazine, "there developed a generalized erythematous rash and cutaneous hyperesthesia of the lower limbs." Generalized and localized eruptions have been observed, also, in patients taking therapeutic doses of the drug. (See page 122).

According to Sidi and Bourgeois-Spinasse (252), numerous cases of alopecia have been noted, after a reducing diet, use of thyroid or phenmetrazine.

Gastrointestinal disturbances

There have been reports of gastric hyperacidity (201), occasional epigastric pain (19), sensations of gastric heaviness or fullness, "heartburn" (201), indigestion (108), gas, malaise, nausea and vomiting (19, 33, 56, 108, 220, 244). Five patients complained, during one study, that the drug caused a sensation of "butterflies in the stomach" (201). Appetite has been so effectively curbed that certain patients experienced a "flare-up" of ucler syndromes (201). When ulcer therapy was re-instituted, symptoms subsided.

There have been reports of constipation (90, 201); more rarely, of diarrhea (19, 108), and instances of definite increase in hunger sensations, increase in appetite and increase in weight (220).

31. The Pharmacological Basis of Therapeutics
(Fourth Edition, The MacMillan Co., first printing 1970, Chapter 24, pages 501–523)

AMPHETAMINE

Amphetamine, racemic β-phenylisopropylamine (Table 24–1), has powerful CNS stimulant actions in addition to the peripheral α and β actions common to sympathomimetic drugs. Its pressor effects were first described by Piness and associates (1930). Alles (1933) observed its bronchodilator, respiratory stimulant, and analeptic actions and, comparing it with epinephrine, found its cardiovascular effects to be of much longer duration but its potency to be only about 0.5 to 1.0%. The central stimulant effects of amphetamine were first used clinically by Prinzmetal and Bloomberg (1935) to treat narcolepsy and have since been employed in a variety of conditions, including obesity, fatigue, parkinsonism, and poisoning by CNS depressants. Unlike epinephrine, it is effective after oral administration and its effects last for several hours.

Pharmacological properties

Cardiovascular Responses. In man and animals, amphetamine given orally raises both systolic and diastolic blood pressures. The pulse pressure is usually increased, since amphetamine has β- as well as α-receptor activity. Heart rate is often reflexly slowed; with large doses, cardiac arrhythmias may occur. Cardiac output is not enhanced by therapeutic doses, and cerebral blood flow is little changed. The *l* isomer is slightly more potent than the *d* isomer in its cardiovascular actions.

Other Smooth Muscles. In general, smooth muscles respond to amphetamine as they do to other sympathomimetics. Bronchial muscle is relaxed, but the effect is not sufficiently marked to be of therapeutic value. The contractile effect on the urinary bladder sphincter is particularly marked, and has been used in treating enuresis and incontinence. Pain and difficulty in micturition occasionally occur. The gastrointestinal effects of amphetamine are unpredictable. If enteric activity is pronounced, amphetamine may cause relaxation and delay the movement of intestinal contents; if the gut is already relaxed, the opposite effect may be seen. The response of the human uterus varies, but usually there is an increase in tone. Contraction of the spleen probably accounts for the transient erythremia observed in some species but not in man.

Central Nervous System. Amphetamine is one of the most potent symathomimetic amines with respect to stimulation of the CNS. Many experimental and clinical studies of its central excitatory and analeptic properties have been made, comparing its potency with its congeners and with such other drugs as strychnine, picrotxin, pentylenetetrazol, nikethamide, methylphenidate, and caffeine. The results vary with the investigator, the species, the doses employed, the index of recovery selected, and the depressants against which the analeptic is measured. However, there is little question that amphetamine is an effective agent for stimulating the medullary respiratory center, lessening the degree of centrol depression caused by various drugs, and stimulating the normal cerebrospinal axis. Animals given sufficient doses of amphetamine show tremor, restlessness, increased motor activity, agitation, and sleeplessness; these effects are thought to be due to cortical stimulation and possibly to stimulation of the reticular-activating system. In contrast, the drug can obtund the maximal electroshock seizure discharge and prolong the ensuing period of depression; these properties may be related to the usefulness of amphetamine in certain cases of epilepsy. In elicitation of CNS excitatory effects, the *d* isomer (dextroamphetamine) is three to four times as potent as the *l* isomer.

In man, the marked *analeptic* action is exemplified by the fact that anesthesia produced by 0.5 g of amobarbital sodium given intravenously can be greatly lessened by 10 to 30 mg of amphetamine injected intravenously. The *psychic* effects depend on the dose and the mental state and personality of the individual. The main results of an oral dose of 10 to 30 mg are as follows: Wakefulness, alertness, and a decreased sense of fatigue; elevation of mood, with increased initiative; confidence, and ability to concentrate; often elation and

euphoria; increase in motor and speech activity. Performance of only simple mental tasks is improved; and, although more work may be accomplished, the number of errors is not necessarily decreased. Physical performance, for example, in athletes, is improved. These effects are not invariable, and may be reversed by overdosage or repeated usage. Prolonged use of large doses are nearly always followed by mental depression and fatigue. Many individuals given amphetamine experience headache, palpitation, dizziness, vasomotor disturbances, agitation, confusion, dysphoria, apprehension, delirium, or fatigue. (*See* review by Weiss and Laties, 1962.)

Fatigue. Prevention and reversal of fatigue by amphetamine have been studied extensively in the laboratory, in military field studies, and in athletics. In general, the duration of adequate performance is prolonged before fatigue appears and the effects of fatigue are at least partly reversed. The most striking improvement due to amphetamine appears to occur when performance has been reduced by fatigue and lack of sleep. Such improvement may be partly due to alteration of unfavorable attitudes toward the task. However, amphetamine reduces the occurrence of microsleeps, the brief losses of vigilance that impair performance after prolonged sleep deprivation, and thus improves execution of tasks requiring sustained attention. The drug is effective in postponing sleep and promoting wakefulness. Rapid-eye-movement (REM) sleep is reduced to about 9%, less than half the normal proportion of total sleeping time. The need for sleep may be postponed, but it cannot be indefinitely avoided. When the drug is discontinued after long use, total sleep increases, and REM sleep appears more rapidly than usual and is unduly prolonged. The pattern of sleep takes as long as 2 months to return to normal. Because the beneficial effects of the drug have to be repaid in the coin of fatigue and often depression, and because of the variable reactions in patients, amphetamine should not be used indiscriminately. (*See* reviews by Weiss and Laties, 1962; Oswald, 1968.)

Analgesia. Amphetamine and certain other sympathomimetic amines, such as causes a shift of the resting EEG toward the higher frequencies in man, but to pain threshold in dogs (Kiessig and Orzechowski, 1941). Analgesia also occurs in man and amphetamine enhances the analgesia caused by morphine and meperidine and may decrease their sedative effects. It largely eliminates the analgesic action of nitrous oxide. Amphetamine has been used in conjunction with antipyretic analgesics, but a therapeutic advantage in the use of amphetamine for analgesia, either alone or given with other drugs, has not been established.

EEG. In general, amphetamine accelerates and desynchronizes the EEG. It vauses a shift of the resting EEG toward the higher frequencies in man, but to a smaller degree than that occurring during attention. It reduces the amplitude and the duration of the large delta waves that are present during sleep after prolonged insomnia and in narcolepsy. The postconvulsive confusion and slow-wave EEG observed after electroshock seizures in monkeys are counteracted by amphetamine. In some children with petit mal and typical 3-per-second spike-and-dome dysrhythmia, amphetamine may abolish both the seizures and the abnormal EEG discharges; this may be due, in part, to an effect on alertness and activity. In children with behavorial disorders and abnormal EEG (6-cycle-per-second rhythm), amphetamine may improve behavior with or without altering the EEG. The EEG cannot be fully relied on as a criterion for the effects of amphetamine since the drug can cause behavorial arousal even when desynchronized by the EEG is prevented by atropine (Bradley, 1958). (*See* review by Toman and Davis, 1949.)

Spinal Cord, Reticular Formation, and Respiratory Center. Amphetamine facilitates monosynaptic and polysynaptic transmission in the spinal cord. In common with ephedrine, it enhances excitatory activity, promotes righting movements and postural activity, and speeds the recovery of responses in spinal, decerebrate, and decorticate animals. Amphetamine can reverse the depressant effect of barbiturates on the reticular formation, and it lowers the threshold for arousal by electrical stimulation of this region (Bradley and Key, 1958).

The *respiratory center* is stimulated by amphetamine in animals, and the rate and depth of respiration are increased. In normal man, usual doses of the drug do not appreciably increase respiratory rate or minute volume. Nevertheless, when respiration is depressed by centrally acting drugs, amphetamine may stimulate respiration, an action that has been used in the treatment of poisoning by anesthetics and hypnotics.

Depression of Appetite. Amphetamine and similar drugs are widely used in the treatment of amphetamine, first reported by Nathanson (1939), was investigated by Harris and associates (1947), who demonstrated loss of weight in dogs and in normal and obese humans treated with amphetamine. The weight loss was almost entirely due to reduced food intake and only in small measure to increased metabolism. It was concluded that the site of action was in the brain, since the drug did not reduce food intake in a small number of patients with frontal lobotomy and since sensory loss by denervation of the gastrointestinal tract in animals did not prevent the anorexigenic action. The precise central site of this action of amphetamine has not yet been established, but it may be in the lateral hypothalamic feeding area since the drug reduces food intake of rate with the ventromedial satiety area destroyed (Stowe and Miller, 1957). In man, some drug-induced loss of acuity of smell and taste has been described, and increased physical activity may also contribute to the loss of weight. In dogs, the effect is powerful and may lead to complete starvation if amphetamine is given each day 1 hour before the daily meal; food is refused even if offered for 45 minutes. Man however, develops tolerance to the drug with continued administration. The degree of appetite suppression is not enough to reduce weight continuously in obese individuals without additional dietary restriction. Amphetamine has little effect of reducing food intake in those persons whose overeating is impelled by psychological factors.

Mechanisms of the CNS Effects. Several mechanisms for the CNS effects of sympathomimetic amines have been suggested, each based on an analogy with known effects of these drugs on tissues other than the brain. Amphetamine depolarizes and then blocks cells in autonomic ganglia, and Reinert (1960) has suggested that a similar nicotine-like action may account for its central effects. This is unlikely, since ephedrine, which has similar although less marked central effects, does not share the depolarizing action of amphetamine. An indirect action by the local release of norepinephrine, as in peripheral tissues, has been suggested. However, amphetamine still exerts its central stimulant effects in animals and patients treated with reserpine, a drug that depletes the brain catecholamines. The possibility that amphetamine acts centrally by inhibiting MAO and thus enhancing the actions of brain norepinephrone has already been mentioned. There are many reasons to reject this hypothesis, among them the fact that amphetamine still stimulates subjects who have previously received MAO inhibitors. With amphetamine, as with other drugs, here is no advantage in postulating an indirect mechanism of action until a direct action on the cells has been disproved. The possibility that amphetamine may act on 5-HT receptors in the brain, as it does on several varieties of smooth muscle (Innes, 1963), has been discussed by Vane (1960). The central effects do not depend on changes in blood pressure and occur without an increase in total cerebral blood flow.

Metabolic Effects. Although large doses of amphetamine markedly increase oxygen consumption in animals, conventional therapeutic doses cause either no change, a small fall, or a modest rise (10 to 15%) in the metabolic rate in man. When an increase does occur, it is neither as constant nor as significant as that caused by epinephrone, but it is more sustained. Some patients show a slight increase in body temperature. The apparent calorigenic action may be due to restlessness caused by the drug. Amphetamine increases the plasma concentration of free fatty acids but, in contrast to epinephrine, does not modify carbohydrate utilization or increase blood glucose or lactate, and the respiratory quotient is unaltered.

Preparations, Administration, and Dosage. *Amphetamine Sulfate*, N.F., is a white, water-soluble powder, available in 5- and 10-mg tablets. The *d* isomer is

available as *Dextroamphetamine Phosphate*, NF., in 5-mg tablets; and as *Dextroamphetamine Sulfate*, U.S.P. (DEXEDRINE), in 5-, 10-, and 15-mg capsules, in 5-mg tablets, in an elixir (1 mg/ml), and as an official injection (20 mg/ml). *Amphetamine base* is a volatile liquid that changes to the carbonate when exposed to air; it was formerly used in inhalers to treat nasal congestion. For this purpose it has been replaced by various sympathomimetic amines that have considerably less central stimulant action. Amphetamine is marketed under a variety of trade names, perhaps the best known of which is BENZEDRINE.

With the usual oral dose of 2.5 to 5.0 mg of dextroamphetamine, the effects appear within ½ to 1 hour. The patient's sensitivity should first be tested with a dose of 2.5 mg. For chronic medication the usual dosage is 5 mg, two or three times daily. The last dose is generally given not later than 4 p.m. to avoid insomnia. For parental injection of amphetamine, the subcutaneous rouse is preferred. Vascular effects appear within 5 minutes. The usual dose of amphetamine is 10 mg, but larger doses are often given in treating poisoning by central depressants. Intravenous injection is not recommended. For local application, a 1% aqueous solution of amphetamine sulfate may be used as a mydriatic or as a nasal decongestant.

Toxicity and Side Effects. The *acute toxic effects* of amphetamine are usually extensions of its therapeutic actions and, as a rule, result from overdosage. The *central effects* commonly include restlessness, dizziness, tremor, hyperactive reflexes, talkativeness, tenseness, irritability, weakness, insomnia, fever, and sometimes euphorit. Confusion, assaultiveness, increased libido, anxiety, delirium, hallucinations, panic states, and suicidal or homicidal tendencies occur, especially in mentally ill patients. Fatigue and depression usually follow the central stimulation. *Cardiovascular effects* are common and include headache, chilliness, pallor or flushing, palpitation, cardiac arrhythmias, anginal pain, hypertension or hypotension and circulatory collapse. Excessive sweating occurs, and symptoms referable to the *gastrointestinal system* include dry mouth, metallic taste, anorexia, nausia, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma, and cerebral hemorrhages are the main pathological finding.

The *toxic dose* of amphetamines varies widely. Toxic manifestations occasionally occur as an idiosyncrasy after as little as a mg, but are rare with doses of less than 15 mg. Severe reactions have occurred with 30 mg, yet doses of 400 to 500 mg have been survived. Death has followed rapid injection of 120 mg. Larger doses can be tolerated after chronic use of the drug.

Treatment of acute amphetamine intoxication should include acidification of the urine by administration of ammonium chloride. Excretion of amphetamine is negligible in alkaline urine, and is vastly increased in acid urine. Sedation with barbiturates and especially with chlorpromazine (Espelin and Done, 1968) is usually indicated, and a nitrite or a rapidly acting α-receptor blocking agent should be given if hypertension is marked.

Chronic amphetamine intoxication causes symptoms similar to those of acute overdosage, but abnormal mental conditions are more common. Weight loss may be marked, and occasionally dermatitis occurs. A psychotic reaction with vivid hallucinations and paranoid delusions, often mistaken for schizophrenia, is the most common serious effect. Recovery is usually rapid after withdrawal of the drug, but occasionally the condition becomes chronic. In these persons amphetamine may act as a precipitating factor hastening the onset of an incipient schizophrenia.

Precautions and Contraindications. Abuse of amphetamine by the laity as a means of overcoming sleepiness and of increasing energy and alertness should be discouraged. The drug should be used only under medical supervision. The additional *contraindications* and *precautions* in the use of amphetamine are generally similar to those described above for epinephrine. The drug should be used with care in patients with anorexia, insomnia, asthenia, psychopathic personality, or a history of homicidal or suicidal tendencies.

Addiction and Tolerance. *Addiction* often occurs to amphetamine and dex-

troamphetamine, as discussed in Chapter 16. *Tolerance* almost invariably develops to the anorexigenic effect of amphetamines, and it often seen also in the need for increasing doses to maintain improvement of mood in psychiatric patients. A period without the drug usually restores the patient's sensitivity. Tolerance is striking in addicts, and a daily intake of 1700 mg without apparent ill effects has been reported. Development of tolerance is not invariable, and cases of narcolepsy have been treated for years without an increase in the initially effective dose.

Therapeutic Uses. Amphetamine and dextroamphetamine are used chiefly for their CNS effects. They have been largely supplanted by other sympathomimetic agents for their peripheral effects. Dextroamphetamine, with greater CNS action and less peripheral action, is generally preferred to amphetamine; it is used in obesity, narcolepsy, parkinsonism, depressive syndromes, behavior disorders, and petit mal epilepsy, and in conjunction with supportive therapy for central depressant drug intoxication. These uses are discussed later in this chapter.

METHAMPHETAMINE

Methamphetamine is closely related chemically to amphetamine and ephedrine (Table 24–1) Its *pharmacological actions* are similar to those of amphetamine, but it exhibits a different ratio between central and peripheral actions. Small doses have prominent central stimulant effects without significant peripheral actions; somewhat larger doses produce a sustained rise in blood pressure due in main mainly to cardiac stimulation. Cardiac output is increased, although the heart rate may be reflexly slowed. The drug has considerable β-receptor activity, and increases blood flow in skeletal muscle. Peripheral venous pressure is increased and venous constriction occurs. These factors tend to increase the venous return and, therefore, the cardiac output. Pulmonary aterial pressure is raised, probably secondary to increased cardiac output. Renal blood flow is also enhanced. Although moderate doses stimulate cardiac contraction, excessive doses depress the myocardium. The cardiovascular effects of methamphetamine are compared with those of several other pressor amines in Table 24–3. (*See* Aviado, 1959; Ekestein and Abboud, 1962.)

Preparations and Dosage. *Methamphetamine Hydrochloride*, U.S.P., is the *d* isomer; it is marketed under a confusing number of trade names, including DESOXYN, EFROXINE, METHEDRINE, NORODIN, and SYNDROX. It is available in tablets containing 2.5, 5, 7.5, and 8 mg of drug; in sustained-release tablets containing 5, 10, and 15 mg; as an elixir (0.66 and 1 mg/ml); and in sterile solution (20 mg/ml). The usual oral dose for central effects varies from 2.5 mg daily to 5 mg three times daily. For the pressor effect, a dose of 10 to 30 mg is given intramuscularly.

TABLE 24-3.—EFFECTS OF SOME SYMPATHOMIMETIC AMINES THAT RAISE BLOOD PRESSURE BY ALTERING VASCULAR TONE OR CARDIAC OUTPUT, OR BOTH

	Effective doses in adult man (mg)	Heart rate		Force of cardiac contraction		Cardiac output	Coronary blood flow	Total peripheral resistance	Blood pressure
		Reflex activity		Small doses	Large doses				Systolic/diastolic
		Normal	Blocked						
Epinephrine	0.5–1.0 s.c.	+ or −	+	+	+	+	+	−	+/−
Norepinephrine (Levarterenol)	0.002–0.008/min i.v. infusion	−	+	+	+	0 or −	+	+	+/+
Ephedrine	15–50 s.c., i.m., 8–10/min i.v.	+ or −	+	+	−	+	+	+ or −	+/+
Methamphetamine	10–30 i.v., i.m.	+ or −	+	+	−	+	----------	0, +, or −	+/0
Mephentermine	10–30 i.v., i.m.	+ or −	+	+	−	+	+	+	+/+
Hydroxyamphetamine	5–10 i.v., 10–20 s.c.	+ or −	+	+	−	+	+	+	+/+
Metaraminol	5–10 i.v., i.m.	+ or −	+	+	−	0 or −	+	+	+/+
Phenylephrine	0.5–1.0 i.v., 3–10 s.c.	−	0	0	+	−	+	+	+/+
Methoxamine	5–10 i.v., 10–20 i.m.	−	0 or −	0	−	0 or −	0	+	+/+

Note: 0 = no effect; + = increased; − = decreased; s.c. = subcutaneous; i.m. = intramuscular; i.v. = intravenous.

This compilation is from data obtained under various experimental conditions either in dogs or in normal human subjects. (Modified from Aviado, 1959, and Zaimis, 1964.)

Therapeutic Uses. Methamphetamine is principally used for its *central effects*, which are more pronounced than those of amphetamine and are accompanied by less prominent peripheral actions. It is also employed to maintain blood pressure in certain *hypotensive states* (*e.g.*, in spinal anesthesia). These uses are discussed below in the therapeutic section of this chapter.

EPHEDRINE

Ephedrine occurs naturally in various plants. It was used in China for over 5000 years before being introduced into Western medicine in 1924 (*see* Chen and Schmidt, 1930). Prepared synthetically in 1927, it has since been used extensively for clinical conditions in which either peripheral or CNS actions of sympathomimetic drugs are desired. Its central actions are less pronounced than those of the amphetamines, which have therefore superseded ephedrine for all except peripheral effects. Ephedrine stimulates both α and β receptors and has clinical uses related to both types of action. The drug owes part of its peripheral action to release of norepinephrine, but it also has direct effects on receptors and exhibits substantial effects in reserpine-treated animals and man (Krogsgaard, 1956). Tachyphylaxis develops to its peripheral actions, and rapidly repeated doses become less effective, probably as a result of the depletion of norepinephrone stores. Small doses of ephedrine increase and large doses reduce the excitatory effects of catecholamines and sympathetic nerve stimulation; the mechanisms involved, although much studied, are as yet incompletely understood.

Since ephedrine contains two asymmetrical carbon atoms, six compounds are possible. Only *l*-ephedrine and racemic ephedrine are commonly used clinically; their pharmacological properties and uses are essentially similar. The structure of ephedrine is depicted in Table 24–1.

Pharmacological Actions. Ephedrine differs from epinephrine mainly in its efficacy after oral administration, its much longer duration of action, its more pronounced central actions, and its much lower potency. *Cardiovascular effects* of ephedrine are in many ways similar to those of epinephrine, but they persist seven to ten times as long. The drug elevates the systolic and usually also the diastolic pressure in man, and pulse pressure increases. Pressor responses are due partly to vasoconstriction but mainly to cardiac stimulation, provided venous return is adequate. The heart rate may not be altered, but it increases if vagal reflexes are blocked. The force of myocardial contraction and cardiac output are augmented by the drug; the renal and splanchnic blood flows are decreased whereas the coronary, cerebral, and muscle blood flows are increased. The pressor responses to ephedrine are blocked by α-blocking agents, but reversal, if it occurs, is slight. The cardiovascular effects of ephedrine are compared with those of other sympathomimetic amines in Table 24–3. *Bronchial muscle* relaxation is less prominent but more sustained with ephedrine than with epinephrine. Consequently, ephedrine is of value only in milder cases of acute asthma and in chronic cases that need continuel medication. *Mydriasis* occurs after local application of the drug to the eye. Reflexes to light are not abolished, accommodation is unaffected, and intraocular pressure is unchanged. Ephedrine and other sympathomimetics are of little use as mydriatics in the presence of inflammation. The drug is less effective in individuals who have heavily pigmented irides than in those in whom the iris is light colored, a difference attributed by Angenent and Koelle (1953) to a greater content of dopa oxidase and other enzymes in heavily pigmenter irides. Other smooth muscles are generally affected by ephedrine in the same manner as by epinephrine. However, the activity of the human *uterus* is usually reduced by ephedrine, regardless of the effect of epinephrine, and thus the agent has been used to relieve the pain of dysmenorrhea. Ephedrine is less effective than epinephrine in elevating the level of *blood sugar*. The *central nervous system effects* of ephedrine are similar to of amphetamine but are considerably less marked.

Preparations, Administration and Dosage. *Ephedrine Sulfate*, U.S.P., is the *l* isomer. It is available in 25-mg tablets and in 25- and 50-mg capsules; the oral dose varies from 15 to 50 mg. For continued medication small doses are given at 3- to 4-hour intervals. Sterile solutions (25 and 50 mg/ml) are available; in hypotensive states, 15 to 50 mg may be given subcutaneously or, if a rapid

response is necessary, 20 mg can be injected intravenously. Solutions of 1 and 3% in water and 1% in jelly are available for nasal mucosal decongestion, and aqueous solutions of 3 to 5% are applied to the eye to produce mydriasis.

Toxic Reactions. These are similar to the untoward reactions observed after epinephrine, with additional reactions referable to the CNS effects of ephedrine. Insomnia is common with continued medication, but it is readily counteracted by barbiturates. *Precautions* in the use of ephedrine are similar to those outlined for epinephrine and the amphetamines.

Therapeutic Uses. The main clinical applications of ephedrine are in *bronchospasm*, in *Stokes-Adams syndrome*, as a *nasal decongestant*, as a *mydriatic*, and in certain *allergic disorders*. The drug has also been employed as a *pressor* agent, particularly during spinal anesthesia, and for its central stimulant action in *narcolepsy*. These uses are discussed below in the threapeutic section of this chapter.

MEPHENTERMINE

Mephentermine is N-methylphenyl-*tertiary*-butylamine (Table 24–1). It is one of several pressor agents currently used in various hypotensive conditions. Its duration of action is prolonged, pressor effects lasting 30 an 60 minutes after subcutaneous doses and up to 4 hours after intromuscular doses. Its peripheral actions and effects appear to be very similar to those of methamphetamine, but its central actions are relatively feeble and of no clinical use. Mephentermine increases blood pressure in *man* mainly by cardiac stimulation. Cardiac contraction is enhanced and cardiac output increased. The change in heart rate is variable, depending on the degree of vagal tone. α-Receptor activity of the drug appears to be relatively weak, and its contribution to the pressor effect is as yet unclear. Peripheral resistance increases in normal subjects, but may be unchanged as lessened in patients with hypotension. In such patients the blood pressure may not increase in spite of a greater cardiac output, indicating a vasodilator effect (Udhoji and Weil, 1965). Cerebral and coronary blood flows are increased, forearm blood flow is reduced, and venous tone is increased. In *dogs*, coronary and splanchnic blood flows increase, there may be some reduction in renal blood flow, and blood flow to the foreleg is decreased; excessive doses depress the myocardium. Tachyphylaxis occurs readily with repeated large doses in dogs, but it has not been reported in man. Enough α-receptor activity (vasoconstriction) is present for the drug to be used by inhalation to cause nasal mucosal decongestion. CNS effects may occur with large doses of mephentermine. These include drowsiness, weeping, incoherence, and convulsions, and rapidly disappear on withdrawal of the drug. In Table 24–3 the cardiovascular effects of mephentermine are compared with those of some other pressor amines. (For references, *see* Aviado, 1959; Eckstein and Abboud, 1962; Zaimis, 1968.)

Preparations and Dosage. *Mephentermine Sulfate*, U.S.P. (WYAMINE), is available in sterile solution (15 and 30 mg/ml) for parenteral injection. Given *subcutaneously* or *intramuscularly* the dose is usually 10 to 30 mg. Slow *intravenous infusions* are also given, the rate being varied to produce the desired pressor effect. Oral tablets (12.5 to 25 mg) are also marketed.

Therapeutic Uses. Mephentermine is mainly used as a pressor agent in various *hypotensive states*, as discussed below in the therapeutic section of this chapter.

HYDROXYAMPHETAMINE

Hydroxyamphetamine, synthesized in Germany in 1913, came into clinical use only after reinvestigation 2 decades later (Alles, 1933; Alles and Prinzmetal, 1933). Its chemical structure differs from that of amphetamine only by the addition of a 4-OH group (*see* Table 24–1).

Pharmacological Actions. In many respects the actions of hydroxyamphetamine resemble those of ephedrine, with the exception that the drug almost entirely lacks CNS stimulant activity. The duration of action after oral or subcutaneous administration is from 90 to 120 minutes; after intravenous injection, 20 to 30 minutes.

Cardiovascular Actions. In man, as in other special, the drug elevates systolic and diastolic pressures; the increase is apparently due more to cardiac stimulation than to enhanced peripheral resistance, although the latter does occur. Heart rate is often reflexly slowed at the height of the pressor response, and cardiac irregularities, probably due to reflex vagal activity, have been reported. The cardiac stimulant action of the drug has been used to maintain an

adequate ventricular rate in Stokes-Adams syndrome. Reflex vagal activity does not, of course, alter the effects of hydroxyamphetamine or other sympathomimetic drugs on the ventricle when complete heart block is present. In dogs, cardiac output and coronary blood flow increase, while cutaneous, splanchnic, and renal blood flows decrease. Pulmonary vessels are not constricted by the drug. The effects of hydroxyamphetamine on various vascular beds in man have not been established. Responses of cutaneous blood vessels in man are anomalous in that they are not effectively constricted by the drug, and systemic doses do not lower skin temperature. The duration of local anesthesia is not prolonged when the drug is injected with local anesthetics. However, hydroxyamphetamine constricts the vessels of the nasal mucosa, and this property has been used clinically. Venous constriction may play a role in causing the pressor response (Stead and Kunkel, 1939). In Table 24–3 the cardiovascular effects of hydroxyamphetamine are compared with those of other pressor amines. (*See* Abbott and Henry, 1937; Iglauer and Molle, 1943; review by Aviado, 1959.)

Smooth Muscle. Hydroxyamphetamine exerts both α and β activity on smooth muscle. Actions on α receptors are put to effective clinical use for mydriasis, by instillation of the drug in the eye, and for nasal decongestion, by application of nasal drops or a spray. The β-receptor activity of the compound is reflected in relaxation of bronchial muscle, but this is too feeble to be of value.

Preparations and Dosage. *Hydroxyamphetamine Hydrobromide,* U.S.P. (PAREDINE HYDROBROMIDE), is available in 20-mg tablets and as a 1% ophthalmic solution. The oral dose in Stokes-Adams syndrome varies from 20 to 60 mg, three to five times daily.

Therapeutic Uses. The clinical applications, mainly in *hypotensive states,* in *Stokes-Adams syndrome,* as a *mydriatic,* and as a *nasal decongestant,* are discussed below in the therapeutic section of this chapter.

METARAMINOL

Metaraminol, 3-hydroxyphenylisopropanolamine (Table 24–1), is used almost exclusively for the treatment of hypotensive states. Its action is mainly direct and, therefore, does not depend on release of norepinephrine. It is primarily a pressor agent with actions similar to those of norepinephrine, but it is much less potent and has a more prolonged action. It lacks CNS stimulant effects. Metaraminol is absorbed after oral administration; however, for equal effects, oral doses must be five or six times greater than doses given intromuscularly or intravenously. The pressor effect of an intramuscular dose of 5 mg lasts for about 1½ hours.

Pharmacological Actions. The *cardiovascular* actions in man are reflected in a sustained rise in systolic and diastolic pressures, almost entirely due to vasoconstriction and usually accompanied by a marked reflex bradycardia. Occasionally sinus arrhythmia also occurs. In normotensive subjects, cardiac output it unchanged or may decrease slightly, but the force of myocardial contraction is enhanced. Cardiac output increases strikingly when slowing of the heart is prevented by atropine. Increased cardiac output may play a larger role in patients with hypotension and shock, in which conditions the drug increases cardiac output as well as peripheral resistance. Metaraminol increases venous tone and recreases renal and cerebral blood flows, the latter even when blood pressure is raised as much as 40%. In dogs, limb and splanchnic blood flows are also decreased and coronary blood flow is increased, but these effects have not yet been confirmed in man. Pulmonary vasoconstriction occurs in man, and the pulmonary blood pressure is elevated by the drug even when cardiac output in reduced. Systemic pressor responses to metaraminol appear to be mainly due to peripheral vasoconstriction, but cardiac stimulation can also be demonstrated and may play a small role in the pressor effect. In Table 24–3 the cardiovascular effects of metaraminol are compared with those of other sympathomimetic amines. (For references, *see* Aviado, 1959; Eckstein and Abboud, 1962; Zaimis, 1969.)

Preparations and Dosage. *Metaraminol Bitartrate,* U.S.P. (ARAMINE BITARTRATE), is available in 1-ml ampuls and 10-ml vials as a sterile solution (10 mg/ml) for intramuscular injection, usually in a dose of 5 to 10 mg, or, after suitable dilution, for intravenous infusion. The rate of administration is regulated according to the individual's response to the drug. Subcutaneous injections should be avoided since tissue sloughing may occur.

Therapeutic Uses. The principal use of metaraminol is as a pressor agent in certain *hypotensive states,* the treatment of which is discussed below in the therapeutic section of this chapter.

PHENYLEPHRINE

Phenylephrine differs chemically from epinephrine only in lacking an OH in the 4 position on the benzene ring (Table 24–1). It was first studied by Barger and Dale (1910), but was not used clinically until years later when it was found to have greater potency than other monohydroxyl derivatives. Phenylephrine is a powerful α-receptor stimulant with little effect on the β receptors of the heart. A direct action on receptor accounts for the greater part of its effects, only a small part being due to its ability to release norepinephrine. Central stimulant action is minimal, and the clinical applications of the drug depend on α-receptor activity.

Pharmacological Actions. The predominant actions of phenylephrine are on the *cardiovascular system* (*see* Table 24–3). Intravenous, subcutaneous, or oral administration causes a rise in systolic and diastolic pressures in man and other species. Responses are more sustained than those to epinephrine, lasting 20 minutes after intravenous and as long as 50 minutes after subcutaneous injection. Accompanying the pressor response to phenylephrine is a marked reflex bradycardia that can be blocked by atropine; after atropine, large doses of the drug increase the heart rate only slightly. In man, cardiac output is slightly decreased and peripheral resistance is considerably increased. Renal and cutaneous blood flows are reduced. Circulation time is slightly prolonged, and venous pressure is slightly increased; venous constriction is not marked. In experimental animals, most vascular beds are constricted, and cerebral, splanchnic, and limb blood flows are reduced but coronary blood flow is increased. Pulmonary vessels are constricted, and pulmonary arterial pressure is raised. Not all the effects of phenylephrine on the various vascular beds observed in experimental animals have yet been confirmed in man, but it is clear that the drug is a powerful vasoconstrictor, with properties very similar to those of norepinephrine but almost completely lacking the chronotropic and inotropic actions on the heart. Cardiac irregularities are seen only very rarely even with large doses, and the reflex slowing is sufficient to permit use of the drug to end attacks of paroxysmal atrial tachycardia. (For references, *see* Aviado, 1959; Eckstein and Abboud, 1962.)

Preparations, Administration, and Dosage. *Phenylephrine Hydrochloride*, U.S.P. (ISOPHRIN, NEO-SYNEPHRINE), is the *l* isomer. It is available as sterile solutions (2 and 10 mg/ml) for parenteral use, 10- and 25-mg oral capsules, an elixir (1 mg/ml), various nasal (0.125, 0.25, 0.5 and 1.0%) and ophthalmic (0.125, 2.5, and 10%) solutions, and an ophthalmic emulsion (10%). Roughly equipressor doses are 0.8 mg intravenously, 5 mg subcutaneously or intramuscularly, and 250 mg orally. However, absorption after oral administration is unreliable. For treatment of hypotension during spinal anesthesia, the usual dose is 5 to 10 mg, administered intramuscularly. The rate of intravenous infusion in hypotentive states should be regulated according to the patient's response.

Therapeutic Uses. Phenylephrine is used mainly as a *nasal decongestant*, a pressor agent in *hypotensive states*, a *mydriatic*, a local vasoconstrictor (0.05%) in solutions of local anesthetics, and in the relief of *paroxysmal atrial tachycardia*. These uses are discussed below in the therapeutic section of this chapter.

METHOXAMINE

Methoxamine is β-hydroxy-β-(2,5-dimethoxyphenyl) isopropylamine (Table 24–1). Its pharmacological properties are almost exclusively those characteristic of α-receptor stimulation. The outstanding effect is an increase in blood pressure due entirely to vasoconstriction. The drug has virtually no stimulant action on the heart and lacks β-receptor action on smooth muscle. It causes little or no central nervous system stimulation.

Pharmacological Actions. Methoxamine, given intravenously or intramuscularly in man, causes a rise in systolic and diastolic blood pressures that persists for 60 to 90 minutes. The pressor effect is due almost exclusively to an increase in peripheral resistance. Cardiac output is decreased or unchanged. Renal blood flow is reduced in man to a greater extent than after equipressor doses of norepinephrine or metaraminol. Cerebral, splanchnic, and limb blood flows are reduced in dogs, and coronary blood flow is unchanged; whether the effects are similar in man is not yet known. In man, the venous pressure increases, but the constrictor action on forearm veins is feeble. Methoxamine has no significant stimulant action on the heart, and does not increase the ventricular rate in patients with heart block. Reflex bradycardia is prominent, and, therefore,

the drug is used clinically to relieve attacks of paroxysmal atrial tachycardia. When the vagal effects are blocked by atropine, methoxamine often slows the heart slightly. This residual slowing may be due to the β-receptor blocking property of methoxamine, as shown in dogs by Imai and associates (1961); this blockade would antagonize any direct cardioaccelerator effect of the drug. Methoxamine does not appear to precipate cardiac arrhythmias and can even improve rhythm in patients with certain ventricular arrhythmias due to myocardial infarction or digitalis toxicity (Brill *et al.*, 1959). In contrast to epinephrine, methoxamine prolongs ventricular muscle action potentials and refractory period and slows A–V conduction (Gilbert *et al.*, 1958). In Table 24–3 the cardiovascular effects of methoxamine are compared with those of other drug pressor amines. Tachyphylaxis to the drug occurs in experimental animals, but has not been reported in man. (*See* reviews by Aviado, 1959; Eckstein and Abboud, 1962; Zaimis, 1968.)

In man, pressor doses of methoxamine cause pilomotor stimulation and often a desire to micturate. Occasionally tingling of the extremities and a feeling of coldness follow intravenous injection of the drug.

Preparations, Administration, and Dosage. *Methoxamine Hydrochloride*, U.S.P. (VASOXYL), is available in 1-ml ampuls (10 or 20 mg/ml) as a solution for intramuscular injection. The dose varies from 10 to 80 mg. Intravenous injections of 5 to 10 mg may also be given with the precautions properly accorded to intravenous injections of sympathomimetic amines. The drug is also marketed as a nasal solution (0.5%).

Therapeutic Uses. Methoxamine is almost solely used as a pressor agent in *hypotensive states* and to end attacks of *paroxysmal atrial tachycardia*. It is also employed as a nasal mucosal *decongestant*. These conditions are discussed below in the therapeutic section of this chapter.

METHOXYPHENAMINE

Methoxyphenamine, β-(σ-methoxyphenyl) isopropylmethylamine, differs from methamphetamine only in having a methoxy substituent in the 2 position on the benzene ring (Table 24–1), but its pharmacological properties differ greatly. Its main sympathomimetic action is on β receptors of smooth muscle. By this action, the drug causes *bronchodilatation*, its usual clinical use. Its bronchodilator effect is greater than that of ephedrine, and the accompanying cardiovascular effects are considerably less. The α-receptor and central stimulant actions of the drug are minimal. Methoxyphenamine also exhibits weak antihistaminic properties.

Preparations and Dosage. *Methoxyphenamine hydrochloride* (ORTHOXINE HYDROCHLORIDE) is marketed in 100-mg tablets and in a syrup (10 mg/ml). The usual oral dose is 50 to 100 mg, repeated every 3 or 4 hours if necessary.

Therapeutic Uses. Methoxyphenamine is used mainly in mild cases of *asthma* and other *allergic conditions*, as discussed below in the therapeutic section of this chapter.

Nylidrin and isoxsuprine

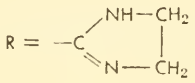
These two sympathomimetic agents are the outcome of a search for long-acting, highly selective, β-receptor stimulants that would dilate blood vessels supplying skeletal muscles and exert a minimum of other typical sympathomimetic actions. Both drugs have large substituents on the amino group (conferring β-receptor activity) and a methyl substituent on the side chain (permitting oral absorption and long action). Their chemical structures are shown in Table 24–1. The pharmacological actions of nylidrin and isoxsuprine are similar and typical of β-receptor stimulants. The main actions are dilation of blood vessels in skeletal muscle and stimulation of the heart. In normal subjects, the mean arterial pressure is little changed; systolic pressure is usually slightly raised, while diastolic pressure falls. Heart rate and cardiac output increase. Blood flow in muscle increases, and peripheral resistance falls. Nylidrin has also been reported to increase cerebral blood flow in man (Eisenberg, 1960). Both drugs relax smooth muscle in most organs, but this effect is insufficient for clinical use. The uterine relaxant action of isoxsuprine has been advocated for *dysmenorrhea* and *threatened premature labor*, but the value of the drug for these purposes has not been established. *Disturbing side effects* occasionally occur, including nervousness, trembling, weakness, dizziness, palpitation, nausea, and vomiting. Both drugs have been proposed for the treatment of a variety of *peripheral vascular disorders*. (*See* Freedman, 1955; Caliva *et al.*, 1959; Hyman and Winsor, 1969.)

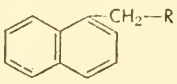
Preparations, Administration, and Dosage. *Nylidrin Hydrochloride*, N.F. (ARLIDIN), is available in 6-mg oral tablets. *Isoxuprine Hydrochlodire*, N.F. (VASODILAN) is marketed as 10-mg oral tablets. Both are well absorbed after oral administration. The usual doses are 6 mg, three to six times daily, for nylidrin; and 5 to 10 mg, three or four times daily, for isoxsuprine. Both drugs are available in sterile solutions (5 mg/ml) for intramuscular injection; the dose is 2.5 to 5 mg for nylidrin and 5 to 10 mg for isoxsuprine.

Miscellaneous sympathomimetic drugs

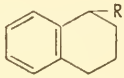
Several sympathomimetic drugs are used primarily as vasoconstrictors for local application to the nasal mucous membrane or the eye. Their structures are depicted in Tables 24–1 and 24–4. They cary from simple aliphatic amines to complex imidazoline derivatives. Their nonproprietary and trade names as well as available preparations are as follows: *Propylhexedrine*, N.F. (BENZEDREX), nasal inhaler (250 mg); *Tuaminoheptane Sulfate*, N.F. (TUAMINE), 1% nasal solution; *Naphazoline Hydrochloride*, N.F. (PRIVINE), 0.05% nasal jelly, nebulizer, or nasal solution and 0.1% ophthalmic solution; *Tetrahydrozoline Hydrochloride*, N.F. (TYZINEC), 0.05% nasal solution and 0.1% ophthalmic solution; *Oxymetazoline Hydrochloride*, N.F. (AFRIN), 0.05% nasal solution; *Xylometazoline Hydrochloride*, N.F. (OTRIVIN), and 0.05 and 0.1% nasal solution.

Table 24–4. IMIDAZOLINE DERIVATIVES USED AS NASAL DECONGESTANTS

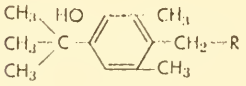




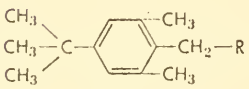
Naphazoline



Tetrahydrozoline



Oxymetazoline



Xylometazoline

Cyclopentamine Hydrochloride, N.F. (CLOPANE), is available as a 0.5 or 1.0% nasal solution. It has been used as a pressor agent and causes little central excitement. The intramuscular dose is 25 mg.

Phenylpropanolamine Hydrochloride, N.F. (PROPADRINE), shares the pharmacological properties of ephedrine and is approximately equal in potency except that it causes less CNS stimulation. The drug is marketed as such, and it is also the ingredient of numerous proprietary mixtures that are marketed for the oral treatment of nasal and sinus congestion, usually in combination with an antihistaminic drug.

Metaproterenol and *protokylol* are long-acting derivatives of isoproterenol. Like the parent compound they selectively stimulate β-receptors and are used as bronchodilators in the treatment of bronchial asthma. Compared with isoproternol, they are more stable in the body, a property permitting oral administration, and have a longer duration of action. Side effects are similar to those of isoproterenol. Given orally they may reduce the frequency and the severity of asthmatic attacks but do not abort an acute attack. Inhaled as an aerosol, metaproterenol acts as promptly and efficiently as isoproterenol, and remains effective for 3 to 6 hours (Holmes and Morgan, 1968). *Metaproterenol* (*Orciprenaline*, B.P. [ALUPENT]), is marketed in Europe as a 20-mg oral tablet, a syrup (2 mg/ml), a metered aerosol (0.75 mg per dose), a 5% inhalant solution, and a solution (0.5 mg/ml) for parental use, but it is not yet available for general use in North America. *Protokylol* (CAYTINE) is available in 2-mg oral tablets, a solution for injection (0.5 mg/ml), and a 1% inhalant solution. Usual oral doses, given four times daily, are 20 mg for metaproterenol and 2 to 4 mg for protokylol. Intramuscular doses are 0.5 mg for metaproterenol, repeated after 30 minutes if necessary, and up to 0.5 mg for protokylol.

Dopamine (*3,4-dihydroxyphenylethylamine*) is the immediate precursor in the synthesis of norepinephrine in the body. It increases blood pressure in *man*, mainly by enhancing cardiac contraction. Peripheral resistance is not increased. Cardiac output, renal blood flow, and sodium excretion increase in normal subjects and in patients with congestive heart failure. The renal vasodilatation, which is unusual in that it is not blocked by either α- or β-blocking agents, presents possible advantages in the treatment of hypotension and shock, and the drug is being used experimentally for these conditions. (*See* MacCannell *et al.*, 1966.) Its possible role in basal ganglia function is discussed alsewhere (see *Index*).

THERAPEUTIC USES OF SYMPATHOMIMETIC DRUGS

As a result of the ubiquitous distribution of sympathetic nerves and adrenergic receptor systems in the body and their involvement in a variety of clinical disorders, and because sympathomimetic agents not only exhibit α- and β-receptor activity but also exert, in several instances, prominent CNS excitatory effects, it is not surprising that drugs in this class have a large number of important therapeutic uses. These clinical applications are considered in the following pages, under appropriate headings related both to the disease states and to the locus and mechanism of action of sympathomimetic drugs.

Use of Vascular Effects. *Control of Hemorrhage.* The vasoconstrictor action of epinephrine may control superficial hemorrhage from skin and mucous membranes when the drug is applied topically as a spray or on cotton or gauze pledgets. It is effective only against bleeding from arterioles and capillaries and does not control venous oozing or hemorrhage from larger vessels. Obviously there is no rationale for systemic use of the drug in internal hemorrhage. Given orally in gastric hemorrhage, it is of questionable value and can act only locally by constricting small mucosal vessels. Sympathomimetics other than epinephrine are seldom applied to bleeding surfaces.

Decongestion of Mucous Membranes. Sympathomimetic amines with α-receptor action cause marked vasoconstriction and blanching when applied to nasal and pharyngeal mucosal surfaces. They are therefore useful in the treatment of mucosal congestion accompanying *hay fever, allergic rhinitis, acute coryza, sinusitis*, and other respiratory conditions. The short duration of action of many of the amines, such as epinephrine, limits their value in shrinking the nasal mucosa, and longer-acting congeners are more commonly used in these conditions. Some of the sympathomimetic amines more widely used for nasal decongestion are indicated in Table 24–4, and as *N* in Table 24–1. All have the disadvantage that their use may be followed by "aftercongestion" and that

prolonged use often results in chronic rhinitis. Some (*e.g.*, naphazoline) also irritate the nasal mucosa, causing a brief but sharp stinging sensation when first applied. Naphozoline and tetrahydrozoline should not be administered to children, since CNS depression leading to coma and marked reduction in body reduction in body temperature may occur, especially in infants. CNS depression has not been reported with oxymetazoline or xylometazoline, which have the imidazoline group common to the two above-mentioned nasal decongestants but lack the naphthyl group. The structural similarity suggests that these drugs should not be used in children. Amphetamine was formerly used widely as a nasal decongestant, but inhalers containing this drug were withdrawn from use, since they provided a ready supply of the drug for abuse of its euphoric effect. Some nasal decongestants and their usual concentrations as nasal drops or spray are as follow: amphetamine, 1%; ephedrine, 1%, hydroxyamphetamine, 1%; mephentermine, 0.5%; methoxamine, 0.5%; naphazoline, 0.05%; oxymetazoline, 0.05%; phenylephrine, 0.25%; tetrahydrozoline, 0.1%; and xylometazoline, 0.1%. Propylhexedrine and tuaminoheptane are marketed in inhalers containing the volatile base.

Epinephrine is used in many surgical procedures on the nose, throat, and larynx, to shrink the mucosa and improve visualization by limiting hemorrhage. Since epinephrine is relatively nonirritating, it is especially suitable for use in treatment of congestion of the conjunctiva.

The efficacy of locally applied sympathomimetic vasoconstriction in shrinking the nasal mucosa has led to the use of amines that may have this effect when given orally. Since the vessels of the nasal mucosa have not been shown to be more sensitive than most other vessels to sympathomimetic drugs, doses of orally administered sympathomimetics large enough to afford relief from nasal congestion will be expected to constrict other vascular beds and to raise the blood pressure. Ephedrine and pseudoephedrine have been given orally as nasal decongestants; their effects on nasal congestion due to colds are not of much consequence, but *allergic rhinitis* often responds well. While they do not raise blood pressure to any marked extent in doses that have this decongestant effect, they redistribute blood flow and cause cardiac stimulation. Several oral preparations promoted for the relief of colds and other upper respiratory conditions contain a sympathomimetic amine in combination with a variety of other agents (*e.g.*, antihistamines, antimuscarinic drugs, antipyreticanalgesics, caffeine, antitussives). Benefit from these blunderbuss preparations depends largely on the effects of the other drugs. In addition, the placebo effect in improving the patient's feeling of well-being should not be underestimated. No convincing evidence of benefit from oral use of sympathomimetics to relieve nasal congestion in colds has yet been presented.

Use with Local Anesthetics. Epinephrine is widely used in concentrations of 1:100,000 to 1:20,000 in solutions of local anesthetics. It slows absorption of the local anesthetic by local vasoconstriction and thus prolongs the duration of anesthesia, decreases the amount of anesthetic needed, and lessens the danger of systemic toxicity. Furthermore, hemorrhage from surgical procedures in the area of infiltration is decreased. However, careful surgical hemostatis is more necessary than ever because small vessels, which have been cut but are constricted by epinephrine, may escape detection. Stronger concentrations may cause tissue damage from ischemia. The total amount of epinephrine injected with a local anesthetic solution should not exceed 1 mg. Small amounts of epinephrine can also be added to the local anesthetic solution injected intrathecally for spinal anesthesia. Here also it delays absorption of the local anesthesia. Since epinephrine is the most potent α-receptor stimulant, smaller concentrations of epinephrine than of any other sympathomimetic have been added to local anesthetic solutions in the past, but only nordefrine and phenylephrine are now used as alternative to epinephrine. The combined use of epinephrine and local anesthetics is further discussed in Chapter 20.

Hypotension. The use of sympathomimetic amines to relieve hypotension occuring during spinal anesthesia and after sympathectomy, or from overdosage of ganglionic blocking agents, antiadrenergic agents, or veratrum alkaloids has a rational basis in temporarily constricting resistance vessels relaxed by release from adrenergic vasoconstriction. Such use has given satisfactory results. Agents with predominantly α-receptor action are clearly the most suitable for this purpose, but levarterenol is not frequently used because its intra-

venous administration demands attention that is not necessary with sympathomimetics that can be given intramuscularly.

Given before *spinal anesthesia*, intramuscular injections of ephedrine, hydroxyamphetamine, mephentermine, metaraminol, methamphetamine, methoxamine, or phenylephrine are often effective in preventing a substantial fall in blood pressure (*see* Aviado, 1959). Where hypotension is marked in spite of the initial prophylactic injection, a second intramuscular dose may be required to restore blood pressure. However, if the operative conditions permit, the blood pressure may usually be restored to an acceptable level without drugs by tilting the operating table to elevate the legs and thereby improve the venous return to the heart. Persistent hypotension during operation usually indicates hypovolemia and should be treated by replacement of the circulating blood volume with blood or plasma volume expanders. Treatment with sympathomimetic is unwise in cases of hypotension occurring in patients under *general anesthesia* with cyclopropane, halothane, and other drugs that sensitive the heart to the arrhythmic action. Even the feeble cardiac-stimulant action of phenylephrine may then be enough to precipitate ventricular arrhythmias. If administration of a pressor drug appears to be imperative, the choice of a sympathomimetic should be limited to one with minimal cardiac excitatory actions, such as phenylephrine or methoxamine. Methoxamine has been reported to inhibit the development of cardiac arrhythmias, perhaps by its β-receptor blocking action.

Administration of sympathomimetic agents for their pressor effect may be a useful *emergency measure* until other therapy can be instituted in certain hypotensive states (*e.g.*, in acute hemorrhage). Sympathomimetics may be used to raise the blood pressure and sustain the coronary and cerebral circulation until measures can be taken to restore an adequate circulating blood volume. However, this therapy must be regarded as only a temporary expedient that can obscure the extent of blood volume replacement required and can in itself cause loss of fluid from the vascular compartment. Vasopressor therapy can thus increase the risk of further circulatory deterioration.

The release of large amounts of catecholamines during operation on patients with *pheochromocytoma* can lead to a considerable decrease in the circulating blood volume, and the blood pressure may drop precipitously as soon as the tumor has been removed. Levarterenol infusion has been used to sustain the blood pressure postoperatively, but adequate fluid-volume replacement appears to be more rational therapy. Alternatively, the loss of circulating volume can be largely prevented and the postoperative fall in pressure much reduced or eliminated by inhibiting the vasoconstriction due to released catecholamines with an α-adrenergic blocking agent (*see* Chapter 26).

The blood pressure of patients with *orthostatic hypotension* due to various factors, including neurological diseases such as syringomyelia and tabes dorsalis, may be supported by treatment orally with ephedrine, amphetamine, or other long-acting pressor sympathomimetic agents. However, responses are highly variable and control of the blood pressure in these conditions remains a very difficult problem.

Shock. Intravenous infusions of levarterenol or of other sympathomimetics have been widely used in the treatment of shock associated with trauma, hemorrhage, speticemia, or myocardial infarction. This treatment is directed toward raising the blood pressure on the assumption that this will improve nutrition of vital organs. The rationale, however, is questionable. Shock of other than cardiogenic etiology is usually characterized by a relative deficiency in circulating blood volume, and compensatory mechanisms will have already initiated intense peripheral vasoconstriction. Renal and splanchnic blood flows are already much reduced, and further vasoconstriction in these regions by the action of a sympathomimetic can seriously impair the blood supply to the kidney, liver, and other vital organs. In addition, it is probably of importance that sympathomimetic vasoconstriction can itself reduce circulating blood volume. Continuous infusion of levarterenol in animals can cause lethal shock, and the injudicious use of this drug or other sympathomimetic agents in man can produce the same effect. (Spoerel *et al.*, 1964). The first consideration in the treatment of most types of shock should be adequate replacement of blood volume; this tends to reduce sympathetic tone and restore adequate circulation to vital areas. Administration of an α-adrenergic blocking agent may supplement fluid therapy in some cases by further reducing adrenergic vasocon-

striction. This aspect of shock therapy is discussed in Chapter 26. Successful results in treating shock with levarterenol or other vasopressor agents are the subject of many reports; however, assessment of such results is notoriously difficult, and it is seldom clear whether survival was due to or in spite of this treatment. (*see* Nickerson, 1962).

Shock following *myocardial infarction* differs in that reduced cardiac output is probably primary and not, as in other types of shock, secondary to inadequate venous return. A suitable vasopressor agent can raise the blood pressure although the latter point has not been proved unequivocally. The elevated blood in most cases of myocardial shock and may somewhat improve survival, pressure increases coronary flow and presumable the nutrition of uninvolved myocardium and areas of marginal viability. However, it also increases the myocardial work required for any given level of cardiac output, and the effect of sympathomimetic vasopressor agents on the balance between these two opposing agents on the balance between these two opposing factors doubtless varies with patients. Sympathomimetic agents that stimulate the heart are generally agreed to be the most appropriate therapeutic agents, but myocardial infarction predisposes to the arrhythmic action of these drugs. It is undecided whether sympathomimetics that cause peripheral constriction in addition to myocardial stimulation are more effective. Isoproterenol and mephentermine stimulate the heart without causing peripheral vasoconstriction; levarterenol and metaraminol have both actions. Both types of agent have strong advocates, but the fact that other agents, including dopamine, are being tested reflects the inadequacy of the presently used drugs. Metabolic acidosis due to poor tissue perfusion adds to the cardiac depression and should be corrected. It also inhibits the cardiac response to norepinephrine but not to isoproterenol (Silberschmid *et al.*, 1968). Isoproterenol may therefore be a better choice if severe acidosis is present. Additional measures may include the use of α-blocking agents if vasoconstriction is severe. These may aggravate the hypotension, leaving the indication for myocardial stimulation unchanged. For patients with inadequate venous return, a plasma volume expander may also be used, with due care to avoid circulatory overload leading to acute heart failure. Despite all measures, therapy of myocardial shock has only limited success and the mortality rate remains very high. (*See* Kuhn, 1967.)

Peripheral Vascular Disease. Nylidrin and isoxuprine, long-acting, orally effective sympathomimetic amines with predominant β-receptor action, have been used in the treatment of intermittent claudication due to peripheral vascular disease. Although both drugs increase the resting flow of skeletal muscle in normal persons, clinical results have been disappointing, probably due to the fact that control of the blood flow in skeletal muscle normally depends largely on dilatation of the blood vessels by locally produced metabolites. Such metabolites maximally dilate the blood vessels before symptoms of claudication appear. There is no evidence that blood vessels maximally dilated by local factors can be further dilated by sympathomimetics. In addition, only those vessels least affected by the pathological changes in diseases such as arteriosclerosis obliterans can be expected to dilate, and benefit can be obtained only when there is an element of arteriolar spasm. This view is supported by a study made by Caliva and associates (1959) on the effects of nylidrin in normal persons and in patients with peripheral vascular disease. Doses of nylidrin that normally increased blood flow in the calf by 33% had no effect on the blood flow in eight patients with arteriosclerosis obliterans; in patients with venous disease and segmental atherosclerosis, the flow at rest was increased but there was no improvement in tolerance to walking. There is no rational basis for the use of these drugs in conditions where the blood supply to the skin is reduced, since their effects on cutaneous blood flow are negligible.

The use of nylidrin has been proposed to increase cerebral blood flow in cerebrovascular disease. However, it is not likely that severely sclerotic cerebral vessels are capable of dilatation. In addition, the degree of dilatation of cerebral vessels depends largely on local factors that will already have induced the greatest dilatation of which these vessels are capable. No evidence of improvement due to nylidrin has been found in patients with long-standing hemiplegia; the value of this type of therapy has not been assessed in recent cerebral infarction (Eisenberg, 1969).

Use of Reflex Cardiac Effects of Pressor Drugs. Attacks of *paroxysmal acrial* or *nodal tachycardia* may be ended by reflex vagal discharge caused by pressor

responses to phenylephrine or methoxamine, drugs without significant cardiac excitatory action. The dose, given slowly intravenously, should not raise the blood pressure above 160 mm Hg; for phenylephrine, the dose may be 0.15 to 0.8 mg; for methoxamine, 3 to 5mg. These drugs have the advantage over parasympathomimetic agents in that they produce fewer unpleasant effects.

Use of Cardiac Effects. *Cardiac Arrest and Heart Block with Syncopal Seizures.* Syncope in *Stokes-Adams syndrome*, generally occurring at the transition from partial to complete A-V block, may be due to ventricular standstill or to prefibrillatory rhythm leading to ventricular fibrillation. Epinephrine and isoproterenol are of value in prophylaxis and symptomatic treatment of the attacks, but physical measures should be applied first in the acute attack. Circulation may sometimes be restored by a precordial blow followed by external cardiac compression or, if readily at hand, by an electrical pacemaker or defibrillator. Next, cardiac puncture with or without intracardiac injection of epinephrine may be effective and, as a last resort, thoracotomy and manual cardiac massage may rarely be required. External cardiac massage by compression of the chest can maintain circulation for considerable periods. To restore the intrinsic cardiac rhythm once some circulation has been reestablished, intravenous infusion of epinephrine or isoproterenol may be necessary. These catecholamines are likely to precipitate ventricular fibrillation if injudiciously used in patients with prefibrillatory rhythm, and, therefore, extreme care should be taken in their *intravenous* administration. When the indications are less urgent, repeated subcutaneous injections of epinephrine, intramuscular injections of epinephrine in oil, or sublingual doses of isoproterenol may give the desired results. Epinephrine has been used to maintain an adequate ventricular rate (30 to 40 beats or more per minute) for as long as a week, but other sympathomimetic amines are more suitable for prolonged and prophylactic treatment. Isoproterenol can be given sublingually or in sustained-action oral tablets, but absorption, especially after its oral administration, is unreliable. Ephedrine and hydroxyamphetamine are both orally effective and longer acting. Either can prevent recurrence of syncopal attacks. However, drug therapy is now regarded as a temporary measure only to be used until an electrical pacemaker can be fitted to supply optimal and reliable ventricular regulation.

The problem of reviving patients apparently dead from *drowning, electrocution*, and *anesthetic accidents* is not substantially different from that of the syncope in Stokes-Adams syndrome, and the same principles apply. In all cases of cardiac arrest, hypoxia is an important additional factor necessitating adequate artificial ventilation. Anesthetic cardiac accidents may be due either to asystole or to ventricular fibrillation. Since the heart is sensitized to the arrhythmic action of epinephrine by many anesthetics, the drug may convert asystole to ventricular fibrillation. Physical measures, especially the use of an electrical pacemaker, which should be available in the operating room, are obviously more appropriate. Electrical countershock followed by mechanical compression of the heart is indicated in ventricular fibrillation. Although the use of epinephrine in anesthetic accidents is theoretically inadvisable in cardiac arrest or after defibrillation, many patients have recovered when the drug has been administered. It is impossible to decide whether recovery is due to the drug, to mechanical stimulation of the myocardium by the needle prick, or to other procedures simultaneously applied. Recovery from such anesthetic accidents is achieved in less than 25% of cases: in patients who do not respond to other measures, it is not unreasonable to resort to the cardiac excitatory action of epinephrine. (*See* Bellet, 1960; Zoll and Linenthal, 1963; and many others.)

Acute Cardiac Failure. The treatment of acute cardiac failure does not include the use of epinephrine or other sympathomimetic drugs. The drug treatment of the acute attack of left-heart failure characterized by "*cardiac asthma*" or *pulmonary edema* is primarily with morphine, aminophylline, and oxygen. Emergency treatment with epinephrine to stimulate the heart should be avoided, since this procedure increases the demand of the heart for oxygen. A more effective and rational emergency measure is the application of venous tourniquets to the limbs, thereby reducing venous return and decreasing the load on the heart. A mistaken diagnosis of dyspnea due to bronchial asthma has sometimes led to treatment of cardiac asthma (dyspnea due to left ventricular failure) with epinephrine, in some cases with benefit. This can be expected

only when there is a degree of bronchospasm superimposed on the basic pulmonary vascular congestion due to the cardiac failure and cannot be relied on as a basis for routine treatment of acute cardiac failure with epinephrine.

Uses in Allergic Disorders. *Bronchial Asthma.* Epinephrine and isoproterenol, drugs with a powerful action on β receptors, are the mainstay of the symptomatic treatment of respiratory distress due to bronchospasm. Acute asthmatic attacks are usually relieved within 3 to 5 minutes after subcutaneous injection of 0.2 to 0.5 mg of epinephrine. The decrease in vital capacity and increase in residual air characteristic of these attacks are rapidly corrected. Vital capacity, maximum breathing capacity, and velocity of air movement, especially in the expiratory phase, increase equally well after peroral inhalation of a 1% solution of the drug from a nebulizer, and many clinicians now use this method of administration, often with an intermittent positive-pressure breathing machine, in preference to parenteral injection. Although airway obstruction is relieved the lowered Po_2 is generally not increased, indicating that the ventilation-perfusion disturbance is not remedied (Palmer and Diament, 1967). Relief with epinephrine is due to the β-receptor action, which relaxes bronchial smooth muscle, and to the α-receptor action, which constricts bronchial mucosal vessels and thereby reduces congestion and edema. Since epinephrine inhalation shows no obvious superiority to isoproterenol inhalation in relieving the acute attack, the major part of the benefit is probably due to their common relaxant action on bronchial muscle. Although isoproterenol is the more potent cardiac stimulant, palpitation after inhalation of isoproterenol appears to be less disturbing than after epinephrine.

Whatever the drug or route of administration, the smallest dose affording relief should be used. Smaller doses given early in an attack are more effective than larger doses given later. Inhalations of isoproterenol or epinephrine may have to be repeated at intervals of 2 or 3 minutes, and subcutaneous injections of epinephrine may have to be given at 15- to 20-minute intervals until relief occurs. If symptoms recur, massage of the site of injection may give relief by enhancing absorption of the drug. *Very slow intravenous infusion* of epinephrine has been used in patients who failed to respond to subcutaneous injection, but *this procedure is hazardous* and presents no advantage over the simpler and much safer method of aerosol inhalation, which applies the drug in the greatest concentration where its actions are desired, provided mucus plugs do not completely block constricted regions and proper technics of administration are used. Tolerance to epinephrine may occur after repeated use, and larger doses are then needed.

Epinephrine refractoriness is not uncommon in protracted severe cases and in status asthmaticus. In such cases bronchospasm is often secondary to or associated with the presence of viscid mucus plugs in the bronchi, and the action of epinephrine in reducing bronchial secretion may have an adverse effect by making these plugs more viscid and difficult to dislodge. Measures to facilitate removal of mucus plugs are important in these cases and include expectorants and increased hydration of the patient to liquefy the plugs, and mechanical removal of retained secretion by bronchoscopic suction. Suitable chemotherapy is used to combat respiratory infection when this common precipitating cause is present. The element of bronchospasm secondary to the presence of plugs may often be relieved by inhalation of epinephrine or isoproterenol as an aerosol, even in patients in whom subcutaneous epinephrine has failed.

Pressurized aerosols containing isoproterenol or epinephrine have been available for several years and are widely accepted as an effective and convenient therapy. In several countries the mortality from asthma has recently increased, an increase that coincides with the growing use of pressurized aerosols (Speizer *et al.*, 1968). Although the use of sympathomimetics has not been established as the basis of the increased mortality, these drugs can cause several kinds of cardiac toxicity, as already discussed. Development of compounds such as α-[(*t*-butylamino)methyl]-4-hydroxy-*m*-xylene-α',α^3-diol (SALBUTAMOL), which appear to act primarily on β_2 receptors and thus are powerful bronchodilators with little action on the heart, may obviate the problem of cardiac toxicity; however, a drug of this type is not as yet available for general use. Excessive use of the aerosols should be discouraged, and therapy should be supplemented by the other procedures outlined.

In cases of *refractory asthma,* intravenous administration of aminophylline is sometimes useful, but intravenous injection of adrenocorticosteroids is often required to break into the severe asthmatic cycle. Because of the serious side effects of prolonged use of such steroids (*see* Chapter 72), their administration should be discontinued as early as practicable; fortunately, such discontinuation is possible in virtually all cases. Withdrawal from steroids becomes exceptionally difficult if delayed. Susceptibility to small doses of epinephrine and other sympathomimetric amines is usually restored once repeated and progressive bronchial relaxation has been achieved. For prolonged relief from bronchospasm, usually in chronic asthma, *epinephrine in oil* is sometimes used, and a dose of 1 ml may permit a night's sleep free from attacks. The longer-acting oral sympathomimetics with prominent β-receptor action are commonly used to prevent attacks. Ephedrine, 20 to 50 mg given at 4-hour intervals, is an effective prophylactic. Methoxyphenamine, metaproterenol, and protokylol are effective but more expensive substitutes. The CNS stimulant action of ephedrine tends to cause wakefulness and irritability, and a barbiturate is commonly given in addition. Many drug mixtures have been proposed for the treatment of asthma; they have the obvious disadvantage of all mixtures in that the dose of each ingredient cannot be individually regulated to the patient's specific and changing requirements.

Miscellaneous Allergic Disorders. Epinephrine is the drug of first choice to relieve the symptoms of acute hypersensivity reactions to drugs (*e.g.,* penicillin) and of other acute reactions to sera and other allergens. A subcutaneous injection of epinephrine rapidly relieves itching, urticaria, and swelling of lips, eyelids, and tongue, and the drug may be lifesaving when edema of the glottis threatens suffocation. Only epinephrine is administered to relieve these acute reactions since it acts particularly rapid; however, ephedrine, having a more prolonged action, can be used for the continued treatment of allergic disorders, such as hay fever. Epinephrine may also give symptomatic relief in certain forms of eczematoid dermatitis. When skin tests are performed for hypersensitivity to various foods, drugs, pollens, or other allergens, epinephrine should always be at hand to control acute untoward reactions. If chronic medication with ephedrine is being given for at least 12 hours before sensitivity tests are made; otherwise, positive reactions may be prevented. When conjunctival tests for serum or drug hypersensitivity are made, epinephrine solution instilled into the eye readily controls the local discomfort of positive reactions.

Ophthalmic Uses. Local application of various sympathomimetic amines to the conjunctiva is used to dilate the pupil, mainly to permit adequate examination of the fundus. The mydriatic effect of these drugs, notably ephedrine (3 to 5%), amphetamine (1%), hydroxyamphetamine (1 to 3%), and phenylephrine (1 to 2%), lasts for only a few hours, in contrast to the long duration of action of the belladonna alkaloids. The sympathomimetics have the additional advantage that they do not cause cycloplegia and usually do not increase intraocular pressure. Sympathomimetic mydriatics are also used to reduce the incidence of posterior synechiae in uveitis, and epinephrine (1 to 2%) or phenylephrine (10%) is used to treat open-angle glaucoma, reducing the intraocular pressure by their local vasoconstrictor action, which decreases production of aqueous humor.

Uses of Central Effects. Apart from a series of drugs used only as anorectics (*see* below), the main sympathomimetics used for central effects are ephedrine, amphetamine, dextroamphetamine, methamphetamine, and mephentermine. Of these, dextroamphetamine and methamphetamine are most widely employed. The peripheral actions of ephedrine, mephentermine, and, to a lesser extent, amphetamine are disproportionately great, and central effects cannot be obtained without side effects from the peripheral actions.

Narcolepsy. Ephedrine, amphetamine, and dextroamphetamine have been used to treat narcoleptic patients. The amphetamines largely prevent attacks of sleep in nearly all patients, and cataplexy is often much improved. The usual dose of dextroamphetamine varies from 30 to 50 mg daily, in divided portions, the last dose being taken not later than 4 P.M. so that the nocturnal sleep is not prevented. Tolerance does not appear to develop to these agents in the treatment of narcolepsy.

Postencephalitic Parkinsonism. Dextroamphetamine is of considerable value

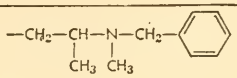
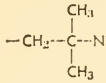
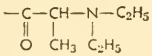
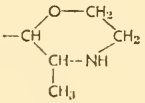
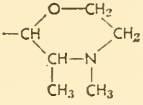
in relieving the symptoms of parkinsonism. It has little effect on tremor, but decreases rigidity in many patients and frequently relieves *oculogyric crises.* The drug brings about a better sleep cycle, a subjective improvement in muscle strength and rigidity, and elevates the mood, a most important objective in the treatment of these patients. Dextroamphetamine is especially valuable when given in conjunction with a belladonna alkaloid or with certain of the synthetic antiparkinsonism drugs. There is little improvement when organic defects are marked and in arteriosclerotic parkinsonism, and accompanying personality changes and psychotic states are not always helped. The total daily dose varies from 10 to 50 mg or more. In certain other diseases of the extrapyramidal system, such as *spasmodic torticollis* and spasmodic movements of a limb, dextroamphetamine may relieve symptoms.

Obesity and Weight Reduction. Whatever the etiology of obesity, a factor common to all cases is necessarily an intake of food that supplies more energy than the body uses. Of the two possible measures to correct this imbalance, attempts to reduce food intake have been more popular in Western civilization. Persistent dietary restraint has proven both essential and difficult to achieve, and various sympathomimetic and related drugs that depress appetite have been used to make a low-calorie diet more tolerable. These appetite depressants are of no value without an accompanying stringent dietary regimen, and it has been regularly demonstrated that, without consistent supervision, no prescribed regimen of drug or diet is predictably successful. Several factors have a part in determining this unsatisfactory situation. In many patients the etiology of obesity is psychological, and compulsive overeating is difficult to eradicate even with psychiatric help. The central effects of anorexia and wakefulness have proven inseparable in all currently available anorectic drugs. This prevents their use in the latter part of the day; given after 4 P.M., they interfere with sleep at night. Since much of the overeating takes place in the evening, their value is obviously limited. The anorectic agents are often given with a barbiturate to overcome this difficulty, but without conspicuous success. In addition, tolerance develops with a few weeks and increased dosage is limited both by the peripheral actions that these drugs exert and by such symptoms of central stimulation as nervousness and irritability. Even during the early period of administration, peripheral effects, although seldom pronounced, are rarely completely absent. However, the use of an anorectic by obese individuals who are well motivated to reduce their food intake may ease the discomfort of adherence to a restricted diet, and may be of help in the earlier part of a regimen while new dietary patterns are being established. Drugs used in obesity are listed in Table 24–5; none has as yet proven to be superior to dextroamphetamine or methamphetamine, either in effectiveness or in lack of side effects. In contrast to other amphetamine derivatives, fenfluramine (Table 24–1) causes drowsiness and does not interfere with REM sleep. This drug is used in Europe and may prove more acceptable for evening use, but it is not yet available in North America. (*See* Modell, 1960.)

Depressant Drug Poisoning. The value of amphetamines and other analeptic agents in treating poisoning by central depressant drugs has been the subject of much debate. The central stimulant sympathomimetics can lessen the degree of depression caused by moderate doses of anesthetics and hypnotics, but it is questionable whether they have any significant effect in persons poisoned with large doses of depressants. There is little need for their use in patients with adequate respiration and active reflexes. In patients in whom central depression is greater, maintenance of adequate ventilation and general measures to support the circulation should be the primary objective. There is little evidence that this objective is better attained when a sympathomimetic or other analeptic is added to supportive measures. However, if a central stimulant is to be used, an agent such as dextroamphetamine is probably easier to control and poses less hazard to the patient than do most other types. This subject is further discussed elsewhere (*see* Index).

Psychogenic Disorders. A large and controversial literature has accumulated concerning the use and value of amphetamine and dextroamphetamine in a variety of mental diseases. These drugs have been used in mild mental disorders such as mood disturbances, chronic nervous exhaustion, and psychoneuroses,

Table 24–5. CHEMICAL STRUCTURES AND DOSAGES OF SOME ANORECTIC DRUGS*

NONPROPRIETARY NAME	TRADE NAME	R	USUAL SINGLE DOSE (*mg*)	TABLET OR CAPSULE CONTENTS (*mg*)
Benzphetamine	DIDREX		50	25, 50
Phentermine	IONAMIN WILPO		15-30	8
Diethylpropion	TENUATE TEPANIL		25	25
Phenmetrazine	PRELUDIN		25	25
Phendimetrazine	DIETROL PLEGINE		35	35

*Not included in this table are dextroamphetamine, methamphetamine, chlorphentermine, and fenfluramine, the structures of which appear in Table 24-1.

as well as in major psychoses such as schizophrenia and the depressed phase of manic-depressive psychosis. Children with behavior problems generally become more easily managed. This is particularly true in certain cases of *hyperkinesis* in children; the basis for improvement is not understood, and the phenomenon is often referred to as the "paradoxical effect" of amphetamines. The immediate results may be quite satisfactory in cases of simple depression and chronic exhaustion; in some instances improvement may be spectacular. Some patients with the depressed type of manic-depressive psychosis may be improved, but endogenous depression is not relieved and may be aggravated. Anxiety states may be worsened, and patients with involutional melancholia do not respond well. Apathy in some cases of schizophrenia may be favorably influenced, but these drugs cannot be regarded as an effective treatment for schizophrenia. Further investigation is required before the value and dangers of the centrally acting sympathomimetics in psychogenic disorders can be fully assessed. Their indiscriminate use in patients with mental disorders should be avoided (also *see* Chapter 12).

The amphetamines are sometimes used in conditions in which there is a physiological as well as a psychic component. Nocturnal enuresis is sometimes successfully treated with these drugs, and dextroamphetamine may be helpful in relieving premenstrual tension, nausea and vomiting of pregnancy, and menopausal symptoms.

Epilepsy. In *grand mal*, dextroamphetamine is a valuable adjunct to phenobarbital, counteracting the ataxia and drowsiness produced by the barbiturate and thus allowing effective amounts to be given. It is also useful in *petit mal* to counteract the sedative effect of trimethadione if this is troublesome. In some cases of petit mal, dextroamphetamine, either alone or in conjunction with an oxazolidinedione or succinimide, may prevent the attacks and restore the EEG to normal.

Alcoholism. The amphetamines often benefit patients with hangover or depression after drinking. They may also shorten the period of recovery in acute alcoholic stupor. Their value in chronic alcoholism is not established, but they may be of use as an adjuvant to psychotherapy.

Fatigue. The effects and limitations of amphetamines in preventing and alleviating fatigue and sleepiness have already been discussed. The drugs should be used for such purposes only sparingly and with medical advice.

Miscellaneous Uses. Ephedrine and amphetamine have been reported to prevent *syncopal reactions* of the vagal or vasodepressor type due to abnormal sensitivity of the carotid sinuses. Ephedrine, amphetamine, and other sympathomimetics have been used with variable success to treat *urinary incontinence* and *nocturnal enuresis.* The benefit may be due partly to central effects of the drugs and partly to contraction of the vesical sphincter. Ephedrine and amphetamine, although quite unreliable as uterine relaxants and often excitatory, have been reported to relieve the pain of *dysmenorrhea.* Both these drugs have an inconstant and unreliable relaxant action on the alimentary canal; they have been used in spastic colitis and to assist x-ray diagnosis, but are of little value in these situations. In severe *hypoglycemia* due to hyperinsulinism or overdosage with insulin, epinephrine may, as an emergency measure, raise blood sugar pending administration of glucose; little reliance should be placed on this procedure since the drug is effective only if the liver contains adequate glycogen; a subcutaneous dose of 0.5 mg, if ineffective, should not be repeated.

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32. Abuse of Amphetamines and Related Stimulants

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Amphetamine[1] and chemically related drugs are widely used in medicine for the treatment of fatigue, minimal brain dysfunction (hyperkinesis) in children, in narcolepsey; as mood elevators in mild depression, and very extensively for appetite suppression.

Although amphetamine and related drugs have been clearly shown to elevate the mood, and are readily obtainable through illicit channels, increased abuse of these drugs in the United States has been only recently recognized. This is in contrast to widespread amphetamine abuse in post-World War II Japan and currently in Sweden and England.

In this chapter, the nature of amphetamine abuse will be discussed with specific consideration of the following questions:

1. Who are the amphetamine abusers?
2. What are the pharmacological effects of amphetamines, and how do these drugs effect one's overall performance?
3. How are amphetamines used medically?
4. What are the specific characteristics of amphetamine dependence?
5. How might we classify and distinguish different types of amphetamine abusers?
6. What are the effects of intravenous injections of amphetamine?
7. What are the characteristics of an "amphetamine psychosis," and why is this the most serious consequence of amphetamine abuse?
8. Is it easy to "kick" the amphetamine habit? Is there an established relationship between amphetamine and crime?
9. What is the extent of amphetamine abuse in Japan, Great Britain, and Sweden? Do we have similar problems in the United States?
10. What is the incidence and nature of amphetamine abuse among our college and high school, and grade school students?
11. How does the pusher, and ultimately the user, get the drug?
12. How can we curb this potentially explosive problem?

THE AMPHETAMINE USER

Prior to discussing amphetamine abuse, it is imperative to consider the nature of the abusers. Whereas, the public generally envisions typical heroin users as members of the "hippie" subculture or from the lower socioeconomic classes of large cities, a large number of amphetamine users are members of the vast middle class—that is, they include the housewife who is attempting to lose a few extra pounds, the business executive who is seeking that enthusiastic start in the morning and vibrant personality to captivate his clients, the serious college or graduate student who is "cramming" all night prior to a final exam, or the truck driver who requires that additional physical and mental stimulation to enable him to drive non-stop from coast-to-coast.

All these individuals pass unnoticed as our friends and neighbors. Public attention, however, is generally directed toward the thrill-seeker who attempts to change his perception of society via a drug-induced elevation of his mood and outlook. In 1966, Sadusk[14] suggested that thirty-five tablets of amphetamine-like drugs were legally produced for every man, woman, and child in the United States Moreover, he estimated that one-half of all this amphetamine enters illegal markets. (Note: See section titled "Illegal Procurement of Amphetamines.") Abuse by the vast middle class has been emphasized because it enables one to understand who is at least partially responsible for the enormous consumption of stimulants.

Angrist and Gershon[1] recently interviewed the backgrounds of 60 patients, all high abusers of amphetamines, who were admitted over to a 22-month period

[1] The term "amphetamine" will be used to denote the specific drug amphetamine and other chemically related drugs with similar pharmacological properties.

to Bellevue Psychiatric Hospital. The patients ranged from 17 to 41 years of age, with an average age of 25; of these, 70% were males and 30% were females; fifty-two were white. 7 were Negro, and one was a Puerto Rican. The duration of amphetamine usage varied from 20 years down to one time only, with a mean of 3.7 years.

With this general background, the actions and therapeutic uses of amphetamines will be discussed in an attempt to better understand the nature and characteristics of drug abuse.

PHARMACOLOGICAL EFFECTS OF AMPHETAMINES

Amphetamines act by stimulating the central nervous system and the sympathetic division of the autonomic (involuntary) nervous system. Such stimulation prepares the body for greater physical and mental efforts, as well as for "fight or flight."

Amphetamine-induced effects may be conveniently divided into those producing stimulation of the central nervous system (brain and spinal cord) and those that have a peripheral site of action. The majority of clinically available amphetamine-like drugs act more selectively on the central nervous system; hence, with therapeutic doses, the user is alert, has a decreasd sense of fatigue, elevated mood, and has enhanced initiative, confidence and the ability to concentrate; he is elated and experiences euphoria (a feeling of well-being); increased motor activity and talkativeness is observed; appetite is suppressed.[8]

The peripheral effects become manifested with high doses, as noted by an increased heart rate, elevation of blood pressure, flushed warm skin, sweating, widely dilated pupils, and dryness of the mouth. Often this last effect produces soreness of the tongue with possible ulceration. The user is frequently observed to rub his tongue along the inside of the lower lip. With very large doses, there are alterations in the normal rhythm of the heart (cardiac arrhythmias), involuntary oscillations of the eyes (nystagmus), dizziness, slurred speech, headache, nausea, profound insomnia, and disorientation.[4]

With an average dose, performance of simple mental tasks is enhanced, but, although the output of work is increased, the number of errors is not necessarily decreased (i.e., typing). Physical performance, as in athletic competition, is improved; however, with large or repeated doses, performance is worsened because of adverse effects (headaches, palpitations, dizziness, confusion, irritability, agitation and so on).[8]

One of the most common non-medical uses of amphetamine is to reduce fatigue, and it has been used this way by countless students, executives, truck drivers, athletes, and soldiers. It should be recognized that these drugs superimpose excitation over pre-existing fatigue enabling the individual to temporarily engage in physical and mental activities with greater vigor. The body's normal need for rest and sleep is not removed, but merely postponed. When fatigue does set in, there are brief lapses of alertness, a drooping of the head and an abrupt onset of sleep. Depending upon the dose of stimulant and the duration of drug administration, sleep may last from eight hours to several days.

Recently, several amphetamine-like derivatives of mescaline have been synthesized which are more active than mescaline. The one most widely used by the "hippie" population is 4-methyl-2, 5-dimethoxy-alpha-methyl phenethylamine (DOM), more widely known as STP. It is estimated to be 50 to 100 times as potent as mescaline in hallucinogenic activity. Unlike amphetamine, STP is not used in medical therapeutics; it is exclusively a drug of abuse.

USE OF AMPHETAMINE IN MEDICINE

The amphetamines are widely used in therapeutics. These drugs are helpful in the treatment of narcolepsy, a neurological condition in which the patient is overcome by uncontrollable drowsiness at any time and anywhere. The drowsiness induced by certain drugs that are used in the treatment of epilepsy is reduced by co-administration of an amphetamine. When given alone, amphetamine has afforded some success in the treatment of petit mal epilepsy, in certain behavioral disorders in children, (characterized by hyperactivity or hypoactivity), in Parkinson's disease, and in mild, short-term depression.

At present, the widest therapeutic use (and, in the author's opinion, misuse) of the amphetamines is as appetite suppressants. In this regard, these agents should only be used for the first few weeks of a diet program, during which time the patient is attempting to alter his poor eating habits. Following pro-

longed administration, tolerance to the drug occurs; that is, a given dose produces less of a response than it did initially, thus requiring an increased dose to derive the effects obtained following initial treatment with the drug. This phenomenon of tolerance to appetite suppression, and perhaps the euphoria that accompanies it, often result in medically unsupervised increases in the amount of drug taken.

AMPHETAMINE DEPENDENCE

In the older literature on drug abuse,[9] an attempt was made to differentiate between drug addiction and drug habituation. In 1957, the World Health Organization (WHO) attempted to evolve definitions that would serve to distinguish these two conditions based on the following differences: (a) compulsion versus a desire to continue taking the drug, (b) tendency versus little or no tendency to increase the dose (tolerance), (c) psychic and physical dependence versus psychic but no physical dependence, (d) abstinence symptoms after abrupt withdrawal of the drug versus no abstinence symptoms, and (e) detrimental effects to the individual and society versus detrimental effects to society.

In 1964, the WHO Expert Commitee on Addiction-Producing Drugs recognized that the earlier definitions had failed to clearly distinguish "addiction" from "habituation;" they therefore abandoned the terms and adopted "dependence" as an all-inclusive term. Drug dependence was defined as "a state arising from repeated administration of a drug on a periodic or continuous basis." Further, since the characteristics of dependence differ with each class of drugs, specific types of dependence were described. The characteristics of "drug dependence of the amphetamine type" include:[16]

(a) a desire or need to continue taking the drug;

(b) consumption of increasing amounts to obtain greater excitatory and euphoric effects or to combat fatigue accompanied to some extent by the development of tolerance;

(c) a psychic dependence on the effects of the drug as related to a subjective and individual appreciation of the drug's effects; and

(d) a general absence of physical dependence so that there is no characteristic abstinence syndrome when the drug is discontinued.

It should be noted that the Expert Committee avoided mention of risks to society and/or to the individual. By contrast, opiate (heroin) and alcohol dependence are characterized by an overpowering compulsion to take these drugs, tolerance, psychic and physical dependence on the effects with an abstinence syndrome after abrupt withdrawal, and a resulting detrimental effect on the individual and society.

CLASSIFICATION OF AMPHETAMINE ABUSERS

Connell[5] has classified amphetamine users as being of one of seven types, based on the nature and extent of their drug abuse:

Type 1: Takes the drug only once, as an experiment, in the company of friends, and never takes it again.

Type 2 and 3: Take amphetamines only on weekends and markedly reduce their intake as the weekend draws to an end;

Type 4: Mainly weekend use of the drug, with lesser amounts during the week to combat the rebound depression;

Type 5: Uses amphetamines for only a short period and rapidly progresses to more potent drugs, such as cocaine and heroin;

Type 6: Requires amphetamine to carry out normal activities on a daily basis. This type of individual is generally a middle-aged user whose physician initialy prescribed amphetamines for him for the treatment of obesity or mild depression. His consumption is generally 2 or 3 to 7 or 8 tablets per day.

Type 7: Uses amphetamines for months or years and eventually progresses to more potent drugs.

MAINLINING "METH"

In the previous sections, most of the emphasis was directed toward the weekend drug user, who generally takes amphetamine orally. This class includes middle-aged individuals, who are the very solid members of the vast middle class and the high school and college students who are seeking a diversion from a long week at the books.

Unfortunately, there is still another group—that of the high dose users, who intravenously inject very large doses of methamphetamine (meth; speed) every two hours or less around the clock for 3 to 6 days, with rare individuals continuing this way for as long as up to 12 days.

In 1967, Kramer and co-workers[10] reported that there are 4,000 persons in San Francisco who take amphetamine intravenously, and that this figure approximates the number of heroin users in that city. Occasionally these persons began by taking amphetamine orally in doses which reached 150 to 250 mg (30 to 50 tablets) per day, with this stimulant as only a "part of the scene," i.e., in addition to marihuana or other drugs. In an attempt to improve the quality of the amphetamine experience, they generally switched to injections at doses higher than those taken orally. Because of the rapid development of tolerance to th desired euphoria and stimulation, it was necessary to continually increase the dose. There is far greater abuse potential with drugs administered intravenously than for those taken by the oral route; in fact, such abuse has been suggested to be comparable to that observed with cocaine or heroin.

Following an intravenous injection of methamphetamine, there is a sudden, generalized, overwhelming pleasurable euphoric feeling termed a "flash." During the "run," there is intense fascination with all thoughts and activities, with the pursuit of purposeful activity at first, followed later by more compulsive and ultimately disorganzed acts. This is exemplified by individuals taking apart and repairing radios continuously for hours, although they were originally in perfect working order; others spend an entire day shining shoes. Subjectively, the user imagines that the drug enhances performance; however, objective evaluation has actually shown deterioration of performance.

Under the influence of the amphetamines, some users have alleged that there is a considerable interest in sexual activities. Orgasm is delayed for both sexes, thus permitting marathon sexual relations; when the orgasm is achieved, it is reported to be more powerful and pleasurable than without the drug. These claims have not been documented scientifically, however.

With the development of tolerance, the user finds it necessary to use very large doses to maintain his "run." The highest maximum dosage reported is 1000 mg every two hours or about 15,000 mg in one day. The "run" may continue for 3 to 6 days. After several days of intravenous administration of these drugs, severe tremors, muscle or joint pains begin, indicating drug toxicity from over-dosage; for the user this signals the end of the "run." When the stimulating effects wear off there is profound sleep for 12 hours or more prior to the start of a new round of drug administration.[10]

Whereas the individual who takes relatively low doses of amphetamine orally may often appear normal, there are various physical complications following a "speed run." Amphetamine's very potent appetite suppression effects may result in weight losses of 20 to 30 lbs.; aware of this, the experienced user forces himself to eat. Moreover, food deprivation alters the duration of drug action. The acidosis resulting from starvation creates circumstances within the body that favor the rapid excretion of amphetamine, thus necessitating frequent, high doses to maintain the euphoria. Malnutrition may produce brittle fingernails; abscesses and skin ulcers result from self-injections under less than sterile conditions. There is an obvious neglect of personal appearance.

AMPHETAMINE PSYCHOSIS

Although tolerance rapidly develop, permitting higher, more frequent doses, this adaptation phenomenon does not protect the abuser from developing an amphetamine psychosis which is the most dramatic consequence of amphetamine abuse.

While the findings of investigators vary, Kalant[9] summarized the relative incidence of symptoms of amphetamine psychosis in 94 reported cases: delusions of persecution (83%), visual hallucinations (54%), auditory hallucinations (40%), tactile and olfactory hallucinations (18%), and excitation (41%). Unlike many other drug-induced psychosis, the amphetamine abuser is generally able to think clearly and have an excellent recollection of relevant and extraneous facts during the period of psychosis.[6]

Almost all persons (80%) taking heavy doses of amphetamines become suspicious. In the early stages, users are suspicious of their family, friends, lovers, and especially of strangers. At intermediate stages, they think that they are being followed or pursued by Federal agents or by the police. In very advanced

cases of abuse, patients not only think that they are being monitored, but also that they are being manipulated, i.e., by radio or television, transmitters and by unknown power sources, with which they, in turn, manipulate others.[8, 10]

Similarly, in early stages, visual hallucinations begin as fleeting glimpses, and progress to fully formed, recognizable figures. Auditory hallucinations start as simple noises, whereas in the more psychotic stages, the patient carries on long conversations with his persecutors.

The drug user is aware of his paranoid reactions and learns to live with them. There are no physical signs by which to diagnose amphetamine intoxication, and the mental picture may be indistinguishable from that of acute or paranoid schizophrenia, or of alcoholic hallucinations present during the withdrawal phase of alcoholism, i.e., delirium tremens.[4] These psychotic symptoms generally subside spontaneously about one week after the drug is discontinued.

Most persons who develop an amphetamine psychosis have been shown to have a high instance of pre-existing abnormal and unstable personalities (pre-psychotic disorders, sociopathic, and so on), and they are generally disposed to alcoholism and other drug dependent states. However, these reactions have also been shown to occur in normal, well-adjusted individuals. At present, there is no specific treatment during the psychotic phase; rather, therapy is directed toward curing the dependency state.

"KICKING" AMPHETAMINE DEPENDENCE

A physical abstinence syndrome occurs after abrupt cessation of heroin and barbiturates usage. It is characterized by very violent symptoms, which may have life-threatening consequences. In contrast to these dramatic symptoms, no grossly observable signs have been noted following amphetamine withdrawal. Although some investigators suggest that the general fatigue, sleepiness, and depression that follows an amphetamine "run" are part of an abstinence syndrome [4-5], it appears more likely that they result from the sudden withdrawal of a stimulation which has masked fatigue and made conditions more favorable for an extended sleep. More recently, it has been shown that following abrupt withdrawal from large doses of amphetamine or phenmetrazine, aberrations appear in the normal electrical activity of the brain during sleep; these abnormal electroencephalographic (EEG) patterns meet the usual criteria for a withdrawal symptom.[12]

Kramer et al,[10] noted that 1/3 of the patients who used high doses of amphetamines intravenously, reported impaired memory and ability to concentrate. Objective studies to date have not demonstrated whether permanent brain damage or mental impairment does indeed result. Connell [4-5] has observed marked and permanent changes in personality in many long-term, high dose users.

Because of the relative ease in the illicit procurement of amphetamines, and the less urgent need to sustain drug administration in order to prevent the severe abstinence syndrome (as with heroin), there is a high rate of relapse. No doubt the environment and drug-using friends psychologically influence the user to return to this drug-oriented world.

Kramer [10] and Willis [15] suggest that amphetamine users have a greater potential for violent crimes as a result of drug-induced hyperactivity and psychosis, whereas phenmetrazine abusers in Sweden appear to resort to nonviolent crimes (prostitution and forgery) to support their drug-dependent states.[11] In this country, many men support their drug habits with petty thefts; a majority of the girls are prostitutes. In several instances, violent acts and beatings have been reported when the abuser is undergoing delusions associated with persecution.[13]

At present, however, it is not clear whether there exists a caused relationship between amphetamine abuse and criminal behavior.[6]

EXTENT OF AMPHETAMINE ABUSE

Japan: After World War II, amphetamines, which had been used by the Japanese armed forces, fell into the hands of black market profiteers. One estimate suggested that by 1954 there were 500,000 to 600,000 Japanese amphetamine abusers, and half of these were considered "addicts": [1] the Japan Pharmaceutical Association estimated that these abusers numbered 1.5 million.

[1] Literature at this time referred to amphetamine dependency as "addiction."

In a study of the amphetamine abuse problem in Kurume, Japan, 1,000 of 90,000 (1.1%) of the population were considered "addicts"; most of these persons were males from the lower socioeconomic class, between the ages of 16 and 25, and contstituted 5% of the population of the younger generation. It should be emphasized that most of the abusers were self-administering amphetamines by the intravenous route and were not taking the drugs orally.

In another study consisting of 600 cases, 22% of the patients suffered from "addiction" with psychosis which cleared after drug withdrawal, and 10% developed chronic psychosis.

At present, the Awakening Drug Control Law prohibits the importation of amphetamines into Japan, and severely restricts their manufacture, sale and purchase.

Great Britain: In 1966, it was estimated that 100 to 200 per 100,000 members of the population illicitly used amphetamines in Great Britain. An approximately equal number of persons were using these drugs pursuant to a physician's prescription and were slightly dependent upon them. This very high incidence of amphetamine abuse is more dramatically exemplified by the fact that marihuana and morphile (heroin) abusers respectively number about 30 to 60 and 4 to 5 per 100,000 persons.[15]

A very large number of abusers in Britain are obese women who originally used amphetamines for appetite suppression, and who subsequently developed psychic dependence upon them. Strong intra-professional pressures have been exerted upon British physicians who indiscriminately prescribe these drugs without full cognizance of their inherent abuse potential. By contrast, British teenagers appears to be taking amphetamines and amphetamine-barbiturate combinations for their euphoric effects without medical indications.

Sweden: Sweden now has what is generally regarded as the world's most serious amphetamine abuse problem. It has more addicts than any other country in Europe. One account which appeared in *The New York Times* estimated that there may be 10,000 to 12,000 amphetamine abusers in Sweden, with about half of them found in Stockholm.[11]

In the late 1940's, amphetamines were taken orally by those in circles of artists, actors, and writers. Several years later, the asocial and criminal groups began to use amphetamines intravenously. By about 1958, the intravenous use of phenmetrazine spread throughout the major cities in Sweden.[2] By 1965, one of every five Swedish males who was arrested for any reason was a drug abuser. Two years later, this proportion had risen to one-in-three.[11]

The usual oral dose of phenmetrazine is 25 mg (1 tablet) taken twice daily, but abusers have been known to take, by injection, a dose of up to 20 or 30 tablets every few hours. Abusers inject the contents of 300 to 400 tablets daily for 7 to 14 days with very little sleep or food. Following such a "run," the user rests and eats for a day or two and then resumes this cycle; this may occur for months or years.

A phenmetrazine psychosis has been demonstrated and it is purported to be more acute and intensive than that from amphetamines.[2]

Table 1 compares patterns of amphetamine abuse in Europe with those of phenmetrazine abuse in Sweden.[7] It should be noted that with phenmetrazine, the abuser has an apparently normal personality and is 15 to 30 years old; in contrast, the "typical" amphetamine abuser has an unbalanced personality, and is generally older

At present, Swedish police are directing their efforts against phenmetrazine smugglers and sellers of the drug (sale is illegal in Sweden), rather than against the user; attempts are being made to treat rather than to arrest abusers.[11]

United States: While the nature and extent of amphetamine abuse has been well recognized in Japan, Great Britain, and Sweden, at this time, the extent of the problem in America has not been well defined.

In the late 1930's through the mid-forties, non-prescription Benzedrine inhalers were used to treat nasal congestion. Each inhaler contained the equivalent of about 56 amphetamine tablets, and when broken open, it supplied the needs of an abuser for many hours. To preclude this readily available source of amphetamine, such inhalers have been replaced by another nasal decongestant that lacks abuse potential.

Information on the effects of amphetamines was brought back to our civilian drug-using population by many of our servicemen, who had been stationed in

Japan following World War II and during the Korean War. These ex-servicemen, attending college on the G.I. Bill, continued to use these drugs; now they were being taken to enhance endurance and "performance" prior to examinations. The use of these stimulants spread to include truck drivers, who found it necessary to remain awake and alert for long periods on the road.[13]

By 1966, it was estimated that there was enough amphetamine produced in this country to supply every member of the population with 35 doses per year; furthermore, it was suggested that 50% of the amphetamine produced is being distributed illicitly.[14]

THE STUDENT AS AN AMPHETAMINE DRUG ABUSER

Not long ago Blum[3] conducted a survey of about 1,300 students in five San Francisco area colleges. He reported that amphetamine abuse is apparently a relatively minor problem when compared with the use of other drugs; i.e., only 21% of the students reported to have ever taken amphetamine (incidence of usage?). Of this number, only 8% reported having any difficulty in obtaining their supply of drugs. In this survey, the characteristics of the "typical" college amphetamine abuser included: an individual who was an older, upper classman who began abusing drugs at 18 or 19 years of age; he was an arts, humanities, or biology major; he came from a wealthier family with one or both parents dead or he was from an unsettled family. Except for political interests (generally left wing), the youth had few outside interests, such as sports or religion.

Often the student saw little relationship between studies at school and his life or career aspirations. Understandably, use of amphetamines appeared to be more prevalent among students who had recently taken incompletes in one or more courses, who had dropped out of school earlier, or were contemplating dropping out. Notwithstanding this, the grade point average of users was 2.8, whereas non-users had a 2.7 average.

There appeared to be a variety of reasons for using amphetamines such as: to gain courage, to better understand oneself, to seek religious or spiritual experiences, to relieve boredom, to combat depression, to calm nervousness, to facilitate friendliness, and to improve physical and mental performance.

It is interesting to note the apparent parental influence on paterns of amphetamine use. Whereas this study showed 31% of the parents of intensive users had used amphetamine, only 19% of the parents of light users and 5% of the parents of non-users took amphetamine.

Most amphetamine abusers in the colleges included in this study were observed to use other drugs such as alcohol (99%, tobacco (87%), marihuana (44%), such sedative sand hypnotics as barbiturates (33%), tranquilizers (32%), hallucinogens (17%), and such opiates as heroin (4%).

In another recent study of four San Francisco Bay area high schools involving about 5,500 students, Blum and co-workers[3] observed that only a relatively low percentage of the total students surveyed had ever experimented with amphetamines, and indeed a mere handful of these were using drugs regularly. While amphetamine abuse in the United States appears to be more prevalent among upper class college students, Willis[15] noted that amphetamine use in England usually begins at about 14 or 15 years of age; children as young as 12 years of age have been observed to be amphetamine-dependent.

Although not representative of the normal teenage population, 16% to 18% of the 12 to 17 year old boys and girls in two London juvenile detention homes were shown to have taken amphetamine or amphetamine-barbiturate combinations These youths generally took amphetamine to stay awake, for its euphoric

TABLE 1.—COMPARISON OF PATTERNS OF PHENMETRAZINE ABUSE IN SWEDEN AND AMPHETAMINE ABUSE IN OTHER COUNTRIES[7]

	Ordinary abuse of amphetamine-like drugs	Phenmetrazine abuse
Number of cases	Relavetily few (endemic)	Very large numbers (epidemic).
Geography	England, Central and Northern Europe	Big cities in Sweden.
Participation	Single cases	Groups.
Route of administration	Oral (some intravenous)	Intravenous.
Dosage	Slow increase over several months	Very high doses used at onset.
Repetition of doses	Continually	Continually, but also sporadically.
Reason for abuse	Increase in personal efficiency	Social excesses.
Personality	Unbalanced	Normal.
Age	30–40 years	15 to 30 years.
Sex	Mostly male	Male and female.

properties, and as an aid in overcoming social embarrassment. Most of this drug use was on weekends, with the youths depressed at the beginning of the week. There was no evidence to link amphetamine with delinquncy, although the work and school record of the weekend taker generally declined. At home, parents often observed their child to be out of bed all night, unable to sleep Upon his return home the following morning, after nocturnal drug use with friends, he was wide-eyed (drug-induced dilation of the pupils) and irritable. Unprovoked rages produced a deterioration of favorable relationships with family and friends. Moreover, the user was often restless, constantly moving about, trembling and laughing inexplicably; his lips and tongue were dry and coated with dried saliva. It should be emphasized that with many amphetamine abusers, tolerance to the drug exists, and the patient may appear normal and be indistinguishable from the non-user. Indeed, he may only be detected by chemically analyzing his urine for the presence of the drug.[15]

ILLEGAL PROCUREMENT OF AMPHETAMINES

The pusher obtains his supply of amphetamines by robbing or pilfering from legitimate pharmaceutical supply warehouses, or by inexpensively purchasing them from illicit manufacturers or from smaller manufacturers on the pretense of being engaged in scientific research Less frequently, he gets them from a small group of pharmacists or physicians who sell these drugs illegally.

The user obtains his drugs on a legitimate prescription, or by stealing prescription blanks and forgin them, from a small group of pharmacists who supply them without a prescription, or from the omnipresent pusher "Splash" (amphetamine) parties, originally informal gatherings arising from the user's desire to be among friends, is another channel of distribution. Eventually more enterprising individuals organized these parties with a profit incentive. One such person was reported to have made a $3,000 profit from a $9.00 investment in amphetamine powder.[13]

CONTROLLING AMPHETAMINE ABUSE

Recognizing the increased incidence of amphetamine abuse in this country, the Bureau of Narcotics and Dangerous Drugs (BNDD) is currently seeking to extend the legal controls applying to amphetamine and amphetamine-like compounds. In the proposed law, all manufacturers, physicians, hospitals and pharmacies will be required to maintain a perpetual inventory and submit such an inventory at regular intervals to the Bureau. Without advance notice, they will be subject to inspection by Federal agents. Several states, such as New York, currently have such laws.

The author believes that controlling the amphetamine abuse problem should involve: (a) vigorous inspection of all legal channels of drug distribution, i.e., manufacturers, wholesalers, hospitals, physicians, pharmacies, and so on; (b) an attempt to eliminate illicit manufacture of these drugs in this country and prevent its illegal smuggling from abroad; (c) imposition of strong penalties upon illicit pushers who supply drugs to the users; (d) better education of physicians and the drug-using public about dangers inherent in the misuse of these drugs: (e) supplying of purely objective information about these drugs to students from the elementary school to the university levels without sermonizing, since the facts speak for themselves; and (f) since chronic drug abuse is a medical problem, offer psychiatric help to those who are drug dependent, without police involvement.

Although at present amphetamine abuse is not widespread among youth of high school and colege age in the United States, its incidence appears to be increasing. Every effort should be expended to insure that such use for nonmedical purposes is seen as the very real danger it is to health.

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33. Amphetamine Psychosis: I. Description of the Individuals and Process[1]

E. H. Ellinwood, Jr., M.D.[2]

(Pps. 42–51)

The existence of "amphetamine psychosis" is well documented. Although there is conflicting evidence as to the relative importance of drug effect vs. underlying personality factors in the precipitation of this psychotic state, Beamish & Kiloh,[4] Hampton,[10] and Young & Scoville[18] believe that it is produced primarily in persons who already manifest a personality disorder or predeliction for paranoid reaction. Connell,[5] however, suggests that the phenomenon is primarily precipitated by the effects of the drug itself. There has, unfortunately, been a singular lack of data for comparison of amphetamine abusers who develop psychosis with those who do not. Another equally important and equally uninvestigated problem is whether certain individuals prefer the use of amphetamines over other available drugs. The author believes that these neglected areas must be studied if the phenomenon of amphetamine psychosis is to be fully understood.

The aims of this study, therefore, were threefold: (1) to afford a detailed description of individual reactions to the use of large doses of amphetamines; (2) to investigate and evaluate differences in reaction patterns within the amphetamine addict population and to explore reasons for these differences; and, (3) to differentiate betweeen the types of individuals who are consistently drawn to the use of amphetamines and those addicts who prefer other drugs.

METHODOLOGY

Subjects for this study were selected from the admission wards of the United States Public Health Service Narcotic Hospital in Lexington, Kentucky. The only criterion for selection was the use of large daily doses of amphetamine (exceeding 30 mg.) continued over a three-month period within the past two years. These subjects constituted the amphetamine group or "abusers."

The primary source of data was the patient's responses to a standard structured interview, administered after at least two weeks complete withdrawal from all drugs. The same psychiatrist conducted and evaluated in a similar fashion all interviews, which focused upon: (1) patient's recollection of psychological and physiological reactions during the period of heavy amphetamine abuse; (2) *major patterns of perception and thinking while off drugs*; (3) assessment of personality; and, (4) developmental history. An attempt was also made to identify specific behavioral sequences stimulated by amphetamines. The first half of the interview consisted of a series of nonleading questions designed to establish the presence or absence of specific symptoms and behavioral patterns (Table 1), which had proved significant in previous work with amphetamine addicts. Many items used by Connell[5] were included for purposes of comparison. The latter part of the interview was open-ended to facilitate discussion of unique reactions to the amphetamines. Most patients were well aware of the

1. Reprinted with permission from the *Journal of Nervous and Mental Disease*, Vol. 144, pp. 273-283. (April, 1967).

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TABLE 1

TOTAL AMPHETAMINE AND GENERAL ADMISSION* GROUPS COMPARED

Characteristic	Total Amphetamine Group	General Admission Group
Age Range	18 - 41	18 - 63
Mean Age		
Men	30	31
Women	26	30
Caucasian		
Men	60%	60%
Women	93%	60%
Married		
Men	20%	27%
Women	13%	40%

* From a previous study.[17]

amphetamine psychosis either in themselves or others, and, except in two paranoid patients, there was little or no hesitancy to discuss the psychosis. One noteworthy feature of the interview was the acute memory patients had of the psychotic experience, including places, time and extraneous details. This hyperamnesis facilitated obtaining a detailed description of the psychosis. At least two-and-one-half hours were usually required for each interview.

Psychiatric evaluations and Minnesota Multiphasic Personality Inventory (MMPI) testing at the Lexington Narcotic Hospital are routinely carried out approximately one week after withdrawal from all drugs. All the post-drug diagnoses discussed in this study are taken from this evaluation. The evaluations from both this and a previous comparison study[17] were made by the same group of psychiatrists. The results of individual routine MMPI testing are always compared with a standardized Lexington addict profile. This standardized profile is used in this study as a control with which to compare the amphetamine addict profiles.

Following the interview, patients were categorized as amphetamine psychotic or nonpsychotic according to the presence or absence of all three of these symptom clusters: (1) fully formed visual hallucinations; (2) hallucinations of voices which were perceived as speaking directly to the patient; and, (3) moderately well organized delusions of persecution or gross paranoid reactions. If less than all of these three symptom criteria were present, the patient was assigned to the nonpsychotic group. It is necessary to emphasize that the terms "psychotic" and "nonpsychotic" as used in this paper refer to the status of subjects *while on amphetamines*, not to the diagnosis made after withdrawal from all drugs. Ten of the 25 amphetamine addicts were considered psychotic; eight, nonpsychotic. Of the seven addicts who fell into neither group, four exhibited only one or two of the above symptoms, and three exhibited psychotic symptomatology when not taking amphetamines though they were free of major psychotic episodes when taking the drug regularly. While the latter two groups present themselves, they shall, for the sake of clarity, be omitted from the following discussion, although they are included in the accompanying tables and figures.

To test symptom differences between the psychotic and nonpsychotic groups, the data were cast into two-by-two contingency tables. Significance levels were then determined using the Fisher exact probability test.

SAMPLES

To discover any outstanding differences between the amphetamine addicts and the general addict, the present data were compared with those of a previous investigation[17] concerned with characteristics of the general addict population of Lexington Narcotics Hospital. The sample of general addicts included amphetamine abusers.

The total amphetamine group comprised 25 subjects—ten men and 15 women.* The general Lexington admission population sample included 81 men and 30 women. (See Table 1 for a demographic comparison of the two groups). It was noted in the previous study and confirmed by the present sample that amphetamine users were more withdrawn, sociopathic, resentful of authority and had a higher incidence of nondrug psychiatric hospitalizations than the usual addict. Their incidence of previous juvenile delinquency was higher, and they had been more frequently admitted to reform schools.

RESULTS

Symptomatology.—Many symptoms of amphetamine abuse were common to both psychotic and nonpsychotic states (Table 2) and showed no continuum of severity toward psychosis. Hand-face touching and picking, gritting or gnashing teeth, an acute sense of novelty, distortion of time sense, and depression upon withdrawal were reported by both psychotic and nonpsychotic groups. Many physiological symptoms (e.g., insomnia, alertness, lack of appetite, difficulties in

*Because of administrative convenience, the selection process was begun earlier for women than men, thus accounting for the over-representation of women.

TABLE 2

PSYCHOTIC SYMPTOMS AND BEHAVIORAL CHARACTERISTICS IN THE NONPSYCHOTIC VS. THE PSYCHOTIC GROUP

Psychotic Symptom or Behavioral Characteristic	Non-Psychotic (N = 8) %	Psychotic (N = 10) %	Total Amphetamine (N = 25)† %
Psychotic Symptoms			
Suspicious and aware of being watched (a presence)	50	100*	80
Organized paranoid behavior††	0	100	56
Gross all prevailing paranoia	0	70**	28
Ideas of reference	13	100***	52
Auditory hallucinations (noises)	0	100***	56
Auditory hallucinations (voices speaking to patient)††	0	100	48
Auditory hallucinations (conversations with voices)	0	50*	20
Visual hallucinations (peripheral vision fleeting)	38	100*	60
Visual hallucinations (fully formed and stable)††	0	100	44
Tactile hallucinations	13	70*	44
Olfactory hallucinations	0	70**	36
Change or distortion in body schema	13	80*	44
Persistence of hallucinations beyond 2 weeks of withdrawal	0	70**	36
Felt some of the bizarre experiences were real	0	80**	32
Behavioral Characteristics			
Libido same or decrease	88	10**	52
Libido increase	13	90**	48
Polymorphous sexual activity	13	80*	48
Concern with eyes, faces and their distortion	13	100***	56
False recognition of faces	25	80	52
Attracted to shiny objects and shadows	13	90**	44
Philosophical concerns	38	80	52
Increased deja vu	13	70*	44
Estrangement	0	60*	32
Curiosity, examination and dismantling of objects	25	90*	60
Acute sense of novelty	38	70	60
Attachment to transition objects	13	30	24
Depression on amphetamine	13	30	28
Depression on withdrawal	38	50	52
Terror and fear	30	70	60
Hand-face touching and picking	50	50	56
Gritting and gnashing teeth	63	70	68
Increased activity (task specific)	75	20	40
Inactive diffuse pattern (daydreamer)	0	60*	36
Dominant and aggressive pattern	62	30	52
Passive pattern	38	70	48

† Included in total amphetamine group are seven patients who fit into neither the nonpsychotic nor the psychotic group.
†† Psychotic criterion symptom.
* p less than 0.05.
** p less than 0.01.
*** p less than 0.001.

micturition, thirst, diaphoresis and increased energy, were also noted by both groups. Most addicts noticed loquaciousness, decreased ambivalence, a sense of cleverness and "crystal clear thinking" and an "invigorating aggressiveness," especially during initial amphetamine use. Both psychotics and nonpsychotics appeared to have had a hyperacute memory during the period of abuse both for relevant and extraneous material. Several symptoms that were specifically sought, but which were found to be rare, were synesthesia, micropsia, macropsia, visual perserveration, gross confusion, disorientation, aphasias, and calculating difficulties.

Some characteristics were present in both psychotics and nonpsychotics but became progressively more severe as the psychosis developed. Fear, suspiciousness, awareness of being watched, and visual hallucinations in the peripheral fields were quite definitely progressive. Practically all patients at some time became suspicious. Awareness of being watched was prominent when the patient was in crowds, alone, or in the dark and was not infrequently a ubiquitous feeling that someone was watching from behind or from the side. This symptom, not unlike "a presence" (symptom noted in parietal lobe lesions), became organized in the more serious psychoses. Repeatedly, reports were given of heightened awareness and over-reaction to slight movements in the peripheral vision which became a stimulus for initial illusions.

Over half the patients developed well formed delusions of persecution which appeared to be an extension of this suspiciousness and awareness of being watched. The contents of these delusions were often in keeping with the characteristic objective circumstances of the addict group, such as federal agents and incarceration. Of the few patients that were found to have been paranoid before starting on amphetamines, the drug appeared to have either little effect on the psychosis or to accentuate it. Among these patients, more common delusions were found (e.g., they were persecuted by communists, Martians, evil spirits, racial prejudice, and specific people). They were more often deluded that they were being affected by poisoned gas, or poisoned fruit.

Fear and terror were major symptoms mentioned mainly by psychotics. Frequently, the fear was associated with delusions or hallucinations, but others described a diffuse anxiety, especially over losing control. Occasionally the fear tended to abate as the delusional reasons for the fear were organized. Periods of acute terror were described in which the patient reacted to the slightest stimuli. It was not uncommon for patients to hide alone for weeks from their tormentors. One attempted suicide in a state of acute terror.

Philosophical concerns increased as patients became progressively psychotic. Such concerns were usually unsophisticated dealing with "beginnings, meanings, and essences." Revelations of significant insights were frequently experienced. These eureka experiences often ushered in prolonged periods of thinking about "the meaning of life." One patient's description was "everything became relative to some truth, a light ray would prove unity, a light ray breaking up would prove why men break up . . . I suddenly discovered how the world began." Another patient said, "I began to put details together from the past and present. Now I think I know what is going to happen to this world." Intense religiosity and involvement with Zodiac systems were also noted. Later, philosophical involvements degenerated into delusional systems. Two processes that were common to both philosophical and delusional concerns were sudden insights and compulsions to analyze a variety of details to find meaning and explanations.

Hallucinations occurred in over half of the total amphetamine group. Fourteen patients developed auditory hallucinations; 15 developed visual hallucinations; all but three who had auditory hallucinations also had visual hallucinations. Visual hallucinations started with fleeting glimpses of just recognizable images in the peripheral vision. The hallucinations later became more individualistic: some saw God, people involved in sexual activity, tormentors, buildings crumble, animals, Martians, angels and cities in the sky. Auditory hallucinations began with the patient's perception of simple noises or voices which whispered or called his name. The identity of the voices was usually unknown, but this appeared to be unimportant to the patient. Often psychotic patients perceived voices as either friendly or evil, and they devised elaborate methods to distinguish between them. In the more advanced psychoses, the patient conversed with them. Tactile hallucinations presented in seven patients, but all were incorporated in visual hallucinations. For example, patients reported infestations of microanimals and the presence of vermiform and encysted skin lesions which they felt as well as saw. Three patients had punctate scars incurred when they attempted to dig out these encysted parasites. The hallucinations became integrated into delusional material as the patient became more psychotic.

Gross distortions of bodily image were also highly correlated with psychosis. Such changes varied in degree from slight alterations in size, consistency, or color of the whole person. Some patients alleged that the right and left sides appeared separated at times or that the action of one side was antagonistic to the other. Vivid

autoscopic experiences were reported by five patients. Many patients also experienced a vague loss of body boundaries and described their bodies as ethereal or transparent. They felt that others could see their feelings and read their minds. Overemphasis of visual cues and selective disregard of somesthetic sensation was apparent in the descriptions. Interestingly enough, these same patients felt themselves capable of projecting themselves to distant locales and of controlling by thought people and objects which might in turn control them.

The majority of amphetamine patients exhibited a heightened awareness and concern with faces and eyes. Such concern appeared early in amphetamine abuse, deepened as the psychosis progressed, and gradually degenerated to gross distortions of facial expressions and physiognomy. An evil cast to faces was described by half the patients, but some stated that faces were simultaneously evil and kind. Ten patients reported marked distortions. Faces melted, faded, and appeared with stockings or masks over them; blood and bone appeared; eyes changed slant and shone; faces became hairy, developed deep crevices and lines, glowed and were transformed to witches and monsters.

Both psychotics and nonpsychotics commonly reported the symptom of false recognition. These patients often falsely identified strangers as family or friends. Many accosted strangers on the street and began intimate conversations. When this symptom became more florid, everyone looked like an intimate acquaintance.

Recognition in situations other than facial recognition was heightened and distorted. Deja vu experiences on amphetamines were difficult to evaluate because most patients had noted such experiences both on and off amphetamines. However, 11 patients stated they had an increase in deja vu, and eight reported experiences of estrangement and/or depersonalization. Deja vu experiences were recalled in detail.

Personal reference and significance revealed a biphasic response to amphetamines. Initially, the drug relieved any acute sensitivity to what others thought or felt. The constant reference to one's self seen in many sensitive people was relieved. They felt confident and aggressive. Later, they became suspicious, self-conscious, and self-referent. In some patients, self-reference and the constant searching for significance and meaning in the environment appeared to have a potentiating interaction that often subsequently developed into delusional systems. Ideas of reference developed fully in 13 patients. In the beginning stages, patients over-identified with characters on television, or would hear a reference made to himself or associates. Gradually, the messages became personally directed; finally the news media and others "knew too much." The more psychotic patients moved to talking directly to the television or radio. Television, radio, and electrical equipment were often viewed as vehicles of control and manipulation.

An acute sense of novelty and curiosity presented early in amphetamine abuse. Novelty was less pronounced than curiosity and was related to the heightened awareness of objects especially in the peripheral vision. Curiosity was not related to peripheral vision and did not need an immediate external stimulus for its evocation. Not only was it directed toward people, but also to inanimate objects which were frequently anthropomorphised.

Concurrent with the changes in awareness and curiosity, objects took on new emotional significance; many became "overcathected." As with most paranoid illness, this significance and meaning was eventually referred to the self. Five patients became greatly attached to childhood transition objects, such as small stuffed animals. For others, neutral objects (windows, chairs, pencils) took on an evil cast. The more paranoid patients concretized the experience to poisoned food (especially fruit) and drink. Altered object evaluation was manifest in other ways too. Fifteen patients described a compulsion to take objects apart, to analyze, to sort, and on rare occasion, to put back together. These patients "analyzed" details in a very concrete and repetitive manner. More abstract visuoconstructive trends were noted, such as reading blue prints, analysis of material in terms of color, pattern and weave. The more paranoid patients tended to search intensively for signs and meaning. One patient stated, "I looked everywhere for clues—under rugs, behind pictures—and took things apart. I read magazines looking at periods with a jeweler's glass for codes . . . they were to help me solve the mystery."

Changes in libido were found to vary extensively, corroborating the findings of other investigators (Bell & Trethowan[2] and Fox & Lippert[9]). However, an increase in libido and polymorphous sexual activity most often preceded the psychoses. The nonpsychotic group reported that amphetamine use either decreased libido or had no effect. The increase in libido was described as a driven state, in which orgasm was either absent or prolonged for hours. The polymorphous sexual activity was mainly a marked increase in orogenital activity but also included extreme masochism and other sexual deviations. These changes in sexuality were most striking in those females who were frigid when abstaining from amphetamines.

Different patterns of physical activity while on amphetamine were reported: (1) active (characterized by

obsessions with a specific immediate task), and, (2) relatively inactive (daydreaming, withdrawal or diffuse activity). The nonpsychotic group fit the active category, and the psychotic group the relatively inactive category. While on amphetamines, the nonpsychotics were found to be relatively aggressive and dominant, and the psychotics passive.

Developmental and Personal Characteristics.—A detailed developmental history of parent-child relationships and the patient's preadolescent reaction pattern to his parents was recorded, categorized and rated on a five-point scale. Few differences were found between the psychotic and nonpsychotic groups, although nonpsychotics appeared to rely more heavily on manipulation of parents and tended to become identified with the more aggressive parent.

Female patients were noted to have a high incidence (73 per cent) of first memories involving their father or his surrogate. In several females, these memories, along with reported dreams, seemed related to sexual conflict. The psychotic females were more prone to have first memories about their fathers than the nonpsychotic group (70 vs. 25 per cent). In contrast, 60 per cent of the males (all of whom were in the psychotic group) reported first memories dealing with feelings of helplessness, ineptness, or shame. Only one of the developmental characteristics used by Connell was found to be associated with psychosis in this study, i.e., "No friends at school" (Table 3). The incidence of several personal traits was rated to be high in both groups (Table 4) but, except for patterns of thinking, did not serve to differentiate between the two. In the nonpsychotic group, there was a greater tendency toward verbal thinking with little visual imagery (Table 4). They did not daydream frequently, but when they did, often daydreams consisted of carrying on conversations with themselves. They also appeared more often to remember in sequences and by details. Two of these patients spontaneously mentioned a compulsion to count when anxious, or when others might ordinarily daydream. These compulsions had been present since childhood. A precise and articulate memory was also noted, though to a much lesser extent, in the psychotic patients. Three patients in the psychotic group had strong verbal recall and little, if any, daydreaming, except in the verbal mode. One even had marginal facial agnosia and lack of revisualizing ability. The psychotic group in general had less precise memories, which were more visual, intuitive, emotionally colored, less sequential and detailed. Memory of childhood events, however, was more accessible* in the psychotic group (Table 4).

TABLE 3

CHILDHOOD TRAITS

Trait	Non-Psychotic (N = 8) %	Psychotic (N = 10) %	Total Amphetamine (N = 25) %
Tantrums	25	30	24
Nail-biting	50	40	48
Severely afraid of dark	38	40	36
Severe nightmares	25	20	20
Sleepwalking	13	10	12
Enuresis	13	10	16
Truant	50	70	68
Antisocial activity before age 15	38	60	56
No school friends	13	80*	52
Not keen on games	62	50	56

* p less than 0.05.

TABLE 4

PERSONAL TRAITS

Trait	Non-Psychotic (N = 8) %	Psychotic (N = 10) %	Total Amphetamine (N = 25) %
Poor work record	50	60	64
Ennui	25	60	48
Late Sleeper	38	60	52
Alcoholism	38	40	32
Delerium tremens	0	10	8
"Daydreamer"	25	50	44
Prolonged homosexual relationship	25	10	16
Childhood memory repressed	38	0	24
Childhood memory average	50	30	40
Childhood memory full	13	70*	36
Predominantly verbal memory	75	30	48
Predominantly visual memory	25	70	52

* p less than 0.05.

*Accessibility was evaluated on the basis of age of first memory and fullness of memory for both pleasant and unpleasant events.

TABLE 5

DOSE LEVEL AND DURATION OF AMPHETAMINE ABUSE

	Nonpsychotic (N = 8)	Psychotic (N = 10)
Average maximum daily dose for at least 3 months*	170 mg. (range 60 - 300 mg.	310 mg. (range 120 - 500 mg.
Average duration of abuse	3.1 yrs. (range 4 mos. - 6 yrs.)	2.2 yrs. (range 5 mos. - 6 yrs.)

* The difference between the psychotic and the nonpsychotic groups is significant at p less than 0.05.

Length and Tolerance of Amphetamine Habit.—Eighteen patients had abused amphetamines for at least one-and-one-half years. The nonpsychotic group had taken amphetamines longer, but at lower doses (Table 5). There was no preference for a particular type of amphetamine in either group. Five patients from each group had at times used either barbiturates or narcotics with the amphetamines. The dose relationships raise the question of why the psychotic group continued to increase their amphetamine level in the face of progressive psychosis.

Psychiatric Diagnosis.—Among the post-withdrawal diagnosis, antisocial reaction was the most frequent diagnosis in the nonpsychotic group (Table 6). However,

TABLE 6

DIAGNOSTIC CATEGORIES

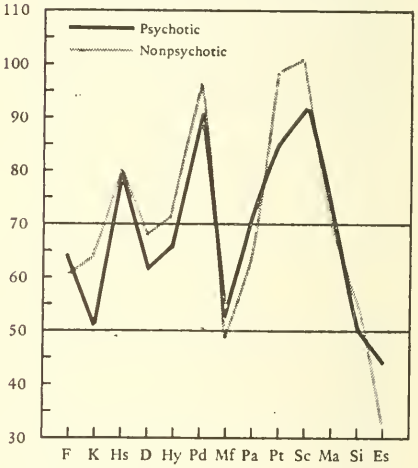
Diagnosis	Non-Psychotic (N = 8) %	Psychotic (N = 10) %	Total Amphetamine (N = 25) %
Schizophrenic reaction	0	40	20
Manic depressive reaction	0	10	4
Antisocial reaction	50	0*	20
Schizoid personality	0	20	20
Paranoid personality	0	0	4
Personality trait disturbance	50	30	28
Adolescent adjustment reaction	0	0	4

* p less than 0.05.

hysteria was noted as a common factor in the four personality trait disturbances in this group. In contrast, the psychotic group received no less than four diagnoses of a schizophrenic reaction: three patients were diagnosed as personality trait disturbances, two as schizoid personalities and one as a manic depressive reaction, manic type. The six patients with a psychotic diagnosis had persistent hallucinations when interviewed. Each also had previously either withdrawn from drugs or had had a prolonged hospitalization with continued hallucinations. Five of these were still convinced that some of their bizarre experiences were real. Composite MMPI profiles for the psychotic and nonpsychotic groups revealed remarkably similar patterns and peaks (Figure 1). Both showed peaks on the psychopathic deviance, psychasthenia, hypochondriasis, and schizophrenic scales in a pattern consistent with a disturbed borderline personality.

FIGURE 1

M.M.P.I. COMPOSITE OF AMPHETAMINE PSYCHOSIS AND NONPSYCHOSIS



Psychiatric diagnoses of patients in both the amphetamine abusers and in the general addict sample[17] shown in Table 7 were made by the same examiners. Because the incidence of psychosis, schizoid and sociopathic personality diagnosis had been high in amphetamine users in a former study,[17] these diagnoses were compared between these two samples. In this sample of

TABLE 7

DIAGNOSTIC COMPARISON OF AMPHETAMINE ABUSERS AND GENERAL ADDICT SAMPLE

Diagnosis	Amphetamine Abusers		General Addict Admission	
	Male %	Female %	Male %	Female %
Schizoid personality	40	13	14	3
Sociopathic personality	0	40	17	3
Psychotic diagnosis	20**	26	0	7

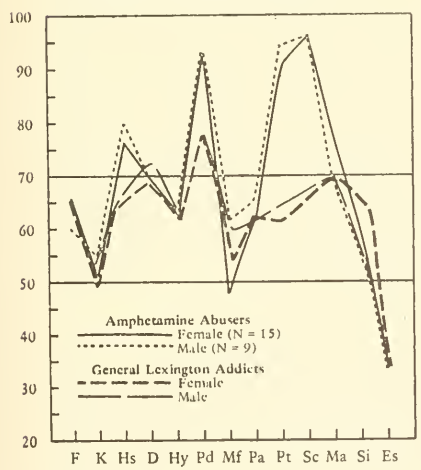
** p less than 0.01.

amphetamine abusers there is again noted the high incidence of these diagnoses except for an unexplainable lack of the sociopathic label among males.

There are differences in the amphetamine vs. the general Lexington addict MMPI profiles on psychopathic deviance, schizophrenia, psychasthenia, and hypochondriasis scales (Figure 2). Two-tailed *t*-tests were calculated for the differences between these peak scores and the average Lexington addict for each sex separately. The hypochondriasis scale was significant at p less than 0.05, and all other peak score differences were significant at p less than 0.005. Thus, from both diagnostic and psychological test data, there is evidence that amphetamine abusers are different from other addicts. Patients drawn to use amphetamines are more sociopathic, and exhibit more eccentric and bizarre behavior.

FIGURE 2

M.M.P.I. COMPOSITES OF AMPHETAMINE ABUSERS COMPARED WITH GENERAL LEXINGTON ADDICTS



DISCUSSION

From the above data, it is clear that many differences exist between amphetamine addicts and a general addict population, as well as between amphetamine psychotics and nonpsychotics. The most notable difference, and the one which provides the most significant clue to the solution to the questions posed in the introduction to this paper, lies in the psychiatric diagnosis of the individuals in the addict groups. It has been shown that antisocial and schizoid personalities, as well as schizophrenic reactions, constitute 60 per cent of the diagnoses of the patients addicted to amphetamines, a far higher percentage than was found in the general addict population.

Why should these individuals be drawn to amphetamines? There are several lines of evidence which suggest reasons why psychopaths prefer to use amphetamines rather than other drugs. Clinicians have reported some success with the administration of amphetamines in the treatment of psychopathic states and behavioral disorders, particularly those involving aggression, hyperactivity, and hypersexuality (Bradley & Bowen,[3] Hill,[11] and Hill & Watterson[12]). This success may be due to the initial calming effect described by the patients in this study. The paradoxical question of why a stimulant drug should produce a calming effect remains unanswered.

Psychopaths have been found to have an almost childlike capacity for novel stimulation. They seek it out. In fact, Quay[16] has explained psychopathic behavior in terms of the need for varied sensory input which leads to an extreme stimulus-seeking behavior. This continued search for new stimuli may stem from insufficiently internalized objects, schema and categories. Because he fails to internalize his experiences, the psychopath's ability to form a self-image is limited. He conditions poorly[13] and shows little anticipation of coming events either psychophysiologically or cognitively.[1] His poor conditioning performance applies to both avoidance and approach tasks, and he conditions best under partial reinforcement.[8] Fox and Lippert[9] found that psychopaths have significantly fewer spontaneous galvanic skin responses, which may be indicative

of internal arousal. Mundy-Castle and McKiever[15] had already shown that subjects with few endogenous galvanic skin responses habituate rapidly to repetitive stimuli. In Pavlovian terminology this could be stated as a predominance of external inhibition and a relative lack of internal inhibition. Thus, the psychopath appears to have reduced internal mechanisms for nonspecific arousal and for retaining the emotional or conditioned significance of stimuli.

Amphetamines may produce their paradoxical calming effect in these individuals by stimulating internal arousal mechanisms and, thereby, reducing the need for novel environmental stimuli. These arousal mechanisms become grossly hyperactive in the psychotic amphetamine abusers. The initial "organizing and energizing" effect of amphetamines described by schizoid and schizophrenic patients may also be due to increased internal arousal, but this needs study. Whether certain schizophrenics and psychopaths have similar defects in their internal arousal and attention mechanisms is unclear, but such a finding would account for the preference for amphetamine noted in both the psychotic and nonpsychotic groups, between whom there are certain common features. Arieti[1] and others have noted that reactive schizophrenics often reconstitute at the psychopathic level. Histories of the schizoid and schizophrenic patients in this study certainly were often remarkably similar to the patients diagnosed as pseudopsychopathic schizophrenics by Dunaif and Hoch.[6]

The separation between the psychotic group and nonpsychotic group of amphetamine addicts also rests primarily, though not entirely, on their psychiatric diagnoses upon their withdrawal from drugs. Patients who had developed the amphetamine psychosis were more often designated as schizoid or schizophrenic, while those who had not were found more often to be psychopathic. Other characteristics appeared to fit this pattern as well. Nonpsychotics tended to be more manipulative, identified with the aggressive parent and had more articulate memories. Psychotics were more passive, sensitive, fearful, felt inadequate and lethargic, were daydreamers and had visual memories. They tended to have been "loners" as children. Since five of the amphetamine psychotic patients continued to experience psychotic symptoms long after amphetamine withdrawal, an underlying psychotic process is indicated. It is unknown whether amphetamine contributed permanent effects to this psychotic process. Based upon the past histories of these five patients, it is the opinion of this investigator that amphetamine abuse was only a moderate contributing factor to this underlying psychotic process. It certainly was, however, the active catalyst in initiating the acute episode.

The amphetamine psychosis that was superimposed on the psychotic process that persisted beyond amphetamine withdrawal was qualitatively different from psychosis seen only with the drugs. As described previously, the amphetamine psychosis of the patients who were mentally clear after withdrawal was less bizarre than those of patients with an underlying psychotic process: their delusions and hallucinations were more reality-oriented. In these relatively more stable patients, the amphetamine psychosis was contiguous with the amphetamine use.

SUMMARY

A detailed behavioral description of amphetamine psychosis is presented. The usual paranoid psychosis is noted and some of the behavioral sequences leading to the psychosis are presented. Vision is the primary sensory mode in hallucinations, thinking disorders and body schema distortions. Vision is also prominent in an affinity for visuoconstructive tasks and in the ubiquitous feeling of being watched. Objects and events take on heightened emotional significance. There is a concern with inner workings and analysis of details, clues and signs. Philosophical excursions are noted often along with a general attempt to add up details in order to see the larger picture. Disorders of recognition are frequent, especially false recognition of faces. Faces are quite often distorted both on others and the patient. Body schema distortions were also frequent. Fear and terror are more prominent than depression. Sexual fantasies become elaborate, and there is a marked increase in libido and polymorphous sexual activity in many.

It was noted that amphetamine addicts differ from their fellow addicts on several variables: (1) they have a higher incidence of antisocial, schizoid and paranoid personalities; (2) they also have proportionately more schizophrenic reactions; and, (3) their Minnesota Multiphasic Personality Inventory profiles are significantly different. Psychosis, triggered by amphetamine abuse, appeared more often in the schizoid group than in the antisocial group. The mean amphetamine dose level was greater in the group of patients who developed psychosis than the group which did not.

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34. Amphetamine Psychosis: II. Theoretical Implications[1]

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(Pps. 52–59)

In a previous paper,[11] a detailed description was presented of the amphetamine psychosis based upon the histories of amphetamine addicts who were questioned extensively about manifested symptoms when taking large amounts of amphetamine. Several symptoms and behavioral antecedents of the amphetamine psychosis were intriguing, but have not been given emphasis in the literature. The present paper will attempt to explore the possible mechanisms in this psychosis, bearing in mind certain symptom complexes. Three groups of symptoms of that present in the amphetamine psychosis appear related to hyperexcitability of: (1) the limbic system including the temporal lobe (e.g., polymorphous hypersexuality, deja vu, fear and defense responses, olfactory hallucinations, extreme curiosity and examination and contralateral touching and picking habits), (2) minor hemispheric temporoparietal areas (e.g., false facial recognition, facial distortions and persistent concern with visuoconstructive activities), (3) unilateral or contraversive attention mechanisms that mediate reaction to peripheral stimuli (e.g., overreaction to auditory and visual stimuli in the lateral periphery, defense and fear reactions evoked by these peripheral stimuli and constant dread or vague awareness that someone or something is present just outside the border of their peripheral vision).

At this point the author would like to present a brief theoretical framework that will attempt to explain the presence of all three symptom complexes in the amphetamine psychosis. Later a more detailed discussion of the amphetamine psychosis symptomatology and of the theoretical framework will be taken up.

This hypothesis is based upon the action of unilateral attention mechanisms governed by visuopostural reflexes that course up and down the central nervous system. These visuovestibular mechanisms, especially the tonic neck and conjugate eye reflexes, direct attention contralaterally when an unknown auditory or visual stimulus appears in the periphery and are part of systems regulating orienting and rapid recognition responses. Tonic neck reflexes which are closely associated with the limbic system, and, with conjugate eye movements, are stimulated in many areas of the limbic system especially the amygdala, hippocampus and cingulate gyrus. The limbic component of unilateral attention may regulate the emotional coloring of recognition. Fear and defense reactions are commonly evoked by a higher voltage from the same stimulation points that evoke unilateral attention. Limbic appetative mechanisms such as curiosity and sexual exploration also may be related to these systems.

In the cortex there are also visuovestibular representations, especially at the temporo-parietal junction. Contralateral head and eye turning is stimulated in several cortical areas that are closely associated with the limbic system, thus the cortex appears to have representation in this unilateral attention system. Attention to one side is mainly subserved by the contralateral cortex. From split brain studies in lower animals it appears that

1. Reprinted with permission from the *Journal of Neuropsychiatry*, Vol. 4, pp. 45-54. (January-February, 1968).

both hemispheres have independent and equal attentive and emotive mechanisms. It can be assumed that the unilateral attention systems not only direct attention in the environment, but also take part in regulating attention between the two hemispheres. In man the gradient of attention appears overbalanced in favor of the dominant cortex, but is probably still dependent on the neural substrates of the tonic neck systems for mutual regulation of attention. The amphetamine psychosis presents certain symptoms referable to the minor hemisphere. Many schizophrenics show disorders of visuopostural mechanisms, and it has been noted that borderline schizophrenics and schizoids develop the amphetamine psychosis. Amphetamines stimulate postural reflexes and may thereby amplify any disorder already present. A shift in the gradient of attention to the minor side could be taking place in the amphetamine psychosis and could be causually related to the psychosis.

Using this theoretical framework, one can explain the simultaneous production of the three symptom complexes presented earlier. Although totally untested, this framework may be useful to the reader in ordering the amphetamine psychosis symptoms discussed below.

DISCUSSION

The symptomatology of the amphetamine psychosis has been found to be strikingly similar to that of the psychosis associated with temporal lobe epilepsy. Complex visual hallucinations, olfactory hallucinations, depersonalization, estrangement, deja vu, "ideas of a presence" and gritting of the teeth are presented in both syndromes. Temporal lobe symptoms, however, are not present in amphetamine addicts after drug withdrawal. This is similar to the depersonalization syndrome recently described by Roth,[43] Davison,[9] and others,[45] which also presents with the above temporal lobe symptoms, though no organic signs can be demonstrated.

Several authors (including Hill,[23] Pond,[42] Slater and Beard,[49] and Goldstone[17]) have described the paranoid psychosis associated with temporal lobe epilepsy, although others[50] report that the psychosis is found with equal frequency in other forms of epilepsy. This syndrome includes paranoid ideas, ideas of influence, auditory hallucinations and thought disorders. Deterioration is less common than in schizophrenia; the affect tends to remain warm and appropriate, and paranoid ideas are often colored with religiosity. Small *et al.*[50] however, have presented evidence that these symptoms are also noted in other forms of epilepsy. The most extensive description of the symptomatology of the epileptic psychoses (mainly temporal lobe) was made by Slater and Beard in 1963.[49] Several vignettes drawn from their 67 patients illustrate the religiosity, primary delusional experience and revelations which were also found in the amphetamine psychosis. One patient stated, "I had two thoughts side by side," and then he realized the untruth of Christianity. Apocalyptic visionary experiences were reported as that instant coming when everything made sense. The special significance attached to signs and objects was also noted. There were statements, such as "it all falls into a pattern," "things have some kind of connection," "people's Christian names have a significance," "everything has a double meaning—it's very difficult." The heightened significance of thought, insight, the meaning of signs, along with an intense philosophical concern (including cosmic consciousness, mystical and "eureka experiences") reported by amphetamine abusers is almost identical to the above excerpts.[11] In the amphetamine psychosis philosophical concern appeared to evolve out of a heightened awareness and significance of common objects in the environment. Objects would be noted in minute detail, would suddenly represent the meaning of everything, or they would have an evil, strange, sexual or familiar appearance. It is currently thought that the emotional elaboration of images is a function of temporal lobe areas. Irritative lesions of the temporal lobe and certain psychotomimetics would appear to distort these functions.

The Slater and Beard report,[49] in relating derealization experiences, presents several statements about faces—"her father was not her father, had lines on his face, her mother was wearing a mask, her clothes were not her own." "The doctor is not the doctor but the devil, people in the street look like foreigners, everybody dressing up in pantomime." Roth[44] also presents descriptions of distorted faces reported by patients with the depersonalization syndrome which are not unlike those noted in the amphetamine psychosis. False recognition of faces as seen in the amphetamine psychosis is not reported as a common symptom in temporal lobe epilepsy or the depersonalization syndrome. However, Milner[36] reported right temporal lobectomy patients are defective in facial recognition. Agnosia for faces (prosopagnosia) is usually found with a lesion of the minor occipital lobe (Hecaen and Angelergues,[19]). These patients cannot recognize family, friends or themselves by physiognomy. Even pictures of persons present are frequently not recognized. The impairment in recognition may extend to animals, and frequently revisualization is disturbed. There is a paroxysmal form of the disease (migraine and epilepsy) in which faces are warped, torn, distorted. The systems ablated in facial

agnosia may well be the same that are over stimulated in the amphetamine psychosis. Bodamer,[5] considering recognition of faces to be a quite primitive ability which preceded the recognition of objects, pointed out that in incomplete prosopagnosia attention was levied on the "ocula." Ahrens[2] noted increased cathexis of eye area by infants. Hypercathexis of faces, especially of eyes, the primary area of individual recognition, was noted in the amphetamine psychosis.

Depersonalization and estrangement experiences are basic symptoms in temporal lobe epilepsy; Mullan and Penfield[38] elicited both these experiences and also deja vu with stimulation of the temporal areas mainly on the right side. Estrangement experiences were usually described by amphetamine abusers as events that seemed strange, uncanny, peculiar and queer, and that things, events and people appeared different or foreign. An increase in deja vu was also noted in the early stages of the amphetamine psychosis. The sense of familiarity in deja vu is like the emotional counterpart of recognition and the assimilation of present experiences into past categories. Jamais vu emotive experiences may occur when one is unable for various reasons to find a framework for the present experience. Thus, deja vu and jamais vu may be associated with orienting and recognition.

The orienting response is succeeded by recognition of the new but familiar and assimilation of this perception into variously significant categories or by nonrecognition of the strange, different or uncanny. The unplaceable object may stimulate avoidance and fear. It may also stimulate curiosity and a search for new categories and significance, or attempts to expand, change and distort the categories or unknown object for mutual reconciliation. In the amphetamine psychosis, there was an incessant attempt to add up all the details past and present, a search for significance, and a striving for universals to explain the uncanny "mystery." Heightened awareness is readily notable in this syndrome, but the most notable theme is recognition and/or search. Recognition attributes stand out in false facial recognition, deja vu, estrangement and the frequent attempts to recognize objects in the peripheral vision. There were common recognition images in the amphetamine psychosis that are noted as illusions or hallucinations in toxic organic states. Snakes, microanimals, spiders, figures and faces presumably are inborn recognition images in man. They are not unlike the so-called innate fear release mechanism in naive monkeys toward snakes. It can be argued that these images are but elaborations of more basic visual perceptual units such as spirals, dots, radiating lines and ovals, but it is the snake and microanimals that elicit recognition with emotional significance. It is just this contingent of recognition, the emotional interpretation of the present experience contrasted against past analysis, that is so hyperactive in the amphetamine psychosis. Distortions follow the hyperactivity; normally bland experiences became fearful, and neutral objects take on an evil cast.

The disturbance may also reflect an inability to recover the past, categories or standards. Goldstone[17] states, "Subjects influenced by lysergic acid diethylamide have difficulty in locating concepts. Their judgments of conceptual standards are characterized by increased variability and their judgment processes are accompanied by long pauses during which time subjects report an intense search for the appropriate standard. This would appear to reflect a disruption in concept availability involving oscillating losses of the appropriate frame of reference." The development of a concrete attitude in the amphetamine psychosis is paradoxical since the comparison apparatus appears to be so stimulated. The oscillatory state of this comparison system is probably the cause of this. The realistic perceptual present, quite blind and binding, is interspersed with sudden intuitive and most incorrect abstractions and insights. In this connection, animals with amygdala lesions react even to familiar objects with curiosity and oral exploration. Past standards for aggression, as well as for food and sexual objects, appear unrecoverable and consumption of bizarre objects is noted. For example, the classical temporal lobe ablated Kluver-Bucy monkeys were tame, curious, constantly searching, hypersexual and polymorphous perverts.

The critical lesion of the medial temporal lobe region apparently is in the amygdala or pyriform cortex (Green *et al.*[18] and MacLean[30]). MacLean has proposed that the amygdala and its projections subserve preservation of the individual since stimulation elicits patterns of behavior that are related to alimentary functions or fighting and defense. He further points out that the evocation of bizarre hypersexuality in the Kluver-Bucy syndrome apparently is due to release of the hippocampus and septal region from restraint.[31] Stimulation in these latter areas is frequently followed by enhanced pleasure, grooming reactions, and sometimes penile erection. This curiosity and hypersexuality are two of the most notable features in the amphetamine psychosis.[11] Curiosity and hypersexuality, as well as oral behavior, may be part of approach and exploration systems that are under restraint of the amygdala and frontotemporal area. The interesting automatism of contralateral searching in temporal lobe epilepsy has yet to be explained. Similar to this is the hand-face touching and picking in

amphetamine psychosis. The hand searching the contralateral side of the body is not searching clothes—one would doubt that a primitive automatism would be dealing with such a civilized item as clothes—but must be searching on the body. Could this be a partial grooming reaction which is primarily directed toward hair matting and microanimals as in lower primates? Patterns similar to grooming reactions, such as picking at microanimals, digging at encysted ones and incessant facial picking, are common in the amphetamine psychosis.

What is the nature of the polymorphous hypersexuality in the amphetamine psychosis? MacLean[32] has drawn attention to the primitive nature of the limbic system which interprets experience largely in terms of feeling. He suggests ". . . that the crudity of the analyzing mechanism and the overlapping incoming impressions from the nose, mouth, viscera, sex organs, eye, ear and body wall might account for the often seemingly paradoxical overlapping of affective reactions such as those associated with orality and sexuality . . ." An alternate explanation of the polymorphous hypersexuality may be that those alienated from their past experience and object categories might frequently seek intimate relationships with even sexually undifferentiated objects (regression) "to fill the void." This would fit in with reports of "desire just to physically be close to someone for hours," which was not unlike oceanic feelings. Thus, in the amphetamine psychosis, the undifferentiated sexual object was more noticeable than a well-defined homosexual object.

If the sexual object is undifferentiated, why should many persecution delusions in males of this study involve explicit homosexual accusations? Many paranoid individuals have difficulty with dominance-submission relationships. Visual sexual signs play a preeminent role in the assertion of primate dominance. MacLean[31] speaks of this in describing how vision is all-important to monkeys especially when considering sexual and aggressive display. Penile display is the expression for both and has the same order of dominance in certain monkeys as pecking order in chickens. MacLean says, "There are other considerations that lead one to wonder if penile display does not generalize to the eye so that the mere act of one animal's looking into the eyes of another becomes in itself an aggressive act. Some monkeys, such as the macaque, seem in general to try to avoid looking each other in the eye or indeed people, in the eye. If one looks the macaque in the eye, he will charge. In this connection it is interesting to recall that looking in the eye spells panic to some patients and particularly some schizophrenic patients." The amphetamine psychotics described eye avoidance; the critical feature being to see others without being seen. Men were especially prone to spy on others while hidden. Even at the time of the interview, these patients had no clear cut idea of their motivation for spying. They would allude first to the scoptophillic, voyeuristic aspect and then to the secret aggressiveness. It was, conversely, quite common for patients to describe their body image only in visual terms and to state their belief that people could look right through them, especially with eye contact. They felt weak, impotent, and ineffectual when others were looking and were afraid that others would see homosexual traits in them. On other occasions, however, sexual promenade and display apparently is evoked in the amphetamine psychosis.

The visual mode was predominant in the amphetamine psychosis. Visual imagery was heightened and there was a pictorial quality to thought. One visual pattern was the patients' proclivity for visuoconstructive tasks, which took the form of dismantling watches, radios, etc., reading blueprints, and analyzing objects in a space for their makeup pattern and "3-D characteristics." Even their language reflected the visuoconstructive attitude (e.g., "putting things together to get the large picture," "placing the details in their place"). Visuospatial and visuoconstructive defects are prominent symptoms of lesions involving the temporoparietal junction of the minor hemisphere (Hecaen *et al.*[20] Hecaen,[21] McFie & Zangwill,[35] and Patterson & Zangill[39]). This would lead one to seek further symptoms of amphetamine psychosis that might be functions of the lesser hemisphere. As mentioned earlier, the false facial recognition is probably due to stimulation of the same areas that are related to the facial agnosia in minor hemisophere lesions. Reviews by Milner[37] and Piercy[41] summarized the effects on intellectual function of temporoparietal lesions in the nondominant hemisphere. Unilateral neglect of body and space, hemidepersonalization, visuoconstructive agnosia, apraxia for dressing and loss of topographic memory are the primary symptoms. Specific tests that are performed inadequately by patients with these lesions are porteus maze, map drawing and block design, as well as the McGill Picture Anomaly and the Wechsler arrangement both of which involve complex picture material dealing with everyday social situations.[37] The McGill Picture Anomaly test is specific for right temporal lobe lesions and tests the ability to see the picture as a meaningful whole scene in which the separate objects are only parts, the task being to pick out the one incongruous object. Milner[37] states, "It seems that the deficit appears when attention has to be given to many aspects of a complex picture or when different pictures have to be arranged in a meaningful

order on the basis of slight differences in detail." Statements by patients in this study (e.g., "I could see everything at once when reading blueprints" and "I looked for days for elusive clues or signs") sound much like an amplification of the quality described by Milner.

Several investigators (Hecaen,[21] Mullan & Penfield,[38] and Tueber *et al.*[51]) report that visual fits are localized predominantly in the right occipital or temporal lobes. These seizures commence either with visual manifestations (e.g., hallucinations) or are entirely confined to the visual sphere. Mullan and Penfield noted visual illusions not only with epileptic auras from right-sided foci, but also from stimulation of the right cortex. These were visual illusions of speed, dimension and perceptual intensity. Auditory illusions were produced from bilateral stimulation. Deja vu is reported to have been observed mainly in right temporal lobe lesions (Cole & Zangwill,[7] Hecaen,[21] and Mullan & Penfield[38]). Difficulties in appreciating time, particularly with a shortening of time, also are described as a rightside function (Hecaen,[21] and Mullan & Penfield[38]). These symptoms are also prominent in amphetamine psychosis,[11] however hemidepersonalization, a frequent symptom of right side lesions, was noted in only four of the amphetamine psychotics.

Negative findings are also reported. Slater and Beard[49] found no lateralization prominent either in psychosis or symptoms in their epilepsy study. Hecaen[21] insists that, from their large collection of patients in disturbances of activities of synthesis (such as the personality disturbances derived from cerebral lesions), no differences were found between right and left side lesions. They could find no differences of frequency or quality in the psychical disorders according to lesion site except for a singificantly greater percentage of euphoric, indifferent or denial reactions on the right side and catastropic reactions on the left. Others[40] have reported similar findings following Amytal injections into the right and left carotid arteries. Indifference and denial are, of course, the qualities seen in hemiasomatognosia, anosognosia and neglect of one-half extracorporeal space.

A question can be raised as to the nature of this organic denial, namely whether it presents elementary paradigms of cerebral programming, and whether it offers any further explanation of the amphetamine psychosis. Denny-Brown[10] has demonstrated in both man and monkey that temporoparietal lesions regularly present release symptoms, namely the postural changes he calls avoiding and labyrinthine symptoms. The avoiding represents an adversive turning from the side of the lesions, or, conversely, a turning to the contralateral side. Avoiding probably has its basis in postural reflexes similar to the tonic neck reflex. Gesell[15] has repeatedly pointed out that the tonic neck reflex (T.N.R.) is the first reflex or complex movement to show laterality preference and apparently was the scaffolding around which prehension and cerebral dominance developed. Postural control of head and eyes is an important feature of these patterns. Unilateral regard or attending must be viewed against a background of the contralateral neglect, inattention, inhibition or adversive turning. Concurrently, attention is primarily focused in one hemisphere and moderately inhibited in the other. The T.N.R. is also similar in several respects to the orienting reflex in which, among its many manifestations, is noted the turning toward a novel stimulus, with the orientation of eyes, head and body. The T.N.R. is but one of postural reflexes on which orienting responses and attention are organized and is especially concerned with unilateral attention.

As was noted in the introduction, unilateral attention mechanisms were hyperexcitable in patients taking large amounts of amphetamine. They were hyperalert to peripheral stimuli which frequently evoked a gross fear reaction. Hallucinations and illusions initially appeared only in the peripheral vision. One of the most ubiquitous symptoms was the constant notion that something was beside them (a presence). Although it is generally agreed that disorders of attention and awareness are involved in hallucinatory states, little is known of the varieties of attention or the systems subserving them. Since manifestations of unilateral attention were so pronounced in the amphetamine psychosis, the author would like to pursue the attention mechanisms represented by the T.N.R. further.

The T.N.R. sets up a unilateral regard especially in visuomotor attention. A six-week-old infant regards movement in the peripheral field of the extensor side, but takes no notice of similar stimuli on the flexor side.[16] Although at this age the T.N.R. and contralateral attention are probably represented anatomically no higher than the pallidum, the cortex later manifests considerable control of movement associated with contralateral attention.[8] At sixteen weeks an infant is bidextrous, tends to move his arms in unison and makes bimanual approaches, and regards stimuli in both visual fields. The patterns of unilateral and bilateral attention appear from behavioral observation to be refined at successive stages of development. In animals, destructive lesions and stimulation at successive levels in the central nervous system also demonstrate evolving unilateral attentive mechanisms,[13] in contrast to the generalized alerting from midline reticular and thalamic systems.

Contraversive turning is evoked by stimulation of extrapyramidal, limbic (Anand & Dua,[1] Bender & Shanzer,[4] Gabor & Peele,[14] Kaada,[27] and MacLean[33]) and certain cortical areas (Anad & Dua,[1] and Crosby *et al.*[8]).

On the basis of stimulation of wide cerebral areas in the cat, Flangel and Kaada[13] suggested that alertness and contralateral head turning are parts of a behavioral attention response. They noted that many cortical areas (especially area 24) presenting these responses are related to the limitrophic type of associational cortex. It is also notable that the orienting reflex has been linked to the hippocampus and possibly other areas of the archicortex. Together with characteristic aroused electro-encephalographic patterns, the orienting reaction is invariably associated with head and eye deviation. At the cortical level, other mechanisms may be also involved in regulating unilateral and bilateral attention processes. By varying the frequency of stimulation across the corpus callosum, Jung[26] achieved both facilitation and inhibition of the opposite cortex. A critical unanswered question is whether both hemispheres are simultaneously attending, alternating attention or whether one hemisphere controls the bilateral approach. The early scaffolding of attention has a direct bearing on the later complex vicissitudes of attention. Since at present the attentional relationships between the two hemispheres in the child, as well as in the adult, are esentially unknown, the author would like to propose a hypothetical model.

The main control of attention at any moment in time probably resides in one hemisphere. With development, the major hemisphere increases its gradient of control, although the non-leading hemsiphere may maintain a background attention and at times take a partial lead. This would involve a simultaneous attending to the sequential details and the verbal articulate program while at the same time maintaining a dim awareness of more global but necessary background visual and emotional material in the minor hemisphere. With recognition and visuoconstructive problems, the minor hemisphere lesions, the attending process is further overbalanced to the major side with a concurrent avoiding of the side contralateral to the lesion, or, in Denny-Brown's terms,[10] the postural reflex (T.N.R.) has been released. The preponderance of indifference, denial and avoidance in the somatognosia and anosognosia syndromes may offer insight into these psychological processes.

With unilateral loss of sensation or motor function due to lesions in the right hemisphere, there may be a perceptual flooding of the centers in the left hemisphere that conserve bilateral body schema. This rush of perceptual information concerning the loss of function is in overt conflict with the body chema. Cognitive or perceptual dissonance possibly also potentiates the attentional shift to the left hemisphere and resolves the conflict by denying the left side. Thus, the bilateral body schema is preserved. This concept that "discrepant sets of associates do not neutralize each other or mix and make a blur" is expressed in James'[25] "Law of Figured Consciousness." Hemispheric inhibition may also be one of the ways repression and denial function under ordinary circumstances. Thus, the minor hemisphere complements, alternates with and enlarges upon major hemisphere function, except at moments of cognitive dissonance or conflict when repression or denial resolves the conflict. In this connection it could be noted that conversion reaction is the par excellence example of denial and indifference. Neurophysiological substrates must underlie the attentional patterns present in this disorder. Unilateral attention mechanisms and the gradient to the left hemisphere may relate to many hysterical disturbances of sensibility, since as Schiller[47] pointed out, most of these lie on the left side of the body.

How does one explain the amphetamine psychosis and its tendency toward hyperactivity of minor hemisphere functions? Righting and postural reflexes are facilitated by amphetamine (Macht,[29] and Maling & Acheson[34]). If the tonic reflex systems are stimulated by amphetamines, one would expect either that the gradient of attention will be directed even more to the left hemisphere or that an indiscriminant stimulation of both hemispheres will result. With initial low doses, amphetamine users noted clarity and preciseness in their thinking, and they became much more loquacious. In the psychotics, both major and minor temporal lobes may be stimulated for longer intervals without the clear-cut dominance of the major lobe or with frequent alternation between the two. Therefore, there are many symptoms referable to the minor hemisphere and its prolonged stimulation without counterreference from the major hemisphere. Another possibility is that in psychosis-prone individuals amphetamine stimulates an already defective cortical attention regulating mechanism.

It was reported previously that many of the patients who developed the amphetamine psychosis were either schizoid or schizophrenic.[11] Why should these individuals be susceptible? Bender[3] has emphasized that schizophrenic children frequently show lack of integration or repression of the tonic neck reflex even as late as seven years of age. There is much evidence that visuopostural reflexes are disturbed in many schizophrenics and that this is accompanied by abnormal ocular deviation responses; there is also much evidence that similar distur-

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bances are noted in temporoparietal lesions. Lowenbach[28] repeatedly observed caloric nystagmus responses in thirty of Gjessing's cases of periodic catatonia and found that shortly before and during periods of stupor the vestibular reactivity diminished and sometimes only slow deviations were elicited. Fitzgerald and Stengel[12] studying a composite of schizophrenics noted the diminished response in some and also directional preponderance (mainly to the left). Direction preponderance is usually seen in unilateral temporal and parietal lobe disease. Both these caloric studies found ocular deviation in the direction of the slow phase. It was further noted by Fitzgerald and Stengel that such deviation secondary to caloric stimulation occurs in unconsciousness and semiconsciousness and is thought due to cortical depression.

Other visuopostural disturbances found in both parietal lesions and in certain schizophrenics are spontaneous turning around the longitudinal axis[24] and difficulty in aligning a rod to the vertical while seated in a tilted chair.[52] As previously presented, these visuopostural systems take part in regulating unilateral attention and are often mutually inhibitory. With stimulation by amphetamine in large amounts, any disturbance in the mutual regulations of right and left attention systems may result in a shift in the gradient of attention of the minor hemisphere.

Stimulation of the unilateral attention systems would help also in explaining why patients when addicted to amphetamine were so hyperalert and reactive to stimuli in their peripheral vision.[11] These unilateral attention systems are probably used for fast recognition in the peripheral visual fields. An animal or person turns quickly and without conscious effort to unknown auditory or visual stimuli. Danger especially requires fast recognition, and thus these contraversive visuopostural systems are not only associated with orientation but also with fear and defense reactions as Flangel and Kaada[13] have demonstrated so well in animals. The fear component is extremely prominent in the amphetamine psychosis and most patients reported repeated incidences of terror in response to peripheral stimuli.[11]

It should be reiterated that the above model of unilateral attention is a possible explanation for but one of the specific systems that are set into action at various levels of arousal. There is a need for further dissection of the varieties of attention and levels of arousal, especially as they relate to psychotic states. It would be productive to take a fresh look at our psychiatric syndromes by detailed description either from a phenomenological basis or with an eye sharpened by our present knowledge of neurophysiology. Nature and society perform certain experiments that we cannot. In the case of amphetamine abusers, it was previously demonstrated that specific types of persons are drawn to use amphetamines, and that only certain persons develop a psychosis.[11] The development of this chemical psychosis occurs over time and is not laboratory set dependent. A focus on behavioral antecedents and sequences can also afford some insight into this paranoid psychosis.

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35. Introduction to Amphetamine Abuse

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(Pps. 8–13)

Stimulants have been used for centuries if not millenia. Xanthine bearing plants are used by a majority of mankind, and produce a dependency which does not usually interfere, and may, in fact, enhance the efficiency of the users.

In a separate category, the juices of coca leaves have provided a sense of well-being and endurance to Andean Indians since before the Conquistadors. Less well known, the fresh leaves of the Khat[1] plant have been chewed in East Africa and the Near East for centuries. If the followers of Al Hasan used any drug to enhance their appetite for assassination and battle, one might speculate that they used Khat rather than Cannabis. When taken in the leafy form, though both coca and Khat may produce a dependency clearly detrimental to the user, it often does not. Extracted from the plant, cocaine is much more likely to create a damaging dependency, as are phenethylamines (amphetamines in this report), the synthetic equivalents of Khat.

Among the synthetic stimulants, amphetamine itself was first prepared in 1887 by Edeleano and methamphetamine in 1919 by Ogata,[2] but it was not until 1927 that the psychopharmacological effects of amphetamine were first described by Alles. From the 1930's through the 1950's, medical use of amphetamine became extensive and it was looked upon as a useful and relatively safe agent though some toxic effects and some tendencies to produce dependence were described.[3] As recently as 1963[4] the AMA Council on Drugs, while recognizing the great potential for abuse of amphetamines, stated that "at this time, compulsive abuse of the amphetamines [constitutes] a small problem [in the United States]." By 1966 concern was greater. In that year the AMA Committee on Alcoholism and Addiction and the AMA Council on Mental Health[5] took note of the information that sufficient amphetamine products were available in the United States to supply 25 to 50 doses to every man, woman and child in the country. In 1966 Griffith[6] and Lemere[7] further warned of the extent and dangers of amphetamine use and in 1967 Kramer[8] described the pattern and effects of high dose intravenous use.

PATTERNS OF USE

Though regular, oral use of amphetamines may cause difficulties, including paranoid psychosis and a disabling dependence, it is less likely to lead to these effects than intravenous use. Colonies of intravenous stimulant users have gathered in such areas as San Francisco, New York, Los Angeles, and elsewhere. At present the developmental history of the intravenous amphetamine user is typical enough to warrant a general description.

He has tried amphetamines orally; he may have liked them or not. He has used other drugs perhaps moderately, perhaps extensively, and he has been moving either in marijuana-psychedelic drug-using circles or in heroin-addict circles. His first intravenous use of amphetamine is an ecstatic experience and his first thought is "where has this been all my life." The exper-

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ience somehow differs from the effects of oral amphetamines not only quantitatively but also qualitatively. Early his use of the drug is intermittent; doses probably equivalent to twenty to forty milligrams per injection may be taken once or a very few times over a day or two. Days or weeks may intervene between sprees. Gradually the sprees become longer and the intervening periods shorter; doses become high and injections more frequent.

After a period of several months, the final pattern is reached in which the user (now called a *speed-freak*) injects the drug many times a day, each dose in the hundreds of milligrams, and remains awake continuously for three to six days getting gradually more tense, tremulous and paranoid as the "run" progresses. The runs are interrupted by bouts of very profound sleep (called "crashing") which last a day or two. Shortly after waking after crashing, the drug is again injected and a new run starts. The periods of continuous wakefulness may be prolonged to weeks if the user attempts to sleep even as little as an hour a day.

Though amphetamine used intravenously is a powerful reinforcer, there are individuals who have tried it once or several times and have chosen not to continue. Nevertheless, like heroin or cocaine, it is a form of drug use which may overwhelm even a casual dabbler.

It is interesting to note that in experiments[9, 10] in which rats had the opportunity for self-injection of amphetamines intravenously, the drug proved to be strongly reinforcing and the self-administration was characterized by periods of intake and abstinence entirely analogous to that seen in human amphetamine users.

EFFECTS

The intravenous use of amphetamines produces a syndrome with a variety of behavioral and physical effects some of which, particularly insomnia and anorexia, may themselves produce symptoms or alter the effects specifically attributable to the drug. The high dose user thus is not merely responding to a drug, but also to altered sleep patterns, to undernourishment, to malnourishment, and often to infection. And amphetamines are seldom, if ever, used exclusively: "downers"—opiates, phenothiazines and sedatives—are regularly used, as is cannabis and occasionally psychedelics. A surprising miscellany of other substances may be used experimentally and the "speed" itself is seldom pure and probably contains by-products not extracted during illicit manufacture, as well as those added afterward to "cut" the product.

The Flash and the Euphoria.—A few seconds following the injection, the user experiences a sudden, intense generalized sensation which has both physiological and psychological characteristics. It is ineffable and ecstatic, yet may differ in intensity and quality of flash and because the pure, commercially produced products do not give a good flash, it seems likely that the flash may to a great extent depend upon substances other than the methamphetamine.

The euphoria can be viewed as having both primary and secondary characterstics. Part of the sense of well-being seems purely internal and part stems from the feelings of ability and of invulnerability which are produced. Suddenly, magically volubility and gregariousness appear and boredom departs.

These desired effects are extremely vulnerable to the impingement of tolerance. It takes ever more drug to recreate this chemical nirvana. It is the desire to re-experience the flash and the desire to remain euphoric, and to avoid the fatigue and the depression of the "coming down" which drives the users to persist and necessarily to increase their dose and frequency of injection. And it is this persistence of use and these large doses which bring on all the other effects of these drugs.

Anorexia.—One of the medical uses of amphetamines is to induce anorexia to aid in weight reduction. In doses ordinarily prescribed, five to thirty milligrams per day, the anorexia produced is moderate and some have questioned whether a placebo effect is responsible rather than a drug effect. With the large doses taken during abusive use, there is no question but that anorexia is produced. Users uniformly lose weight during periods of abuse. Appetite suppression may be so profound that users may find the very act of swallowing difficult. Some users diligently force themselves to take small amounts of highly nutritious foods or inject themselves with vitamins and other dietary supplements.

Upon arising from the profound sleep which follows a run, either immediately or perhaps a few hours later, the user becomes voraciously hungry. Though he has eaten little or nothing for several days, bulimia like this seems to be related to release from the drug effect in large measure, because in the instance of non-drug assisted starvation, appetite is diminished after several days starvation. Undernutrition and malnutrition result and undoubtedly complicate all the other effects of high dose amphetamine use.

In an unpublished study[12] Seevers, Gantz and Deneau found in monkeys given high doses chronically that as the dose was raised past 32 mg./kg. per day the animals became polyphagic rather than anorexic, but continued to lose weight though eating more than three times their usual daily ration.

Insomnia.—Even early in this pattern of drug abuse

the users remain awake for a day or two at a time. These periods gradually become longer so that the runs tend to last three to six days. Though longer runs have been reported, they are generally isolated events. Some users will force themselves to lie down, close their eyes and drift into a half-sleep for perhaps an hour or two. With this the user may be able to persist in a run for several weeks before crashing.

There is no question but that sleep deprivation (or perhaps dream deprivation) alone can produce deterioration in performance, misperceptions, hallucinations and other phenomena. All these occurred in one sleep deprivation experiment,[11] but it was the impression of Pasnau *et al.*, that withholding all stimulants from their subjects during the eight-and-one-half days of wakefulness, permitted the subjects to cope better with these effects.

It is likely that both the insomnia and the drug contribute to the syndrome, and as with other aspects of this phenomenon, are inextricably intertwined. The observation that many of the physical and psychological symptoms are largely dissipated after sleeping for a day or two suggests that the insomnia alone is a major contributor to the syndrome. The fact that some symptoms persist after weeks or months of abstinence indicates that sleep deprivation is not alone responsible.

Considering that the usual pattern seen during well established high dose abuse is of three to six days of wakefulness followed by one to two days of sleep, then users spend about one-fourth of their time in sleep, about the same proportion as non-users only distributed differently. Whether the REM time is different has not been investigated and may be of consequence even if the total sleeping time of users equals that of non-users.

Tolerance develops to many of the effects of amphetamine, including that of producing wakefulness. When drug use is well developed very large doses will be necessary to keep the user awake. At times when tremulousness develops after several days of wakefulness, users describe taking a moderate dose of their drug to calm them sufficiently so that they can relax and sleep. A "moderate" dose in this instance may be as much as several score milligrams.

Paranoia.—A paranoid psychosis can be precipitated by either a single large dose or by chronic moderate doses of amphetamines. Two surveys of patients entering psychiatric units have suggested that amphetamines may be causal or at least a precipitating event in the psychiatric hospitalization of patients not otherwise identified as users of amphetamines.[13, 14] The presenting symptoms are those of paranoid psychosis.

High dose intravenous users of amphetamines generally accept that they will sooner or later experience paranoia. Aware of this, they are usually able to discount for it. Moderate persecutory ideas and visual illusions will seldom be acted on because of their intellectual awareness of their nature and origin. However, when drug use has become very intense or toward the end of a long run, even a well practiced intellectual awareness may fail and the user may respond to his delusional system.

Leake[15] has suggested in the past and Ellinwood[16, 17] more recently, that the effect of amphetamine is to release underlying psychotic trends. Griffith, Cavanaugh and Oates[18] however, precipitated a paranoid psychosis in all four subjects given *d*-amphetamine (120-220 mg. per day for 24-120 hours) inciting psychosis. All had previously been diagnosed as having a moderate personality disorder.

Though there may be individual differences in sensitivity to the psychotogenic effects of amphetamines, it appears that anyone given a large enough dose for a long enough time will become psychotic. Though this hypothesis may be untestable, given the experiences of a large number of high dose amphetamine users, it seems likely, more so than the view that psychosis is precipitated only in those already so inclined.

As mentioned earlier, the paranoia does not usually start during the first few months of high dose intravenous use. When it does finally begin, it is mild, easily controlled and is largely dissipated upon waking after crashing and it usually does not start again until after two or three days on a new run. As time goes on, it may start earlier in a run and may persist to some extent even after crashing. In some instances, the first injection after a period of sleep will bring about a return of the paranoia. Once an individual has experienced amphetamine paranoia, it will rather readily return even after a prolonged period of abstinence.

Violence.—Public concern over use of psychoactive drugs often centers on the assumption that among the effects of a specific drug is its tendency to induce unwarranted violence. Clearly, opiates do not possess this characteristic pharmacologically. Though an opiate user could, for instance, commit an act of violence during a robbery, there is nothing in the drug effect which would so incline him. If anything, opiates are more likely to inhibit any tendency toward violent behavior.

From all evidence, amphetamines tend to set up conditions in which violent behavior is more likely to occur than would be the case had an individual not used it. Suspiciousness and hyperactivity may combine to induce precipitous and unwarranted assaultive behavior.

Under the influence of amphetamines liability of mood is common—the user abruptly shifting from warmly congenial to furiously hostile moods for the most trivial of reasons.

Most high dose amphetamine users describe involvement, either as aggressor or victim, in episodes in which murder or mayhem was avoided by the slimmest of margins. There are, of course, instances in which violence actually occurred. From descriptions of a number of these events, it is clear that they would not have taken place had it not been for the use of amphetamines.

The role of barbiturates in this is difficult to assess. Paradoxically, when barbiturate use is not followed by sleep they often induce considerable irritability (though opiates, cannabis and phenothiazines are calming). Users of amphetamines often use barbiturates for sedation and may thus unknowingly add to, rather than diminish, a tendency toward angry or perhaps violent behavior.

Compulsivity.—Perhaps the most curious effect of amphetamine is its capacity to induce behavior which is persisted in or repeated for prolonged periods. If the user is not too disorganized the activity may, on the surface at least, be useful. Dwellings may be cleaned, automobiles polished or items arranged to an inhuman degree of perfection. Or these activities may be partially completed when another compulsively pursued task intervenes. The behavior may be bizarre as in the elaborate but nonfunctional reconstruction of mechanical or electrical devices, or it may take on a destructive character as in skin picking which may produce extensive ulcerations.

Analogous to this compulsive behavior in man is what has been termed stereotype in animals. Rats, mice, guinea pigs, cats and squirrel monkeys[19] almost without exception performed repetitive acts, which though not unique for the species, were characteristic for each animal.

Over-amping.—The term "over-amping" was probably derived during the year when commercially produced ampules of methamphetamine were widely used. Users prefer this word to the word "overdose" which carries the connotation of an overdose of heroin, a condition which produces an entirely different set of symptoms. A variety of events may occur when the dose of amphetamine taken far exceeds the tolerance of the user. Descriptions have been too few in number for a clear pattern to emerge. One or several symptoms may occur, including chest pain which lasts minutes or hours. Unconsciousness, again lasting minutes or hours, may occur, the user waking and occasionally finding himself aphasic or paralyzed for hours or days in a manner suggestive of the pattern seen following a cerebral-vascular accident. More frequent is the situation in which the user remains conscious, his mind racing with a myriad of thoughts, often in an ecstatic mood but unable, or perhaps unwilling to move.

Under these circumstances the user's friends attempt to nurse him and may use opiates or sedatives in an attempt to counteract the effects of over-amping.

Death.—The motto *Speed Kills* is cute, short enough to fit a button, and carries a message of concern. It is not altogether accurate. Very few deaths have been recorded in which overdose of amphetamines has been causal.

Though viral hepatitis and other infections are common and persistent among intravenous amphetamine users, again, only a few deaths related to infection have been recorded. Death by violence might add still a few more names, and the San Francisco County Coroner revealed that only one or two deaths per year in each county could be attributed to overdose and a like number to other events which might be related to amphetamine use.

The rarity of death may be due to the tolerance produced by these drugs and the relatively high ratio of effective dose to fatal dose. Dr. David E. Smith of the Haight-Ashbury Clinic and Amphetamine Research Project indicates that the two deaths he has seen were relative novices in amphetamine use.

Chlorpromazine (and probably other phenothiazines) have been shown to be effective in suppressing amphetamine effects both clinically[20] and in animals[21] while barbiturates, though not without effect, are less valuable and introduce the hazard of barbiturate toxicity. These findings have been confirmed by acute, intravenous injection of methamphetamine, *d*-amphetamine and *d,l*-amphetamine. Each produced rapid death in toxic doses (usually within 2-3 minutes, though 10 minutes was allotted for experimental purposes). Those animals which did not succumb promptly usually survived for at least six hours. Because of the rapidity of death, such conditions as grouping, room temperature, or activity did not enter into consideration. Several findings of interest emerged: unlike the results found with i.p. injection of amphetamine the LD-50 curves were sharp and consistent; in addition, the lethality of each of the three substances was approximately the same; and chlorpromazine (CPZ) effectively raised the LD-50 to about 55 mg/kg (with 5 mg/kg of CPZ), from the usual LD-50 of about 35 mg/kg.

Besides confirming the usefulness of chlorpromazine in antagonizing the effects of phenethylamines, these experiments also suggest that the antagonism is not merely based on the tendency of CPZ to diminish hyper-

activity (though this may be one mechanism of action), but also by altering biochemical events within the tissues.

Pathology.—Though human deaths due to amphetamines are not common, some clinical and pathological descriptions have been published. In a recent report[22] Cravey and Baselt describe a young man who swallowed two packets of methamphetamine when confronted by police. Within a half-hour he appeared delusional and was responding to hallucinations. When hospitalized he was cyanotic, with a temperature of 104°, pulse of 102 and blood pressure of 74/50. He was in severe acidosis. He died 5½ hours from the time of ingestion. This and other reports and unpublished case histories indicate that marked hyperpyrexia and shock are usually noted prior to death from amphetamines. In experiments with mice given amphetamine, Hardings and Peterson[23] found that those whose temperatures rose above 42.4°C usually died while those whose temperatures remained below 41.7°C usually survived. Zalis *et al.*[24] found that dogs given amphetamines developed fevers proportional to dose. He found that pulse rose at first but dropped rapidly in the terminal stage, and acidosis occurred due to the formation of lactic acid and acetic acid.

Pathologic findings in both man and animals are generally nonspecific and show pulmonary congestion and often congestion of other organs including the brain. Petechial hemorrhages in various organs including the brain are frequently but not uniformly described. Only rarely[25] is massive hemorrhage noted.

Histologic examinations of the brain tissues of monkeys, dogs, and other animals[26] has occasionally shown some cellular deterioration, but usually does not. Zalis *et al.* reported mild to moderate deterioration in the cerebral cortex of all 24 of their animals and suggest it was due to a hypermetabolic state associated with hyperpyrexia.

I have found no first-hand reports in the Western medical literature describing a histological picture of damage to human brain cells, though Lemere[7] refers to an article by Tatetsu[27] citing histopathological evidence (lobotomy and postmortem) of permanent organic brain damage. In two of six deaths due to amphetamine overdose reported by the San Francisco Coroner, petechial hemorrhages were noted in brain tissue.

Other Complications.—As in any situation in which hypodermic equipment is shared without proper sterilization, viral hepatitis is common. Evidence of hepatic damage is so common that consideration has been given to the possibility that part of the damage may be due to a direct toxic effect of amphetamines on liver.

Other forms of infection are common. Often the skin becomes shiny and delicate; small injuries may produce ulceration and healing is slow.

Jaw grinding is often described, and like tremors due to lesions of the basal ganglia, can be stopped briefly by conscious control. Mattson and Calverlay[28] report other dyskinesias in some individuals on therapeutic doses of d-amphetamine.

RECOVERY

Though a Japanese report[27] suggests that some high dose amphetamine users may become chronically psychotic, what has been most striking in our experience has been the slow but rather complete recovery of users who, according to their own descriptions and that of others, had become rather thoroughly disorganized and paranoid prior to their detention. Though most of the florid symptoms are dissipated within a few days or weeks, some confusion, some memory loss, and some delusional ideas may remain for perhaps six to twelve months. After that time, though there may be some residual symptoms, they are slight and not disabling and are noticed primarily by the (now abstinent) user himself. Most commonly, ex-users report slightly greater difficulty in remembering.

As a group they describe being more open and talkative than they had been prior to their use of amphetamines. They like the result and declare with certainty that it is due to their experience with amphetamines.

Anyone concerned with the welfare of amphetamine users, and the users themselves, should recognize that most, if not all, can recover from even the most profound intellectual disorganization and psychosis given six months or a year of abstinence.

TREATMENT

The care of amphetamine users poses some special problems. In them are combined the problems of management of the hooked drug user and the paranoid personality. Though suffering with severe medical and psychiatric symptoms, they are generally fearful of hospitalization.

Some crises may yield to phenothiazine tranquilizers or first aid, but abstinence is probably the most important therapeutic device, and this result may be difficult to attain. Many users who attempt abstinence find it difficult because of the fatigue which results, extreme at first, gradually diminishing but persistent, perhaps for months.

Abstinence for many is forced by a stay in prison or jail or commitment to a psychiatric hospital or civil addict program. No data have yet been collected to

indicate the long term value of such enforced abstinence. Certainly, many who have been incarcerated have returned to their drug use upon release. A concerned person is in a bind. Users do not readily volunteer for care, but commitment programs offer little besides enforced abstinence. Should the user be permitted to live in the limbo of his drug or forced into the limbo of an institution? Can voluntary programs be devised which are sufficiently useful and attractive that users will seek them out and persist in their program? Can commitment programs be devised which do not resemble slightly benign prisons? Or, do we just let the user seek heaven or hell on his own terms while the community offers help only on its own terms?

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36. The True Speed Trip: Schizophrenia

By Solomon H. Snyder

(Psychology Today, pages 42–46 and 74–75, January, 1972)

GIVE THE PATIENT 10 MILLIGRAMS OF DEXTROAMPHETAMINE EVERY HOUR, DAY AND NIGHT, AND THE RELIABLE RESULTS IS PSYCHOSIS—"A UNIQUE FEATURE OF AMPHETAMINE PSYCHOSIS IS COMPULSIVE, STEREOTYPED BEHAVIOR THAT THE VICTIM REPEATS HOUR AFTER HOUR"

The patient has just been admitted to the hospital emergency room, so violent that it took three strong men to bring him in.

From relatives and from bits of the patient's incoherent ramblings, the admitting psychiatrist begins piecing together an account. Yesterday John felt that others were looking at him in a peculiar way. He had walked the streets all night and spent this morning looking for gold in the gravel paths of the city park. This afternoon he heard voices talking about him. Hostile, secretive persons were looking at him; he was sure they were planning to kill him.

In an interview, the psychiatrist concludes that John suffers from auditory hallucinations and that he has delusions of persecution, and volatile, inappropriate emotions. The diagnosis is simple: an obvious case of paranoid schizophrenia.

But there is a hooker. John is not schizophrenic at all. After a few hours his wife arrives at the hospital and tells the psychiatrist that John has been injecting methamphetamine into his veins for the past three months. John is a speed-freak, an amphetamine addict, and is suffering the principal hazard of the habit.

Key

For years researchers have been trying to find a chemical key to schizophrenia. The first quest is for a drug that will make normal persons act, temporarily, in the peculiar ways that schizophrenic patients act. Such a drug could provide an important lead to the causes of schizophrenia. And if the drug also will make animals behave schizophrenically, investigators will be able to manipulate schizophrenia in their laboratories. They can explore how environmental, chemical and genetic factors influence schizophrenic behavior, and they can investigate a wealth of possible cures. A growing number of scientists believe that this approach is likely to pay off in the search for a cure of schizophrenia.

Amphetamine offers promise to be this key drug, because it produces patients like John who can trick even experienced clinicians into erroneous diagnosis of schizophrenia. But other chemicals also are under serious study in the search. LSD is the best known psychotomimetic—psychosis-mimicking—drug: LSD, mescaline, psilocybin and other drugs produce effects similar to psychosis. Alcohol is another: an alcoholic in withdrawal undergoes delirium tremens—d.t.s—an agitated state fraught with frequent, frightening hallucinations. And many drunks have heard nonexistent voices and seen occasional elephants of unusual colors. Marijuana and its concentrate, hashish, taken in sufficient quantity, can produce hallucinations. And the United States Army, with somewhat different motives, has investigated several highly secret chemicals related to atropine, minute doses of which produce a delirious, psychotic-like state.

Daze

Most of these drugs yield only imperfect approximations of schizophrenia: disoriented and confused—often they cannot say who they are, where they are, or what time of day it is, or what month. The true schizophrenic patient, on the other hand, is likely to be well oriented as to person, place and time. Most drug-produced disorientation resembles the symptoms of brain damage—from accident, stroke, brain tumor, vitamin deficiency, or hormonal imbalance—more than it resembles schizophrenia. Amphetamines provide a much better chemical analog to schizophrenia—speed-freaks are invariably well oriented, perhaps even more when they are under the influence than when they are not drugged.

After recovering from a psychotic episode, an amphetamine user usually retains a detailed memory of the whole experience, as do most patients recovering from schizophrenia. By contrast, the other drugs—possibly excepting

the psychedelics—deaden the mental faculties so that a patient may have partial or total amnesia that covers the episode.

See

Another important difference is that in drug-induced psychosis, hallucinations or perceptual distortions are primarily visual; in true schizophrenia they are almost always auditory.

When a schizophrenic patient does report visual hallucinations, it is usually during the early stages, after an acute onset. This was true in the cases of amphetamine psychosis reported by Phillip H. Connell in London: visual hallucinations occurred primarily in patients whose psychoses developed acutely after a few large doses of amphetamine The patients who had escalated dosage gradually over several months tended to have mostly auditory hallucinations. Another telling link is that the drug therapy most effective for schizophrenia is the one that is most effective for amphetamine psychosis. A barbiturate or sedative may be helpful for a number of drug states, but phenothiazine tranquilizers are uniquely effective in amphetamine psychosis and schizophrenia.

For all of these reasons, it appears that amphetamine psychosis is the best chemical model of true schizophrenia, at least of the paranoid type.

Pills

The average patient with amphetamine psychosis started taking the drug in pill form. Most pills on the market contain five or 10 milligrams of active drug, and are called pep pills or diet pills, depending on the user's purpose. Tolerance for amphetamine builds up rapidly; the pill-popping addict must take more and more pills at shorter and shorter intervals to reach the same high—sometimes more than 100 pills a day. But the typical amphetamine addict tires of pills quickly and begins mainlining: he injects the drug directly into his veins, with perhaps 100 or 200 milligrams of methamphetamine—crystal—in each injection, or hit.

Even before he withdraws the needle he feels an intense buzzing euphoria, called a rush, that users sometimes liken to an orgasm of the whole body. After this, the addict will be elated and hyperactive for several hours, with no desire for food. He may eventually shoot up every three or four hours, on a five- or six-day run, until he crashes, exhausted, to sleep for two to four days. He awakens with a ravenous hunger; after he has eaten as much as he can hold, he goes into profound depression, he seeks the only known cure: more amphetamine.

F.B.I.

Signs of amphetamine psychosis first develop while the speed-freak is under the influence of the drug (they are thus unlike delirium tremens, a withdrawal psychosis). The harbinger is vague fear and suspicion—*What was that? I heard something. Is somebody trying to get me?* Soon the paranoia centers around a specific delusion—for example, that the FBI is out to get him. An amphetamine party may begin with everyone very elated and talkative, and may end with each person stationed silently at a window, peeking through the curtains for signs of the police.

Acting on his delusions, the speed-freak may become violent—*to get them before they get me.* It is in this sense that the slogan speed kills is most accurate: more persons die from senseless and brutal violence associated with amphetamine delusions than from overdoses of the drug itself.

Bag

Another unique feature of amphetamine psychosis is compulsive, stereotyped behavior that the victim repeats hour after hour, apparently without fatigue or boredom. A woman sorted out her handbag over and over for several hours. A man at a table constantly rearranged his knife and spoon. A teen-ager counted cornflakes all evening. While a user is busy at this major repetitive behavior, he may also grind his teeth, lick his lips, or constantly shift his eyes from side to side.

Drugged laboratory animals behave similarly. Under small doses of amphetamine, they become hyperactive and vigilant; with greater doses, they develop repetitive, stereotyped behavior. And Roy Pickens and his colleagues have found that when laboratory rats can dose themselves with amphetamines by pressing a bar, they follow a pattern of intake and abstinence, run and crash, that is similar to the pattern of the human amphetamine user.

Why

Some theorists believe that lack of sleep may cause amphetamine phychosis, not any ingredient of the drug itself. We know that often persons who go without sleep for long periods develop bizarre, psychoticlike behavior. Others speculate that amphetamine's overstimulation of the senses brings on the psychosis. Still others argue that the intense emotional arousal in the amphetamine experience simply triggers a latent psychosis that any stress could have provoked.

The best way to resolve these questions was to produce amphetamine psychosis in human beings—deliberately drive people crazy—and carefully follow the sequence of events.

The first person to essay such an experiment was a physician, John Griffith at Vanderbilt University. He recruited four men in their late 20s and early 30s who already were amphetamine addicts but who had never shown signs of amphetamine psychosis, or any tendencies toward schizophrenia. They were all mildly to moderately psychopathic, a condition that is readily distinguishable from schizophrenia. Griffith relentlessly dosed each man with dextroamphetamine—10 milligrams, orally, every hour of the day and night—until he developed signs of amphetamine psychosis. Griffith carefully monitored each man's physiological and psychological symptoms throughout the experiment.

Cling

Each man exhibited unequivocal psychosis within two to five days and the psychotic symptoms followed the same sequence in each. After the first doses of amphetamine he showed the usual euphoria, excitement and hyperactivity. During this time he was lucid, in good contact with his surroundings, normally boyish and warm. But by the fifth or sixth dose, he had changed: he became quiet, depressed, uninterested in amusement—a hypochondriac who clung dependently to Griffith.

This pattern was not ordinary amphetamine behavior, probably because the subjects were tested in solitude in a controlled hospital environment. On his own, an amphetamine addict would probably increase his dosage before such symptoms developed, and social variables undoubtedly would color the experience. For example, his interactions with other amphetamine users probably would keep him hyperactive longer than Griffth's subjects were.

Signs

The first patient developed psychotic signs after about 24 hours; the last after 12 0hours (five days). In each case the subject began peculiar behavior about eight hours before the explicit psychotic symptoms appeared. He became taciturn, and refused to talk about his thoughts or feelings. He asked guarded questions about the room, the experiment, or unusual noises, but backed off if anyone asked why he wanted the information. In retrospect, the patients recalled that it was at about this time that paranoid ideas first entered their minds. For a while they could recognize that the ideas were unfounded, chemical delusions—familiar and expected side-effects of the drug. Later the ideas were not so easy to dismiss.

"One man believed he was the target of rays from a 'giant oscillator'—Another maintained that his wife planned to kill him"

The florid psychosis commenced abruptly in each man. After being stony-faced and silent for about eight hours, he began discussing his thoughts openly and sharply, though he remained cold and aloof. His paranoid ideas became more elaborate and organized, and he believed them. One man believed he was the target of rays from a "giant oscillator." Another maintained that his wife planned to kill him. Strikingly unlike patients with other forms of drug-psychosis, these subjects could not be comforted easily and they were not at all suggestible. The psychosis dissipated within eight hours of the drug cut-off in three of the subjects; the fourth remained somewhat paranoid for another three days.

Out

Griffith's experiment answers some questions about possible alternative explanations of drug-induced psychosis. First of all, the psychosis can not be

attributed simply to sleep deprivation, because two of the men became psychotic after losing only one night's sleep, which alone is not long enough to produce psychotic symptoms.

Nor can the psychosis be attributed to intense stimulation and arousal—the men never appeared to be overstimulated—in fact, after the first few hours they all appeared to be depressed.

Griffith also was careful to rule out pre-drug personality as a significant factor; he selected subjects who had never shown schizophrenic tendencies either in a drugged state or undrugged.

Order

The amphetamine psychosis that Griffith observed is a good imitation of schizophrenia, probably the best of the drug-induced states. But it isn't perfect; there are differences, the most salient being that Griffith's subjects showed no signs of formal, schizophrenic thought disorder. This is the bizarre mental process that produces crazy associations and meandering, contradictory, hard-to-follow speech (see "Schizophrenia: Carnival Mirror of Coherence," by Donald Bannister, *P.T.*, January 1971). Other researchers confirm Griffith's finding: amphetamine addicts rarely display thought disorder.

The lack would seem to destroy any systematic analogy between amphetamine psychosis and schizophrenia, for many psychiatrists consider thought disorder to be the vital element of schizophrenia (see "The Shattered Language of Schizophrenia," by Brendan A. Maher, *P.T.*, November 1968). But tht issue is not so simple. Doctrinaire diagnosis aside, thought disorder does not invariably accompany schizophrenia. Acute schizophrenics show much less thought disorder than chronic schizophrenics do; and paranoid schizophrenics, with their tight and ordered delusional systems, may show no thought disorder at all. In this connection it is encouraging to note that the amphetamine psychosis usually is both acute and paranoid, and thus resembles the types of schizophrenia with least thought disorder.

"Amphetamine-induced psychosis seems to be the best available chemical imitation of schizophrenia"

Brain

From Griffith's research and from clinical experience, it seems safe to say that large doses of amphetamines will almost invariably produce psychosis similar to acute, paranoid schizophrenia. The clinical picture is not identical to schizophrenia, however, perhaps because amphetamine's grab-bag of side-effects (arousal, sleeplessness, loss of appetite, stereotyped behavior, etc.) may complicate matters. To find out which components of the amphetamine experience are most responsible for the psychosis, we must study the brain to find how nerves, tissues and brain chemicals respond when amphetamine is added to the system.

An obvious clue is that the chemical structure of amphetamine closely resembles the structures of dopamine and norepinephrine, two chemicals that occur naturally in the brain. Dopamine and norepinephrine are found at the brain's synapses, the points at which branches of one neuron come close to but do not quite touch, the sensitive portions of another neuron.

Fire

When a nerve impulse in a neuron reaches a synapse, it triggers the release of chemicals—dopamine or norepinephrine, among others—out of the nerve endings. These wash up against the next neuron and trigger it to renew the nerve impulse and send it on its way to the next neuron link in the chain.

It is through these brain chemicals that one neuron thus communicates with the next, and this neuronal conversation underlies all information-processing, thoughts, plans, and perceptions in the brain. Whether the neurotransmitter is dopamine, norepinephrine or some other chemical, it must be inactivated after it has done its job. Otherwise it would continue to stimulate the second neuron and make it continue firing. Some transmitters are inactivated by other chemicals that neutralize them. Dopamine and norepinephrine are inactivated by being transported back into the nerve endings that released them. Julius Axelrod, who discovered this mechanism, called it "reuptake," and won a Nobel Prize in 1970 for his discovery.

One of the ways amphetamine enters the picture is by inhibiting the reuptake mechanism: small pools of used dopamine or norepinephrine built up

at the synapses thereby causing nerves that are sensitive to dopamine and norepinephrine to fire erratically, repeatedly, and without stimulation from other neurons. The resulting behavior depends on whether the stimulated nerves are in dopamine pathways or norepinephrine pathways.

Image

Which pathways are responsible for which symptoms? We get help in answering this question because amphetamine can be broken down into two mirror-image forms that have different effects on behavior and on the brain's transmitter chemicals. One type rotates polarized light to the right, and is called dextroamphetamine; the lefthanded form is levoamphetamine, borrowing *dextro* from Latin to indicate *right* and *levo* to indicate *left*.

It has long been known that dextroamphetamine is by far the more potent of the two forms in stimulating the central nervous system. Smith Kline & French puts out a pill form of dextroamphetamine, under the trade name Dexedrine.

Joseph Coyle, Kenneth Taylor and I have found that dextroamphetamine is 10 times more powerful than levoamphetamine in inhibiting the reuptake mechanism in norepinephrine nerves. When dextroamphetamine is present in a system, there will be more norepinephrine at brain synapses, the nerves triggered by norepinephrine will fire more often than usual, and the behaviors that are governed by these norepinephrine tracts will be exaggerated. And all of these effects will be dramatically more pronounced with dextroamphetamine than they are with levoamphetamine.

In dopamine tracts, on the other hand, dextroamphetamine and levoamphetamine tend to be equally effective: dextroamphetamine produces a slightly greater pileup of dopamine at the synapses than levoamphetamine does, but the difference is nowhere near the order of 10 to one. This suggests that if a given symptom of amphetamine intake appears about as often with dextroamphetamine as with levoamphetamine, that behavior is probably mediated by the dopamine neurons. If a behavior occurs much more readily with dextroamphetamine than with levoamphetamine, the behavior probably is governed by tracts of norepinephrine neurons.

Rats

Kenneth Taylor and I recently studied two typical amphetamine effects—motor activity and stereotyped behavior—in laboratory rats. With relatively small doses the animals appeared to be excited, running about their cages furiously, and this effect was exactly 10 times more pronounced under dextroamphetamine than it was under levoamphetamine. This perfectly parallels the 10-fold advantage that dextroamphetamine has in producing excess norepinephrine, and it strongly suggests that the central-stimulant and heightened-activity effects are probably produced when amphetamine comes in contact with the norepinephrine neurons of the brain.

With somewhat larger doses of amphetamine, animals begin stereotyped behavior similar to the compulsive, repetitive behavior of speed-freaks. Rats tend to stay in one corner of the cage, to sniff and lick repeatedly, and to gnaw incessantly on any available object, such as the bars of the cage. We found that the two forms of amphetamine were fairly close in their ability to produce stereotyped gnawing in rats. This suggests that the brain's dopamine tracts are responsible for repetitious, stereotyped behavior in amphetamine users. Other investigators have reached the same conclusion by showing that, when dopamine areas of the rat brain are cut out, amphetamine does not produce stereotyped behavior as readily as it usually does.

After hearing about our successful experiments with animals, Burton Angrist and Samuel Gershon at New York University asked the next logical question: how do dextroamphetamine and levoamphetamine compare in producing amphetamine psychosis in human beings? They studied three former amphetamine addicts, volunteers, putting them through the 10-milligram-per-hour regimen that Griffith followed. Each subject went through three separate sessions: once with dextroamphetamine, once with levoamphetamine, and once with a mixture of the two.

Both drugs and the mix produced psychosis in each man and none was markedly more powerful than any other. (Dextroamphetamine was slightly faster than the other preparations, levoamphetamine was the slowest, and the mixture, as might be expected, was intermediate.)

Maps

This finding suggests that amphetamine psychosis is produced by excessive activity in the dopamine tracts of the brain, while such other amphetamine effects as hyperactivity and euphoria originate in the norepinephrine tracts. With a chemical stain developed by a group of Swedish researchers, it has recently become possible to map dopamine and norepinephrine pathways through the brain. We have learned, for example, that some prominent dopamine tracts end in areas of the brain's limbic system that regulate a variety of emotional behaviors. The largest dopamine tract has become famous in its own right: it leads to an area that coordinates body movements, and if the tract is damaged so that there is a deficiency of dopamine, the patient is likely to suffer from Parkinson's disease. L-dopa, the drug that is converted to dopamine in the brain, has been hailed as a miraculous treatment for Parkinson's disease.

The major norepinephrine tracts start in the brain stem and ascend through the medical forebrain bundle—the pleasure center. Animals will work very hard to get electrical stimulation in this area, which likely has an important role in the euphoric high of amphetamine use. The norepinephrine tracts also extend into other parts of the hypothalamus, perhaps into the so-called satiety center which, when stimulated, makes a food-deprived animal stop seating.

Several pharmacologists have found that phenothiazine tranquilizers produce improvements in schizophrenic patients by blocking the dopamine receptors in the brain. This fits nicely with our idea that amphetamine produces psychosis by increasing the amount of dopamine around dopamine-sensitive cells. Phenothiazine alleviates symptoms by working in the opposite direction: it makes the dopamine-sensitive neurons less sensitive.

Systems

Amphetamine-induced psychosis seems to be at best available chemical imitation of schizophrenia. But there remains one nagging difficulty; the amphetamine illness resembles paranoid schizophrenia, not catatonic schizophrenia, undifferentiated schizophrenia, or other forms of the disorder. I don't think this means that paranoid schizophrenia is a different disease from other types. I think that if amphetamine were to act solely on dopamine neurons and had no effect on norepinephrine neurons, the result might be the classic, undifferentiated form of schizophrenia, or a form with characteristics determined only by the personality of the patient. But norepinephrine stimulation adds another set of symptoms to the clinical picture—hyperactivity, sleeplessness, and loss of appetite. The alerting effect may make the patient try to find an intellectual framework for the strange feelings that come over him. He searches for explanations and meanings, and this leads to the elaborate system of delusions that is the essence of paranoia. In short, the basic amphetamine psychosis may arise through the brain's dopamine mechanisms, but the specific paranoid solution comes from the contribution of norepinephrine systems.

Investigators are now trying to improve upon amphetamine, to find a drug that will stimulate dopamine systems but not norepinephrine systems. If my reasoning is accurate, such a drug would produce a pure schizophrenia indistinguishable from the disorder that is observed in mental-hospital wards. The drug would be a boon. It would give specific direction to the search for the cause of natural schizophrenia, and would allow investigators to manipulate schizophrenic symptoms in the laboratory and study, in animals, a vast range of possible cures.

Amphetamine—A Sketch

Chemists first synthesized amphetamine in 1887, but no one evaluated it systematically until 1927, when experimenters reported that laboratory animals dosed with the drug became hyperactive and lost all interest in eating or sleeping. Five years later a pharmaceutical house introduced the drug into clinical medicine under the name Benzedrine.

Scientists isolated two different forms of the drug. One of them rotated polarized light to the right—clockwise; the other rotated it to the left. Gordon Alles found that the right-handed *dextro* form was a much more potent central stimulant than the left-handed, *levo* form. Soon dextroamphetamine (Dexedrine) was with us.

Dexedrine and Benzedrine, both marketed by Smith Kline & French Laboratories, were the primary commercial amphetamines until 1945, when Burroughs Wellcome & Co. joined the market with methamphetamine (Methedrine), now notorious under the name *speed.*

The number of amphetamine-related agents proliferated. Some deemphasized the stimulation effects and decreased appetite—phenmetrazine (Preludin) and diethylpropion (Tenuate) are examples. Methylphenidate (Ritalin), on the other hand, made its debut as a potent central stimulant with little or no appetite-suppressing properties. (The researchers discovered that, in a seemingly paradoxical way, it tranquilized hyperactive children; physicians prescribe it widely for this purpose.) Despite their subtle differences, all these drugs are powerful, all lend themselves readily to abuse, and all can lead to amphetamine psychosis.

Astir

Amphetamines have other effects than hyperactivity, sleeplessness, and loss of appetite. Persons under amphetamine are talkative, restless, always in motion, often with repetitive and stereotyped movements. They take on monumental projects and assignments with little sense of fatigue or boredom. They may show improved scores on reaction-time tasks, though this is probably due to increased alertness and scanning of the environment rather than to increased response speed *per se.*

The effect of amphetamines on sexual behavior is not clear-cut. Gosta Rylander, a Swedish physician, thinks amphetamine is the most powerful aphrodisiac known. He quotes a patient who said that an injection of amphetamine "goes straight from the head to the scrotum . . . This wonderful drug is a ——— pump . . . I always need a couple of girls at the same time." But others report with equal conviction that amphetamine dulls sexual sensitivity. Eugene Schoenfeld, M.D., who writes "HIPpocrates," an unorthodox medical-advice column that appears in many underground papers, has noted that "amphetamines commonly make sexual arousal and fulfillment more difficult to achieve."

Amphetamine also dilates the bronchial tubes and it was first used in inhalers for asthma patients. Each inhaler contained the equivalent of 500 milligrams of Dexedrine—about 50 times the average dose for appetite suppression. In the '30s, inhaler containing these massive amounts of amphetamine were sold widely, and the drug could be removed easily from the inhaler.

Doze

Although there were a few cases of amphetamine psychosis in persons who consumed the contents of inhalers, the first reported incidence of amphetamine psychosis was among persons being treated with amphetamine for narcolepsy, an uncommon condition in which the individual goes to sleep at unpredictable times—he can doze off while he is walking, or when he is in the midst of a heated discussion.

Benzedrine proved most useful in keeping these patients awake. In 1938 three narcoleptic patients were reported to have developed temporary paranoid psychoses after they had escalated their daily Benzedrine doses two- to threefold—against doctors' orders. The patients had the major symptoms of full-fledged amphetamine psychosis.

The first epidemic of amphetamine psychosis occurred in Japan. During World War II the German Luftwaffe used amphetamines to keep pilots alert on long bombing missions. Germany's allies, the Japanese, soon began producing large quantities of amphetamines. Toward the end of the war, Japanese munitions-factory workers used these drugs almost compulsively to keep up their spirit and efficiency, and drug companies built up enormous stocks of them. With the war's end, the companies cleaned out their huge stockpiles by advertising "amphetamine for elimination of drowsiness and repletion of the spirit." The ad campaign apparently appealed to many young Japanese who suffered from frustration and loss of self-confidence—because by the mid-1950s amphetamine abuse had reached epidemic proportions. More than 500,000 Japanese were amphetamine addicts, and there were at least 50,000 reports of amphetamine psychosis, in 1954 the government imposed six-month jail sentences for simple illegal possession of the drug, and in three years the epidemic was over.

Hippies

The most massive and systematic intravenous dosing of amphetamines, however, began in the United States in the late 1960s. It started with the

hippies in San Francisco. To heighten the intensity of the psychedelic experience, some bold experimenters added Methedrine to preparations of LSD. Drug users I interviewed said that Methedrine is the favored amphtamine because it produces more euphoria than the others. (It also is the amphetamine most easily synthesized by underground chemists.) In any event, a new class of hippie, the speed-freak, soon emerged. He often could not tolerate the overwhelming self-revelation induced by LSD, and preferred instead to be high, pure and simple. He injected astronomical doses of amphetamine into his veins, and amphetamine psychosis stalked the Haight-Ashbury neighborhood. Most speed-freaks, aware of the effect, expect sooner or later to experience severe paranoid psychosis.

Words

Smart, flip, in-group terminology gathers around a new forbidden fruit the way insects do, and the amphetamines have a considerable collection. Some terms refer descriptively to the uses and effects of amphetamine: *crank, pep pills, uppers, lid-poppers, wake-ups, eye-openers, truck drivers, copilots, coast-to-coasts.* Other terms identify specific pills by their chemistry or appearance: *bennies, dexies, meth, whites, black beauties, purple hearts, greenies, footballs.*

But it is the ultimate frequent effect of amphetamine that has inspired the simplest and most telling catch-phrase of all: *Speed Kills.*

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37. NECROTIZING ANGIITIS ASSOCIATED WITH DRUG ABUSE

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[*New England Journal of Medicine*, 283:1003–1011, Nov. 5, 1970]

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Abstract Fourteen young drug abusers with a necrotizing angiitis indistinguishable from periarteritis nodosa were studied. The six women and eight men had used narcotics, stimulants, hallucinogens and depressants. Methamphetamine, alone or in combination with heroin or d-lysergic acid diethylamide, was used commonly

The clinical presentation varied from a complete lack of symptoms in five patients to pleomorphic systemic signs and symptoms with renal failure, hypertension, pulmonary edema and pancreatitis. The vascular changes of necrotizing angiitis, including arterial aneurysms and sacculations, were noted in the kidney, liver, pancreas and small bowel at selective angiography. Post-mortem findings in four patients revealed generalized vascular changes of differing age, including chronic and healed lesions.

Because of the multiplicity of injected substances with the high probability of contamination the exact etiologic agent in these cases is not clear; however, methamphetamine appears to be a common denominator.

THE existence of a lethal systemic disease associated with drug abuse and with characteristics of periarteritis nodosa has not previously been described. Fourteen drug abusers with necrotizing angiitis (periarteritis nodosa), a disease of pleomorphic clinical manifestations characterized histopathologically by inflammation and fibrinoid necrosis, have been observed and studied. The potential importance and broad implications of this observation warrants a report.

The six women and eight men comprising the study had used a spectrum of narcotics, hallucinogens, stimulants and sedatives. The following list of drugs taken by one patient during a three-year period is not unusual: amphetamines, barbiturates, chlordiazepoxide hydrochloride, diazepam, hashish, hydroxyzine d-lysergic acid diethylamide, marijuana, diacetylmorphine, meperidine hydrochloride, mescaline, methamphetamine, oxycodone hydrochloride preparation, oxymorphone, 2,5-dimethoxy-4-methylamphetamine (STP), strychnine and tetrahydrocannabinol. Although the patients in this study had used many drugs, the basic combinations of heroin and methamphetamine or d-lysergic acid diethylamide and methamphetamine were most commonly involved. All except two of the patients with necrotizing angiitis admitted to the use of intravenous administration of methamphetamine, and one patient had used it exclusively. The duration of drug abuse varied from three months to over five years.

The following four cases, all with a fatal course, illustrate the confusing symptoms and signs involving many systems manifested by these patients.

Case Report

D.G., a 19-year-old man with a 2-year history of daily intravenous administration of methamphetamine, was admitted to the hospital because of nausea, emesis, headache, diminished vision in the left eye and urinary frequency of 2 days' duration. There was no previous history of hypertension or of cardiac or renal disease. The patient had been noted to have had a diastolic blood pressure of 90 mm of mercury several days before admission.

Abbreviations Used

BUN	blood urea nitrogen
SGOT	serum glutamic oxalacetic transaminase
SGPT	serum glutamic pyruvic transaminase

Physical examination revealed a poorly nourished, lethargic, bearded man, who was slow in his response to verbal stimulation. The temperature was 98.8°F by mouth, the pulse 90, and the respirations 18. The blood pressure was 195/135. The pupils were equal in size, and there was blurring of the disk margins bilaterally. Visual acuity was 20/120 in the left and 20/40 in the right eye. The lungs were clear to percussion and auscultation. There was a 4th heart sound at the apex. Abdominal palpation revealed minimal tenderness in the left lower quadrant. There were no localizing neurologic signs or abnormal reflexes.

The hemoglobin was 13.2 g per 100 ml, and the white-cell

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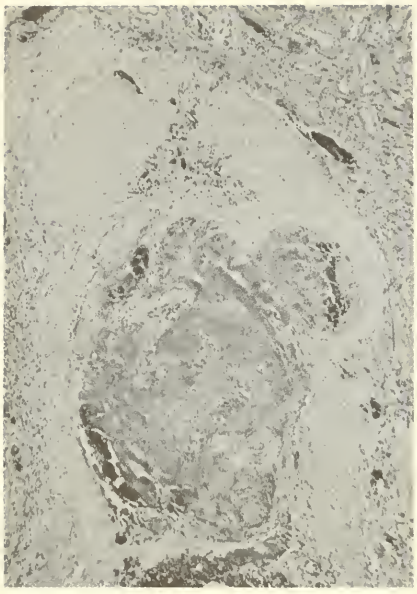

Figure 2. Renal Arcuate Artery in D.G., Showing Aneurysmal Dilatation, with Organizing and Recent Thrombosis (Hematoxylin and Eosin Stain X55).

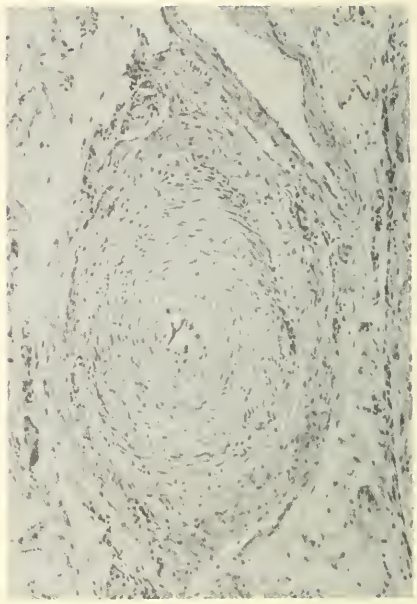

Figure 3. Marked Luminal Narrowing Resulting from Intimal Proliferation and Medial Fibrosis in an Artery of the Colonic Serosa of D.G. (Hematoxylin and Eosin Stain X125).

of her feet that had been present for 3 years. She had noted intense pain in both calves during the 3-week period before admission. No arthritis and no arthralgias were present. The patient was a known heroin addict and chronic alcoholic, who had previously received treatment for pancreatitis and hemorrhagic alcoholic gastritis. She used marijuana on occasion and took several other drugs, which may have included methamphetamine as a diluent in the heroin. She had recently had fever, weight loss and a nonproductive cough. She had noted transient pedal edema for 1 week before admission.

Physical examination revealed a slim, well developed woman in no acute distress. The temperature was 100°F by mouth, the pulse was 100, and the respirations 24. The blood pressure was 130/80. Numerous needle tracts were evident over both arms. The pupils were equal. Examination of the chest and abdomen was negative except for midepigastric tenderness. The neurological examination revealed decreased sensation to pinprick over both lower extremities. The biceps deep tendon reflexes were 3+ bilaterally; the right quadriceps reflex was 1+ whereas that on the left was 4+. The hemoglobin was 11.2 g per 100 ml, and the white-cell count 26,600, with 85 per cent segmented neutrophils, 1 per cent band forms, 10 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. The urine was yellow, with a specific gravity of 1.008 with a trace of protein. Results of laboratory tests obtained at the time of admission included a blood sugar of 108 mg and a BUN of 8 mg per 100 ml, and a potassium of 4.1 mEq and a sodium of 127 mEq per liter. The serum amylase was 530 U, and the urinary amylase 4250 U per 100 ml. The total serum bilirubin was 0.5 mg per 100 ml. The alkaline phosphatase was 3.0 Bessey–Lowry U, the SGOT 55 U, and the SGPT 31 U. The albumin was 1.9 g, and the globulin 4.7 g per 100 ml.

Pancreatitis was diagnosed, and supportive treatment was given. There was a spiking fever, with a maximum temperature of 103°F, and the abdominal tenderness persisted. Antibiotics were administered without response. The hematocrit fell from 26 to 14 per cent without evidence of hemorrhage. On the 62d hospital day the first of many episodes of pulmonary edema developed. The patient had lost 15.9 kg since admission, and at this time weighed 29.5 kg; marked muscle wasting was particularly evident. On the 64th hospital day, bilateral foot drop developed, and sensation over the soles of the feet was noted to be absent. A decrease in pain sensation below the knees was observed. Renal and selective visceral angiography established a diagnosis of necrotizing angiitis (Fig. 5 and 6). A biopsy taken from the gastrocnemius muscle showed fibrinoid necrosis involving the entire thickness of the wall of a small muscular artery with a polymorphonuclear-cell infiltrate in the wall and in the tissue surrounding the vessel.

On the 135th hospital day, steroid therapy was initiated and was followed by a 6.8-kg weight gain. Hypertension developed, and the patient died on the 177th hospital day.

At post-mortem examination, the body was markedly emaciated, with a weight of 31.7 g and a length of 150 cm. The skin and conjunctivas were jaundiced. The heart, which weighed 450 g, showed generalized hypertrophy and slight dilatation, especially on the right. A 2-mm nodose aneurysm was observed in a branch of the left anterior descending coronary artery overlying the left ventricle. Generalized ath-

count 32,000, with 92 per cent segmented neutrophils, 3 per cent band forms, 3 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. Urinalysis revealed a specific gravity of 1.007, a pH of 6.5, a 1+ test for albumin and a 1+ test for sugar, and microscopical examination of the sediment showed occasional red blood cells. Results of blood tests obtained at the time of admission included a sugar of 104 mg and a blood urea nitrogen (BUN) of 47 mg per 100 ml, and a potassium of 2.7 mEq, sodium of 128 mEq, and carbon dioxide of 32 mEq per liter. The calcium was 8.4 mg, the creatinine 3.3 mg, the albumin 3.5 g, and the globulin 3.2 g per 100 ml; the alkaline phosphatase was 3 Bessey–Lowry U, the serum glutamic oxalacetic transaminase (SGOT) 48 U, and the serum glutamic pyruvic transaminase (SGPT) 32 U.

The QT interval was prolonged, with clockwise rotation in the electrocardiogram. Radiologic studies of the skull and chest were within normal limits.

A working diagnosis of malignant hypertension secondary to chronic renal disease was made after a normal, midline echoencephalogram and normal findings at lumbar puncture had been obtained. The patient was treated with alpha-methyldopa, fluid restriction and potassium replacement. Repeat urinalysis showed red cells and red-cell casts in the sediment. Beta-hemolytic streptococci were grown from a throat culture, and he was treated with penicillin.

The first of several episodes of acute pulmonary edema occurred on the 4th hospital day. The BUN rose to 66 mg per 100 ml, and the potassium to 5.5 mEq per liter. From the 5th to the 9th hospital day there was a fall in hematocrit, associated with hemolysis. By the 12th hospital day the BUN was 100 mg, and the creatinine 6.0 mg per 100 ml. Bilateral retinal detachments and 4+ papilledema were observed 7 days later. Renal angiography (Fig. 1) demonstrated a florid necrotizing angiitis of the intrarenal vessels.

Because of deterioration of renal function and progressive encephalopathy, peritoneal dialysis was begun on the 24th day. The patient died 5 days later.

At post-mortem examination, the body was thin (weight of 49.9 kg for a 165-cm length). The heart weighed 590 g and displayed generalized hypertrophy without dilatation. The left ventricular cavity contained an apical mural thrombus, 2 by 3 cm. There was minimal generalized atherosclerotic fatty streaking of large arteries. The right lung weighed 1200 g, and the left 850 g. Both showed patchy confluent consolidation, which microscopically was found to be organizing bronchopneumonia. The spleen weighed 250 g and showed many recent infarcts. No lesions were identified in the splenic artery or vein. The main renal arteries were entirely normal; however, the kidneys were reduced in size, weighing 150 g each and containing multiple old and recent infarcts. Thickened medium-sized muscular arteries were prominent.

On microscopical examination medium and small arteries of many organ systems showed a variety of extensive pathologic lesions (Fig. 2-4). Profound alterations involved the arteries of the esophagus, stomach, duodenum, ileum, colon, pancreas, gallbladder, adrenal glands, subcutaneous tissue, prostate, aortic adventitia, renal arcuate and interlobar arteries and arterioles of the pons. The testes were involved by a patchy interstitial and tubular fibrosis, and spermatogenesis was absent.

M.W., a 21-year-old woman, was admitted to the hospital because of epigastric pain of 1 day's duration. The pain, which was accompanied by nausea, became cramping in nature after the ingestion of food. She complained of numbness

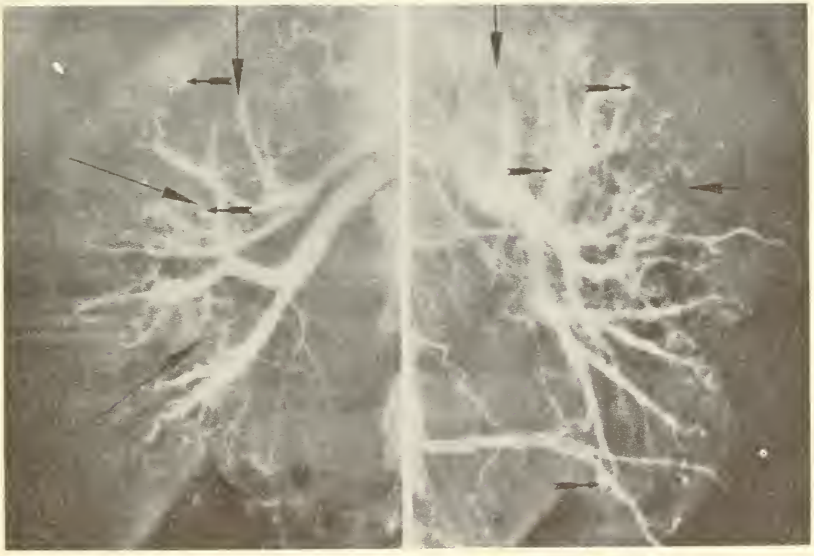

Figure 1. Bilateral Selective Arteriograms of the Kidneys in D.G

Obliteration of many intrarenal vessels is associated with areas of infarction (large arrows). There is no visible perfusion of most of the cortex. The small and medium-sized arteries reveal marked contour irregularity and gross indistinctness. Scattered microaneurysms are designated by the small arrows. This angiographic pattern is consistent with a diagnosis of necrotizing angiitis.

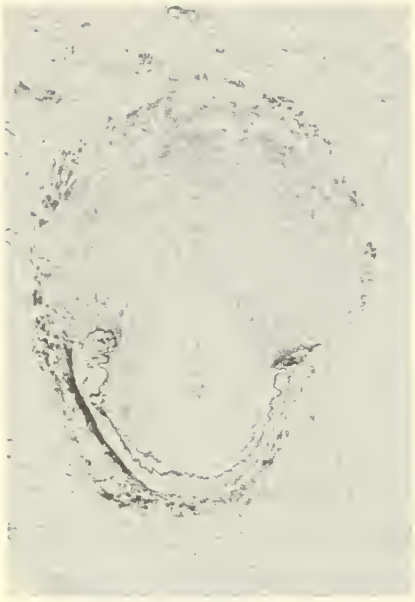

Figure 4. Renal Interlobular Artery of D.G., Showing Eccentric Destruction of Its Wall with Dilatation, Fibrosis and Luminal Narrowing in a Healed Lesion (Verhoeff-van Gieson Stain X100).

erosclerosis was minimal. The right lung weighed 850 g, and the left lung 450 g. A large thromboembolus occluded the artery to the right lower lobe, with resultant infarction. In addition, there was confluent bronchopneumonia and a fibrinopurulent pleuritis. The liver, which weighed 1300 g, displayed central lobular congestion and necrosis. A rare aneurysmal dilatation of the mesenteric arteries was grossly visible. The kidneys (Fig. 7), the most severely affected organs, were moderately reduced in size, the right weighing 135 g, and left 125 g. They presented the nodular appearance of segmental ischemic atrophy. On cut surface, areas of cortical infarction were evident. The classic arteriolosclerosis found in hypertension was not present. Thrombi were seen in the veins of the ovary, gallbladder, neck and urinary bladder.

Arterial lesions involved the pancreas, periadrenal tissues, perithyroid tissues, ovary, appendix, uterine cervix, gallbladder, small-bowel mesentery, heart, liver, lungs, stomach, duodenum and renal interlobar and arcuate arteries.

E.V., a 21-year-old woman with a 3-year history of intravenous use of methamphetamine, heroin, dextroamphetamine and barbiturates, had a sore throat 3 months before admission. During the following week fever, progressive generalized myalgia and painful swelling and tenderness in both ankles developed. The fever, accompanied by anorexia, persisted during the ensuing weeks. There was a 11.3-kg weight loss, progressive weakness of the lower extremities, with dragging of the feet.

Physical examination revealed a thin, emaciated woman, who was alert and oriented. The temperature was 103°F by mouth, the pulse 120, and the respirations 22. The blood pressure was 110/60. The pupils were equal in size. The heart was of normal size and configuration. A Grade 3 of 6 holosystolic murmur was heard along the upper left sternal border. There was severe, generalized weakness of the lower extremities, with marked bilateral foot drop. A stocking-type hypalgesia to the mid-calf was noted bilaterally. The triceps, biceps and patellar reflexes were depressed equally on each side. Ankle reflexes were absent.

The hemoglobin was 10.8 g per 100 ml, and the white-cell count 16,000, with 68 per cent neutrophils, 11 per cent band forms, 5 per cent monocytes and 2 per cent eosinophils. The urine had a specific gravity of 1.015, and both microscopical and chemical examinations were within normal limits. At the time of admission the blood sugar was 77 mg, and the BUN 8 mg per 100 ml. The serum sodium was 132 mEq, and the potassium 3.3 mEq per liter. The albumin was 2.7 g, and the globulin 4.1 g per 100 ml; the SGOT was 34 U, and the SGPT 44 U.

The hospital course was marked by continuous fever, with daily temperature spikes to 105°F. There was progressive weight loss, arthralgia, myalgia and emotional lability. Urine, sputum and blood cultures showed no growth. Skeletal-muscle biopsy (Fig. 8), performed on the 14th day, demonstrated panarteritis with fibrinoid necrosis.

Forty-eight hours after the initiation of steroid therapy, the patient became afebrile, but the blood pressure rose to 180/120. At that time she showed mental obtundation. Her condition steadily deteriorated, and she died 5 weeks after admission.

At post-mortem examination the body showed marked generalized cachexia, with a weight of 29.5 kg and a length of 150 cm. The soft tissues and extremities were profoundly atrophic. The heart weighed 300 g and showed slight left ventricular hypertrophy, with the muscle wall measuring 1.4

Table 1. Clinical Manifestations of Necrotizing Angiitis, Associated with Drug Abuse.*

Patient	Age (yr)	Sex	Systemic				Skin Rash	Cardiopulmonary		Renal		
			Fever	Weight loss	Malaise	Weakness		Pneumonitis	Pulmonary edema	Proteinuria	Hematuria	Azotemia
D. G.†	19	M	+	+	+	+	+	+	+	+	+	+
M. W.†	31	F	+	+	+	+		+	+			+
E. V.‡‡	21	F	+	+	+	+		+				
A. E.†	47	F	+		+	+	+	+		+	+	+
A. L.	30	M		+							+	
S. T.	20	F		+	+	+	+					
V. G.	27	F		+	+	+	+					
R. C.	34	M	+	+	+	+		+				
B. B.	23	M	+	+								

*5 patients (A. B., G. A., S. V., E. J., & E. C.) were asymptomatic. †Death, with autopsy. ‡No angiographic study.

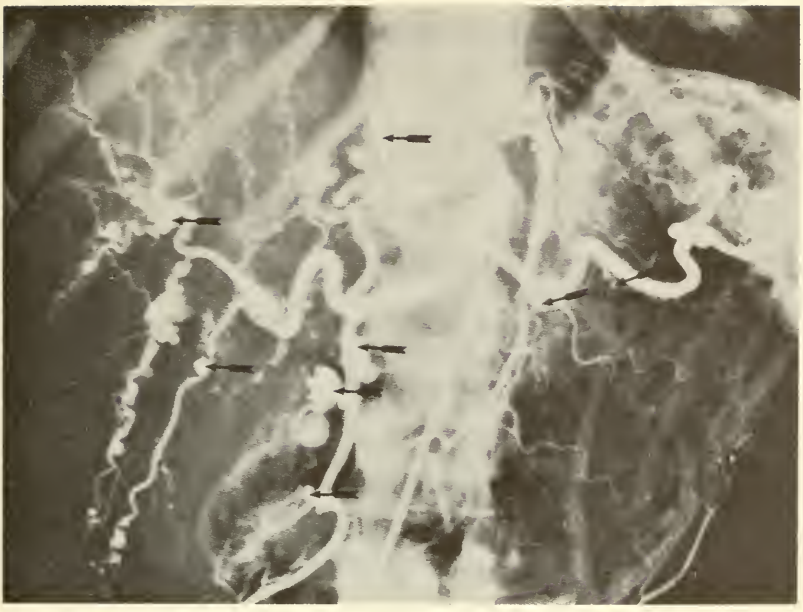

Figure 5 Selective Celiac Arteriogram of M.W.
Multiple small and large aneurysms are present at bifurcation sites of the intrahepatic, gastroduodenal and left gastric arteries (arrows). Microaneurysms also involve the pancreatic blood supply. There is marked sparsity of the intrahepatic vessels.

cm in thickness. There was minimal generalized atherosclerosis. The right and left lungs weighed 150 and 300 g, respectively, and were normal except for acute hemorrhage in the left. The kidneys, which weighed 100 g each, contained numerous segmental old infarcts. The adrenal glands displayed cortical atrophy bilaterally. There was marked cerebellar hemorrhage and recent and resolving cerebral and pontine infarction.

Destructive arterial lesions involved the coronary, hepatic, renal interlobular and arcuate arteries (Fig. 9), as well as arteries of the stomach, appendix, vagina, periadrenal tissue, esophagus, pancreas, skeletal muscle, spleen, fallopian tube, colon, cerebrum, cerebellum and brainstem.

A.E., a 47-year-old woman with a history of drug abuse, was admitted to the hospital because of confusion and disorientation and with complaints of progressive muscular weakness accompanied by pain and burning of the legs and feet.

Physical examination revealed an obese, confused woman in no acute distress. The oral temperature was 105°F, the pulse 86, and the respirations 30. The blood pressure was

Table 1 (Concluded)

Patient	Renal		Gastrointestinal			Musculoskeletal		Neurologic	Hematologic		
	Renal failure	Hypertension	Abdominal pain	Pancreatitis	Hemorrhage	Arthralgia	Myalgia		Anemia	Leukocytosis	Hemolysis
D. G.†	+	+	+			+	+		+	+	+
M. W.†	+	+	+	+	+			+	+	+	+
E. V.†‡		+				+		+	+	+	
A. E.†		+	+	+	+	+	+	+	+	+	+
A. I.		+	+	+							
S. T.						+	+		+		+
V. G.			+		+	+	+				
R. C.						+	+	+			
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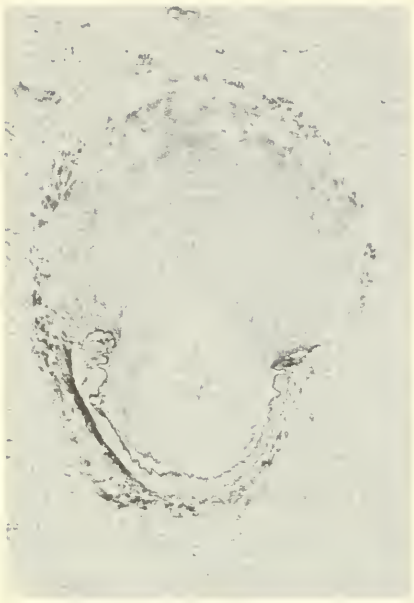

Figure 4 Renal Interlobular Artery of D.G., Showing Eccentric Destruction of Its Wall with Dilatation, Fibrosis and Luminal Narrowing in a Healed Lesion (Verhoeff–van Gieson Stain X100).

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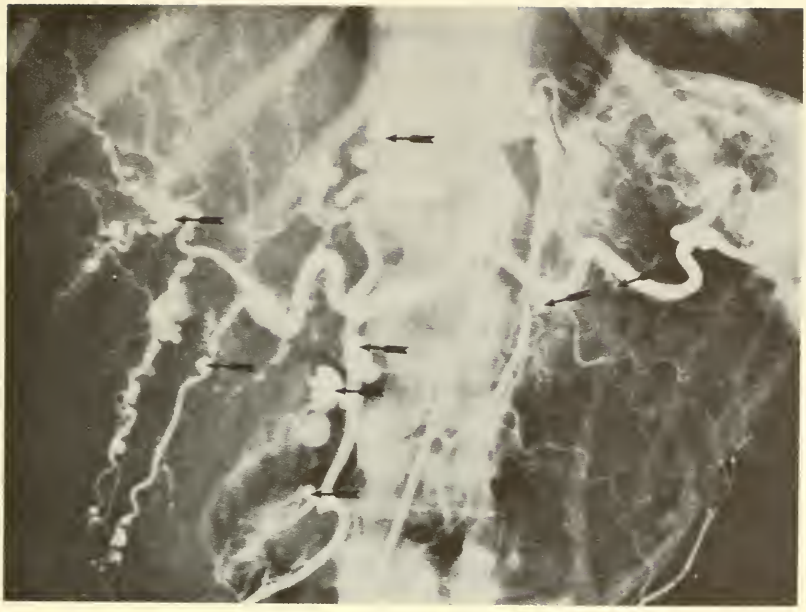

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A. I.		+	+	+							
S. T.						+	+		+		+
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*5 patients (V. B., G. A., S. V., E. J. & E. C.) were asymptomatic. †Death, with autopsy. ‡No angiographic study.

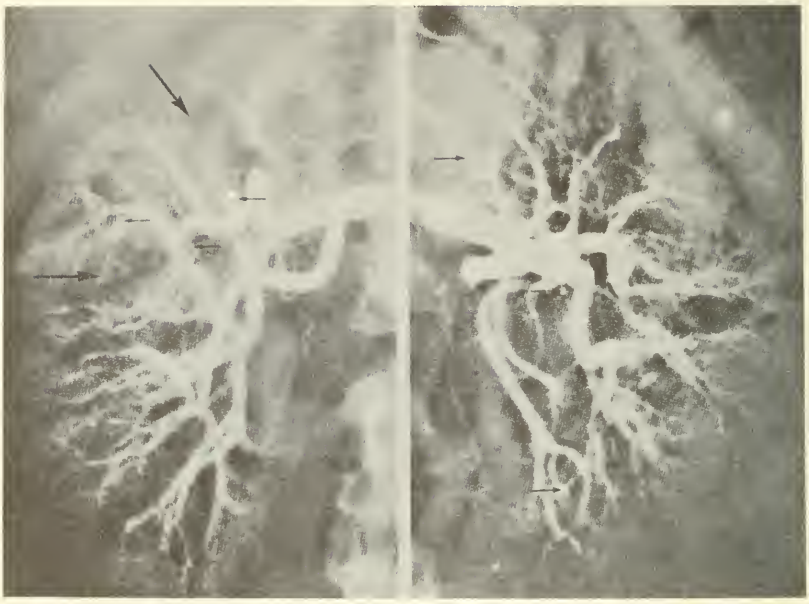

Figure 6. Bilateral Selective Renal Arteriograms of M.W.
Many intrarenal vessels are obliterated and associated with segmented infarctions (large arrows). There is luminal irregularity and indistinctness of many branch vessels. Scattered microaneurysms are present (small arrows).

140/110. There were bronchovesicular breath sounds but no rales or rhonchi. The abdomen was markedly obese. A large, firm, tender mass was palpated in the right lower quadrant. There was no muscle tenderness, and neurologic examination was within normal limits.

The hemoglobin was 13.1 g per 100 ml, and the white-cell count 17,800, with 91 per cent segmented neutrophils, 2 per cent band forms, 3 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. The urine showed a specific gravity of 1.015 and contained a trace of protein, with 4 to 6 white blood cells and an occasional red blood cell per high-power field in the sediment. At the time of admission the blood sugar was 135 mg, and the BUN 73 mg per 100 ml; the potassium was 3.4 mEq, and the carbon dioxide 26 mEq per liter, and the calcium 9.5 mg, and the creatinine 2.2 mg per 100 ml. Urine culture grew *Escherichia coli* and paracolon bacilli.

A working diagnosis of chronic pyelonephritis was made, and antibiotic therapy was begun. The right-lower-quadrant pain persisted, and there was evidence of increasing distention of the small bowel on repeated x-ray examinations. On the 8th hospital day operation was performed for appendicitis. Examination of sections of the appendix demonstrated fibrinoid necrosis and inflammatory-cell infiltration of the walls of the small arteries.

The initial postoperative course was unremarkable, except for persistence of the fever and infection of the surgical wound. On the 18th hospital day there was a complete absence of deep tendon reflexes. Without evidence of blood loss the hemoglobin demonstrated an abrupt fall to 8.7 g per 100 ml. The white-cell count was 8700, with 70 per cent segmented neutrophils, 13 per cent band forms, 2 per cent lymphocytes and 15 per cent eosinophils. Renal arteriography on the 25th hospital day was interpreted as being consistent with necrotizing angiitis.

The patient's condition steadily deteriorated. She was treated with antibiotics for pneumonia due to a combined beta-hemolytic streptococcus and pseudomonas, and blood replacement for a subsequent gastrointestinal hemorrhage. She died on the 37th hospital day.

At post-mortem examination the body was obese, weighing 129.3 kg for a length of 160 cm. The right-lower-quadrant wound was infected. Severe atherosclerosis was generalized. The heart weighed 530 g and showed generalized hypertrophy and dilatation. The right and left lungs weighed 900 and 750 g, respectively, and microscopical examination disclosed pulmonary thromboemboli and edema. A large duodenal ulcer penetrating into the pancreas was found in association with 150 ml of old blood in the stomach. The pancreas was calcified, firm and necrotic on gross inspection; microscopical examination revealed fibrosis, inflammation and fat necrosis. The gallbladder had a thickened wall and contained 20 calculi. The spleen weighed 400 g and was soft, with microscopical features of acute splenitis. The kidneys, weighing 210 and 180 g, had coarsely granular surfaces, with microscopical features of arteriosclerosis and arteriolosclerosis.

Marked changes involved the arteries of the pancreas, periadrenal tissue, small-bowel mesentery, colon, ileum, fallopian tube, ovarian ligament and skeletal muscle and the renal interlobar, arcuate and peripelvic arteries.

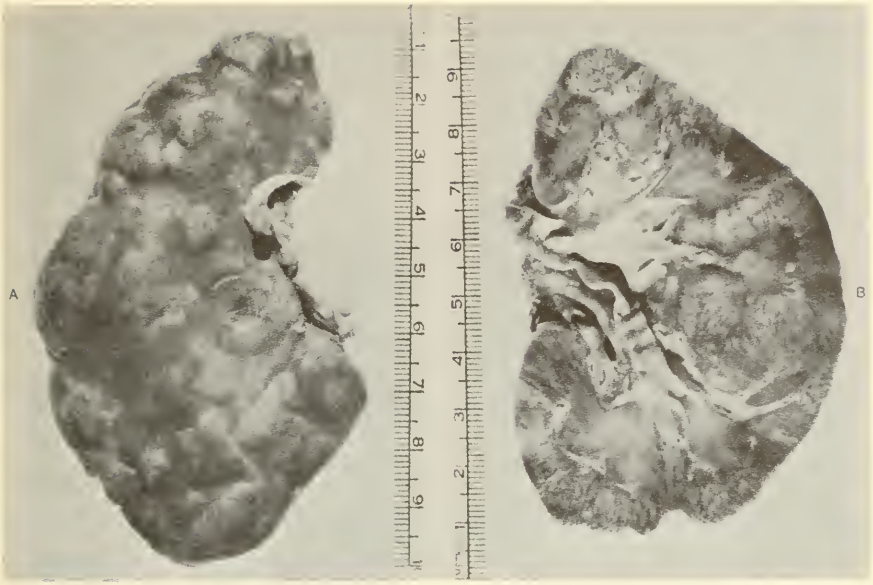

Figure 7. Scarred Subcapsular Surface Clearly Seen in a Kidney Fixed in Formalin from M W (A). This finding classically occurs in periarteritis nodosa The cut surface shows prominent thickened arteries, particularly at the corticomedullary junction and the infarctions (B).

Pathological Observations of Vascular Lesions

All lesions in these four cases were studied after fixation with hematoxylin and eosin, Masson trichrome and Verhoeff-van Gieson elastic-tissue stain and were viewed with polarized light.

The diseased vessels included medium-sized and small arteries in most organs and arterioles in the brain. Elastic arteries, capillaries and veins were spared. In acute lesions, fibrinoid necrosis of the media and intima was prominent, with a neutrophilic, eosinophilic, lymphocytic and histiocytic infiltrate (Fig. 8). Fresh occlusive thrombosis was common in early and later lesions (Fig. 2). The involved arterioles displayed fibrinoid necrosis of their walls and had fibrin thrombi in their lumens. Subacute lesions were characterized by florid intimal proliferation with marked luminal narrowing. In some cases this lesion occurred in arteries with no other apparent damage, and in others, marked medial and adventitial alteration accompanied this proliferation, with delicate interweaving of medial musculature with new fibrous tissue (Fig. 3). Older (healed) lesions demonstrated marked destruction of muscular and elastic components of the arterial walls, with replacement by collagen and a striking luminal narrowing. Destruction was either circumferential or eccentric, with sparing of remaining wall (Fig. 4). The lesions were prominent at bifurcations. In many cases the defective area of the wall showed a nodular (nodose) bulge with nearly aneurysmal dilatation (Fig. 9).

In the four patients studied at autopsy, rare minute refractile foreign particles were found in pulmonary capillaries on viewing with polarized light. No such material was observed in any vascular lesions or in other organs.

Discussion

The diverse clinicopathological syndrome of necrotizing angiitis associated with drug abuse reported here is strikingly similar to periarteritis nodosa with severe renal, gastrointestinal, cardiac and neurologic involvement. These patients had pancreatitis, renal failure, hypertension, pulmonary edema and neuropathy. The relation of the hemolytic episodes to the basic pathologic process is unclear.

The histologic picture is indistinguishable from that of classic periarteritis nodosa and does not resemble hypersensitivity angiitis, in which small arteries, capillaries and venules are involved. Also, in hypersensitivity angiitis the spleen and lung are

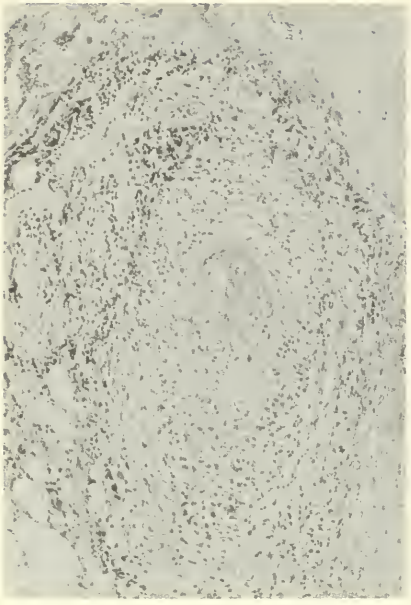

Figure 8 Artery in a Skeletal-Muscle Biopsy from E.V., Demonstrating Fibrinoid Necrosis, Luminal Thrombosis and Panarteritis of Mixed Inflammatory Cells (Hematoxylin and Eosin Stain X125).

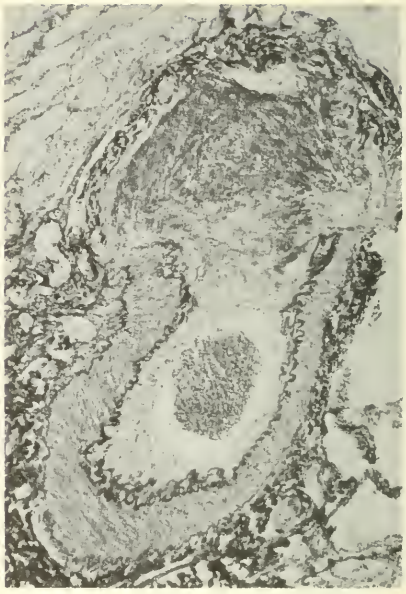

Figure 9 Healed Eccentric "Nodose" Lesion Shown in a Renal Arcuate Artery of E.V. (Verhoeff-van Gieson Stain X75).

often affected, and intestinal lesions are rare.[1,2] Although several of the patients with necrotizing angiitis have presented a typical clinical picture, in most the diagnosis was suspected from the history of drug abuse alone and subsequently confirmed by angiography. Selective renal and visceral angiography has been crucial in the diagnosis of necrotizing angiitis, autopsies provided confirmation in the above cases. None of the patients had a history of noteworthy allergy such as asthma or of previous drug reactions. Important clinical manifestations of the 14 cases are summarized in Table 1. Five patients with a history of methamphetamine abuse were without symptoms of necrotizing angiitis. These patients had been hospitalized for diverse medical problems: E.J., for a fractured thumb; F.C., for heroin withdrawal; S.V., after an overdose of barbiturates; A.B., for evaluation of iritis; and G.A. for evaluation of renal trauma after a stab wound of the abdomen.

One patient, A.L., was initially admitted to the hospital for hypertension of 15 years' duration; pancreatitis and an abnormal urinary sediment later developed. Another (S.T.) had hemolytic anemia and initially was without other complaint. V.G. had a bleeding gastric ulcer. B.B. was admitted to the hospital after an overdose of barbiturates, and R.C. had alcoholic withdrawal symptoms.

Although it is not possible to establish a single etiologic agent from the complex of drugs used by these patients, methamphetamine among the various candidates may have been a common denominator. Methamphetamine was used in large dosage by 12 of the patients with necrotizing angiitis and exclusively by one of them. There was no evidence of necrotizing angiitis either clinically or on selective angiography in four patients who had taken multiple intravenous drugs but not methamphetamine or in five persons who had used intravenous heroin or cocaine alone. D-lysergic acid diethylamide also may be suspect as a causative agent of vasculitis. The widespread abuse of marijuana makes it imperative that its potential role be evaluated. Study of the contamination of "street" and "home-made" drug preparations and the reproduction of the angiitis in laboratory animals are important parts of this continuing investigation.

Deaths occurring in young people using a large variety of drugs have often remained unexplained. The occurrence of necrotizing angiitis, which resulted in the deaths of four patients reported in this study,

brings into sharp focus the lethal character of this disease. It is important to stress the fact that five of the 14 patients were completely asymptomatic. An inescapable inference from this report is that drug abuse may be a factor in necrotizing angiitis.

We are indebted to John C. Norris, M.D., for assistance.

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38. Abuse of Barbiturates and Amphetamines

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[*Postgraduate Medicine*, pps. 45–51, January 1965]

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Patterns of drug abuse in the United States have undergone significant changes since World War II. A prominent feature has been a shift from alcohol and heroin to the barbiturates, amphetamines and related substances. Dependence on these drugs may create serious medical and sociologic problems which the pharmacist and physician can minimize by knowledgeable and thoughtful control of the prescription.

SINCE World War II, the pattern of use and abuse of drugs which are capable of creating behavioral problems by exerting a toxic effect on the nervous system has changed so significantly as to require a re-evaluation of concepts and definitions in this whole field. National recognition was given to these changes by the White House Conference on Narcotic and Drug Abuse held in September 1962[1] and the subsequent appointment of a Presidential Advisory Commission on Narcotics and Drug Abuse.[2]

Three principal factors have contributed to these changes: (1) altered social patterns in large urban areas, especially among juveniles, (2) wide dissemination of information, factual and otherwise, about drugs which are purported to produce pleasant subjective effects, and (3) the relative scarcity of illicit narcotics of the morphine type due to punitive legislation and diligent control measures.

Drug abuses are so varied that the terms "habituation" and "addiction" are no longer adequate to describe them. "Drug dependence," a term adopted by the World Health Organization,[3] is broad enough to include not only chronic abuse but also single and intermittent use of excessive quantities on a "spree" basis. Drug sprees often create sociologic and criminologic problems more serious

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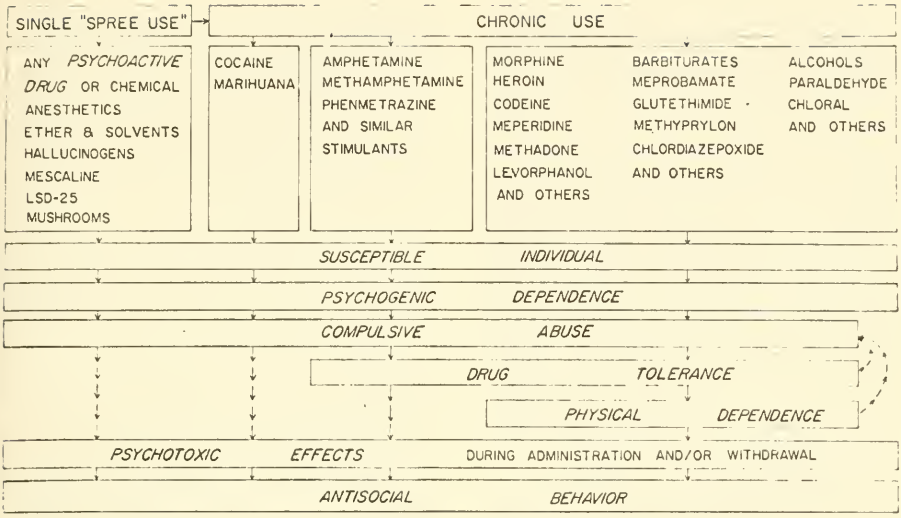

FIGURE 1. Elements of drug abuse.

than those stemming from chronic drug abuse. For example, a person who takes a large amount of cocaine or amphetamine intravenously may become violent while in a hallucinatory or delusional state.

In much of the literature "addiction" has been inextricably linked to tolerance and physical dependence. These two biologic phenomena are physical factors which influence significantly the course of chronic intoxication with certain drugs and reinforce the psychologic factors involved in dependence. However, they are not essential to creation of psychic dependence on a drug, its compulsive abuse, or the induction of psychotoxic effects that may lead to antisocial behavior.[4] Neither cocaine nor marihuana, for example, produces tolerance or physical dependence, yet abuse (especially of cocaine) may give rise to dangerous antisocial behavior. Limitation of space precludes a detailed discussion of even the principal (and interrelated) factors in this complicated medical and sociologic problem[5] (figure 1).

Drug abuse, although fairly widespread, involves only a small fraction of the population. Only certain emotionally maladjusted persons seek this form of escape, and many factors (genetic, medical, psychologic, cultural, sociologic, economic) are contributory.

Every psychoactive drug or chemical is potentially subject to abuse. Although attention recently has been called to abuse of solvents (model airplane glue) by teen-agers and of hallucinogens (LSD-25, mescaline) by "long-hair" and beatnik groups, the major problem of drug abuse in the United States at present, excluding alcohol and the morphinelike substances (heroin, opiates, synthetic narcotic analgesics), involves the barbiturates, amphetamines and pharmacologically related substances—the "dangerous drugs." Accurate information concerning the extent of their abuse is unavailable, but calculations based on production suggest a comparatively large excess in relation to the estimated legitimate medical needs. Careful epidemiologic studies are badly needed.

Despite the fact that these drugs are legally available only by prescription, the incidence of abuse has risen steadily. Experience with existing narcotic laws strongly indicates that it would be unwise to introduce similar legislation to control the "dangerous drugs." The ensuing discussion is an attempt to outline the general patterns of abuse of these two classes of drugs. It is hoped that pharmaceutical manufacturers, pharmacists and physicians will recognize the scope and significance of the problem and will take steps to avert this form of punitive legislation, which not only fails to prevent abuse but also opens a Pandora's box of evil consequences.

Dependence on Barbiturates and Related Drugs

The abuse characteristics of barbiturates and drugs producing similar pharmacologic effects have much in common with those of ethyl alcohol, but there are also several distinctive properties. These drugs exert effects on mentation and somatic functions which are often pleasurable to neurotic and irritable persons and lead to strong psychic dependence. Alcoholics may use them as substitutes for liquor in attempts to conceal their habit. The drugs are effective when taken orally and do not produce gastric irritation or other significant side effects. Physical dependence requires the use of large doses but is associated with a life-threatening withdrawal syndrome marked by delirium and convulsions. Perceptual distortion of time coupled with slow absorption may lead to "involuntary" suicide.

Psychic dependence is a formidable factor in the habitual use of this class of substances. It may exist in all grades and does not necessarily lead to abuse. Prescription of sedative or hypnotic doses to be taken daily over a long period, even many years, is not inconsistent with good medical practice. Many patients have been denied the benefits of proper sedative medication because physicians have been misinformed in this regard. Although the patient may become psychologically dependent on such medication, this is not harmful by itself if certain conditions are maintained. It is the physician's obligation to prescribe suitable doses to be taken at wide enough intervals so that the subjective effects are limited to those required to achieve the therapeutic objective. It is also his responsibility to dispel any misconception the patient may have concerning the actions of the drug. Patients who take excessive amounts of these drugs often cite as a reason the fear that they will be unable to sleep; as tolerance develops, they take the drugs more and more frequently until toxic symptoms and signs appear.

The early diagnosis of barbiturate abuse is difficult. In many instances, severe dependence is discovered only when the patient is hospitalized.[6] The condition may be erroneously diagnosed as acute barbiturate poisoning (largely from accidental or intentional overdosage), acute depression, neurosis, schizophrenia, brain tumor, or other neurologic or psychiatric disorder. Symptoms and signs include various degrees of clouding of consciousness, euphoria, irritability or depression, dysarthria, ataxia, tremor, nystagmus, prosis, pupillary changes, and hyporeflexia or areflexia, either symmetric or asymmetric. Determination of the concentration of barbiturate in the blood is helpful under some circumstances but is not of value in estimating the total amount taken or the duration of administration. Many patients attempt to conceal their dependence, and the information furnished by them may be unreliable or misleading. Suspicion of drug dependence may be aroused if the family reports that the patient is often confused at home.

Two general types of severe barbiturate abuse are common. Some patients stay in bed, seeking oblivion and semipermanent stupor and arising only to answer nature's demands or to obtain more drug. A second and paradoxical type of reaction occurs in some persons in whom tolerance has developed following prolonged use; the drug has

a stimulatory effect and is taken to "increase efficiency." A type of abuse practiced especially by juveniles involves intravenous self-administration of illicitly obtained barbiturate to the point of unconsciousness.

The difficulties in diagnosis emphasize the physician's obligation to follow carefully the course of sedative therapy. Only in this way can he evaluate a patient's susceptibility to drug abuse and take the necessary preventive measures. *It is improper medical practice to write prescriptions for large quantities of barbiturates or other drugs of this general class. The prescriptions should be "nonrefillable."* The laxity of physicians in this regard is one, if not the primary, cause of abuse during or following therapy.

Abuse of Barbiturates and Amphetamines

There are three important reasons why patients should not have access to large quantities of these drugs.

1. Physical dependence will not develop if a controlled, small-dose regimen is followed. Comparatively large doses of barbiturates are necessary to induce physical dependence, and these doses are often sufficient to induce psychotoxicity and detectable symptoms and signs even in tolerant individuals.

2. Availability of large quantities may lead to "involuntary" suicide. This danger is related to the perceptual distortion of time which occurs at a given level of barbiturate (or alcohol) intoxication and to the slow absorption and delayed pharmacologic effects after oral administration. The presence of a large quantity of barbiturate in the stomach also diminishes gastric and intestinal function and further delays absorption. The barbiturate user who fails to obtain the desired effect from a prescribed dose within what seems to him to be a long period of time will ingest tablet after tablet. Slow absorption makes it possible for him to take a lethal dose before he becomes unconscious. The alcoholic may also "pour it down" when in a semiconscious state, but the absorption of alcohol is sufficiently rapid so that coma usually supervenes before a lethal dose is taken. Moreover, the irritating properties of alcohol in large amounts may evoke emesis.

3. Voluntary suicide with barbiturates is facilitated by the availability of large quantities, commonly accumulated by "hoarding." Avoidance of this risk requires comprehensive and coordinated efforts by physicians, nurses and pharmacists.

Although some tolerance develops to the short-acting barbiturates, it does not increase significantly the size of the lethal dose. Tolerance is probably the result of an increased rate of enzymatic breakdown and is measured in terms of reduction in sleeping time and a lessening of symptoms and signs of toxicity. Paradoxically, persons who have received large amounts of barbiturates and are then given the drugs again after a "free period" are likely to exhibit an exaggerated response the second time; this is termed post-tolerance sensitivity. Comparatively little tolerance develops to barbital and phenobarbital, whose detoxication depends largely on renal elimination.

Physical dependence on barbiturates differs significantly from physical dependence on the morphinelike analgesics. The response to the morphine drugs parallels the amount given until a comparatively high dosage is reached. Then it levels off, and little further increase occurs even when maximum tolerated doses are given. The barbiturates, like alcohol, must be given continuously for months (minimum effective quantity, possibly between 0.3 and 0.5 gm. in 24 hours) before an abstinence syndrome is detectable on withdrawal. Maximum physical dependence develops only if large quantities are used (1 to 2.5 gm. per 24 hours). Dependence on barbiturates, when fully developed, is a greater threat to life than dependence on morphine. The barbiturate must be with-

horses. Abuse has been fostered in some large urban centers by irresponsible and immoral physicians who operate "antiobesity" clinics whose main function is to dispense amphetamines legally on a mass basis, often without examination or follow-up observations. Fortunately most of these activities have been suppressed by warnings from local medical societies or by revocation of licenses.

There has also been an appreciable increase in the use of these drugs as stimulants by persons who abuse alcohol and barbiturates. Many times they become part of the picture of mixed addiction. The prognosis is poor, the relapse rate is high, and continued dependence on these or other drugs is the rule, especially among prepsychotic persons or those with latent schizophrenia.

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39. A SAN FRANCISCO BAY AREA "SPEED" SCENE*

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[*Journal of Health and Social Behavior*, 9(2):164–174, June 1968]

This study explores the physical, psychological and social effects of massive doses of amphetamines among a group of heavy users in Berkeley, California, their round of life, and the effect of the law on these social relations. Data were gathered through interviews with users, reports of key informants and participant observation. The findings suggest that the behavior reported is a result of the interaction of three factors: the chemical effect of the drug, the setting within which it is used, and the impact of the law.

Social scientists, medical researchers and law enforcement personnel have noted the wave of illegal drug use that has been building in the United States since the early 1960's. (Goddard, 1962; Kramer, 1967; Larrick, 1964; Sandusk, 1966; Seevers, 1965.) One unique feature of this development is its middle-class character. Numerous middle-class youth who use and have access to mind-altering drugs not only make a free choice to violate the law, but also choose the drugs they will experiment with and later use regularly.

Once they choose to alter their minds, the personal and social consequences of drug-taking depend largely on the chemical impact of the drug as well as the broader context—such as laws against drug use and the attitudes of peers and authorities—in which drug-taking occurs. Some drugs actually diminish otherwise "criminal" tendencies, others cause a flood of experience or more energy and willingness to cope with everyday reality. Little has been written to-date which describes what actually occurs among people who freely choose to commit felonies in order to experience a different, desired, chemically-produced "new state of mind." In this article we will describe some users of *massive* doses of amphetamines or "speed." This investigation grew out of two parallel studies which explored the social world of two different strata of youth on the West Coast. One explored the patterns of drug usage among Negroes and Mexican-Americans of high-school age in a low-income neighborhood in Oakland, California (Blumer, 1967). The other inquired into the pattern of drug use among college-age persons in Berkeley, California, several miles north (Carey, 1967). Heavy amphetamine users, young, white and lower-middle to middle class were interviewed at the fringes of these two groups, moving in and around them. It is this group, consisting of a collection of heavy using amphetamine settings, which is the focus of this inquiry.

Scope of Inquiry

We will discuss only those who regularly take 100–1,000+ mgs. of amphetamines (compared to prescribed daily dosages of 5–10 mgs.) via intravenous injections.[1] Those we describe are taking so much amphetamines in the form of Methedrine crystal (methamphetamine hydrochloride) that they experience qualitatively different lives than they did previous to massive amphetamine use, and they are probably much different than they would have been had they not chosen this type of drug. Methedrine comes to dominate much of their lives, their choice of friends, life rhythms, and their job (or lack of it).

Method

In the depiction of life styles of persons defined as deviants, a major source of distortion has been

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[1] This excludes dieters, students who are cramming, people who take amphetamines to improve their work (e.g., pilots, truckers, Madison Avenue executives, prostitutes), even when the pills are obtained illegally and regularly taken at several times the normal dosage.

the condition under which information was gathered. Lindesmith (1940; 1963) pointed out initially that the manner in which heroin users were characterized was strongly influenced by the nature of the observer's relation to them. More recently, Polsky (1967) has made the same point about career criminals, i.e. they are studied in captivity. Apart from sampling bias, the relation of researcher to respondent is suspect. The disparity in status hinders the respondent's freedom to disagree or to develop the kind of trust in the investigator that would enable him to disclose himself and act "normally."

Using random sampling to get information on illegal drug use, let alone those who inject massive doses, is a costly way to obtain a little data of questionable validity. Yet how can one get "hard data" about heavy drug use or drug trafficking? Even a selected sampling would not help much, except at the end of a study with a "stable" population hardly likely among heavy amphetamine users. There is also the problem of what to ask. Contemplating a survey of drug traffic is putting the cart before the horse, especially if the drug being studied generates unique and extreme behavior. There is further difficulty in getting reliable information pertaining to higher levels of trafficking. The number of large amphetamine deliveries is simply too small to permit a very systematic "sampling" of such behavior.

The social scientist interested in styles of drug use and dealing must rely on field observation if his account is to reflect reality. He must become part of the world of users and dealers. Our information is drawn primarily from what users and dealers say and do in their daily round of life. This has been supplemented by official statistics, and professional and mass media reports deemed relevant. An observational or "knowledgeable informant" approach can be justified on its own merits as proper for this subject, but a simpler justification is one of expediency: What or who else can be consulted?

It is difficult to describe our sample because most contacts were not made on a formal interviewing basis. Such procedures often destroyed the very things we were after. We personally spoke to and obtained abbreviated life histories on 20 people who regularly used marijuana but used Methedrine occasionally. We had access to interviews and recorded group discussions of 30 East Oakland juveniles (lower socioeconomic status, primarily from a Negro ghetto) who used amphetamine pills in heavy doses, and occasionally Methedrine, plus the field observations related to this style of drug use. Our key informants on the world of "Meth heads" were 11 heavy Methedrine users; five large dealers trafficking regularly in amounts of over $500, who stocked Methedrine but did not deal exclusively in it; two interviews with dealers who handled speed exclusively; and two informal second-party interviews with others dealing at this level. The dealers were queried about the volume of traffic in methamphetamine and the motives and life style of those involved in heavy use. Twenty drug agents working for the Bureau of Drug Abuse Control in the Food and Drug Administration were also interviewed about the traffic in amphetamines and their own observations about heavy Methedrine users with whom they had contact. The interviews were supplemented with observations of one scene for much of one summer and fall. Apart from the East Oakland juveniles, almost all our information came from persons in, or close to, Berkeley's colony.

The following description of Methedrine usage is based on 50 interviews with casual users, 11 extensive descriptions of participants in a speed scene, 20 federal agents involved in enforcing the laws against amphetamine usage, and seven user-dealers. In short, our report is based on 88 interviews and extensive field observations over a six-month period.

The Effects of Massive Doses of Amphetamine

There are only a few, and mostly very recent, studies of the effects of massive dosages of amphetamines. When the drug was developed, just before and during World War II, limited doses were used mainly to keep pilots alert and improve combat performance.[2] Experimental studies indicated that amphetamine improved perform-

[2] Laurie (1967) notes that the first non-medical use of what the English call "thrusters" was in ships' survival packs during the Spanish Civil War, and were issued to German paratroops as standard equipment about that time. During World War II the maximum military dosage supposedly allotted British soldiers was 10 mg. in 12 hours, 30 mg. a week.

ance when subjects were fatigued or suffering sleep deprivation, and that limited dosages elevated mood and induced a state of well-being. Increasing dosages, however, seemed to evoke apprehension, volubility, tremor and excitement. (Cuthbertson and Knox, 1947). Prior to 1966 little was reported about regular users taking massive amphetamine doses for "kicks," primarily because medical researchers assumed such large quantities to be dangerous. Most of the few persons observed taking massive amphetamine doses had developed tolerance for the drug over many months or years. Goddard (1962) and his associates summarize the effects of amphetamines and related compounds on humans:

> Drugs of this class * * * cause wakefulness, some increased physical activity, and, in moderate doses euphoria * * *. Tolerance is developed * * * the ordinary therapeutic dose of 10 to 20 mg. can be raised to * * * 500 mg. or more a day without producing serious physical disability or significant hypertension. Larger doses may induce a toxic psychosis characterized by physical hyperactivity, delusions and hallucinations.

Beginning in 1966, and increasing the following year, a few medical and mass media reports about "street level" Methedrine shooting appeared. (Brody, 1967; Kifner, 1967; Kramer, 1967; *Look,* 1968; Sandusk, 1966; Seevers, 1965).

As the dosage of amphetamine is significantly increased beyond the usually prescribed 10 mg., the behavior of the user becomes so quantitatively different that qualitative differences emerge. Heightened alertness and energy change to jumpiness. Reactions to close-range immediate stimuli are enhanced, but in getting engrossed in the immediate there is a falling off of awareness of distant stimuli:

> All the time (we were listening to the radio, talking, and drawing) I had no idea what was going on in the other side of the room, even if people were arguing or someone was crying.

The immediate experience, however, is one of intense pleasure.

The Rush. Methedrine crystal has its own peculiarities which must be described since it is the drug of choice in the scenes we are describing. It comes in powder form and can be prepared and injected like heroin to get a quick, powerful and direct "high." It can also be "sniffed" but this is not usually done because it does not have the immediately powerful effect of an injection. Because Methedrine crystal is so strong, it must be diluted. If one wants to go "higher now" he can; if he wants to put off coming down for a few hours he can; if he wants to take no more and ride out the high until it ends, he can do that also. With pills, especially spansules, the user doesn't have such direct control. Heavy users like the rushing effect of shooting Methedrine, within seconds actually feeling the impact. One can compare it to an electric shock or the sensation of being splashed with cold water.

The extreme pleasure reported seems directly related to the "rush" or "flash" seconds after the Methedrine is injected. The full effect of the massive quantity of amphetamine hits almost instantly, before the needle is removed from the arm. The intense pleasure of the rush is difficult to describe. One of our respondents reported the sensation as follows:

> The first time I rushed I thought it was nirvana. I was tired and suddenly my head was light. All the heaviness and dust in my brains cleared out. Everything was empty. Anything that was to happen was fine, because it was so easy to do anything.

Some report orgasms, or near orgasms of a good rush.[3] A 20-year-old woman reported:

> When it is done right, when the needle goes into your arm, it hurts but it's like a sexual excitement—when the speed goes into your veins, you flash out—that's sort of like a shock—like an electrical shock or any kind of shock. It jars you but it's a speed shock. Then you get the rush which is accompanied by a feeling of euphoria. Rush is like a buzzing; where the whole surface of your brain is vibrating—it's, you know, hi frequency sometimes accompanied by a rushing sensation up your back this is the adrenalin being shot in your system. During this you're entirely in your own world. Your communication is limited although

[3] Brody (1967) describes the rush as "a sudden overwhelming pleasurable feeling * * *. This feeling has been compared to 'an orgasm all over your body.'"

you can understand precisely what the people around you mean — their various levels.

Physical Hyperactivity. Meth-heads while high are usually active bodily, though they are seldom doing hard physical tasks. Rather they often have the "fidgets," unable to sit still under heavy doses. It is not uncommon for them to stay awake two, three or four days. The duration of the drug-induced experience is characterized as a "run." During this run a person's appetite for food is severely suppressed, despite the activity and energy generated. Weight loss of 10 to 20 pounds or more is not uncommon during a run.

One of our older respondents reported one instance of the heavy user's hyperactivity:

> I was working in a prison and one inmate, who was the most manic person I had ever seen at that time, was causing trouble in every job assignment because of his excess energy. He was reassigned to sweeping cell block floors, a job hated by almost all prisoners, and proved to love it. He was the swiftest, most thorough sweeper in anyone's memory. Of course, several rules were suspended due to his efficiency. He was allowed to sing on the job and could do cell floors a second time if he finished early.

Things are simply happening too quickly in one's head. Thinking directed toward solving a long-run problem with no side adjuncts along the way is nearly impossible. Pure quietness and stillness—often a goal of LSD users—is virtually unheard of in speed scenes.

If used in great quantity, on many long runs, with few intervals between the crash and a new run, the person will not only become emaciated but will report feeling muscle and joint pains, and possibly twitches. These—and not the reflection he sees when he looks in the mirror— may be enough to make him lay-off. Often the brain, as well as the body, feels the strain after awhile:

> I was a grad student when I was 19, and going so fast that only speed could keep me "up" with the pace. Naturally, I dropped out of school that year and was simply a speed freak for three years. I quit because I was seeing movies of myself projected on all the walls in my apartment, only I was the only person in the room and there was no camera. I laid off three months ago, and I'm just beginning to learn how to add and subtract again, and I'm learning typing again so maybe I could get a job.

There are occasional reports of overdosing where numbness occurs. Some reported they were paralyzed and afraid to move. Their racing thoughts either went too quickly or stopped; their hearts throbbed. For others the racing world gets out of control, leading to what is characterized as a "freakout," a temporary psychosis.

There are also reports of heavy users' "brains getting scrambled." Meth-heads, after many months of regular use, simply fail to make certain connections that those in the larger world make. They seem to forget recently past events or remember them in a haze.[4] Things are frequently misplaced and forgotten. One of our respondents reported that a Meth-head friend of his, believing drug agents were "casing" his apartment, went outside to bury his drugs in the backyard and within an hour had completely forgotten where he buried them.

"Compulsive" behavior. Concentration is enhanced, so long as it is on a narrow path. Any number of immediate occurrences can lead the mind to wander along in that direction. There are reports of bizarre group behavior consisting of actions which are repetitive, immediate and small, and which might be considered compulsive. One of our informants described several young women acting compulsively:

> I knew four chicks who were on Meth all the time and they used to sit around and they'd get loaded and they'd string beads * * * yeah, I know some head freaks too * * * big boxes of beads and all this glass—hours and hours.

The compulsivity of heavy users is vastly different from past clinical descriptions of that phenomenon. The Meth-heads' compulsion is not focused on a single behavior, like washing one's hands over and over again. The act of stringing beads, carving a wooden knife, memorizing the plots of all Italian operas, and doodling for four consecutive hours are all intrinsically liked. Attention can easily wander, and one can become wrapped up for hours in another "compulsive" behavior. There is no necessary utility in the acts

[4] Kramer (1967) reported that one third of the former amphetamine abusers they interviewed state that memory or ability to concentrate has been permanently impaired.

performed. The action is its own reward since it is so enjoyable.

Some paintings and writings of our respondents were similar to reports of other heavy users. The drawings are usually filled with hundreds of objects, or thousands of lines, or both, and convey a very two-dimensional world of enormous energy and action. Not atypical is the story reported by Griffith (1966):

> A graduate student hired as a temporary employee was discovered to be a chronic amphetamine user. This was first suspected when, after being asked to comment on a minor research project, he turned out a 453 page book which was largely unintelligible.

The enhanced concentration, coupled with high distractibility, leads to rapid mood changes. Under LSD, to take a comparative example, a person is often deeply "into" himself and reports picking up deep vibrations from others. On Methedrine, a person seems to sail along without going very deeply into himself and deals with others in a swift but surface manner. The mood swings reflect neither deep internal conflict nor deep mixed feelings about one's setting. Rather, the Meth-head is engrossed in the here-and-now and exaggerates or invents flows in the social setting. These mood swings are quicker and stronger as the person's body wears out.

Aggressiveness. Hyperactivity often leads to a kind of "reaching out" that appears aggressive. Enforcement officials have reported on the unpredictable character of the person who has taken massive doses of amphetamines. One official we interviewed described what he characterized as a typical Methedrine addict:

> One of the main problems we've got to face is this damned aggressiveness—these amphetamine users, they're all this way. This is the common denominator. I've seen guys that would pop fifty ten milligram pills or shoot some Meth and they're just all over—they can't stand still—they just can't keep from doing things and they're jumping around all the time. If they've got something in their hand they'll hit you without realizing what they're doing—and they'll—if they've got a flashlight they're likely to go like that (swings) and hit you with it.

It should be noted, however, that drug agents tend to come into contact with heavy users under the least tranquil conditions—as in making arrests or in transactions for large quantities of the drug. Their very presence may trigger an aggressive response. Nonetheless reports are frequent of sporadic violence which could be considered unprovoked under conventional circumstances. We observed, and had reported to us first-hand, 30 violent incidents, but their occurrence more than once during every 2 or 3 runs would be unusual. The acts are usually not premeditated but triggered by perceived insults or inconveniences.

Examples of such behavior might include a person striking a crying child while he was coming down from a trip, or a man slapping his girlfriend for no apparent reason. One of our older respondents reported this most bizarre incident:

> I let this couple crash at my house, and the next morning as I was about to say "good morning" to her she put her head down and smashed into my stomach like a goat. . . . It knocked me down. Then they grabbed their belongings and left. . . . Two weeks later she appeared at my door with another friend, and just asked for a room they could stay . . . like nothing had happened, and she probably didn't even remember it.

Possibly the extent and character of aggression vary for persons when high or when coming down. It also seems that the extent and degree of violence increase with the duration of a person's run and the number of consecutive runs he has made. For heavy users, who keep their first five or ten runs not much over two days in duration, the incidence of violence may not be much higher than average.

"Paranoia." Massive dosage of amphetamines seems to induce a kind of "paranoia" which builds up over the duration of a run and during several weeks or months of running-crashing-running. Meth-heads report hearing police running down the hall to arrest them, or little men with machine guns on the opposite roof-tops moving in for the big kill. Others report fear of "moving trees" or suspicion of friends who are sitting with their backs turned to them.

Recently, a committee of the American Medical Association (Committee on Alcoholism and

Addiction, 1966) reported that amphetamine-induced paranoia "lacks certain features of organic delirium since there is no disorientation or true confusion * * *. Usually patients do not exhibit the specific dissociated and autistic disorganization of thinking associated with schizophrenic states." Often the crystal shooter believes he sees something dangerous, but is not sure. Yet the belief can linger despite apparent "evidence" to the contrary:

> I finally decided last week (fifteen months after last shooting crystal) that I really had a delusion under speed. I saw a police car pull up in front of the house, two men get out and walk up the street. I ran to look out the rear window, and when they didn't show up in a minute or so, returned to the front window. There was the same car, only it wasn't a police car, in the same spot, and the same two men walking further up the street * * * only they weren't policemen either.

Volubility. The most typical report of heavy-using amphetamine scenes is of a group of people in a room who simply talk away at each other for hours or days at a time. Verbosity is so intense that four-person conversations are often impossible because everyone is speaking at once. The conversation is often small-talk chatter, there being little discrimination among those on Methedrine between what straight people consider serious or enlightening and utterly banal.

The Meth-head has little desire to talk to conventional people in conventional ways. A self-characterized Meth-head, age 20, reported:

> I take it especially because it creates within me this need to talk for hours. In fact, that's the quality of it. Lord help you if you ever have a friend who likes Methedrine and get on it and comes over and talks to you the entire night.

Massive doses of amphetamines seem to create the desire to be outgoing on the part of the heavy user, but there is the realization that there are a markedly small number of people who will interest and tolerate him. The Meth-head also knows, at least when he is not utterly confused, that his outgoing energies will still be strong when the normal person is running down. Thus, finding good straight company becomes extremely difficult after midnight.

The Crash. The crash, like the rush, is so extreme that the person who has had a really good sleep after long exertion only has a glimmer of what occurred. Total sleep may occur for a day or a day and a half. Shortly after, or even shortly before awakening slight inconveniences greatly disturb the "crasher." Irritability is so intense that it appears to the outsider as intolerant selfishness. Arguments, to the point of yelling and occasional hitting occur for what appear to the outsider to be fairly insignificant reasons. The crasher feels that demands made on him are inconsiderate, insufferable, and impossible. Crashing is so unpleasant an experience that many persons who try Methedrine a few times, and like it, forego future trips because of the after-effects.

> I had a great trip, but my body can't take the crash. I had tranquilizers around, and a quiet apartment, but it didn't work. My head and body ached, I got into a silly argument with my girl and pushed her. She left. I'm over 30 years old, with a license to practice clinical psychology, and here I am pushing the girl I love over something I can't even remember. Never again, until they develop a crash-proof chemical.

The intense pleasure of the rush, and the intense discomfort of the crash, explain why the regular user chooses to run even when he feels his body worn down. It seems to be the opposite of postponed gratification.

The User's Perception of the Effects of Methedrine. Much of what the outsider considers "bad"—hyperactivity, extreme talkativeness, waste of time—the user considers the successful pursuit of pleasure. The more serious medical effects leading to body deterioration that were reported were discounted as fallacious exaggerations. Heavy users pointed to the absence of published reports on massive amphetamine use or street users. The Meth-heads in our study believed they had seen and experimented with large amounts of speed and knew as much about it as any doctor or researcher. Further they were very pharmaceutically oriented, testing for impurities, experimenting with various dosages and different length runs, investigating the proper

foods to stock to counter serious loss of interest in eating during the run (even if these investigations were seldom followed up by actually using these foods) and constantly checking the body for unusual symptoms and reporting these to friends for comments.

Stories of deleterious effects after massive doses of amphetamines or prolonged use were not completely ignored, however, and only the very inexperienced and naive seem to discount completely the horror stories. Rather, many Meth-heads felt that they had personally worn out or overdosed and had lived, not only to tell the tale but to return to shooting, none the worse for wear in their own eyes—or at least still getting more pleasure from it than from anything else.

Social Relations and Round of Life

In view of the effects of massive doses, the people who like to take Methedrine, and the atmosphere in which they enjoy taking it, are unique. The scene is a youthful one. Older persons simply do not have the bodies or body rhythms to cope with it as well. They wear out sooner and crash harder and longer. Also the concern about success, "feelings" or responsibility is greater among older persons and conflicts with the world of shooting speed.

Those heavily involved in this speed scene cannot function in the straight world, at least not in many capacities. They may be able to manage walking along the street, but a normal task will be difficult unless it is something engrossing, intrinsically interesting and motion-effort-consuming.

A scene typically involves persons who go on long trips—36 to 72 hours, usually. Consequently, it is frequented by very few persons who have a steady job, for it is not only the duration of the high which mitigates against a steady job, in the square world, but also the intensity and duration of the crash. The "week-ender" on a speed trip is probably far less common than even the occasional user of heroin. If he goes "up" on Friday night, he must be sure to crash by Sunday morning—hard to do when everyone around him is so high, preparing to go even higher, and the immediate future looks so unpleasant.

The scene is so unique and time-demanding that it tends to become engrossing. The friendships of Meth-heads are oriented around and within the scene. Nowhere else can he find others whom he likes when high, or who understand his situation enough to leave him alone or ease his agony when crashing. Only those in the speed world will tolerate, understand, and accept him for whatever untoward aggressiveness may come while "up" and for the general irritability when coming down or riding out the crash. The type of friendships are also unusual. Users spend an enormous amount of time in the company of other users, but often focus on the relation of that person to drugs, particularly speed.

> There was Larry. He was a pig. One time they ran out of speed and he crawled on the floor trying to gather up every bit of white powder there was.

Given the scarcity of companions, the members of a group might not like each other very much, yet they continue spending huge blocs of time with each other. Even those suspected of being informers are often tolerated.

Due to the demands of the speed world, users tend to be people who might be characterized as "structurally irresponsible"—often young, jobless, living away from home, virtually propertyless, lacking "ambition," not holding an on-going reputation anywhere outside a scene or two. A 20-year-old, at the fringes of the scene, characterized the participants as follows:

> These are street people on Methedrine. Seldom does anyone going to school or who makes a lot of money ever get involved with it, and so they're running around in the dope scene and they aren't honest. They'll burn you or take your money for drugs and think nothing of running off with it and never seeing you again.

Whether heavy users are "street people" to anywhere near the same extent before (or after) their full entry into the world of Meth-heads is problematic. Several we had contact with were ex-students, talented artists or writers, apparently equipped to be as "successful" as the average 20-year-old college student.

The Flash House. All this suggests what actually occurs: collections of "speed freaks" and "freak houses" where like-minded people get together to while away the days. A 28-year-old

former Meth-head characterized one of the houses he had moved from:

> Like everybody was sleeping in one house, in one of their houses. There'd be ten or twelve, or God knows how many, people would just zonk out. Shooting up and staying up. Kind of a weird running party, you know. It lasted for four or five months.

Such congregating in residences devoted mainly to shooting amphetamines has been reported in other research studies on users of massive doses of amphetamines (Griffith, 1966; Fiddle, 1966; Rawlin, 1966).

Speed freaks seem to drift and form flash houses. When a residence becomes "open," the word gets around and the crystal shooters flow into it until the particular limits of the house are reached. Houses develop reputations—as to how pleasant the atmosphere is, how fast and frequent the action is, and what types of persons on the periphery of a particular scene would be welcome. Common to almost all flash houses are frenetic action and crowded living conditions. If this is not so at first, it develops this way in what one writer calls a "spiralling intensity" (Fiddle, 1966). There is always a shortage of money and meeting places, so Meth-heads seem to move in and assume squatter's rights. If the person in charge of a given residence is not fully committed to the world of speed, he will quickly be forced into a decision to get in or out as Meth-heads flow in and take over.

> I let a girl who had babysat for me crash in my pad, so long as she wasn't seeing her ex-boyfriend who was an impossible speed freak. One day I walked in and they were flaked out in *my* bed, and it was impossible to even get them up to move out. So, I literally rolled them off onto the floor and covered them with blankets. A few nights later, they returned only with 2 more guys and they all crashed on the floor. I told them they had to get out by that night, and they said "sure," and it was so unpleasant I left for the day. When I came back that night there were five of them, all as high as can be and you can't talk to them and I was afraid of them. They knew I'd never call the cops, so there was nothing I could do but beg. And they were high the next night, and all five crashed the day after that. When they woke up I told them they *had* to be out that night, and all day I was telling them and they said "sure" and around 9:30 my boyfriend said "half hour or else I'm going to throw your stuff outside," and before he finished the sentence they had gathered up their belongings and were going out the door, cursing and bitching and terribly indignant about my selfishness. They took some records, and left a $30 phone bill, but I'll never get that back, so * * *.

Who runs the flash house? Heavy users pooling their money for rent and bills are rare. Who will trust someone else with his share of the rent money? Who could remember who paid and who didn't? Occasionally a flash house develops when roommates take to using speed and the process of chipping in to meet expenses works out for a few more months. Occasionally dealers will open their own houses, but this seemed to us to be less frequent than others have noted.[5] Dealing will automatically occur within the flash house. Supply rushes in to meet demand. If a new dealer can make enough in a house, he might contribute to paying the bills to keep his "thing" going for another month. Sometimes a tolerant occasional user lets others use his residence.

Obviously, flash houses don't last very long. They get too "hot," i.e., known to the police. Other times users will fall behind in their rent and abscond. Tolerant users and outsiders who have let Meth-heads use their residences quickly reach a breaking point. Occasionally a scene will disintegrate as users become antagonistic toward each other, violence flares up, accusations of theft and unpaid loans are made. However, there is such transiency that the scene will regroup with slightly different characters around the same house or houses.

Crashing in the midst of continual action is painful and users often wish to come down in quieter surroundings. At first straight friends may be asked to provide a bed for a day but even the most tolerant will not often put up with the useless, irritable, selfish crasher whose main interests are his last and next rush. Social relations of "you give, I take" do not last long. Yet there is a

[5] It is true that money can be made by having a house which will attract the market (cf. Fiddle, 1966; Rawlin, 1966), but it can also be made without the residence, and the flash house used for continual dealing is an easy target for drug enforcers.

residence shortage, and the speed freak toward the end of a run becomes alert for any possible offer of a place to crash. People crashing in the room next to people shooting up is common.

The Law, Drug Agents, and the World of Speed. The assumptions behind the antiamphetamine laws are that the traffic can be slowed down and that by pursuing users and sellers and penalizing them severely a number of persons can be discouraged from trying the drug. This assumption seems irrelevant in the case of methamphetamine hydrochloride. It is easy and inexpensive to make, and scores of persons seem willing to risk arrest to manufacture it if profit expectations are high enough. Making and selling Methedrine crystal can be a very profitable venture. After one or two pounds are made the cost of production drops to about $25 a pound and yields up to $1,000 in profits. Necessary laboratory equipment costs only several hundred dollars. Despite local arrests, the profits are so appealing that enforcement seems to have no more than a minimal and temporary effect on supplies. The fear of imprisonment is largely mitigated by the fact that almost everyone is also carrying marijuana, which is punishable by even more severe penalties, so the perception of users is that nothing new is introduced by the anti-amphetamine laws.

The usual effects of illegality—limiting demand among most young people, while heightening it among those who are rebels—does not seem to operate so predictably with Methedrine use. The fact that the law makes use illegal, and that the police and their avid supporters look down on speed freaks, is of no importance to Meth-heads. The realization of the risks and the fear of getting caught, however, do heighten the clannish, furtive atmosphere under which Methedrine is shot. The particular kind of paranoia among Meth-heads focuses on narcotic agents. There are reports of continual fear of agents which persist or recur after other anxieties have been forgotten during the course of a run. Much of the paranoia which is acted upon, i.e. the "dangerous" episodes, involves erroneous perceptions of agents. Social relations within the speed scene are continually eroded by anxieties and accusations about informing within the group. A counter tendency stemming from the illegal status of amphetamines can also be noted. There seem to be strong bonds of trust and camaraderie among Meth-heads which grow out of their sense of uniqueness, their "criminality" and shared personal experiences.

Summary

The physical effects of massive doses of amphetamines—the extremes of elation and depression combined with hyperactivity—make it a drug of choice for younger people, or for those who have the stamina to absorb its physical impact. The frenetic action characteristic of the person high on speed, his compulsive behavior, aggressiveness and suspiciousness, disable him for functioning in most conventional capacities. This means that he is unlikely to have a job. Scenes involving persons who go on very long trips are frequented by few who have anything resembling a steady job. Meth-heads congregate in special areas and special houses because travel problems become enormously difficult after the first day or two on speed. The demands of the scene are totally engrossing. Those who become part of it are (or become) virtually propertyless, seem without ambition in the conventional sense and do not hold on to any identity outside the scene. The friendship of Meth-heads is oriented around and within a speed setting. There is nowhere else that one can find persons with whom one can stay when high or who understand the Meth-head's situation enough to leave him alone when he is crashing.

Living for the moment is a requirement of participation in the speed scene. The demand for drugs, combined with the fact of poverty, encourages a considerable amount of theft. The theft of the property of an amphetamine shooter cannot be reported to the police. Violence and "burns" occurring within the world of speed can be taken care of only by informal measures. Resort to harsh and immediate retribution thus becomes common. To prevent theft requires constant watchfulness. This contributes a pervasive sense of suspicion to the scene. One must also be concerned about the possibility that another's actions, or one's own, might draw the attention of the "nares." This aggravates suspicion and increases the efforts spent at concealment. The obviousness of someone who is high in public creates a dan-

ger and fear known only to the Meth-head and the drug agent. Also, the consequences of being caught with needles and the apparatus that goes with the preparation and injection of Methedrine crystal are very high. A major part of the lives of young people who participate in the speed scene is lived outside of and behind camouflage from the law. This leads to the perception of one's activity as thoroughly illegal, and heavy users tend to think of themselves as "criminal." It is in this context that the toleration of theft and the measures devised to deal with it can be viewed.

The overall effect of the anti-amphetamine laws, in short, is to underline those features of the speed scene which are recognized as undesirable by participants in it and to encourage even more extreme behavior.

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40. AMPHETAMINE ABUSE

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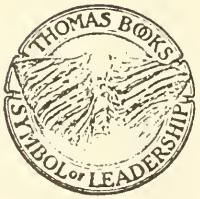

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Chapter III

PSYCHIATRIC IMPLICATION OF AMPHETAMINE ABUSE

JOHN D. GRIFFITH

UNDERSTANDING DRUG DEPENDENCE

The Problem of Observer Bias

ALTHOUGH DRUGS HAVE been available to most civilizations throughout history, it has been only during the twentieth century and with the advent of a modern technology that drugs have been made available in great varieties to large numbers of people. When properly used, the value of these drugs in the control of physical disease, pain and emotional illness is unquestioned and substantiated by much scientific data. On the other hand, it is also well recognized that a number of drugs developed to alter mood or state of consciousness can induce a state of drug dependency with attendant medical, psychological and sociological problems. Unfortunately, the exact causes for drug dependency are not clearly understood. This has led to a scientific vacuum filled by considerable observer bias. Usually this bias takes the very human form of seeking someone to blame. In the past, blame for drug misuse has been placed on either the criminal underworld, the drug user, the drug industry, a careless medical profession, faults in society, or law enforcement techniques. Finding blame is no substitute for scientific inquiry, it merely impedes the scientific process. However, the careful student is well advised to be aware of this blame-finding in his formulations.

The problem of observer bias is further compounded by exploitation of public attitudes about drug dependency. These exploitations are usually harmless exercises in which the problem of drug abuse is used to expand hospital budgets or police protection. Occasionally, however, this exploitation can reach impressive proportions. The American Temperance movement is a case in point. Although begun by a handful of individuals concerned

with the problem of alcoholism, it was soon turned into a powerful force used to control, not alcoholism, but the voting behavior and church attendance of a rapidly emerging educated middle class.[9] As a political movement it was a resounding success; as an alcoholism prevention program it had no demonstrable effect. Interestingly, temperance attitudes are now, in turn, rapped by critics who vehemently condemn any form of prohibition (including restricted distribution of drugs) as ignorant, ineffective, hypocritical, or puritanical. Again, since the distribution of drugs has neither been rigidly controlled nor promiscuously permitted in our contemporary society, the effect of either procedure remains a debatable issue and a potential source of bias.

The scientific community, also, is subject to a form of bias. Generally, scientific conclusions are based on observed facts. However, it is not unusual for scientists to differ in their interpretations. Nor is it unusual for interpretations to shift as new data are obtained. This is perhaps best illustrated by a shift in emphasis that has occurred in medical texts on drug dependency. Until the last decade, there was an almost unanimous emphasis on the *differences* among the various types of drug problems. This emphasis on differences was perhaps unintended and may have been the result of nothing more than the pedagogic choice to consider drug dependency as a function of drugs rather than a type of human behavior. The practical result, however, has been that the average physician thinks of alcoholism in one context while he considers narcotic use in another. He also conceives of some drugs as being "habituating" and others as being "addicting." In addition, he may consider one drug as being "mildly" addicting; another as being "strongly" addicting. Observations also indicate that differences among the various types of drug dependence are more often quantitative than qualitative.

The emphasis on drug chemistry, at the expense of social chemistry, has led to another type of bias in the medical community. Characteristically, as each new drug is introduced to the public it is assumed to be "nonaddicting." This assumption has been made for morphine, intravenous narcotics, heroin, Demerol®, several tranquilizers and the amphetamines. The sequence

of events which followed, once amphetamines became available in American drug stores in 1936, is typical for most drugs and will be cited as an example. Ironically, the first misuse of amphetamine reported in this country occurred in Minneapolis while the psychological effects of the drug were being evaluated at the University of Minnesota. Students, learning by word of mouth about this new stimulant, surreptitiously obtained amounts to use as a supposed study aid.* Student use of stimulants was promptly criticized in an editorial in the *Journal of the American Medical Association*[3] and, later, when the drug was included in the National Narcotics Registry, amphetamines were specifically "not recommended for developing a sense of increased energy or capacity . . ."[2] Thereafter, dissension occurring in the medical ranks led on one hand by Waud, Guttman, Reinfenstein and Davidoff opined that amphetamines might prove to be genuinely addictive despite the lack of withdrawal symptoms. On the other hand, a group of authors represented by Myerson, Leake, Grahn and Nyswander hypothesized that amphetamine misuse was either uncommon, occurred only in maladjusted individuals, or was on the decrease. Punctuating both views were increasing reports of amphetamine psychosis, which have been reviewed by Bell.

Despite these medical opinions, however, amphetamine usage, both clinical and illicit, became widespread during and following World War II. This has been documented by Monroe and Drell, Seevers, the United States Food and Drug Administration and the present author. It is now generally accepted that amphetamine and combined amphetamine-barbiturate dependency is much more widespread in the United States and most Western countries than narcotic dependency. This has posed, for the FDA, a most difficult problem which must carefully balance the usefulness of a drug with its capacity for misuse and the skill of physicians to prescribe it.

As a sociological phenomenon, illicit traffic in amphetamines is also interesting because it defies three rules once thought etiologic in the development of widespread use: (1) public attitudes

*This is reminiscent of the experiments with cocaine by the famous surgeon, Halstead — experiments which led to his addiction.

were at first either humorous or neutral, and therefore, did not reinforce the antisocial attitudes of the drug user; (2) withdrawal from the drug was without important side effects, and (3) being a new synthetic compound there were no historical antecedents, such as with the opium trade.

Thus, it is apparent that the psychiatric implications of drug dependency may be considered a twofold problem. One part of the problem involves the psychiatric problems of the drug user. The other part concerns understanding the biases of the society which surround the drug user. It is impossible to divide the two since each has a marked influence on the other.

Is There a Basic Cause for Drug Dependency?

Definitions. It is often presumed that drug dependency can be defined either in terms of the type of drug used or the amount of drugs consumed. However, this cannot be done in any simple way. It is common knowledge that many people consume alcohol, sometimes in large quantities, but sustain no important ill effect. Less commonly recognized, but observed nevertheless, is that some individuals use morphine or heroin (both very addicting drugs) yet do not become drug dependent in every sense of the term.[11] Therefore, it is not accurate to describe a patient as drug dependent merely because he uses a drug, even if he uses this drug in large quantities. This is especially true of patients who use amphetamines.

Instead, most definitions of drug dependency focus on the peculiar *manner* in which the drug is used. These peculiarities are as follows:

1. The drug is used to obtain a psychic experience, not always described as pleasant. This may explain why those dependent on drugs consume large quantities during short periods of time and may prefer intravenous administration. .

2. The need to use drugs is frequently *compulsive*. That is, the drug user is much like the compulsive hand washer. Consciously, both can enumerate why they need not take drugs or wash their hands. In practice, both report great anxiety if prevented from carrying out their compulsive behavior.

3. The use of drugs is not easily altered by usual life experiences, however pleasant or unpleasant. In cybernetic terminology, it is presumed that unpleasant consequences of behavior tend to exert a "feedback" which extinguishes the behavior. Pleasant consequences have the opposite effect. In drug dependent individuals, as with many other psychiatric syndromes, this feedback is either highly attenuated, reversed or both. Therefore, it can be predicted that drug dependent patients will not respond to techniques which merely punish or reward the patient. This is observed to be the case.

4. Most young people who begin using drugs frequently stop using them once they are middle aged. The reasons for this phenomenon are not entirely clear.

Because etiologic factors in the causation of drug dependency are not yet clearly understood, the medical profession uses a descriptive definition of the syndrome. Drug dependency is considered an illness characterized by the compulsive, repetitive use of a drug, for considerable periods of time to achieve an emotional experience resulting in significant social, domestic and occupational impairment. Admittedly, this definition has many shortcomings. It is not dimensional. It does not recognize the continuum of drug dependent states, nor does it furnish a prognosis with comparison to similar patients. Nevertheless, it is practical because, except in incipient cases, the syndrome is usually quite vivid and can be differentiated from simple drug use with little difficulty.

Causation. Essential to this discussion is the understanding that medicine no longer considers a disease state to be the invariable consequence of one parameter change. For example, the disease tuberculosis is not "caused" by the presence of the tubercule bacillus.[4] Tuberculosis is, instead, a statistically probable future event resulting from the interaction of a number of hereditary, environmental, dietary and physiological events each having their own boundary of indeterminacy. As a disease state, drug dependency follows similar laws. Unfortunately, many of the factors which result in this state are matters of current research and are

not well understood. At present, three main concepts are emphasized by the scientific community.

One such concept is that constitutional factors influence susceptibility to drug use. Theorists who discuss this concept treat the human organism as a biological machine — complex, but a machine, nonetheless. They suggest that this machine has a structural or biochemical flaw (genetically determined, perhaps) that under proper conditions will cause it to seek and consume drugs. Although elegantly simple, this concept is difficult to test because other factors cannot be easily controlled. The concept appears to operate in the case of patients who consume drugs to avoid painful withdrawal symptoms. It finds added support in the observation that a sizeable minority of human test subjects describe their subjective response to drugs as being unpleasant. This is true for all drugs tested, including amphetamines.

Mechanistic concepts of drug dependency are also useful when designing animal experiments, where environmental or constitutional factors are more easily controlled, or in certain types of psychopharmacological research. It has been found, for example, that several stimulant and psychotomimetic drugs, including amphetamine, have the common property of influencing brain catecholamine levels and that the euphoric effect is most likely tied in with altered brain norepiniphrine metabolism. Amphetamine is interesting in that it has four possible modes of action on norepinephrine metabolism as follows: (1) indirectly causing the release of norepinephrine; (2) as a monoamine oxidase inhibitor; (3) by possible conversion to a false neurohumoral transmitter, and (4) directly on the receptor site.

Sociologists, on the other hand, emphasize the concept that individual behavior is profoundly influenced by social and cultural factors which may be etiologic in the problem of drug dependency. This view has led to several valuable studies which indicate, for example, that one's attitude toward drugs is determined by the attitude of others. And also, that the initial introduction to drugs is part of a familiar social setting.[16] It has even been suggested that the drug user might function as a scapegoat for society; that is, the "very good" must have someone they can

think of as "very bad." Most important, however, is the fact that studies which take social factors into account demonstrate that although poverty and cultural deprivation increase the likelihood of drug abuse, income, education, or social status in society do not confer an absolute immunity against drug involvement.[11] One possible exception is intelligence, as only a very small percentage of those who use drugs are mentally retarded.

Psychiatrists, as a rule, tend to emphasize personality factors in disease. Generally, when the psychiatrist uses the term *personality,* he is referring to characteristic, recurring patterns of behavior, diagnostic for each individual, which are evident in response to both the sudden and persistent stresses of life. *Personality theory* (psychoanalysis is one example of a personality theory) is thought to be the deviation of principles which explain the phenomena of behavior. Several psychiatric illnesses characterized by inflexible modes of behavior are termed *personality disorders.* Because the drug dependent individual rigidly adopts the use of drugs as a response to even minor life stresses, he is usually described by psychiatrists as having a personality disorder. Some terms which have been used to describe facets of this personality are *sociopathic, neurotic, paranoid, infantile, narcissistic, hedonistic* and *criminal.* These imply that the drug user is not only unpleasant but unable to assume a productive role in society. Although it has been assumed by some psychiatrists that this disturbed personality antedated the use of drugs, other investigators have suggested that perhaps the observed personality dysfunction should be attributed, instead, to drug involvement. Both views are probably valid in given cases. However, there is no doubt that once the compulsive use of drugs is established, the patient will risk losing life, family, job and social status rather than give up his drug.

The basis for the use of drugs and the attendant personality change is discussed in detail by the psychoanalyst, Otto Fenichel. He conceptualizes the use of drugs as a pathological "impulse" and sees this type of impulsive behavior as also characteristic of certain types of perversions such as voyeurism or homosexuality. However, the drug dependent individual is attempting to obtain

something more than sexual satisfaction. He is attempting to find a feeling of intense security which he may have enjoyed at only one other time in his life — as a suckling child. Fenichel estimates that one who finds satisfaction from drugs lacks strong emotional ties with people in his external reality. Therefore, by default, drugs take on an additional meaning. Complicating the picture, however, is the chemical effect of the drug. He explains:

> All strivings become gradually more and more replaced by the pharmacotoxic longing. Interests in reality gradually disappear, except those having to do with procuring the drug. In the end, all of reality may come to reside in the hypodermic needle. The tendency toward such a development, rooted in an oral dependence on outer supplies, is the essence of drug addiction. All other features are incidental.

Fenichel also explains that normal individuals may develop a temporary need for drugs if, for example, they experience severe pain or similar stress.

Winkler's theory is similar in that the specific actions of drugs are based on the primary needs of man: hunger, sexual urges, aggression and the removal of anxiety or pain. Thus, when the addict says he feels "normal" on drugs, he does. He feels satisfied in these spheres of human need. This is not to imply that his behavior would appear normal to an outside observer, however.

Berne, on the other hand, has recently popularized a theory to explain group behavior. His idea is that interpersonal "transactions" can be conceptualized as games, and he has described alcoholism and criminal behavior in these terms. It would appear that the behavior of drug dependent individuals might be explained in a similar manner. Indeed, addicts themselves have described stereotyped aspects of their group behavior as "games." The author has found himself playing the role of a "chump" with them on more than one occasion.

Although several explanations for drug dependency have been offered, each has one shortcoming in common. None has evolved a treatment method which is simple, inexpensive and successful with most patients. Since the dependency is usually of long duration and not easily susceptible to treatment, it is not surprising that over a period of years a backlog of untreated patients can accumulate.

SPECIFIC CLINICAL AND FIELD OBSERVATIONS OF AMPHETAMINE DEPENDENCY

It has been suggested that the behavior of drug dependent individuals is quite similar, despite the variety of drugs that may be used. Studies of amphetamine dependent individuals in Oklahoma City, conducted by the author, tend to substantiate this view. In these studies observations were made of amphetamine dependent individuals by direct observation in clinical practice; field observations and interview with amphetamine dependent individuals derived from lower socioeconomic groups; with drug peddlers; with physicians who had treated such patients in Oklahoma City, and observations of volunteer test subjects who were given massive doses of *d*-amphetamine in a hospital.[7] Although not a true epidemiological study, the design was such as to obtain instances of drug use in a variety of occupational and social classes in Oklahoma City.

It was anticipated by the research staff that distribution of illicit narcotic drugs in Oklahoma City would be scanty and rigidly controlled since this is typical for most inland southwestern cities. This proved not to be the case. The illegal distribution of amphetamine and barbiturate drugs, however, was both voluminous and widespread. According to law, amphetamine drugs were to be prepared only by licensed firms who sell to a chain of regulated outlets. The drugs are then to be dispensed to a patient under the careful supervision of a physician and a druggist. This study indicated, as have others, that although the vast majority of individuals who participate in this legal system are very careful and aboveboard, large quantities of drugs manage to "leak" from these supervised channels of distribution. In addition to a loosely organized system of peddlers, these leaks included such sources as one small drug wholesaler, druggists who would refill prescriptions carelessly, some students who would sell pills on campus, an occasional hospital or pharmacy employee, and the availability of a nonprescription inhaler containing 150 mg of desoxyephedrine.

These observations suggested that drugs were available to a wide range of the criminal and noncriminal population. They did not explain why individuals would first use drugs, however.

Lindensmith and Scher have commented that the initial introduction to narcotics often begins innocently and as part of the social experience of the individual, whether he is already involved in crime or not. Scher quotes a narcotic addict as describing the introduction of addiction as being "just like the introduction to the Cub Scouts or roller skating." This similarity between initial narcotic use and initial amphetamine use was observed.

College students stated that they first began using amphetamines to stay awake while studying for exams. While most did not seem to be troubled by this occasional drug use, student health physicians indicated that they would have two to three cases a year of amphetamine dependence from among several thousand students. Such students would usually be presented to the health service with acute depressions and as academic failures. Ironically, one member of the research staff, a graduate student hired as a temporary employee, was discovered to be a chronic amphetamine user. This was first suspected when, after being asked to comment on a minor research project, he turned out a 453-page book which was largely unintelligible.

Patients who sought treatment from physicians for amphetamine dependence were usually middle and upper class adult females. None of the women interviewed had had prior knowledge of amphetamine drug dependence, but they did know that medications were available to change mood and suppress appetite. Their first contact with drugs resulted after consulting a physician for an emotional or weight problem. None were told that the prescribed drug might be habit-forming. All stated that they had little difficulty persuading druggists to dispense amphetamines in excess of amounts stated on the prescription written by a doctor dead seven years. These occurrences may change, for Federal law now makes such prescriptions expire at the end of six months. Also, recent court decisions have indicated that a physician may be held liable if he does not explain the possible hazards of his treatment to a patient. This may cause more doctors to warn patients that some drugs may be habit-forming.

The person who purchases drugs from peddler sources has a different sort of introduction to drugs. He is almost always from a lower socioeconomic stratum where knowledge of drug use, com-

plete with undisguised clinical examples, is ubiquitous. If his history can be believed, he begins taking drugs shortly before or after he drops out of school. The sequence of events seems to be the following: feelings of estrangement at school beginning soon after puberty, followed by poor academic achievement and a spotty attendance record, resulting in a search for new friends, whether in or out of school. These new acquaintances either used drugs or would do so. The reasons given by amphetamine users for first using drugs were that they either observed the use of drugs and became curious, wanted to imitate older members of their set, or were persuaded to take drugs by their friends. Some others were introduced to drugs while inmates of prisons or reformatories. None stated they had been encouraged to take drugs by a professional peddler.

Several other impressions that relate to initial drug use among lower socioeconomic users should be added. Although exact figures could hardly be obtained, the staff impression was that relatively few members of the lower socioeconomic group in Oklahoma City use drugs. Our impression was 5,000 individuals out of approximately 65,000. Neither do all of those who are initiated to drugs continue use. Some give up after occasional use. Others use drugs but do not seem dependent in the clinical sense. Some, of course, do become truly drug dependent. A common practice is to use amphetamines in combination with barbiturates or alcohol.

Also important is that an individual who elects to experiment with drugs is faced with a special set of social attitudes in a slum environment. Rarely is he regarded with revulsion. To the contrary he is perceived as different, amusing, or unreliable.

Lastly, although amphetamines and barbiturates are available from peddlers, it is not always easy for the younger user to obtain drugs, especially large, expensive amounts. Incidentally, it is not easy for the noncriminal user to obtain drugs from illegal sources. This was tested by persuading a medical student to try to buy drugs in a slum area. He tried for two weeks with no success.

Based on the previous observations, it would appear that a significant number of individuals from a variety of social classes will at least experiment with amphetamines if the drug is available. These people appear to share a common need to find a

chemical avenue toward a goal which is just beyond their grasp: for the student, better grades; for the housewife, an improved appearance or disposition; for the young slum dweller, an alleviation of a sense of estrangement. Interestingly, although it is assumed that society has a strong sanction against drug use, one who wishes to experiment with amphetamines can find at least tacit support for his behavior.

The use of amphetamines poses several social and medical problems to the abuser which again, is quite similar to the impairment noted from narcotic abuse. One example studied was the "housewife" type of user who obtained amphetamines from a physician. Although she might experience a slight degree of tension when first taking amphetamines, the overall effect of the drug was exhilarating. Loss of appetite, elation, an increased sense of energy and freedom from accustomed lassitude were reported. After approximately three days of drug use, these pleasant drug effects would be present only a short time after drug ingestion. During the next few days or weeks she would then experiment with increased or more frequent doses. Again, however, she would become tolerant to the effects of the drug and increase the dose. To her husband, she would appear tense, irritable, forgetful, preoccupied and neglectful of her home or job. Questions such as, "What's bothering you?" would be greeted with explosive outbursts or circumstantial answers. Since those we interviewed had been prescribed an amphetamine-barbiturate combination, she might also appear unexplainably "drunk." Despite almost incontrovertible evidence that she was drug dependent, she would deny this to herself and to her family. She would become secretive about drug use, and hide tablets, or be fearful that she might "run out." But she would not return to the physician who prescribed the drugs. Usually a psychotic episode, an embarrassing social incident or a severe anxiety attack (frequently interpreted as a heart attack) would cause the patient to be seen by a physician for treatment.

Those obtaining amphetamines from peddler sources appear to abuse drugs in a variety of ways for different reasons. It is difficult to visualize this type of drug abuser without first under-

standing his environment. Detective stories would have one believe that it is a raw and exciting existence. It is not. The architecture is cheap; colors are garish; and personal exchanges — including displays of anger — are almost ritualistic. Even sexual exchanges are performed with the enthusiastic warmth of empty Pullman cars coupling or uncoupling in some dingy switchyard. In this subculture empty of meaningful human relationships, some people seek pleasure and are content with little. Others attempt to enhance the few pleasures they have by using drugs. This category of drug user may not be drug dependent. To him drugs are incidental agents used to enhance his mood as reflected in his intense conversation, dancing or other activities not infrequently terminated by assorted states of intoxication. To the same category might be assigned the prostitute who indicated she took drugs to insulate herself against the rigors of her profession. Each considered themselves to be different from their "pill head" acquaintances. Some of these may, however, represent a stage in the evolution of the drug dependent state.

Another category of amphetamine abuser, however, does consider himself drug dependent. He characteristically takes large amounts of amphetamines, perhaps intravenously, and is frequently incapacitated from drugs. Amounts of amphetamines consumed ranged up to 1.0 gm/day. A single oral dose of 250 mg is not unknown, and a single intravenous injection of 150 mg of desoxyephedrine was observed with some trepidation. Again, barbiturates and alcohol usually accompany amphetamine abuse. In contrast to the amphetamine abuser described above, the individual who admits drug dependency shows evidence of personal neglect. He is invariably emaciated and may have lost his fingernails. His clothes are usually dirty and unironed. He has few personal attachments except those necessary to obtain money to buy drugs. Although solitary use is common, frequently several individuals like himself will get together for a drug "party."* This latter

*Editor's Note: Some areas of the Midwest have organized *Splash houses*. *Splash* is one street term for amphetamines because of the almost incredibly strong cold flash reaction the abuser feels upon intravenous injection. Splash houses are sometimes run by peddlers who instead of peddling, have the customer come to him in a specified location.

term is a misnomer for very little happens. Such "parties" may drag on for several days with various participants coming and going. The principal activity is taking drugs, accompanied by a minimum of conversation and occasional hostile outbursts. After three or more days of continuous amphetamine use, however, a psychotic state resembling a florid schizophrenic episode with paranoid features might insidiously develop in a member and terminate the party. Drugs are usually not taken again for at least twenty-four hours.*

Several comments about these types of amphetamine abusers are in order. Each is frequently incapacitated or "hung over" from drugs and does not hold a job for long. Consequently, crime and prostitution are a usual source of income. On the other hand, not all abusers appear to use amphetamine for its stimulant action. This is especially true for those who use large amounts. Instead, they describe the desired effect in such terms as, "It freezes my brain," or "Keeps me from thinking." Their thought content reflects this retardation and emotional flattening. Apparently, the effects of large amounts of amphetamines are different from prescribed amounts. Lastly, those who seem clinically drug dependent are intensely preoccupied with drugs to the exclusion of almost all else. This, too, is in contrast to the individual who is seeking a stimulant effect in a social setting.

MEDICAL TREATMENT OF AMPHETAMINE DEPENDENCY

Like most psychiatric illnesses, amphetamine dependence is best handled early before the dependence becomes well established by long-term abuse. Unfortunately, most patients do not seek treatment early. Instead, they usually appear when the abuse of drugs has led to a crisis in their lives. This crisis may be a violent rage or panic episode, a suicide attempt, loss of a job, or the onset of a psychosis resulting from either amphetamine or from other drugs that are abused, such as alcohol or barbiturates. Since most patients, and sometimes their families, are reluctant to discuss the use of drugs, it is not unusual for this to go unsuspected. For

*Editor's Note: The dullness and duration of such parties is detailed in a different way in Chapter VII.

these reasons, medical centers, which have to deal with drug problems in a constructive way, organize their facilities to handle psychiatric emergencies on a twenty-four-hour basis.

Another problem is that most individuals who abuse drugs are not wealthy, and, although the doctor may forego the fee, hospitalization is expensive and charity hospitals are crowded. However, hospitalization is frequently necessary because the patient is disturbed and may have a number of medical problems which complicate treatment. Dependence is most often associated with the abuse of other drugs such as alcohol or barbiturates. Withdrawal from these drugs can be a hazardous procedure and often should be carried out in a hospital.

Psychiatric treatment itself is not without considerable discomfort to the patient. Deprived of drugs, he frequently becomes depressed and withdraws. Upon emerging from this depression he is often overcome by guilt which he tries to hide behind rationalizations. For these reasons, many psychiatrists are discovering that such patients are better handled in group therapy situations than individual, face-to-face encounters. Even when given expert care, however, the patient may not do well. If he should impulsively abuse drugs even once, it appears that he will lose control of his drug intake and rehospitalization may become necessary. This control is no easy matter once the patient leaves the hospital and must face getting a job, putting his family back together, and rebuilding his reputation.

A last problem concerning the treatment of the drug dependent person is that the physician himself may have certain prejudices about treating addicts. This is probably based on lack of training. *Most medical schools devote no more than two clock hours of classroom time to the treatment of drug dependency.* Those who specialize in psychiatry receive more training than this, but usually not a great deal more. Increased medical and public interest in drug problems may serve to improve this situation.

Recommendations. Society has found no good solutions for many of its problems. Some mentally ill go to hospitals: others to the electric chair. If this point is moot, the solution for drug problems is even more enigmatic. If experience is any teacher,

however, little will be solved by merely depriving the drug abuser of a few months of his freedom from time to time. Neither will it help to give the hospital label to a large, understaffed mental institution and hope that it will solve the problem.

The author is of the opinion that drug dependence is an illness and that it should and will someday be treated in the same hospitals, clinics and offices that serve for most other illnesses today. The process could be accelerated if some public or private method were devised to underwrite treatment. It could also be accelerated if all physicians, including psychiatrists, were better trained in the area of the drug dependent patient.

Better laws and law enforcement are also needed. Some experts say that strict enforcement of drug laws is no solution, and perhaps their hypothesis deserves testing. But from the Oklahoma City study, it is difficult to see how the distribution of amphetamines could have *fewer* controls. Nor would merely offering treatment to drug dependent individuals have helped, since they rarely sought treatment. The author cannot say what the solution to amphetamine traffic is, but he suggests strict legal controls. There is a moral issue, however, in that those who use drugs are not strictly responsible for their actions. Perhaps this could be resolved by substituting parole-with-treatment for jail-without-treatment.

As a physician who has prescribed amphetamines occasionally and carefully at one stage of his training, this author also suggests that more attention should be given by the medical profession to the fact that many of the drugs now in use are prescribed without proper precautions. There are few, if any, medically legitimate reasons for the prescription of amphetamine-barbiturate combinations. This combination has been outlawed in Norway, and it is hoped that the United States will soon follow suit.

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41.

The Amphetamine Abuse Problem

(By the staff of the Amphetamine Research Project, Department of Pharmacology of the University of California Medical Center, San Francisco, published by American Social Health Association, August 1969)

CONTENTS

FOREWORD

This pamphlet was prepared by the staff of the Amphetamine Research Project, a National Institute of Mental Health sponsored program being conducted in San Francisco by the Department of Pharmacology of the University of California Medical Center, San Francisco. The project, working in close cooperation with the Haight-Ashbury Medical Clinic, has had contact with hundreds of individuals using a variety of amphetamine drugs. In almost every instance, staff members have been struck by patients' lack of information about the amphetamines and the possible consequences of extended use. Non-users and even former users are often uninformed.

The pamphlet is divided into two parts. While both parts derive from the same source, they are edited for separate audiences. The first part was written for junior and senior high school students and the second was prepared for parents, teachers, physicians and others concerned with youth.

John Luce, public information director of the Haight-Ashbury Medical Clinic, drafted the text under the supervision of Roger Smith, project director of the Amphetamine Research Project. Other contributing authors include:

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The pamphlet is published and distributed by the American Social Health Association as part of its program in drug dependence and abuse.

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SPEED KILLS!

A DECLARATION

"Let's issue a general declaration to all the underground community, **contra speedamos ex cathedra.** Speed is anti-social, paranoid making, it's a drag, bad for your body, bad for your mind, generally speaking, in the long run uncreative."

— ALLAN GINSBERG

(In an interview with The Electric Newspaper of Salt Lake City, Utah)

As poet Allan Ginsberg suggests, among those who use drugs like marijuana, LSD, and other drugs that have come to be associated with "turning on," one drug recognized even by them as a real problem and a definite "bummer" is "speed," a common designation for the amphetamine family of drugs. This family of drugs is a "drag" for many reasons. One of the reasons is that the people who use it are unable to remain cool about speed. It's well known in drug circles that only "speed freaks" can stand other speed freaks — and even then, not for too long.

Yet, many people use speed, and many of their friends or former friends wonder if they know what they're doing, what they're getting themselves into, and what happens to people who shoot speed for any length of time.

In a recent survey of a San Francisco Bay Area high school, some students said, "I wouldn't touch that garbage if you paid me! I would rather die than try speed or any other drug." But others wanted to know what speed was all about. Some were just curious and asked, "Is it really that dangerous, more dangerous than pot and LSD?"

When young people were asked how to inform others about speed, a 17-year-old boy user said: "Some organization should find scientific facts about all drugs used today and distribute them throughout the county and city in mailboxes or doors."

He believed his suggestion should be used to let unknowing people in on "what it's all about." This is what the following text does with respect to the amphetamine family of drugs, including speed.

People of all ages and from many walks of life have become involved with these drugs, and their high abuse potential constitutes an alarming medical and social problem. This pamphlet replaces myth and folklore with the most valid information available. It distinguishes between amphetamines used under medical supervision and those substances sold as speed on the black market. It describes the physical and psychological effects of these drugs and some of the possible consequences of their abuse.

WHAT IS SPEED?

Speed is a street name for any number of substances that produce the same central effect as pharmaceutical amphetamines.

The name **Speed** derives from the drugs' fast stimulative action on the central nervous system. The name can be extended to cover any chemical compound that produces a euphoric "high" when taken. (**Speed** is used in this pamphlet to cover substances described in this paragraph, as well as the intravenous use of amphetamines and amphetamine-like agents.) Today, the word is used to describe many drugs that bring a person "up," through stimulation of the central ner-

vous system, just as "downer" is applied to barbiturates and other depressants. The vagueness of these words stems from their prevalence on the black market, where hearsay and slang are often substituted for scientific precision.

In the black market or underground vocabulary, speed is also called "splash," "crank," "rhythm," "meth," or "crystal," the latter term applying particularly to the powdered form of methamphetamine hydrochloride.

HOW IS SPEED MANUFACTURED?

Speed generally finds its way to the black market in two ways. It may be pharmaceutical methamphetamine hydrochloride, dextroamphetamine sulfate, phenmetrazine or another stimulant obtained from a forged doctor's prescription or acquired through robbery of a drugstore or pharmaceutical company. Very often, however, it is a facsimile produced by persons with the requisite knowledge of chemistry.

These underground chemists, often called "cooks," may affix counterfeit labels or stamp trade names on the products they sell in bulk or tablet form. They sometimes say that the drugs are legitimate pharmaceutical products or insist they are of comparative purity, but buyers have no way of determining either their quality or origin.

Street speed is often found to contain ether, which is added to the liquid speed to hasten the crystallization process, or mixed with other impurities. What is advertised as "U.S.P." (official standard) methamphetamine hydrochloride by some illegal chemists may turn out to be methamphetamine sulfate, baking powder, monosodium glutamate (e.g., Accent), or, in one reported case, insecticide.

HOW IS SPEED ABUSED?

Sometimes, speed is used in a quasi-medical fashion by individuals who are depressed, fatigued, or overly sedated by

barbiturates, opiates or other "downers." However, speed is more often abused. It is generally taken in large doses to produce a characteristic high. Some persons take speed once or twice for "kicks," and then abandon the drug; others continue abusing it over longer periods.

Users interviewed by the Amphetamine Research Project and the Haight-Ashbury Medical Clinic indicated their long-term abuse was motivated by a desire for euphoria, escape from tensions and suppression of psychic difficulties and physical needs.[1] A few of their observations are:

> "My boy friend got messed up with speed — and his best friend went to the state mental hospital for it," said one 17-year-old girl.
>
> A 16-year-old girl defended her use of speed: "Oral speed is good for fat girls — and makes working easier," she said.
>
> One mini-skirter reported: "For me, personally, it helped to get along with other people and not be so tensed up. But when you stop speed — man, you get nerves."
>
> From a girl cheerleader: "The advantages of losing weight — of having a good mood while up — of pleasing physical conditions — none of these is worth the breakdown of general physical health. Mentally, you don't function well; the more you use speed, the worse the condition becomes."
>
> An 18-year-old boy remarked: "I use speed orally. It provides insight on your problems. But not an escape. Excessive use is psychologically bad if a person is trying to block something within himself."
>
> One speed user described his trips up and down: "I make lots of plans, but I don't ever carry any of them out. I get in this

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1. See also: Carey, James T. & Mandel, Jerry. A San Francisco Bay Area Speed Scene, *Journal of Health and Social Behavior,* 9 (2), 164-174, June 1968.

   Kramer, John C., Fischman, Vitezslav S., & Littlefield, Don C. Amphetamine Abuse. Pattern and Effects of High Doses Taken Intravenously, *Journal of American Medical Association,* 201 (5), 305-309, July 31, 1967.

megalomaniac bag, about five days into it, and I'll build these mountainous castles in my mind, all the far out things I'm going to do, and all the money I'm going to make. I'll be driving a Rolls Royce and have two speed labs going at once, a heroin refining plant, my own private two-engine airplane. I'll be running the Mafia, and then when I start to come down I realize that none of this stuff is existing and that none of it is going to exist and it's like you pull the bottom out of your brain. I feel empty and suicidal in about four or five hours."

WHAT IS THE SPEED HIGH?

Persons who inject speed in high doses usually experience a pleasurable "rush" or "flash" as the drug reaches their central nervous system. They remain high for several hours. The high is characterized by feelings of self-confidence and mastery, and by greatly increased motor and psychic activity. Persons in this state often "rap" or talk rapidly and may become agitated or violent. They are likely to do or say things not expected by others or themselves.

The high is usually followed by a reaction phase or depression when the effects of the drug wear off. The depression may be so acute that users "shoot" more speed to get high again. Many repeat this cycle until they launch into speed "runs" lasting as long as seven or eight days. During this time they rarely sleep or eat. As their bodies develop tolerance for the drug, they use increasingly higher doses at more frequent intervals. By the end of a run, they may be injecting several hundred milligrams of speed 10 or more times a day. The Haight-Ashbury Medical Clinic has reported cases in which 15,000 milligrams per day were injected.

HOW ARE ADVERSE REACTIONS TREATED?

Persons with acute anxiety reactions should be treated in a supportive environment. Anti-anxiety agents such as chlorpro-

mazine can be applied effectively, but physicians are advised against aggravating the situation by threatening attitudes, and over-medicating patients with sedatives. The anxiety reaction is often followed by depression.

The paranoid-schizophrenic reactions are much more difficult to treat. After prolonged usage, abusers experience auditory and visual hallucinations; they may become convinced of elaborate plots directed against them. They can become violent and require restraint; often they must be hospitalized. Physicians should administer anti-psychotic agents, such as phenothiazines, and isolate patients in supportive environments. Such isolation is necessary because of the phenomenon of group toxicity associated with speed. Studies conducted on laboratory rats at the University of California Medical Center indicated that grouping the animals and injecting them with amphetamines increases the toxicity of the drug by four times. Significantly, it lowers their lethal dose effects.

Persons who take speed in group settings show a marked increase in their psychic responses and are much more likely to become violent than when they take the drug by themselves.[2]

WHAT ARE THE PHYSICAL EFFECTS?

The risk of these many forms of psychic distress from speed is directly proportionate to the frequency and size of doses involved. So is the risk of serious physical damage.

Since speed masks the true physical state, abusers may overexert themselves and fail to recognize the bodily harm incurred. Not eating, they become undernourished, and consequently more vulnerable to disease.

Habitual speed abusers rarely observe proper dental hygiene or nutritional standards. Tooth decay and gum infections may develop. Abscesses or cellulitis often occur because of using

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2. Smith, David E. Behavioral Mediators in the Polyphasic Mortality of Aggregate Amphetamine Toxicity, *Journal of Psychedelic Drugs*, Haight-Ashbury Medical Clinic, San Francisco, November 1968.

contaminated needles, missing the vein when injecting the drug, or using speed which contains impurities. Blown or ruptured veins are common among persons who use poor quality substances which do not completely dissolve in water and may be difficult to force through a needle. Their lips become cracked due to the drugs' constricting effect on mucosal surfaces. They often injure their facial tissue by picking at "crank bugs," imaginary black bugs which seem to be crawling under the skin. But there are no bugs. It's a hallucination. This reaction is common among intravenous speed abusers.

The destructive liver disease known as serum hepatitis is not a specific accompaniment of amphetamine abuse, but is a risk incurred by any drug abuser using the intravenous route. Although many persons recover from hepatitis infection, there remains the possibility of severe complications and the development of acute or chronic liver damage.

HOW IS HEPATITIS RECOGNIZED AND TREATED?

The principal symptoms of hepatitis are nausea, vomiting, loss of appetite and stomach pains with cramps. In less severe cases, weakness and a tired feeling may be the only symptoms. If the liver is damaged sufficiently, it can no longer remove toxic substances from the bloodstream and a material called bilirubin may back up in the system, giving a yellow color to the skin and eyes. In more severe cases of hepatitis, the whites of the eyes and the skin may become jaundiced; the urine becomes dark brown, and the stools turn gray.

When these symptoms are evident, one should seek medical aid immediately. Patients usually require hospitalization during the acute phase, when they require bed rest, cannot eat, and must be nourished by intravenous fluids. Other cases can be treated on an out-patient basis, but should be followed in order to determine any complications that may arise.

Serum hepatitis ordinarily is transmitted only by penetration of the skin by a needle or by an object that has been in contact with a carrier of the virus. Serum hepatitis has a long carrier

state; persons may remain carriers for five years — in some cases, for life. The symptoms of serum hepatitis usually manifest themselves from two to five months after the virus enters the body.

Serum hepatitis spread by unclean needles is very prevalent among speed abusers. Many persons living in a high abuse population, such as that in San Francisco's Haight-Ashbury district, have had the disease. Physicians working at the Haight-Ashbury Medical Clinic see severe forms of liver disease in that community. They believe that high doses of speed may produce an additional toxic effect in those persons whose liver is already damaged by hepatitis.

If you think you have hepatitis, see a doctor or go to a clinic or hospital. Plenty of bed rest will be prescribed because inactivity lowers the amount of stress placed on the liver. A high protein, high carbohydrate diet will be advocated, consisting of meat, fish, eggs, bread, potatoes.

If you think you have hepatitis, do **not:**

1. Donate blood
2. Share a needle with anyone else
3. Drink alcohol
4. Use heroin, morphine or other opiates which are particularly toxic to the diseased liver.

To avoid serum hepatitis: Don't share needles. If you suspect that you are infected, a shot of gamma globulin from your doctor or clinic will modify and reduce the severity of your possible case of hepatitis.

Infectious Hepatitis is a separate viral disease spread in unhygienic surroundings by contaminated water, food or eating utensils.

WHAT ARE THE PSYCHOLOGICAL EFFECTS OF SPEED?

Some people say that speed acts as an aphrodisiac. Others report that it impairs sexual potency. Usually there is a slackening of sexual interest in speed abusers. As their abuse steps

up, their interest in members of the opposite sex often decreases proportionately.

Their interest in social relationships and intellectual or physical pursuits of any kind also declines proportionately to their involvement with speed. Habituated persons usually live solitary lives distinguished only by alternating cycles of depression and euphoria. It is difficult to tell whether speed abuse leads to, or reinforces an already-existing readiness for, such behavior.

WHO ABUSES SPEED?

Most speed abusers are immature. They try to make up for the limitations of their lives by chemical means. Many become involved with speed when they are about 16 years old, an age when adolescents are likely to be facing up to the challenges of maturity. Many suffer from personality disturbances so severe they try to block out reality and its commitments and decisions.

Most of the young people interviewed by the Amphetamine Research Project came from emotionally inconsistent backgrounds, fatherless homes in which the mothers were often depressed and resented supporting their unwanted children. At an early age, many of these potential speed abusers found it difficult to tolerate the "down" atmosphere of their homes and sought any kind of activity, however aimless and compulsive, to get "up" again. Their early lives were barren of affection. They were almost literally starved and needed to fill themselves up in any way they could. They felt great emptiness, overwhelming oral longings. They also felt cheated by the world and wanted others to help them get their "due."

Many speed abusers resemble abusers of other substances in being unable to tolerate frustration. Feeling themselves cheated, they expect immediate gratification for their desires. Speed can make them think they are supermen who can do or have anything they want. The speed flash, which many abusers compare to a sexual orgasm, often becomes a substitute for sexual gratification with another human being. Speed abusers

do not have to risk being refused sexual relations with others. Even if they do have intercourse, it is usually just a form of mutual masturbation, with little shared tenderness or love.

After the flash, speed abusers float on fantasies of conquest, totally divorced from the reality of their actual lives. They feel none of the depression and anxiety that usually overwhelm them. When they start coming down from the drug, they must shoot up again to ward off despair.

High dose speed abusers often brag about how much of the drug they can take in a single injection. Sometimes, they compete with one another to see who can sustain the longest speed runs. Such activity constitutes a form of status in some areas. It is possible that many speed abusers are psychotics who require such competition and danger. The drug helps them to project their inner confusion into the external world and create chaos in their daily lives in order to feel they are actually mastering their confusion.

Whatever psychic needs speed satisfies, its abuse has become increasingly widespread in this country over the past several years. Many persons who once abused marijuana, narcotics, and cocaine have switched to speed. A sizeable number of long-time narcotics addicts must be counted in the national speed abuser population. More and more persons are varying their consumption of speed with barbiturates and other downers in a cyclical pattern.

Many school students without previous drug experience are becoming involved with speed and pharmaceutical amphetamines. A recent survey conducted at a suburban high school in the San Francisco Bay Area revealed that 22 per cent of the 11th and 12th graders had used one or more of these drugs orally one or more times. Three-fourths of the 22 per cent had taken these substances three or more times. Since oral use generally pre-dates intravenous abuse, it is safe to conclude that a number of these students may eventually become habituated to speed.

Although the specific experiences of the speed freak vary, depending on the person and the area in which he lives, all

tend to have certain things in common. They are eventually likely to be excluded from such normal activities as jobs, school, family life, meaningful friendships or love relationships. Speed is a total "ego trip," and the speed freak has little time for anything or anybody other than his love affair with speed.

RESEARCH IS URGENTLY NEEDED

Recognizing the alarming spread of speed and amphetamine abuse in America today, young people, as well as their physicians, teachers, counselors, public officials, parents and law enforcement agencies should familiarize themselves with the patterns of abuse of these substances. More research is urgently needed to determine the social and psychological factors prompting the spread of drug abuse. Treatment facilities must be established to deal with these drug problems.

At the same time, persons curious about speed and amphetamines and wishing to experience their effects should seriously consider the probable psychic and physical danger from such experimentation.

"Speed Kills" is neither an idle threat nor an unsubstantiated warning. Indiscriminate use of these drugs can only lead to harm.

The Amphetamine Abuse Problem

WHAT ARE AMPHETAMINES?

Amphetamines are related chemically and pharmacologically to a large group of compounds, generally known as sympathomimetic amines, that act like adrenaline on the body. They have a pronounced stimulating effect on the central nervous system, as well as certain peripheral effects, and are classified under the broad category of central nervous system stimulants.

Amphetamine equivalents have the same approximate pharmacological properties. They are often erroneously called amphetamines, although they may or may not be properly classified as sympathomimetic amines.

Amphetamines are prepared for pharmaceutical purposes in many forms, the most common of which are amphetamine sulfate, dextroamphetamine sulfate, and methamphetamine hydrochloride. They are manufactured by several large pharmaceutical companies and marketed under such brand names as Benzedrine (amphetamine sulfate), Dexedrine (dextroamphetamine sulfate), and Methedrine and Desoxyn (methamphetamine hydrochloride). Methedrine, a term often used synonymously with amphetamine, is a brand name for one particular form of an amphetamine (methamphetamine hydrochloride).

The combination of methamphetamine hydrochloride and the barbiturate, phenobarbital sodium, is marketed under the brand name Desbutal. A combination of dextroamphetamine sulfate and the barbiturate amobarbital is marketed under the brand name Dexamyl. Two amphetamine equivalents, phen-

metrazine and methylphenidate hydrochloride, are marketed under the brand names Preludin and Ritalin. These drugs are usually sold in tablet form on a prescription basis.

HOW ARE THEY USED?

The peripheral effects of amphetamines include an increase in blood pressure as a result of a step-up in heart rate and vascular tone; dilation of the pupils; relaxation of the smooth muscle of the gastrointestinal tract and urinary bladder; and secretion of sparse, thick saliva.[3]

The drugs also have a constricting effect on blood vessels when applied to such surfaces as the lining of the nose and the bronchial passages. Because of this effect, amphetamine inhalers were once used to treat fever, but widespread abuse of the inhalers led to their withdrawal from the market.

Today, amphetamines are employed therapeutically for their profound stimulative effect on the central nervous system rather than for their peripheral action. The most marked and consistent effect is the production of a state of arousal and wakefulness which may be accompanied by a feeling of increased psychic and motor activity. It is much more often a feeling than a measurable increase. This effect is used medically in the treatment of narcolepsy, a disease characterized by an uncontrollable desire to sleep.

Amphetamines are also used occasionally for the improvement of performance and endurance. Doctors have been known to prescribe amphetamine sulfate or dextroamphetamine sulfate, for example, to students wishing to stay awake while studying for examinations or to truck drivers who must travel long distances late at night. When used as prescribed, these drugs are usually taken orally in 5 to 15 milligram doses once every eight hours. They have a high abuse potential, however, and many physicians now prescribe other stimulants or recom-

3. Kalant, Oriana. *The Amphetamines, Toxicity and Addiction*, Charles C. Thomas, Publisher, Springfield, Ill., 1966, 151.

mend the caffeine available in coffee or various over-the-counter products.

Another prominent central effect of amphetamines is the inhibition of appetite. This effect is the basis of the drugs' most common medical use, the treatment of obesity. Doctors may prescribe methamphetamine hydrochloride in tablet form for weight control and advise that it be taken in single 5 to 15 milligram doses daily. Methamphetamine ampules were once prescribed for the same purposes. Informed physicians now rarely resort to the amphetamines for weight reduction because their side effects are disadvantageous, and their abuse potential high.

The central stimulative effects of amphetamines are usually perceived subjectively as a sense of increased energy and self-confidence, and of faster thought and decision making. Users of the drugs often experience feelings of well-being and even euphoria. These effects are employed in the psychiatric treatment of some forms of depression.

HOW ARE AMPHETAMINES ABUSED?

Drugs are considered to be misused and abused when their persistent or sporadic use is excessive, inconsistent with, or unrelated to acceptable medical practice. Such use interferes with the physical, psychological and social well-being of an individual. With amphetamines, such abuse stems from the drugs' stimulative and psychic effects and is complicated by the fact that as the body develops a tolerance to the amphetamines, higher doses are required to maintain the drugs' effect.

Amphetamine abuse may evolve from therapeutic use. Some housewives who initially try amphetamines to hold down their weight become psychologically dependent on the drug to lift up their spirits. As their bodies develop a tolerance, they increase their doses and/or frequency of ingestion. Eventually, they may become dependent upon the drug and abuse it in a cyclical fashion, alternating between psychic depression and chemically-induced euphoria.

College students and truck drivers can become dependent in a similar manner. They may originally take amphetamine sulfate or dextroamphetamine sulfate to stay awake for a single night and then employ these drugs to deny their need for sleep over a longer period of time. Some also try to deny their need for nourishment or mask their true physical condition. Others employ amphetamines to suppress their anxieties as well as their appetites, and become abusers in a cyclical pattern.

Abuse of amphetamines can lead to erratic behavior and serious mental disturbance. Prolonged high dose consumption usually causes auditory and visual hallucinations and severely impairs judgment. Medical records reveal cases of truck drivers, for example, who have swerved off highways to avoid imaginary obstacles in their paths.

Going the same route, students have reported similar states of confusion or overconfidence, induced by amphetamines, that actually impair their performances on tests. Some have taken high doses of amphetamines to help study and discovered, during the examination, they have forgotten all they have learned. One young man who stayed awake for several days with dextroamphetamine sulfate wrote a long and largely incoherent book in response to a simple examination question.

High dose amphetamine consumption can also produce toxic psychoses and precipitate or aggravate chronic neurotic and psychotic behavior. Housewives who use amphetamines occasionally for intoxication may become disoriented and require hospitalization. Others who take the drugs compulsively over extended time periods can become severely disturbed. There is a greater prevalence and severity of psychotoxic effects when the amphetamines are taken intravenously.

DOES ABUSE LEAD TO PERSONALITY CHANGE?

Some physicians believe that extended abuse can lead to pronounced personality change. Persons who become dependent upon amphetamines usually exhibit increased restlessness and irritability and often become aggressive and violent. When not stimulated by the drugs, they can become withdrawn,

depressed and even suicidal.

Others have argued that such persons are predisposed to such behavior patterns and that amphetamine consumption only reinforces already existing personality defects. Although little research has been conducted to determine whether amphetamine abuse causes or reinforces personality change, it can be stated that most abusers do have certain personality traits in common. Those housewives who abuse the drugs are often passive, unhappy persons. They employ the drugs to deal with their personal problems or to make up for deficiencies in their personalities. Students who become dependent on amphetamines are usually withdrawn individuals who do poorly in their studies and cannot tolerate the tensions of a highly competitive academic atmosphere.

The possibility of personality change from abuse of amphetamines is alarming. More tragic is the possibility that excessive amphetamine consumption can lead to permanent organic damage to the brain. Studies of methamphetamine hydrochloride abusers in Japan and animal studies conducted in this country suggest that irreversible brain damage can be caused by the drugs, and research is now under way to explore the likelihood of this effect.[4]

Because of these dangers, amphetamines should be prescribed only under the strictest medical supervision. In fact, many doctors urge that amphetamines should be removed from the commercial market and replaced by other stimulants with comparable therapeutic effects and significantly lower abuse potential.

Their position is supported by physicians familiar with widespread abuse of amphetamines and amphetamine equivalents in other countries. The rise in methamphetamine hydrochloride abuse in Japan since the Second World War and the recent wave of phenmetrazine abuse in Sweden have convinced many doctors that amphetamine abuse is a most serious international, as well as American, problem.

4. Lemere, Frederick. The Danger of Amphetamine Dependency, *American Journal of Psychiatry*, 123 (5), 569-572, November 1966.

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42. Putting Some Limits on "Speed"

By Rush Loving, Jr., Fortune, pages 99 and 127–128, March 1971

Unlike marijuana, the amphetamines are man-made drugs that can be legally sold in this country. More than 100 U.S. companies, some of them of the highest repute, make amphetamines, and many doctors regularly prescribe them. But the misuse of this stimulant drug—by businessmen and housewives as well as young people—has become a pervasive phenomenon that many medical experts and law-enforcement officials say is more dangerous to society than the spreading use of marijuana.

Amphetamines give hours of extra energy; they keep the user alert and seem to sharpen one's wits. For years truck drivers, students, and others have relied on "pep pills" to ward off fatigue. For many of these users, amphetamine represents only an occasional crutch, but its overuse can have dire consequences. "Like heroin and cocaine, [intravenous injection of amphetamine] is a form of drug use which may overwhelm even a casual dabbler," said Dr. John C. Kramer, former chief of medical research at the California Rehabilitation Center, in a report on "high dose" (i.e., heavy) users.

Amphetamine users, including some who obtain the drug legally, are frequently subject to insomnia, malnutrition, respiratory difficulties, and hallucinations. A person taking large repeated doses may talk incessantly and be hyperactive for days at a time. Some heavy users have killed themselves during the severe depression that follows the euphoria of a prolonged speed trip—"speed" being the name generally given in the new youth culture to all amphetamines. Victims of psychological dependence and massive overdoses—men and women in a continuing state of paranoia, young people in the group of uncontrollable, drug-induced rages—are crowding psychiatric wards and drug clinics. Numerous violent crimes have been committed by amphetamine users; for example, Senate investigators found that Charles Whitman, who shot forty-four people—fifteen of them fatally—at the University of Texas in 1966, was a user.

Federal records show that licensed drug houses turn out the equivalent of 81,400 pounds of amphetamines annually, or 3.7 billion doses of 10 milligrams each—enough to supply every man, woman, and child in the U.S. with eighteen doses. In one recent year, a startling 16 percent of the total legal output wound up recorded as "unaccounted for" in a report prepared by the Federal Bureau of Narcotics and Dangerous Drugs. The bureau believes that the current rate of diversion of legitimate production may be much higher, perhaps 30 percent. In addition, there is a vast, although unmeasurable, production of bootleg amphetamines. The drug is so simple to compound that even a college freshman with a basic knowledge of organic chemistry can produce it.

No one knows how many Americans use amphetamines illicitly, although one drug expert estimates that there are at least as many high-dose amphetamine users as there are heroin addicts (perhaps as many as 100,000 in New York alone) Surveys of U.S. high-school students indicate that an alarming number of them have tried the drug on their own at least once: nearly 8 percent in Montgomery County, Maryland; 10 percent of 47,000 Utah students (including some eighth-graders); 21.5 percent of the junior and senior boys in three California high schools. Not all of these students were regular or heavy users, of course, but the numbers appear to be rising. For instance, a 1968 survey of students in San Mateo, California, showed 16.3 percent had used amphetamines during the preceding year; a 1969 survey in the same county showed that the percentage had risen to 20.8.

The widespread diversion and misuse of amphetamines have prompted Congress, the Federal Bureau of Narcotics and Dangerous Drugs, and the Food and Drug Administration to seek tighter controls on the production and sale of the drug And many medical authorities are questioning whether there is *any* legitimate need for amphetamines. Some favor a total ban on their production. Meanwhile, major companies continue to turn out amphetamines and doctors continue to prescribe them under such brand names as Dexedrine, Desoxyn, and Obedrin.

WHY DOCTORS PRESCRIBE THEM

Amphetamine is a synthesis of basic chemicals like phenylacetic acid and ammonia. It comes in a variety of forms, including racemic amphetamine and

the salts of dextroamphetamine and methamphetamine. It is liquid methamphetamine thta hardened users ("speed freaks") shoot directly into their veins, and originally the term "speed" referred only to this form of the drug.

Amphetamine made its medical debut in 1932 as a decongestant, via the famous Benzadrine inhaler, a product of Smith Kline & French, which quit making it in 1949. Since then the drug has been used medically for treating such diverse ills as alcoholism, Parkinson's disease, mild depression, and epilepsy. Because amphetamines tend to suppress the appetite—at least for the first weeks of use—they are heavily prescribed for obesity; in fact, more than 80 percent of all amphetamine prescriptions are for weight control. Although doctors may still prescribe amphetamines freely, the FDA now recognizes only three possibly effective uses: for narcolepsy, a disease that is characterized in part by excessive sleeping; hyperkinesis, or overactivity in children, often due to mild brain dysfunction; and obesity.

But even these uses have come into question. The Department of Health, Education, and Welfare has already stopped authorizing the purchase of certain amphetamines in government health programs, and the FDA has ordered manufacturers to prove that their drugs are indeed effective in all three of the uses that it currently recognizes. One possible outcome of this would be for the FDA to rule that the use of amphetamines in treating narcolepsy—a relatively rare condition—and hyperkinesis is justified, but that their effectiveness in the control of weight is overshadowed by the danger the drug poses for its users. The Narcotics Bureau, using powers granted it by Congress last year, is taking steps to put amphetamines in the same category as "hard" narcotics, like opium and methadone. This reclassification would mean that quotas would be imposed on legitimate production, and every pill would have to be accounted for at every step in the distribution chain from manufacturer to user.

Still another threat to the amphetamine market may come from a new anti-obesity drug called fenfluramine. A 1968 British Medical Association study concluded that fenfluramine is an effective anti-obesity drug that is not a stimulant and does not cause dependence. Fenfluramine was developed by Servier, a French drug house. The American licensee, A. H. Robins, of Richmond, Virginia, is seeking approval to market the drug in the U.S., but the FDA has withheld permission pending further investigation of its safety and efficacy.

WITHOUT THE HOLY GRAIL

Some of the registered drug houses that turn out amphetamines are quite small, grossing less than $100,000 a year on their output of the drug, which they sell under generic names at lower prices than the trade-name amphetamines marketed by the bigger houses. But nearly one-third of the amphetamine production is from about fifteen of the larger companies that belong to the Pharmaceutical Manufacturers Association, the drug industry's leading trade group.

By far the largest producer is Smith Kline & French, a venerable Philadelphia drug house that sold $20 million worth of preparations containing amphetamines last year. Strasenburgh of Rochester, New York, now a part of Pennwalt Corp.'s Pharmaceutical Division, is second in dollar volume, with about $9 million in sales last year. Abbott Laboratories is third, with amphetamine sales of just under $8 million a year. Next, with volumes of less than $5 million apiece, come S. E. Massengill of Bristol, Tennessee; American Cyanamid's Lederle Laboratories division; and A. H. Robins.

Amphetamines make up almost all the sales of some very small drug companies, and are important for some of the better-known houses. For example, they bring in 18 to 20 percent of Massengill's annual volume If the FDA and other government agencies restrict or ban amphetamine production, it would cause some damage to some firms. "It'll have ramifications unless we have the Holy Grail or something to throw in its place," says Frank W. DeFriece Jr., president and cheif executive of Massengill; the company is "well along" on research on a substitute product. On the other hand, a ban would bring little financial pain to the very large drug houses like S. K. & F.; amphetamines account for less than 6% of its sales and earnings.

All the legitimate manufacturers are registered and inspected by the government. Many of them store their amphetamines in locked, guarded cages; they check on the legitimacy of each customer; they even turn down orders that are

suspiciously big. "We're not shooting it out the back door as fast as it can be made," says Massengill's DeFriece. But even so, some of their pills and capsules and chemicals get into the wrong hands. Abbott Labs, a most scrupulous manufacturer, unwittingly sold two million doses of methamphetamine powder four years ago to a Long Island man who was bootlegging speed pills to the illicit market Last year a Tennessee grand jury indicted a Massengill employee on charges of stealing some 380,000 tablets.

Not all manufacturers have been scrupulous about screening their customers. For example, Bates Laboratories was a small Chicago drug maker with annual sales of only $1,500,000. In 1969 narcotics agents and investigators for the House Crime Committee reported that Bates had sold about 15 million amphetamine doses over a ten-year period to a bogus company in Mexico. The street address on the firm's letterhead turned out to correspond to the eleventh hole of a Tijuana golf course.

Much of the diversion of legitimate production comes at the wholesale drug house, the corner drugstore, or even the doctor's office. The Narcotics Bureau says that two New York wholesalers, Paramount Surgical Supply Corp. and Sherry-Blank Drug Co., sold about five million doses in 1966 and 1967 to Horn Drug Co. of Donalsonville, Georgia, but apparently neither questioned Horn's legitimacy or the unusual size of its purchases. The fact was that Horn's license had been lifted in 1965 because of illegal drug sales. One druggist, Raymond Poynter, owner of the Laurel Pharmacy in London, Kentucky, was supplying amphetamines to pushers in at least two states when narcotics agents closed in on him. Doctors have been caught, too. In 1968 federal agents arrested Dr. Robert N. DeVore, a Jackson, South Carolina, physician, after he had carelessly sold an undercover agent 32,000 amphetamine pills.

Illicit users often obtain their amphetamines through legitimate prescriptions. Some doctors, especially specialists in the treatment of obesity, have been so reckless that almost anyone who wanted a supply of amphetamines could go in, complain of being too fat, and get regular supplies of diet pills. Some users visit more than one doctor in order to get extra doses. Others alter their legitimate prescriptions so that they can get extra refills or more pills.

"WE HAVE CHILDREN, TOO"

The drug industry is acutely aware that there is indeed a problem of amphetamine misuse "We are as much concerned as anyone could be," says Elwood A. Garner, president of Pennwalt's Pharmaceutical Division. "We have children, too." Companies like S. K. & F. and Abbott send out lecturers and movies to schools and civic groups to warn of the hazards of amphetamines. They also caution doctors that amphetamines are no more than a short-term crutch in weight control. "For some time we have been urging doctors not to overuse our product," says an Abbott executive.

In balancing amphetamines' medical usefulness against public welfare, the companies say that they themselves have faced up to the same judgment. For the most part, they have found in favor of continued amphetamine production, though two of the larger firms, Eli Lilly and Burroughs Wellcome, have dropped amphetamines. Some smaller firms may have got out of the market also. Lilly stopped production in 1967 because its share of the market was too slim. Burroughs Wellcome quit because of bad publicity after one of its trade names—Methedrine—became identified with amphetamine abuse among young people, particularly in Haight-Asbury, San Francisco's hippie community.

But the companies still making amphetamines insist that the products are needed. "The medical usefulness of amphetamines in their present indications have been amply demonstrated over the past thirty-five years," says Thomas M. Rauch, president of S. K. & F. Says Bruce Brennan, general counsel for the P.M.A.: "I don't see that as long as there is a recognized medical need that there is any question of morality in making it." But Brennan adds: "I do think that there is a moral responsibility in seeing where it goes."

The larger firms helped shape the federal drug law that Congress passed last year to tighten surveillance of amphetamine makers and distributors and place new restrictions on purchasers of the drugs. The companies say the new law should do much to curb diversion. But they oppose the Narcotics Bureau's move to classify amphetamines with the hard narcotics—a step made possible by the new law. The manufacturers argue that the auditing system required would be unduly expensive, and would not serve to halt the flow of amphetamines from bootleg factories. The illicit flow would continue even if production quotas,

or a total ban, were imposed on amphetamine production. After all, the manufacturers say, heroin is banned, yet addicts manage to get it. Further, says Fred A. Coe Jr., chairman and president of Burroughs Wellcome: "Alcohol is a lot harder to make, but during prohibition they weren't able to stop that."

A NEEDED TREATY

One recurring proposal is that amphetamines should be banned altogether in this country. Japan and Sweden, which have had serious problems with amphetamines, already have imposed strict controls on the drug. In Japan the controls have virtually wiped out amphetamine abuse. But in Sweden abuse is still widespread, largely because of smuggling.

To be effective, limitations on legal manufacture in the U.S. would have to be backed up by a new international protocol restricting the world traffic in amphetamines. John E. Ingersoll, forty-one, director of the Narcotics Bureau, led a delegation of U.S. Government and industry representatives to Vienna in January to negotiate just such an agreement covering all mind-affecting drugs. Neither a domestic ban nor an international treaty would wipe out smuggling and bootlegging, of course, but at least narcotics agents could then concentrate on eradicating the illicit side of the market.

RUSH LOVING JR.

(C) CORRESPONDENCE: SUBCOMMITTEE TO INVESTIGATE JUVENILE DELINQUENCY, COMMITTEE ON THE JUDICIARY, VIEWS OF CONSTITUENTS, PRO AND CON, RELATING TO CONTROLS FOR DIET PILLS

1. LETTER FROM "A CONCERNED MOTHER," TACOMA, WASH., TO SENATOR BIRCH BAYH, FEBRUARY 11, 1972

February 11, 1972

DEAR SENATOR BAYH: I was much interested to read in a Seattle newspaper that you have opened hearings on the abuse of diet pills in treating obesity.

If you can take any action to prevent unscrupulous doctors from indiscriminately handing out prescriptions for these drugs, I will bless you forever. Let me give you an example of the tragedy and heartache that can result from "diet pills."

We have a daughter of 23. She is lovely, personable, and was a perfect joy to raise She was to be married last year and a few weeks before the wedding, decided to lose some weight. She went to our doctor, a fine ethical internal medicine man. He gave her a physical, told her she was perfectly healthy and since she was less than 10# overweight, a little sensible dieting was all that was necessary and that she had no need of diet pills.

She then heard of a "wonderful" doctor who without appointment, examination or questions, would prescribe diet pills. This man, who I will call Dr. X, is a member of the Pierce County Medical Society and is listed in the phone book with the other physicians as a general practitioner. (However, I have heard other doctors refer to him as "that damn quack.")

My daughter went to Dr. X's office and he wrote her a prescription for a large supply of amphetamine diet pills. In a few days she was so "high" and nervous she could not sleep She want back to Dr. X and he promptly gave her a prescription for a large supply of valium.

I can only describe the period that followed as a living hell. She underwent a complete personality change She was either highly irritable and erratic or else stuporous. She attended a company party with her fiance, a fine young man, during which the pills she was taking, combined with cocktails caused her to create a scene so hideous and humiliating before his superiors, her fiance broke their engagement and had himself transferred to another city.

This was just the beginning. I cannot tell you the agony of mind we went through watching this girl destroy herself as she continued on the diet pills and valium. She seemed to lose all sense of self preservation and the strain of never knowing what would happen next was agonizing. I will not go into all that happened—a call at 2 A.M. telling us our daughter had driven her car over an embankment and was in a hospital many miles from home—the loss of her job, a high paying position of prestige and authority because she became so erratic and quarrelsome. There were many other incidents that I still cannot bear to think of, much less put on paper. At this point it was impossible to talk to her sensibly and get her to seek the professional help she so obviously needed.

Finally my own health broke under the strain and I was hospitalized with bleeding ulcers. This acted finally as the catalyst that made her seek help and

she got established with a fine mental health clinic. She was counselled by a very competent therapist who got her off the pills at once almost. Among other things, he was able to show her how she was ruining herself mentally and physically with the diet pills and valium neither of which were necessary. (By that time she was actually underweight.) After a few sessions with him, she became her original warm, lovely self. She became re-established in her job and life returned to normal.

When I recovered from my own illness, I called Dr. X and asked him why he had ever prescribed such large quantities of diet pills and subsequently the valium for a girl who obviously did not have a genuine obesity problem. I told him of the chaos and tragedy he had caused this girl and the family with his prescriptions. He was quite unconcerned, telling me it was not his fault—that he did not know she was going to "abuse" the pills by taking too many. I told him I realized my daughter was at fault for taking them at all but the fact remained that he was the one who needlessly started her on them, that she had to get them somewhere and he was the one who continued to supply the prescriptions. I told him I wanted him to promise me that he would never again give her a prescription of any kind and he promised he would not. This was late in August.

Everything was fine until mid-December. At this time my daughter told me she was engaged in an especially important project at work and had developed a tic from "nerves" and felt she needed a tranquillizer. She went to our doctor who told her that life holds problems for everyone but that she was young, healthy and stable enough to cope with ordinary problems without the crutch of transquillizers and refused to prescribe any.

She left his office and went back to see Dr. X. This man, after all his promises to me in August, without any exam, promptly gave her a prescription for a 5 months supply of 10 mg. valium. In a few days she had herself tranquillized into a robot like state. During this period we were experiencing the worst snow storms in 18 years Driving conditions were so hazardous our schools and stores were closed down and my husband was taking the bus to work rather than risk driving and yet, loaded with valium, my daughter was out driving every day quite oblivious and uncaring about any danger to herself or others. I felt had she gotten into an accident Dr. X would have been just as guilty as though he had been at the wheel.

Since she was taking only valium and not diet pills at this time, she was more amenable to reason and realizing she was living in a vegetable like state, agreed to return to the clinic. She was assigned the same therapist and on her first visit, noting her dilated eyes and dream-like state he recognized at once that she was overloaded with valium. He ordered her to get rid of them at once and she did. He had her tested and told her she is not psychotic, but immature. He also told her she has no need of pills of any kind and this time he intends to extend her therapy period until such time as he is convinced she will never return to them. I cannot say how thankful to God we are for this.

Understandably, this has been a difficult letter to write but I have done it not only for our sakes but others who have been put through the same wringer. I plead with you, in the name of God, please do something to stop these heartless, inethical doctors from so indiscriminately handing out prescriptions for diet pills and tranquillizers regardless of the havoc they cause.

I dislike anonymous letters but feel we have suffered enough pain and humiliation without having to expose our name or receive any publicity so I will sign myself simple as,

A Concerned Mother.

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2. Selected Letters to Senator Birch Bayh Expressing Pro and Con Sentiment Regarding Stricter Control of Amphetamine Diet Pills

Pro letters:

(a)

Hanahan, S.C., February 8, 1972.

Senator Birch Bayh,
Chairman, Juvenile Delinquency Subcommittee, Senate Office Building, Washington, D.C.:

My wife has attended a local Charleston fat-doctor (a licensed M.D.) for 10 years. She's lost 30 pounds. Some months she takes 460 pills, plus shots, which this doctor sells her at his office. Many of these pills are amphetamine. South

Carolina law permits a doctor to prescribe as much amphetamine as he thinks the patient needs. For 3 years I've asked her, and this doctor to discontinue this treatment but to no avail. My wife now suffers from insomnia, hypertension, nose bleeds, and our life together is a wreck. How does America allow these doctors to prostitute their profession just to make a fast dollar? Let's make America work for all our people not just for the privileged few—please. You may forward this to anyone you feel could use this information. If you need any more information regarding this I would be glad to oblige.

J. P. STRANEY.

(b)

February 10, 1972.

Honorable BIRCH E. BAYH, JR.,
Senate Office Bldg., Washington, D.C.

DEAR SENATOR BAYH: I must congratulate you for your efforts in investigating and trying to control Amphetamine and associated reducing pills.

A source of trouble that is being overlooked, is the prescribing Doctor himself, who is cajoled and even forced to prescribe these pills in 100's and even larger quantities. His patients think they save money.

All this is brought about by your Phase II program which forces Pharmacists to post their drug and Prescription prices prominently, so the people can shop around.

Next we will have Doctors and Lawyers forced to follow suit.

It is a very unhealthy situation.

Keep investigating—it will eventually solve the big problem.

Cordially,

MORRIS SHUMAN, *Ph. G.*

(c)

February 7, 1972.

Senator BIRCH BAYH,
Senate Office Building, Washington, D.C.

DEAR SENATOR: I congratulate you on your investigation of diet pills. In the hopes that my experience may add fuel to the fires, I would like to recount the following:

In 1964, when preliminary tests by an M.D. could find no reason for my depression and fatigue, I was sent to a psychiatrist who plied me each week with various amphetamines until he found that dexadrine gave me the "high" I was looking for. I was just starting out as a teacher and as long as I took those pills, I sailed through each day. And I could get by on almost no food. How lucky I thought I was! When I could no longer afford the psychiatrist but found that I was hooked on the dexadrine, I was desperate. I finally found a druggist who was willing to supply me with the pills if I would date him. And so I had an easy source for the next two years. My needs increased and the let down when the effects wore off became more and more miserable. Once I fell asleep at the wheel of my car as I was coming "down" and crashed (at 50 mp.h.) into a line of cars stopped for a light. After that I somehow found the strength to go "cold turkey" and stopped taking the pills. After moving to California, I found a doctor who has been trying to put my body back together after the effects of 4 years on dexadrine. The toll was high: my heart, liver, kidneys, pancreas, etc.—indeed, my whole body seemed to have been ravaged by the dexadrine. This doctor found that I had a serious case of hypoglycemia—which had undoubtedly been the cause of my fatigue and depression in the first place. And he inquired into my diet—which no other doctor had ever taken the time or interest to be concerned about. He found that the combination of amphetamines plus a poor but typically American diet (pepsi, hamburgers, etc.) were the culprits. Now, with proper diet—and NO DRUGS—I am finally beginning to feel healthy and strong for the first time in years.

I think one of the problems with amphetamines is that they're so easy to give and seem so harmless on the surface. Patients go away happy, never thinking of the consequences. A doctor gave my sister—at the age of 11!!—amphetamines for a weight problem. Thank God she took them only for a short time.

Good luck with your investigation.

Sincerely,

MIRIAM ADAHAN.

(d)

CHICAGO, ILL., *February 7, 1972.*

The Honorable BIRCH BAYH,
The United States Senate, Washington, D.C.

Sir: I was delighted to read in the newspapers this morning that at last someone is blasting the use of diet pills!

As a teenager, I was addicted to these pills. I had gone to a "diet doctor" at the suggestion of a high school physical education teacher and was given an unlimited, easily refillable, and not too closely supervised supply of this drug. I was told, of course, to report any difficulty I had with the pills, but I certainly didn't interpret the great feeling they gave me as a "difficulty." In fact, they made me feel so good I soon began taking double, triple more than the recommended dosage. During this time, I ate almost nothing, smoked constantly, slept little, and couldn't understand why my parents were so upset; I was so high I didn't even know that every word I said to them came out a scream. My parents believed, however, that surely the doctor knew best, so they did not interfere.

Finally, fortunately, I ran out of pills one day and had to do without for a few hours. It was then I realized my dependence on the drug. My craving for a "diet" pill was so strong I would have cut off my arm to get one, yet, because of this very craving, I was so terrified of what had happened to me that I never touched them again. This wasn't easy, mind you; I *wanted* those pills. But fortunately I was simply too frightened to buy any more.

Did they help me to lose weight? Yes, while I was taking them, since I existed almost totally on cigarets and sugarless soda. However, as soon as I quit I gained back the few pounds I had lost, plus about one hundred more over the next several years. I've now, at 25, lost over 80 pounds on the Weight Watchers program with no drugs, no fad foods, no "magic"—just a nutritionally balanced eating program. And believe me, as one who's tried it both ways, this is the *only* way to do it.

Bless you for speaking out on the dangers of this drug! I sincerely hope you are successful in getting them away from the public and also away from the doctors who haphazardly prescribe them. As a teenager I watched my friends get hooked on other types of drugs and I vowed it would never happen to me—and yet it did, without my even knowing what was happening till it was almost too late. I'm so thankful that the drug store was closed that day I ran out of pills or God only knows what I'd be addicted to today.

Sincerely,

BONNIE LOVEJOY.

(e)

COTTAGE GROVE, MINN., *February 15, 1972.*

Senator BIRCH BAYH

DEAR SENATOR: I read an article in the February 7th edition of *The St. Paul Dispatch* about the Senate's probe on diet pills. I would like to add my remarks to the article.

I took diet pills at various times for over a period of ten years. Three years ago, I stopped because one pill wasn't enough and so I would take two of them. My thoughts became muddled and it was difficult for me to express my thoughts in a normal conversation. I also became very depressed. I decided to stop the pills. It took a long time to clear my head; almost six months.

I feel that the so called "diet pills" in their various forms should be banned from sale. Most doctors don't even bother to give adequate check-ups during their use or before they give you the pills. There is a doctor in St. Paul that sits behind a desk and dispenses pills at a cost of $20.00 a month. (This was the cost four years ago.) This cost included your weekly visits and your supply of pills. During the month, one visit was used to take a blood sample . . . that's all.

Instead of pills to lose weight, which usually isn't very much, may I suggest that the government set-up clinics to diagnose the "obese" person. Most doctors tell the person that they are fat because they overeat. Most overweight people that I know don't eat any more than their thinner friends. I feel that complete physical and psychological tests should be taken. I feel that with the results of these findings, maybe the person can be helped.

Obesity and over-weight is one of our nation's biggest problems, physically and psychologically. We need help that doesn't cost a fortune, because obesity is not just an illness of the well-to-do but all classes of people; young and old; men and women.

I hope that the Senate's probe will result in a ban of diet pills in all forms. I also hope that some serious consideration can be given to diagnostic centers for the overweight child and adult in the United States.

Sincerely yours,

PATRICIA E. GOETZ.

(f)

WINTHROP, MASS., *February 8, 1972.*

The Honorable BIRCH BAYH,
United States Senate, Washington, D.C.

DEAR SENATOR BAYH: According to *The Boston Globe*, you have been holding hearings on the effects and abuses of diet pills. I would like to share with you my experiences with them.

I am a student presently, and, at 210, at least 50 lbs. overweight, according to the current "charts." I discussed this with my family physician, and he put me on a 1000-calorie-a-day diet. I had the same problem four years ago, and he did the same thing, and prescribed the same drug, pre-ludin Endurets. In 1968, those pills, which I was allowed to refill, controlled by appetite as long as I took them. If I missed a day, I went into a severe depression, and began "eating to beat the band". One month ago, the same pills, which the doctor ordered as non-refillable, did generally the same thing, except that they kept me awake. And when I tried to stop taking them, I found that I began eating more than I was before!

Between those two doctor visits, I will confess (though my friend, the pharmacist will be angry) that I refilled the (first) prescription for pre-ludin twice. I have found that taking them on the morning of a test (early in the morning, so that they will have worn off by bedtime), I stay more alert, and awake. Needless to say, however, that I do become quite nervous with them, also. In fact, one day, when I though that they were becoming ineffective, I took 1½ tablets, and developed earaches, headaches, and chronic nausea.

As a student, I also believe that I can attest to the widespread abuse of this particular drug in the schools. Since they are amphetamines, they are bought and sold in school like any of the other misused prescription, illegal, and over-the-counter drugs. I personally have never, though, abused any drug, because I get higher on reality. Students use this drug in large quantities, and frequently have four tablets or so with a bottle of Coke, thus combining the caffeine effect also. I worry about the kids who use it while driving, though, since they claim that they are too wide-awake (actually spaced-out) to get into an accident. It does, I have observed, make them extremely dangerous drivers, needless to say. One accident I know of was caused when the driver in question thought that the person passing him on the road was "going after" him.

In my opinion, this drug, and others like it, are extremely dangerous, and that certain things should be done to slow down their abuse: 1) A limit on the number of tablets that can be bottled by a pharmacist at one time. 2) A four-month life for any prescription. 3) More stringent regulations on pharmacists in filling these prescriptions. 4) Reports to the government by all pharmaceutical manufacturers, monthly, giving the merchants sold to, accounting for every pill made.

I hope that you will keep me informed on the results of your hearings, and would appreciate hearing from you about any related legislation. From someone who wanted to see a President Bayh and is presently Boston area assistant in Youth Coalition for Muskie, and the Boston Chairman of the successful Let Us Vote campaign, I thank you very much for your time and consideration.

With best wishes, I remain

Sincerely yours,

DAVID P. BRILL.

(g)

THE CANTRELL MEDICAL CLINIC
Little Rock, Ark., February 7, 1972.

Senator BIRCH BAYH,
Senate of the United States, Washington, D.C.

DEAR SIR: I wish to congratulate you on your investigation into the need of diet pills for use in medical practice. I make no pretense at being an authority

on all of the medications prescribed by physicians, but I can state without hesitation that during my six years of medical practice, I have found the amphetamines deadly and totally worthless.

Three months ago, I treated a young lady that had been on amphetamines for five years. She was suffering from atrial fibrillation, liver damage, an altered EEG, plus other findings detrimental to her health. Certainly the most tragic cases have been the pre-teen and teenage groups.

Several patients have sought care from another physician because of my refusal to prescribe these damn suicide pills. With this type of drug on the market, every conscientious physician finds himself in constant battle with what I call the pill pushing doctors.

If you can successfully have all of these drugs removed from the market and make their production illegal, you will have done as much for the health of America as Dr. Salk.

Very truly yours,

EDWIN N. BARRON, Jr., M.D.

(h)

MEMPHIS, TENN., *February 14, 1972.*

Senator BIRCH BAYH,
U.S. Senate

DEAR SENATOR BAYH: In the newspaper I read that you are chairman of the hearing on diet pills. I know the senate has also investigated birth control pills, etc.

I am writing to you in the hopes that an investigation can be made of tranquilizers. I understand that the Federal Drug Administration investigates this sort of thing before it goes on the market, but they also investigated diet pills.

When tranquilizers were first put on the market, it was said that they were not habit forming. Now more and more articles are appearing on the dangers of these pills. Some authorities say they are habit forming and some will also go so far as to say they are addictive.

I, of course, am no authority on these pills and do not have the facilities to do anything about my beliefs. I only know in my own case I took one pill a day for eight years. There were a few minor side effects, but I was well for eight years. Seven months ago I consulted a competent physician to help me get off these pills. I could spend hours telling you of the physical reactions I have had, and I am still not off the pills. I feel as if I have a monkey on my back, but I am still fighting to get off these tranquilizers.

I write you this letter not in my behalf, but with the idea an investigation might help others in years to come.

Very truly yours,

MRS. THOMAS DAVIS.

(Pro Response)

March 6, 1972.

MRS. PATRICIA E. GOETZ,
Grospoint Avenue, South,
Cottage Grove, Minn.

DEAR MRS. GOETZ: Thank you for your expression of concern regarding the abuse of diet pills. Our diet pill hearings are part of the Juvenile Delinquency Subcommittee's coninuing inquiry into the abuse of psychotropic drugs, particularly by our youth. We hope to create an awareness of the potential danger of amphetamines and barbiturates and to develop a fair and effective means to monitor these drugs, which are currently so readily available.

Our investigation has revealed that diet pills, like barbiturates, are highly dangerous when taken without proper medical supervision. Increasing use of these pills quickly produces tolerance. When an abuser attempts to withdraw from these drugs, acute psychological withdrawal symptoms often occur. To ease the agony of "coming down" from the diet pill high, one may turn to heroin or barbiturates. This completes the cycle of drug abuse from which one may never escape.

Unfortunately, in many homes some degree of diet pill abuse is common, and usually unrecognized. Most Americans simply do not reallze the terrible

consequences of abusing these drugs. Children grow up watching their parents indiscriminately taking pills, and they generally develop an unhealthy and often dangerous acceptance of drug use. Thus, casual attitudes towards these potentially destructive drugs coupled with a readily available supply, often the family medicine cabinet, appear ultimately connected with the abuse of diet pills.

While current national concern is focused on heroin addiction, it would be folly to overlook the present and prospective abuse of diet pills.

I appreciate your concern for this problem and your support of the Subcommittee's work.

Sincerely,

BIRCH BAYH,
Chairman.

Con Letters:

(a)

MARCH 27, 1972.

DEAR SIR: I am writing with regard to the F.D.A.'s recent announcement of possible restrictive measures against the use of appetite suppressant medications by overweight patients.

Until a year ago, I kept trying a number of gimmicks, "crash" diets—anything to lose weight; but nothing helped. Finally, I visited a very reputable physician here in San Francisco. After a thorough examination, we discussed the fact that my overweight condition was not injurious to my happiness and emotional welfare; but also, and more importantly so, to my health.

Since then, I have lost a great deal of weight with the help of these appetite suppressants. I am both happier and healthier now, and I don't feel that the medication has been at all dangerous to me. I can eat properly now, without the fear of seriously endangering my health with the crash diets I had tried in desperation.

I still see my doctor twice a month, and at that time, I receive thorough instruction on the use of my medication.

Please urge the F.D.A. not to change the label or do anything to make this medication unavailable.

I see no reason for these drugs to be restricted from the vast majority of responsible patients, in order to pay for the mistakes of a few.

Sincerely yours,

MELISSA BOSTER TIDD.

(b)

MUNCIE, IND., *March 20, 1972.*

DEAR SIR: I understand that some one is trying very strongly to have reducing aids and medicines removed from the market, or either priced so high that a poor person cannot afford it. I do not think this is right. Because I have trouble keeping a normal weight in regards to my health and I never have had any other health problems. And I attend a qualified physician which is tops in his field I think because his medicine has kept my weight down and my health perfect. But my last two visits there has been an increase in the cost, and the products stand a chance to be removed from the market, like many others I can't afford price increases I feel the medicine should not be taken from the market especially when it doesn't injure a person's health.

I would appreciate what attention or help that you could give me and many other people that is in my same situation.

Thank you very kindly for your help in this situation.

MRS. VERMADELL COOPER.

(c)

MODOC, IND., *March 21, 1972.*

DEAR SIR: Today I was informed the government is going to crack down hard on weight control doctors.

I went to one today, the first time since last September. Do you call that being hooked? They aren't habit forming and I certainly want you making a lot of noice about their continuance, please!

They are the lesser of several evils that are a direct cause of overweight. A crutch, perhaps for a lot of people but if it helps some poor unhappy fat person

to loose weight, why knock it? I'm sure you know the pills serve as an incentive to eat less, they will not make one loose weight all by themselves.

The doctors that give them out have to account to the government monthly (I'm quite sure monthly or perhaps everytime they order, they have to send a duplicate) I can't help but be concerned about the millions of tranquilizers that seem to be so freely given.

The last year and a half, I've been to my Doctor (family) and was given a handful of prescriptions to have filled. When I went to the drug store to have them filled, I had 5 prescriptions for tranquilizers and I told him I didn't want those. I'm afraid of them, that I might become dependent on them.

I wouldn't take anything that I thought would hurt me and I know I can stop taking these at anytime without any side effects.

Thank you.

SHIRLEY DEATOR.

(d)

ANDERSON, IND.

DEAR SIR: I live in Anderson, Indiana and attend the Diet Specialist, Zamber, in Ohio. On my last visit I was informed the medication I receive from him will end unless interested people try to speak to their representative on the subject.

I am only 20 but I do not take his medicine as dope or pep pills. I was very heavy and have lost a considerable amount of weight since I first had a visit with him three months ago.

I am asking as a young voter and a 20 lb. less adult, who is not a dope addict, to keep his medication on the market. It has help me lose considerably and I know many of my relatives, also.

I wish you would try to keep this medicine on the market. It would be appreciated greatly by me and many others.

Thank you.

BRENDA WILLIAMS.

(e)

CHICAGO, ILL., *February 8, 1972.*

Hon. BIRCH BAYH,
Washington, D.C.

DEAR SENATOR BAYH: It is fervently hoped that my thoughts on the subject of diet pills—dope, etc., will reach you not to be flung aside to be forgotten but to be added to others' opinions and measured and weighed as each persons concerned words combine into something meaningful on this subject. I am home maker—age 34. Weight decreasing.

Periodically over the span of ten years I have taken a small amount of biphetamines (excuse the spelling) UNDER THE SUPERVISION OF MY TRUSTED FAMILY DOCTOR Mar. 3, 1972. I'm afraid I'm a person who needs a "crutch" when I diet. I have no other vices like a couple of martinis before dinner or smoking a pack or two a day.

There are many elements on this earth that aren't very good for us but it is up to an individual to think for himself. I would hate to fill my diet requirements (dosage under 15 miligrams or whatever) at the friendly corner junk peddler who will definitely continue to flourish (our's is 106th and Ewing Avenue) for a lot of money and risk. My dose wouldn't be a big sale for him.

People have taken away cyclamate drinks, which I enjoyed and helped me keep my weight down but sacharrine leaves a bitter taste for me.

Today's paper says four drinks harm your heart but I doubt that the liquor is going to be limited or taken away like the cigarettes. Next on the list of harmful exercises will probably sex. And I certainly would like to see anyone take that away from the public.

How about a stronger surveillance on the drug producing companies and crackdown on the "Ewing Ave." junk dealers and not on me and my trusted physician who is honest in his reports.

After all I figure I'm ahead, a little bit of drinking, no smoking, no birth control pills, no sacharrin, a moderate amount of sex, three sons to activate my adrenlin and let me scream so I don't look an idiot and one week's vacation away from home to let me live awhile but who knows how much time we have here.

I know it is hard to visualize the innermost feelings of a person experiencing something you can not physically attained like give birth to a child or may not

desire to experience like being fat or like taking the hard drugs, therefore you truely cannot say you know what the person's thoughts and feelings are. Some have different degrees of pain and joy.

I was a fat child not a large one but you couldn't see too many bones sticking out.

Later I slimmed and starved. Right now I guess I eat because I'm hungry, love sweet things and have problems.

It's frustrating to see how short a lifetime is. We have three healthy sons but several years before #3 arrived I ferventy desired a lovely daughter to complete our family. Adoption is not an answer for us too many objections. Now we can't support another child even if it were to be a girl so I sort of mop about my lost cause. Being around four healthy males of various ages who are "always" eating doesn't help my will power. Also, I worry about the future needs of my family as well as my husband's widowed mother and spinister Aunt undergoing treatment for tumors in her throat, and my parents and my sister and her family and my husband's brother and my hubby drinking. Also I worry about the tragedy of others like in Virginia because "somebody" didn't give a "dam" but just wanted to see a few more bucks in his pocket. I worry about living in the pollution laden air of the steel makers shadow (the Republic steel plant expanded toward our community) turtling their way to install devices to contain or eliminate the errors and evils.

And lastly I worry about the paltry sum of $200 in the bank and if it will some day grow back. If when 25 or 30 years have passed if my hubby and I will be able to live happily and decently without fear.

There seems to be too many top dogs in power who are running around chasing their tails encircled by a similar circle of small subordinate dogs doing like wise. What would happen if a whip cracked. Amen.

P.S.—I don't believe in any scientific monkey test reports because the animal is similar but not same. And many tests are not controlled accurately to substantiate them "I called them Irvings" after Hughes.

P.P.S. It would be quite a sight after the Black Power and the Youth and Hippie Power but look out for the Pudgy Power. They will really overflow the streets of Washington, D.C. should they organize and march. An irrate woman is bad but a fat irrate woman is full of power and pent up emotion and pounds.

I know of a number of people, some my relatives who sometimes take diet pills.

Sometimes rules are really crazy like a certain menutral cramp prescription because of 1 milligram of biphemamine my doctor has to write it on a narcotic form. You certainly are not going to stop the young people from take two of a one kind, three of another kind to get high but you are making it impossible for a law abiding citizen as well as her doctor to comply.

When the new law went into effect my doctor forgot to put his narco number and I couldn't, although they have filled my prescription before, receive my pills until three days later. I don't take my pills each day but I'd like to know they are not going to be snatched from my grasp because of some nonsense.

I can't go to Elizabeth Arden Main Chance Fat Farm or the like like some well moneyed person so I use the pills.

Lift the restrictions on the doctors, clamp down on the drug companies selling the surplus to the putting cup of a Mexico golf course.

Bring back cyclamate to help the fat people after, all there is a thin person inside waiting to be set free.

Please answer as to how many other letters you received to express the same opinion as mine and what the results of your committee.

I haven't time to rewrite but I wanted you to hear from me.

Thank you.

Mrs. Pauline Miller.

Con Response

March 29, 1972.

Mrs. Vermadell Cooper,
R.R. 3 Williamson Road,
Muncie, Ind.

Dear Mrs. Cooper: Thank you for your thoughtful letter regarding the Subcommittee to Investigate Juvenile Delinquency's investigation of diet pill (amphetamine) abuse.

I have been very concerned about the abuse and misuse of amphetamines. The recent action by the government regarding amphetamines doesn't ban

their production but limits production to that amount required to fulfill legitimate medical and research needs. Much of the domestically produced amphetamine has reached the illicit market. Estimates range from 20–50 percent. Thus, a substantial percentage of these dangerous drugs were being used for other than legitimate medical and research purposes. It is hoped that the quotas will eliminate most of the production surplus.

Additionally, stricter prescription controls placed on amphetamines reinforce the basic doctor-patient relationship. All recognized authorities agree that amphetamines should be administered only with the close supervision of a physician.

Enclosed is a copy of our amphetamine hearings. I hope that you find it informative.

I share your sincere concern for this problem and hope you will continue to send me your views on issues of public importance.

Sincerely,

BIRCH BAYH.

(D) SUPPLEMENTAL MAGAZINE AND NEWSPAPER ARTICLES AND PAMPHLETS RELATING TO THE USE AND ABUSE OF AMPHETAMINE DIET PILLS

[Ladies Home Journal, November 1971]

1. WOMEN AND DRUGS, A STARTLING JOURNAL SURVEY

(By Carl D. Chambers, Ph.D., and Dodi Schultz)

THE DRUGS WOMEN USE

This chart lists the 12 drugs most commonly used by women, along with the percentages of usage by women and by the overall population. The figures for marijuana, LSD and other hallucinogens can be considered applicable only to the East Coast, West Coast and major metropolitan areas such as Chicago, Detroit, etc. While the use of drugs available through legal channels now follows a nationwide pattern, that of illicit drugs does not. Also, the reported use of hallucinogens must be considered a minimal indication of actual use, because a certain lack of truthfulness in response must be assumed.

[In percent]

	Have used		Now use (at least once a month)	
	Women	Overall population	Women	Overall population
Relaxants	25	20	14	10
Noncontrolled narcotics	37	34	12	10
Barbiturates	22	20	7	7
Marijuana/hashish	8	10	6	8
Diet pills	17	12	6	4
Nonbarbiturate sedatives	9	9	4	4
Pep pills	6	6	3	3
Antidepressants	4	2	2	1
LSD	2	3	1	2
Controlled narcotics	8	7	1	1
Major tranquilizers	3	4	1	1
Other hallucinogens (mescaline, etc.)	2	2	(1)	1

[1] Less than 1 percent.

A message from the editor

As part of the Journal's continuing involvement in programs to combat our national problem of drug abuse, we offer readers here what we believe is the first definitive study of drug use by women—including the mind-affecting drugs, both legal and illegal, which have become part of the daily life of a frightening number of American women. The study, designed and administered by Dr. Carl D. Chambers, as Director of Research for the New York State Narcotic Addiction Control Commission, covers in-depth interviews with some 4,000 New York State women, but the results with minor exceptions, are believed by experienced researchers to be statistically valid for the nation

as a whole. This report, prepared exclusively for the Journal, will appear in four parts. Future installments will cover drug use among homemakers, working women and young women in high school and college. The result, we hope, will be to help women everywhere realize that the drug problem is not "down the street," but often as near as their medicine cabinets, or in that personal emotional area where it is easy to say, "I'll just take something to tide me over." We welcome comments on the series, and hope it will be a springboard for home and club discussions.

A CHEMICAL LEXICON OF DRUGS WOMEN TAKE

These are the psychotropic—mood-altering or mind-affecting—drugs with which respectable, middle-class Americans are increasingly "turning on." Usually, they are obtained by prescription; often, they are not. You will undoubtedly recognize many of their names. We use the word "abuse" to mean use in excess of prescribed dosage, frequency, and/or duration of time.

Type of Drug	What They Do—And Can Do	Some Common Brand Names
Relaxants ("minor" tranquilizers)	*Reduce anxiety. Even in small doses, react with and boost effects of alcohol. Abuse can cause addiction.*	*Atarax, Equanil, Librium, Meprotabs, Miltown, Valium, Vistaril—also combined with analgesics and other substances in such medications as Deprol, Equagesic, Milpath.*
"Major" tranquilizers	*Modify psychotic symptoms; reduce fear and hostility. Dangerous in combination with alcohol or sedatives. Potentially addictive, but rarely abused due to unpleasant side effects.*	*Compazine, Frenquel, Mellaril, Serpasil, Sparine, Stelazine, Thorazine—also in combination drugs (see antidepressants below).*
Antidepressants ("mood elevators")	*Alleviate serious depression. Interact dangerously with alcohol, amphetamines, sedatives, a number of other substances. Side effects, including blurred vision and dizziness.*	*Aventyl, Elavil, Marplan, Sinequan, Tofranil—also combined with major tranquilizers in drugs such as Estratan, Triavil.*
Amphetamines ("pep pills")	*Stimulate central nervous system, create feelings of confidence, prevent fatigue. High doses can cause toxic psychosis. Abuse can produce psychic dependence, possible addiction.*	*Benzedrine, Dexedrine (also see diet pills below).*
Diet pills	*Reduce appetite, create sense of well-being. Abuse poses all the risks of the individual ingredients.*	*Three major types: 1) amphetamines with barbiturates—Desbutal, Devamyl, Nobese; 2) amphetamines with tranquilizers—Appetrol, Eskatrol; 3) other chemicals with amphetamine-like effects—Preludin, PreSate, Tenuate, Wilpo.*
Barbiturates	*Central nervous system depressants that sedate (calm) or, in larger doses, induce sleep. Can cause psychic dependence. Abuse causes addiction.*	*Amytal, Butisol, Luminal, Mebaral, Nembutal, Sandoptal, Seconal, Sombulex, Tuinal, Veronal—also in combination with antispasm drugs in such medications as Bentyl, Donnatal.*
Other powerful sedatives	*Similar to barbiturates in purpose and in trouble-making potential.*	*Chloral hydrate (Noctec, Somnos), Doriden, Noludar, Placidyl, Valmid.*
Controlled narcotics (opiates)	*Powerful analgesics that relieve pain, produce euphoria. Abuse causes addiction—which can sometimes occur with prescribed dosages as well.*	*Natural substances (opium, morphine, codeine, paregoric) plus semisynthetics and synthetics: Demerol, Dilaudid, Dolophine (methadone), Leritine, Levo-Dromoran, Numorphon, Percodan.*
Noncontrolled narcotics (not legally classed as narcotic drugs)	*Similar to controlled narcotics, except that normal (prescribed) dosages are not potentially addictive.*	*Butazolidin, Darvon, Indocin, Robaxin, Tandearil, Talwin.*

Visualize a blank TV screen. Title: Women and Drugs. Quick: what forms in your mind's eye?

Perhaps a riot of color with a dizzing explosion of sparks. Close-up: rock singer Janis Joplin. Voice: husky, whiskey-coated, wailing of love lost and never known, a voice that tears at the soul. Dissolve. Another close-up: Janis Joplin, her husky voice stilled forever—dead at 27. Heroin, said the autopsy report. Overdose.

Or do you see a meadow with thousands trembling to the beat of the electric guitars throbbing atop a wooden platform in the midst of the human sea. Close-up: a breaded youth next to a roughly lettered sign: Grass, 75¢/ LSD, $1/Mescaline, $1.50. A tent, another sign: Emergency Medical Aid. Inside, a white-jacketed doctor bends over a cot. Close up: a girl, no more than 15—her face twisted in terror, long, blonde hair matted with mud and sweat, ringed fingers clawing at the air. A voice filters tinnily through the loudspeakers: "Your attention, please . . . just had reports . . . the acid being sold in blue paper envelopes . . . at your own risk . . very bad trips . . . repeat . . . very bad trips."

Or maybe it's New York City, Times Square. Dusk, liquid neon, beckoning displays and marquees: Nude Models Inside/Peep Show/Adult Books/Now Showing, N.Y. Premiere: "Frenzy in the Flesh," Over 21 Only. Close-up: a woman. She is young, but her eyes are hard. She lounges against a shop window—hair teased high, long legs receding into satin hot pants. Her gaze flickers over the drifting crowd. Wordlessly, she returns a glance, turns, saunters slowly down the block and through a doorway: Hotel/Transients Welcome/Open 24 Hours. A male figure follows. Close-up: bills passing from stubby male fingers to slim, silver-nailed ones. Cut to second closeup: bills sliding into the pocket of plaid shirt; the silver-nailed fingers close tightly around a small glassine packet.

Mood-altering, mind-zapping, sometimes killing drugs. Chemicals swallowed, sniffed and injected in a frantic effort to cope with a world that frightens, bewilders, depersonalizes. The phenomenon reaches far beyond the headlines, beyond the rock world, beyond the Woodstock Nation, beyond the prostitution marts of Manhattan.

We can now conclude that one-third of our adult population use such drugs on a regular basis . . . that more than half of American *women* have done so at some time in their lives—and that 45 percent of American women are using such drugs right now.

The typical woman who uses drugs to cope with life is not a fast-living rock star, nor a Times Square prostitute, nor a devotee of the drop-out-and-turn-on philosophy of Dr. Timothy Leary. She is an adolescent, confused by the stresses of impending adulthood. She is a newlywed, by turns anxious and depressed by the strains of adjustment to a new relationship and new responsibilities. She is a once-busy housewife, her youngsters grown, who finds her days increasingly empty and her thoughts obsessed with the inexorable passing of the years. She is, in short, an average, middle-class American—one of the folks next door. She could even be you.

American women may take some small comfort from the fact that they are under-represented among the users of *outlawed* drugs. Women as a whole smoke substantially less marijuana, use substantially less heroin, cocaine, LSD, and other nonmedical substances than men do. But women are distinctly *over*-represented in the ranks of those who turn to tranquilizers, antidepressants, strong sedatives, dangerous diet pills and powerful analgesics.

Women comprise approximately 53 percent of the U.S. population. But here are their proportions among the habitual, frequent (six or more times a month) users of these crutches: barbiturates, 54 percent are women; major tranquilizers, 58 percent; pep pills, 60 percent; noncontrolled narcotics (drugs not legally classified as narcotics because normal dosages are not potentially addictive, 63 percent; nonbarbiturate sedatives, 66 percent; minor tranquilizers, 70 percent; antidepressants, 72 percent; controlled narcotics, 76 percent; diet pills, 80 percent.

Before we explore the use of each of these drugs, a brief comment on who's responsible for drug use and abuse. It's true that the dispensing of these powerful medications is a multi-million-dollar business. For example, the quantity of sedatives manufactured annually in this country exceeds 500 tons—enough, if taken all at once, to kill twice the entire U.S. population.

A recent poll of 280,000 doctors tells us that they annually write prescriptions for $20,000,000 worth of nonbarbiturate sedatives; $31,000,000 worth of barbiturates; $56,000,000 worth of antidepressants; $84,000,000 worth of diet pills; and a mind-boggling $126,000,000 worth of minor tranquilizers (which represent 15 percent of *all* prescriptions).

Obviously, either we are suffering from a nation epidemic of mental illness, severe insomia and unbearable pain—or people are taking an awful lot of pills they don't need. If the latter conclusion is the sensible one: *why* is this so?

Cease advertising?

Some observers have leaped to an easy—we think too easy—conclusion. The drugs in question, they point out, are advertised only in medical journals, which, for the most part, are read only by physicians. Hence, the solution is to insist that drug manufacturers cease promoting their products. Then doctors will not be bamboozled into prescribing those risky chemicals.

Aside from the fact that the medical journals provide a valuable service in relaying news of medical advances and scientific information to physicians, and that these publications generally subsist on income earned from selling advertising space, there are several flaws in that thinking. The ban-the-ads argument assumes incredible medical ignorance on the part of physicians, plus patients who are docile automatons (one recent women's magazine article described America's doctors as "duped" by the ads into prescribing these drugs for nonexistent ills—drugs then mindlessly gulped down by "dutiful" patients).

We doubt that the American physician, the world's most highly trained and best informed, is often "duped" into believing that a capsule or pill is a valid substitute for facing up to teen-age troubles, or dealing with the roots of marital discord. We suspect that he sometimes may prescribe such substances because there is an acute doctor shortage; having determined that nothing is physically amiss, he may offer symptomatic relief knowing other, more seriously ill patients await his attention.

And we suspect, too, that many a patient—far from docile—*demands* the "magical" stuff that will blur worries, curb appetite and invite sleep; many doctors have, in fact, confirmed that suspicion. The patient is far from blameless or "dutiful": often, as we'll see, if her doctor won't provide what she asks, she goes elsewhere for it. And she doesn't feel she is committing any particular sin. Heroin may be socially unacceptable, but brand-named "medicines" with similar effects are "respectable"; one of America's most distinguished playwrights recently announced, in print, that he consumes two tranquilizers and half a barbiturate pill each day.

What drugs are favored by the American female? Tranquilizers head the list. The chart on the first page of this article lists the top dozen drugs as they emerged from the Journal survey, along with comparison data for the population as a whole.

Now a picture emerges. Nine of these 12 drugs are perfectly legal. Are they being used for legitimate medical purposes—or at least as a doctor has prescribed them? Or does their use reflect a dependency not medically supervised? Two additional questions were put to women who reported that they took a drug on a regular and fairly frequent basis—at least six times a month.

First: had they always obtained it by a doctor's prescription?

Second: did they always use it as the doctor had instructed—the precise dosage, the prescribed frequency?

Almost all women who take antidepressants or major tranquilizers do obtain them by a doctor's prescription—although one in 25 who regularly take major tranquilizers admitted that she did not always follow doctor's instructions. These drugs are among those least likely to create dependence.

The ubiquitous "minor" tranquilizers are obtained mostly via prescription; one regular user in 10, however, reported that at least some of these drugs had come to her from other sources. The figure was higher (15 percent) among coeds; we know that many a teen gets her first taste of a mood-altering drug from the medicine chest, sampling medications prescribed for an older member of the family. One in five women who regularly take a relaxant admitted using the drug in an other-than-prescribed manner, and the figure was highest (30 percent) among working women.

Three out of every 20 women who use sleeping pills—whether barbiturates or others—regularly confessed to getting some or all of them through channels other than a doctor's prescription. And whether by prescription or not, one in four barbiturate-takers, and one in ten users of other sedatives, admitted that these drugs, with their high risk of addiction, were not being taken as ordered by a doctor. Again, working women led in nonmedical use and abuse, especially of the barbiturates; 40 percent—two out of five—reported that they use these drugs in ways not medically specified.

Diet pills, too, are getting into women's hands and stomachs by nonprescription means. Three of every 20 women who take them admitted they had not obtained them all via personal prescription. And whatever the source, one in five regular users of diet pills admitted using them in doses and frequencies not prescribed by a doctor. Housewives lead in self-medication with these risky substances: one in four regular users does not have a prescription for *any* of the diet pills she takes, and 30 percent choose their own dosages.

Not by prescription

It is clear that these drugs are being extensively abused. It is even clearer when we come to the "legal narcotics." One in five regular users of drugs in the uncontrolled category, and one in four regular users of controlled narcotics, readily admitted that at least a portion of her supply was not obtained by prescription (curiously, more than 85 percent of the latter group claimed to be *using* the drugs just as a doctor had ordered!). Working women lead in extra-legal acquisition of these drugs: 30 percent obtain some or all of their supply through nonprescription channels.

A full 38 percent of the regular pep-pill-popers (nearly two out of five) do not obtain the drugs by prescription—although, again curiously, one-third admit to taking it in a nonmedically-devised regimen. Coeds take the highest risks here: almost 50 percent acquire pep pills without prescription, and only one in three claims to follow a doctor's dosage instructions.

This, then, is the broad picture. In the next installment of this series, we will examine drug use by the American housewife—what she takes, how often, and why. And we will also explore there the extent to which she piles risk upon risk by mixing these mood-altering chemicals with one another.

Test Yourself: Five Facts You Should Know About Drugs

Five questions of fact were put to women surveyed. Decide whether each statement is true or false. Then check the answers on next page—and compare your score with that of other women, and with that of the general population aged 14 and up.

WOMEN AND DRUGS

	True	False	Don't Know
1. LSD can cause chromosome change and birth defects	------	------	------
2. Sniffing glue can damage the brain	------	------	------
3. Amphetamines—popularly known as "pep pills," and also a major ingredient of many diet pills—can produce psychological dependence	------	------	------
4. Barbiturates—a major ingredient in a number of prescription sleeping pills—can lead to physical as well as psychological dependence	------	------	------
5. Marijuana is addictive	------	------	------

Facts About Drugs: Answers to the True-False Test

1. "LSD can cause chromosome change and birth defects." The best answer is really *Don't Know*. Chromosome changes have indeed been seen in users of this illegal hallucinogenic drug, which is a thousand times as powerful as marijuana. However, these changes haven't been specifically observed in germ (egg or sperm) cells, and there is at this writing no proof that offspring can be damaged by LSD use; though birth defects have been recorded in the children of LSD users, a cause-and-effect relationship hasn't been established. Nevertheless, the potential risk remains.

About a quarter of our respondents—23 percent of the women surveyed, 27 percent of the population at large—said they did not know the answer to

this question. But women are perhaps more conscious, understandably, of the possibility of genetic damage; 73 percent of them (versus 69 percent of the population as a whole) were convinced that birth defects are a threat. Interestingly, coeds were more "sure" in this unsure area than other segments of the female population; 80 percent of the coeds answered with a flat "true."

2. "Sniffing glue can damage the brain." *True*, in no uncertain terms. There is a rapid onset of physical damage in the frequent glue-sniffer—not only to the brain, but to other vital organs; a microscopic study of the liver of someone who has sniffed glue regularly for only a few weeks will reveal damage equal to that resulting from any years of alcoholism. Sniffing glue and other toxic vapors can also kill; there are, at last report, at least four such deaths in the U.S. each month.

Seven out of 10 women in our survey were aware of this fact, while another 25 percent weren't sure; only 5 percent gave the wrong answer. No special difference between men's and women's answers, or among women's answers.

3. "Amphetamines—popularly known as 'pep pills,' and also a major ingredient of many diet pills—can produce psychological dependence." *True.* Yes, they can—and recent studies have determined that amphetamines can often produce physiological dependence as well. Physiological dependence is, for all practical purposes, the same as "addiction"; it is defined by two criteria—increased tolerance (larger doses are needed to achieve the desired effect) and distinct physical reactions when the drug is withdrawn.

It should be added that in a medically controlled situation, your doctor may prescribe these drugs with safety, and you should not be alarmed if he has done so; contrary to popular opinion, addiction does not develop overnight. On occasion, these drugs are prescribed for very brief periods (a maximum of two weeks) in weight reduction, though an increasing number of physicians believe this use of amphetamines to be unwise. According to leading neurologists, the drugs are quite properly used in three other situations: to treat a rare neurological disorder called narcolepsy; to counter the sedative effect of anticonvulsive medications in some patients subject to seizures; and—in preadolescent youngsters only—to treat a brain condition called hyperkinesis.

Slightly more women than men knew the correct answer to this question: 63 percent of the female respondents answered "true," against only 60 percent of the survey group as a whole. One in 10, though, believed there is no risk of dependence with amphetamines. Highest right-answer score: working women, with 66 percent.

4. "Barbiturates—a major ingredient of a number of prescription sleeping pills—can lead to physical as well as psychological dependence." *True.* Barbiturates can be addictive in every sense of the word. As with amphetamines, barbiturates don't pose a danger *if* they're cautiously prescribed by a physician —as they properly are when a strong sedative or anticonvulsant is needed— *and* when the doctor's instructions are followed precisely. It's important, too, that even a prescribed dosage not be mixed with other drugs, including alcohol; a safe dose of a barbiturate, combined with an innocuous amount of liquor, can be—and has been—lethal.

Seven out of 10 people polled knew the statement was true. Females as a group scored a little higher, 72 percent; housewives, with 75 percent giving the right answer, scored highest of all. But 8 to 10 percent of all marked false.

Is marijuana addictive?

5. "Marijuana is addictive." *False.* Marijuana *isn't* addictive, in either sense of the word: there is no increased tolerance (in fact, smaller and smaller quantities may achieve the desired effect); there are no pains or other physical withdrawal symptoms upon stopping use of the drug. It has been suggested, however, that psychological dependence may develop in the regular marijuana user, as it can in the tobacco smoker or social drinker; at this writing it is unclear whether observed psychological patterns stem from marijuana use, or were present to start with.

Only about one-third of the population has the facts about this most widely used of all illicit drugs; 42 percent said "true." Women as a whole scored lower on this question: only 30 percent said "false," while 45 percent answered "true." Not unexpectedly, 59 percent of the coeds polled—three out of five—knew the correct answer (although one in four still gave the wrong one). Working women made a poorer showing (35 percent were correct); housewives, the poorest of all (24 percent).

[From The Ladies Home Journal, December 1971]

2. Housewives and the Drug Habit, What They Take—And Why

(By Carl D. Chambers, Ph.D., and Dodi Schultz)

The drug problem is often as near as your medicine chest, or as that personal area where it's so easy to say, "I'll just take a pill to tide me over." Second part of an exclusive report on a definitive, 4,000-woman survey of drug use and abuse by the American woman.

"I know what I'm doing is wrong, in a way—but I don't see how it can really hurt me."

Betty Ann lives in a pleasant, middle-class suburb of a city in the Southwest. Her husband Don is hard-working and ambitious. His family could not afford to send him to college, but they brought him up to earn his own way. He soon found that he was skilled with his hands. As he told Betty Ann when they married in 1962, a year after their graduation from high school, "Maybe being an auto mechanic isn't a big deal—but I'm going to be the *best* auto mechanic around."

Five years passed. Don worked long hours and saved his money; he planned to go into business for himself. He and Betty Ann began to think about buying a house. They found the place they wanted, and Don made some careful calculations. They could swing it if Betty Ann took a job—just for a year. That would let them meet the mortgage payments without digging too deeply into their hard-earned savings.

Betty Ann answered an ad seeking women to sell cosmetics door-to-door. There was just one problem. Betty Ann had put on a little weight over those five years—not much, but enough. Looks are important when you're selling beauty aids. Even the most perfect-looking people sometimes find it difficult to approach total strangers; Betty Ann found it especially hard, even frightening. She needed all the confidence she could get.

Betty Ann recalled glowing tales of a wonder-working specialist in fast weight loss with offices on the outskirts of town. She called him. He assured her that his system involved no difficult diets, no strenuous exercises, no complicated calorie-counting; it would be completely effortless. His special medications did all the work. As a matter of fact, she needn't even bother getting prescriptions filled; she would get the pills directly from him. Betty Ann made an appointment for the next day.

It seemed like a miracle. Not only did the pounds disappear in a matter of weeks, but Betty Ann began to feel brighter, more energetic, newly sure of herself. She told the "doctor" so on one of her regular visits. He was delighted; in fact, he would change her medication to one containing only the "miracle ingredient" that produced the pep and confidence; those feelings would continue to grow, he promised, and her weight would stay down as well.

He was right. Betty Ann kept her new, svelte figure—and Don complimented her on her glamorous appearance. Her work went well; the self-assurance and poise definitely helped. After a couple of months, though, she found herself strangely unable to calm down and relax at the end of the day. She visited her old family doctor and told him about her job, with its stress and long hours, and her difficulty in getting to sleep. She neglected to mention the weight she had gained and lost since she had last seen him; nor did she tell him of her visits to the wonder-working specialist. He wrote her a prescription.

Just as Don had figured, Betty Ann was able to stop working within a year. They bought their new home and things were going well. Don was proud of Betty Ann—her new vitality, her new poise, most of all her new figure. Since she didn't want to lose them, she continued to visit the specialist, and her unwitting family physician was happy to provide more of *his* medications any time she felt too tense. That was three years ago. The pills are putting an increasing dent in Betty Ann's household budget, but as she says, "Don doesn't say much about the cost; we never really discuss it. He likes me thin. And *I* like me better this way, too. I feel pretty, and I'm not afraid of people the way I used to be."

Betty Ann's current daily dose of Dexedrine (see the drug list on page 713) is twenty 15-milligram capsules (*one* of which cuts the appetite for 12 hours) plus ten 5-milligram tablets—a total of about 350 milligrams, the equivalent in central nervous system stimulation of 70 cups of black coffee a day.

Each night she needs two 50-milligram capsules of Nembutal to keep her from lying awake, keyed-up and jittery, unable to close her eyes. On the drug scene, daily ingestion of 75 or 100 milligrams of amphetamine is classified as advance drug abuse. Betty Ann, age 28, is a speed freak.

Betty Ann's case is not an isolated one. Housewives—approximately one-quarter of the U.S. adult population—constitute 36 percent of the habitual users of diet pills. One in four heavy users of such pills admits to obtaining her entire supply without proper prescription. Many graduate, as Betty Ann did, to pep pills—and not all pep-pill devotees are by any means keeping house in grubby East Village lofts.

Just over half the homemakers in our country—52 percent—are middle class or even better off; 82 percent are at least high school graduates. Among housewives who take diet pills, 99 percent are high school graduates and 14 percent went to college. Of those who use pep pills two-thirds are at least middle class, and *all* are high school graduates; three out of five are college graduates.

Betty Ann's story also points up another facet of the pill-popping picture in our society: multiple drug use. All drugs—especially the mood-altering ones—interact with one another to some extent. Some of the interactions are unpredictable. A drug can counteract or negate another—or, conversely, combine with it to produce stronger effects. A physician takes these factors into account when he uses a prescription—unless he doesn't know what drugs the patient is already taking.

Betty Ann is currently taking only two drugs, and her combination is typical: more than three-quarters of housewives who habitually take amphetamines also take barbiturates. Others play this chemical Russian roulette with different weapons: 16 percent take other powerful sedatives; 16 percent take tranquilizers; 22 percent take antidepressants; 38 percent take drugs in the noncontrolled narcotic category (drugs not legally classed as narcotics). The percentages total well over 100 because many housewives actually combine amphetamines with two or more other mind-affecting chemicals.

"I don't really abuse drugs; I use them."

At 47, Margaret is a handsome, well-groomed, serene-appearing woman. Her husband Ray is a highly successful physician whose annual income exceeds $40,000. Their gracious home in a large West Coast city is surrounded by beautifully landscaped lawns. Margaret is educated and knowledgeable.

"It began several years ago," she explains. "Our daughter had married and moved East with her husband. My husband's practice is quite active; he's never home very much. At that point, I found myself alone for the first time. I wasn't involved in anything, not even housework; we've always had someone come in to take care of that. Well, I began to drink. After a while, it got out of hand."

It got sufficiently out of hand that talk began to filter back to Ray; the huge deliveries from the liquor dealer, the stacks of empty bottles that were carted away, were starting to cause comment in the community. Ray insisted that Margaret see a psychotherapist. She agreed.

"I knew the drinking had to stop," says Margaret. "That was the main problem. But without the liquor I was nervous and anxious; I just couldn't relax. My therapist prescribed some tranquilizers—Miltown, Valium, that kind of thing—to help me over the worst times; they worked very nicely. Later, when I was having a bit of trouble sleeping, he let me have a sedative. Not a barbiturate—I told him I didn't want any of those; they can be addicting."

"I'VE TRIED THEM ALL"

Like most physicians, Ray receives frequent visits from drug salesmen, who customarily leave generous samples of their products with him. Ray brings many of those samples home. Margaret still sees her therapist occasionally, when she feels the need. She doesn't feel the need often; the samples she helps herself to from Ray's supplies keep her calm.

"We always have them around," she shrugs, "and I guess I've tried all the brands from time to time. But I'm careful. I read the directions, and I never go over the proper amount. I know that you can get to a point where a particular medication isn't effective unless you increase the dose; that's when I switch to something else. And I know it's dangerous to drink when you're

taking these drugs—so I don't. I guess I'm lucky, being a doctor's wife. Some people might get into trouble with these medications—but I know a little more than they do."

The old adage about the dangers posed by a little knowledge still holds. Margaret believes she is treating herself, creating her own medical regimen, and she believes she is doing so safely. But she knows only what she has gleaned from Ray and from reading labels. On that basis she is playing doctor. It is a dangerous game. She has stopped short of addicting doses—so far. She has avoided developing tolerance to, or serious dependence on, any one of the relaxants or sedatives she has taken—so far.

There are several facts that Margaret is not aware of. Addicting doses and tolerances vary widely from one individual to another. Cross-tolerances and cumulative tolerances are not unknown. Like Betty Ann, Margaret is mixing drugs—and the effect is unknown and unpredictable. Because her self-medication is totally unsupervised, there are no checks, no way of knowing the effects—possibly toxic—on her central nervous system, her heart, her blood pressure. The labels she reads are hardly objective studies; they are self-serving claims by the manufacturers, plus whatever warnings are required by law. And while Margaret proudly claims that she is not dependent upon any one of these substances, she *is* clearly dependent on *drugs*.

While only 10 percent of the U.S. adult population can be counted as current users of tranquilizers, the figure for American housewives is 13 percent. And more than one in ten of these housewives, by their own admission, are deviating from dosages prescribed by a physician. Many are mixing relaxants with other mood-affecting drugs: 17 percent mix them with barbiturates; 11 percent with other powerful sedatives; 16 percent with narcotic pain-killers; 9 percent with antidepressants; 6 percent with diet pills. Again, a goodly number of these are taking not just two, but three or more different drugs.

Margaret's age group is notably overrepresented among housewives who habitually take relaxants. Women from 35 through 49 constitute 29 percent of American homemakers. However, this group accounts for 38 percent of those who regularly use minor tranquilizers, and for even higher proportions of regular users of four other mood-altering drugs: diet pills, 44 percent; antidepressants, 45 percent; pep pills, 57 percent; major tranquilizers, 61 percent.

"I could quit taking the pills any time I want."

Sheila is 32, bright, articulate and very attractive; her lithe figure gives no hint that she has borne two children. She and her husband Ted met in college. Both were good students, popular, active and involved in extracurricular activities. Neither had any trouble finding jobs—Sheila as an art teacher, Ted in the management training program of a large insurance company. They soon were able to buy their own home in an outlying residential area of the Eastern city where both worked. Sheila continued to teach until the birth of their first child. The second child arrived 18 months later.

Ted, meanwhile, had been moving up steadily. By the time the second baby came along, he was a rising junior executive. Increasingly, his new responsibilities involved travel. At first, he was away perhaps one day a week, or two at most. Then the two became three, and often four; sometimes a trip to the Midwest or to the Pacific Coast would keep him away from Sunday afternoon until the following Friday night.

"It was a little rough," Sheila recalls. "You know what a struggle it can be keeping up with two preschoolers—feeding them, chasing after them, keeping them out of trouble. Don't get me wrong: I didn't feel I was being put upon. I love the kids. It was just that by the time I got to bed at night, I was worn to a frazzle, all keyed up and overtired. Too tired to sleep. Ted was away a good deal of the time, and I'd just lie there all alone, tossing and turning all night. I wasn't getting any rest, I was edgy and short-tempered with the kids; it was bad all around."

Sheila mentioned her problem to a neighbor one day as they sat chatting at the playground while the children romped nearby. Her friend had had a similar problem; she offered Sheila a few of the sleeping pills her doctor had prescribed. Sheila accepted, a little hesitantly. They worked like a charm. She was able to sleep. Sheila went to see her family doctor; he prescribed a barbiturate, with strict instructions to take it only at bedtime, and only a single dose.

INCESSANT CRISES

At first, Sheila took Tuinal, then some of the other sedatives—some barbiturates, some not. Just for sleeping at the start, as the doctor had advised. But Sheila found they calmed her during the day, too; they seemed to help her cope with the children's incessant crises without losing her cool or her patience. Later, there were minor tranquilizers—sometimes one, sometimes another, depending on what the doctor prescribed.

The youngsters are seven and nine now, both in school. But Ted still travels, and Sheila's anxieties and her trouble sleeping have persisted. And since those preschool days, other doctors have also seen Sheila. She is persuasive and convincing with them; none has ever denied her request for "just a little something" to help her relax and sleep more easily. Often she simply phones one of them, and the prescription is called in to a pharmacist.

Does Sheila think she has serious problems? "Not really," she says. "Oh sometimes I think to myself, here I am eating my bowl of soup, while Ted's having expensive lunches. But honestly, I don't resent Ted's success. I love him; I *want* him to succeed. And I certainly can't complain about his treatment of me. Ted's a good, faithful husband, and I'm proud of him. He's making more than $20,000 a year now, and that's pretty fantastic for a guy of thirty-four. Sure, I still take the pills, just to relax me a little. But I don't *have* to take them."

At this writing, Sheila is taking one 10-milligram Valium tablet and two 0.5-gram Doriden tablets each night before she goes to bed, with two or three additional doses of Doriden during the day. Ted is totally unaware of Sheila's use of chemicals to cope. Because of his frequent business trips, she pays the household bills; he never sees the checks she writes to the doctors and the drugstores. The drugs are not kept in the family medicine chest, but tucked in one of her dresser drawers.

Sheila, as it happens, could *not* stop taking her pills "any time she wants." She has now developed a strong psychological dependence on them, and a degree of physical dependence as well. She is, in short, on her way to a condition she would never think of attributing to herself: addiction.

BELONG TO MIDDLE CLASS

Like Sheila, most of the housewives who take sleeping pills habitually enjoy at least middle-class socioeconomic status: 73 percent of the regular and 85 percent of those who take other powerful sedatives belong to the middle or upper class. Nine out of ten obtain their drugs by doctor's prescription, and nearly that many follow dosage instructions faithfully.

The problem is that none of the many doctors Sheila has visited is aware that this pretty, well-spoken young woman is flitting from physician to physician and maintaining a drug regimen none of them would prescribe.

The three women we have described are real, and their stories are factual: only their names have been changed. They represent many other, equally real, women in homes across the U.S. Table 1 lists the eight top mood-altering drug types in current use among American housewives, with the percentage of women using each (as we have noted, multiple drug use is frequent).

TABLE 1

[In percent]

	All Housewives	By Age Group*			
		18–24	25–34	35–49	50 and over
Relaxants	13	9	17	13	14
Noncontrolled narcotics	9	13	16	7	5
Barbiturates	7	8	8	5	8
Diet pills	6	5	7	8	3
Nonbarbiturate sedatives	5	1	4	3	6
Antidepressants	2	2	3	2	1
Pep pills	1.5	1.5	2	1	2
Controlled narcotics	1	1	4	(1)	(1)

*The four groups are not equal in numbers, thus rates of use will not "average out" to the overall rate. See, for example, noncontrolled narcotics: since seven out of 10 housewives are over 34, the overall rate is only 9 percent despite much higher rates among the younger women.

[1] Less than 1.

When we come to experimentation, the same eight drug types head the list, though in a slightly different order, and there are small but interesting variations in pattern between housewives and the rest of the adult population. Table 2 lists the proportions of each group who have *ever* used each of the eight drug types.

As a group, housewives are not drawn to mind-affecting drugs that are illegal and available only through sources outside the law. Their sisters' psychotropic horizons are a little broader, however. In the next part of this series, coming in a future issue of the Journal, we will survey the American working woman's chemical predilections—what she takes, how her use of drugs compares with that of her male colleagues and other women, and to what extent she takes the drugs on the job: we'll see, too, what effect the kind of work she does has on her drug-use pattern.

TABLE 2

[In percent]

	Housewives	All women	Overall population
Noncontrolled narcotics	33	37	34
Relaxants	26	25	20
Barbiturates	24	22	20
Diet pills	19	17	12
Controlled narcotics	(1)	8	7
Nonbarbiturate sedatives	9	9	9
Pep pills	(2)	6	6
Antidepressants	4	(3)	2

[1] Over 10.
[2] Under 5.
[3] Under 4.

A Chemical Lexicon of Drugs Women Take

These are the psychotropic—mood-altering or mind-affecting—drugs with which respectable, middle-class Americans are increasingly "turning on." Usually, they are obtained by prescription; often, they are not. You will undoubtedly recognize many of their names. We use the word "abuse" to mean use in excess of prescribed dosage and/or duration of time.

Relaxants ("minor" tranquilizers): Reduce anxiety. Even in small doses, react with and boost effects of alcohol. Abuse can cause addiction. *Examples:* Atarax, Equanil, Librium, Meprotabs, Miltown, Valium, Vistaril; also combined with analgesics and other substances in such medications as Deprol, Equagesic, Milpath.

"Major" tranquilizers: Modify psychotic symptoms; reduce fear and hostility. Dangerous in combination with alcohol or sedatives. Potentially addictive, but rarely abused due to unpleasant side effects. *Examples:* Compazine, Frenquel, Mellaril, Serpasil, Sparine, Stelazine, Thorazine—also in combination drugs (see Antidepressants below).

Antidepressants ("mood elevators"): Alleviate serious depression. Interact dangerously with alcohol, amphetamines, sedatives, a number of other substances. Side effects, including blurred vision and dizziness. *Examples:* Aventyl, Elavil, Marplan, Sinequan, Tofranil—also combined with major tranquilizers in drugs such as Estrafon, Triavil.

Amphetamines ("pep pills"): Stimulate central nervous system, create feelings of confidence, prevent fatigue. High doses can cause toxic psychosis. Abuse can produce psychic dependence, possible addiction. *Examples:* Benzedrine, Dexedrine (see Diet pills below).

Diet pills: Reduce appetite, create sense of well-being. Abuse poses all the risks of the individual ingredients. Three major types:)1 amphetamines with barbiturates—Desbutal, Dexamyl, Nobese; 2) amphetamines with tranquilizers—Appetrol, Eskatrol; 3) other chemicals with amphetamine-like effects—Preludin, PreSate, Tenuate, Wilpo.

Barbiturates: Central nervous system depressants that sedate (calm) or, in larger doses, induce sleep. Can cause psychic dependence. Abuse causes addiction. *Examples:* Amytal, Butisol, Luminal, Mebaral, Nembutal, Sandoptal, Seconal, Sombulex, Tuinal, Veronal—also in combination with antispasm drugs in such medications as Bentyl, Donnatal.

Other powerful sedatives: Similar to barbiturates in purpose and in trouble-making potential. *Examples:* Chloral hydrate (Noctec, Somnos), Doriden, Noludar, Placidyl, Valmid.

Controlled narcotics (opiates) : Powerful analgesics that relieve pain, produce euphoria. Abuse causes addiction—which can sometimes occur with prescribed dosages as well. Natural substances: opium, morphine, codeine, pargoric; semisynthetics and synthetics: Demerol, Dilaudid, Dolophine (methadone), Leritine, Levo-Dromoran, Numorphon, Percodan.

Noncontrolled narcotics (not legally classed as narcotic drugs) : Similar to controlled narcotics, except that normal (prescribed) dosages are not potentially addictive. *Examples:* Butazolidin, Darvon, Indocin, Robaxin, Tandearil, Talwin.

[Medical Tribune, Jan. 26, 1972]

3. Response to "The 'Street' Abuse of Drugs"

Robert Brandon and Steven Wax's article, "The 'Street' Abuse of Drugs" states the usual generalities and arrives at the usual false conclusions that seem so prevalent these days. Starting with a statement of fact—that "the Bureau of Narcotics and Dangerous Drugs reports that 3.5 billion amphetamine tablets and 5 billion barbiturates and tranquilizers are produced annually"—they end with the conclusion that curtailing the prescribing of these items will curtail the abuse. How would they explain the fact that the most widely abused drugs have been heroin, LSD, and marijuana, none of which has been available via the practicing physician? Certainly the complete unavailability, not just partial restrictions, of these drugs has resulted in wider illegal use—and not reduced use.

The oft repeated opinions that "the profession's education about new drugs, or new information about old drugs, more often than not comes from a drug industry source," implies the lack of ability to seek out information about a profession that has spent more years training to seek out information than any other. Certainly an ethical pharmaceutical industry is obligated to disseminate information about their products, and certainly the practicing physician accepts information from this source. But it should be noted that the physician also receives information by way of the tremendous number of available scientific programs organized by physicians, participated in by physicians, and attended by physicians. The vast numbers of scientific journals attest to the unending quest for information by physicians. What other profession can point to comparable amounts of scientific material submitted, processed, compiled, published, consumed, and utilized by members of their own profession?

It seems to be the current fad for the younger generation to throw mud at the pharmaceutical industry, but the facts will show that the major breakthroughs in the development of new pharmaceutical agents have been the result of private enterprise—i.e., the industry's investment of its capital into research. It could be said that you and I, and all citizens, support research either by way of taxes and Government grants—or through product use and the company's private research. It is just a matter of choosing between the two.

One has only to review the decreasing population of mental institutions to assess the beneficial effects of psychotropic drugs. One has only to review the statistics on morbidity and mortality of individuals who are overweight to realize that any assistance in the treatment of this problem should be welcomed. Those individuals, both in and out of the medical profession, who do not get involved in the treatment of such problems are the most vocal in their efforts to remove these pharmaceutical agents from legitimate usage. Regardless of whether such agents are "short-term effective" or "long-term effective," the recommendation being made to discontinue their usage, without supplying an alternative, does not help the patient who would be otherwise benefited.

Obesity, like diabetes mellitus, hypertension, or gout, is a chronic illness. That the short-term treatment of any of these is doomed to failure should not surprise anyone. One does not evaluate insulin on the basis of the patient's blood sugar level six months after insulin has been discontinued. The improper usage of narcotics should not invalidate their use in severe postoperative pain or in the pain of ureteral colic.

It has become the fashion today to remove from usage drugs that are not 100 per cent perfect (i.e., effective without side effects). If this criteria were applied universally, automobiles, airplanes, and all household appliances would disappear from the marketplace. If phosphate detergents are being returned to the consumer because the alternative was worse—until such time as an alternative that is better can be developed, then I would suggest that alternatives to the drugs currently being abused be found that are as good, without the abuse potential, before removing the ones now being used.

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The following are excerpts from a research report:

4. AMPHETAMINE ABUSE

Pattern and Effects of High Doses Taken Intravenously

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by John C. Kramer, M. D., Viteslav S. Fischman, Ph. D., and Don C. Littlefield, M. D.

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A "DO IT NOW" PUBLICATION

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This is one in a series of publications by the DO IT NOW Foundation intended to communicate truthful information about Amphetamines, Barbiturates and Opiates.

Abuse of amphetamines administered intravenously has become a well established and extensive form of drug abuse. The abuse potential of these drugs when taken by the intravenous route is greater than when taken orally and is comparable to that of heroin or cocaine. Tolerance builds rapidly and an abstinence syndrome develops which leads to a typical pattern in which the user takes the drug continuously and in immense doses for about five days during which he does not sleep. During this time he gradually becomes more paranoid and disorganized. He then desists for a day or two and falls into a prolonged semicomatose state. Upon awakening he is still lethargic and feels the need to resume his drug for a new round.

In 1960 and 1961, some physicians in the San Francisco Bay region began prescribing large quantities of injectable methamphetamine to patients who identified themselves as heroin addicts. Evidently these physicians felt that this substitute was safe, preferable to opiates, and would help the opium addict resist the use of his narcotic. In other instances flagrant distribution of prescriptions in a totally unethical manner was engaged in by a few physicians who were later prosecuted and convicted. These prosecutions and the removal of injectable methamphetamine from pharmacies ended this era.

Next, a few users discovered that they could purchase crystalline methamphetamine in wholesale lots from manufacturers by representing themselves as individuals engaged in pharmacological research. Further police action resulted in limiting this source of supply. Most recently, amateur "chemists" have been manufacturing amphetamines for distribution on the illicit market. At the present time these privately manufactured supplies provide the majority of the amphetamines for intravenous use in California, though diversion of commercial preparations still occurs.

All our patients used amphetamines orally at first. In a few instances it had been legitimately prescribed for therapeutic purposes, but in most cases "bennies" and "dexies" were merely "part of the scene" along with marijuana, during adolescense. The amount used orally often reached 150

to 250 mg/day. Progression to intravenous use was at times a direct consequence of the desire to improve the quality of the amphetamine experience. In other instances a period of heroin use or relative abstinence from drugs intervened.

With intravenous use, doses are higher than by the oral route. During early phases of intravenous use, 20 to 40 mg-doses, taken three or four times a day, suffice, but, as tolerance builds, the dose and frequency of injection increase considerably.

Devices Used to Counteract the Toxic Effect

Concern about the disabling effect of the psychotoxic syndrome led to countermeasures. Three were mentioned:

1. Everyone in the sample wished to minimize the dose by "will power", but only very few seriously maintained that they had success.

2. Abstinence from food, liquids, and sleep seemed to exaggerate the psychotoxic effect of the amphetamines. The more experienced users in our sample forced themselves to eat, drink, and sleep regularly but even this failed in the later stages of the cyclic process.

3. Another way to control confusion and paranoid behavior was to use depressants. Barbiturates were used occasionally but opiates were generally preferred. Experimentation with varying combinations was common but only of limited value in achieving the desired control.

Patterns of Use

After initial phases of experimentation with the use of an amphetamine intravenously, a pattern emerges. The drug is injected about every two hours around the clock for a period of three to six days during which the user remains awake continuously. Rarely these "runs" last as long as twelve days. Following a "run" he "falls out", that is, he becomes so exhausted, disorganized, tense, or paranoid he ceases using the drug and goes to sleep. Often barbituates are needed to induce sleep, though some subjects report that drowsiness sets in about three hours after a "fix" and sleep cannot be prevented without recourse to more stimulant. Once asleep the user cannot be awakened. The sleep lasts 12 to 18 hours following a three- or four-day "run". However, the more extended the "run", the longer the recovery sleep lasts. Some patients describe semicomatose states lasting four or five days. Upon awakening he is famished, his paranoid state is largely dissipated,but he is still lethargic. At this point, he is ready to resume use of the drug. Reinjection terminates the lethargy and a new "run" has started. Occasionally the use is somewhat less frequent and the user will spend an hour or two in sleep each day. The brief sleep appears to permit him to continue for a longer period without "dropping out". A few of our subjects use the drug in somewhat more casual ways; one is a "weekend user"; another uses it for the sole purpose of postponing orgasm.

When use becomes well established, individual injections generally range from doses of 100 to 300 mg. The size of the dose increases considerably as a "run" progresses. These are, of course, estimates, but because the users have dealt with crystalline methamphetamine or commercial vials, the estimates appear to be reliable. The highest maximum dose reported is in excess of 1 mg. taken every two hours, probably close to 15,000 mg. in one day. The patient reporting this dose purchased methamphetamine, USP from a manufacturer and repackaged it to retail it to others.

Immediate Effects

After intravenous injection of a drug the user gets a sudden, generalized, overwhelming, pleasurable feeling called a "flash" or a "rush". It has been compared to "an orgasm all over your body". It differs qualitatively from the "flash" of intravenous administration of heroin by producing an abrupt awakening feeling as opposed to the drowsy drifting effect of heroin. This effect is repeated with each intravenous injection, though the intensity of the feeling is diminished after repeated injections.

Though the mood under the use of amphetemines can be described as euphoric, this is too limited a concept. Under the effect of the drug, the user has an intense fascination with all his thought and activities which extends even to the paranoid fear and anger he almost inevitably experiences.

During a "run", the user pursues activity. Though occasionally alone, there is a tendency for groups of users to gather together, mingle, talk incessantly, depart, seek more drugs, and reunite in groups again.

At first the activity is purposeful. As hours and days wear on, it becomes less so. At times, it may become compulsive. Ultimately the activity becomes grossly disorganized.

Appetite for food is suppressed completely. Experienced users make an effort to eat. Liquids and vitamins are taken since solid foods seem impossible to swallow during a period of active drug use.

Seldom in this group was the paranoid state experienced during the phase of oral use, or even during the first few months of intravenous use. Even prior to its occurance in themselves, they are aware that a paranoid state will be a consequence of high-dose use. Though some individuals become paranoid following initial injection on each new "run", in most it does not appear until the second or third day. The state usually intensifies as the "run" progresses. The user realizes that the paranoid symptoms are due to the amphetamine; however, in the last day or two, this idea becomes more difficult to accept. When a "run" is terminated and the subject awakes from the profound sleep, the paranoid state is largely dissipated, though in some cases, a mild degree of suspiciousness persists.

Other Effects

Weight loss, 20 to 30 lbs, occurs during a period of chronic use despite the effort to take nutritious food and supplementary vitamins. Abcesses, nonhealing ulcers, and brittle fingernails appear probably secondary to the malnourished state. Tooth grinding is common during the use of the drug, though it may be controlled for a while by effort. Though tooth grinding seems to be a drug effect, one subject continues with this action many months after withdrawal. Despite familiarity with the drug and the high tolerance which occurs, over-dosing does occur occasionally. The symptoms of overdose are severe chest pain followed in a few minutes by unconciousness which lasts an hour or two. Severe tremors or muscle and joint pain are toxic effects which may occur after several days use. These are signals to the user to terminate a "run".

Comment

From out observations, we feel that we have identified a relatively new phenomenon, that is, extensive use of amphetamines intravenously, a form of drug abuse with an addictive and relapse potential comparable to that of opiates or cocaine and which is favored by many drug-use abusers over heroin. This form of drug abuse is extremely disabling from a social and phychological standpoint in its acute phasea and may lead to prolonged psychosis or brain damage. Because of the relative ease of illicit manufacture and the less urgent need to sustain uninterrupted use, the users will probably not be as extensively involved in crimes against property as are opiate users. The likelihood of crimes of violence, though it has only been suggested so far, may be greater. From descriptions of the intensity of the paranoid state and the hyperactivity associated with amphetamine use, crimes of violence by amphetamine users appear likely in the future.

5. Amphetamine Pill Smuggling Charged

(By Peter Milius, Washington Post Staff Writer)
(page A–3)

The government said yesterday that amphetamine tablets made in Mexico by an American company are being smuggled back into this country, and are a major source of illicit supply in the Southwestern and Southeastern states.

The Bureau of Narcotics and Dangerous Drugs announced it is moving to revoke the amphetamine export license of the company, the Pennwalt Corporation of Philadelphia and its Strasenburgh Prescription Products Division in Rochester, N.Y.

The agency said Strasenburgh has been shipping bulk amphetamine to a Mexico City affiliate, Laboratories Strasenburgh de Mexico, where it has been put into capsule form and marketed as Bifetamina.

A "substantial percentage" of this Bifetamina has then made its way back into this country, according to the bureau—first to six small "pharmacies" on the Mexican side of the Texas border, then into Texas border towns, then "along established truck routes" into at least 11 other states. Some has also been flown across the border to "remote air strips" by "light aircraft," the bureau said.

HIGHLY PRIZED

It said the small black pills, which have such street names as "Black Beauties," "Black Mollies" and "Black Widows," are highly prized by users because of their relatively high amphetamine content, 20 milligrams.

The government said it made 80 arrests during a 10-month investigation of the distribution pattern, and bought or confiscated almost a million Bifetamina capsules with a street value of about $1.5 million.

In a statement issued in Philadelphia yesterday afternoon, William P. Drake, Pennwalt's president, described the bureau's action against the company's export license as "baseless." He said that, "since 1966, Pennwalt has manufactured its amphetamine sold in Mexico in that country." But attorneys in the office of the bureau's chief counsel insisted that Pennwalt is on record there as shipping a total of 900 kilograms of bulk amphetamine to Mexico in 1970 and 1971.

(A total of 900 kilograms is the equivalent of 1,980 pounds, just short of a ton.)

NO EMPLOYEES SEIZED

A Pennwalt vice president, W. C. Willits, said that, in Mexico, "we only sell, to our knowledge, to licensed pharmacies under the jurisdiction of the Mexican government." The bureau said no Pennwalt officials nor employees were among the 80 arrested. It added, however, that its investigation "is continuing." The law makes it a felony to export amphetamine "knowing it will be unlawfully imported" back into the U.S.

Congress and the bureau combined last year to limit legitimate amphetamine manufacture in this country, and to put it under close federal control. Amphetamines can be bought legitimately only by prescription; doctors prescribe them most often now for weight reduction. Illicit users prize them for the "highs" they produce, and some, like truck drivers, as means of warding off sleepiness.

The bureau said it began finding smuggled Bifetamina "in ever-increasing amounts and ever wider areas" in this country after it imposed last year's domestic controls. It said a capsule could be bought illicitly in Mexico for 9 to 13 cents, and sold in the U.S. for about $1.50.

[From the New York Times, Jan. 23, 1972]

6. Amphetamine Maker Will Make Criticized Production in Mexico

(By Boyce Rensberger)

The *Pennwalt Corporation*, whose Mexican subsidiary was said by Federal officials last week to be selling amphetamines that eventually enter the illicit drug market in the United States, has announced *that it is going out of the amphetamine business in Mexico.*

William P. Drake, president of the Philadelphia-based drug and industrial chemical concern, said the action was being taken to comply with a new Mexican *law banning the production and sale of amphetamines in Mexico by July 12, 1972.*

Last week the Federal Bureau of Narcotics and Dangerous Drugs charged that Pennwalt's subsidiary, the Strassenburgh Pharmaceutical Division was exporting bulk amphetamines to its Mexico City plant where the substance was capsuled and sold into a market that eventually returned the drug illegally into the United States.

The bureau began legal action to lift Strassenburgh's license to export amphetamines to Mexico. At the time Mr. Drake denied that his company was exporting amphetamines to its Mexican facility.

On Friday, however, Mr. Drake conceded that the earlier statement had been in error and that amphetamines had indeed been sent to Mexico as charged by the Federal officials.

ALL PRODUCTION TO END

Mr. Drake said, however, that the practice had ended last June when the Mexican plant acquired its own facilities for the production of bulk amphetamines.

Now, as a result of the new Mexican law, which is believed to have been passed under pressure from the United States Government, Mr. Drake said that amphetamines would no longer be produced in Mexico in any form.

Pennwalt is not expected to fight the effort to revoke the company's export license inasmuch as it will no longer be needed.

In a statement released Friday, Mr. Drake said that Pennwalt intended to review its records on the production and distribution of its amphetamine products in Mexico "to ascertain whether there has been any failure on the company's part, through any of its representatives at any level, to maintain effective internal controls against diversion of the company's products into other than legitimate channels."

COOPERATION IS PLEDGED

Mr. Drake said that the company would cooperate with Federal officials in efforts to insure that the distribution of its amphetamine products was properly controlled.

Cooper Willits, a Pennwalt vice president, said that his company was unaware of wrongdoing on its own part. "You have to remember," he said, "that we are operating in Mexico under Mexican law, under Mexican supervision and are selling to Mexican pharmacies. What they do with it is not under our control."

Federal officials have said that the pharmacies, especially those operating near the United States border, were selling the drug without prescription and that huge quantities were entering the United States illegally.

The Mexican ban on amphetamines is part of a standard dangerous drug law containing provision for exceptions in the event of serious emergency needs. *The law applies to seven other drug makers in Mexico: Abbott Laboratories, Smith Kline & French Laboratories, Redefsa, Irwin Neisler Laboratories, Bigaux, A. H. Robbins Company and Lakeside Laboratories.*

[From the New York Times, page 14, Jan. 22, 1972]

7. U.S. Crackdown of Amphetamines Driving Up Prices

(By Martin Waldron)

Juarez, Mexico, Jan. 21—A United States Government crackdown on black-market amphetamine operations along the Mexico border is driving up prices here and threatening to increase them elsewhere in the country. But while the move has reduced the illegal inflow, the pills are still readily available for those who really want them.

On Thursday, in this sparkling clean border town across the Rio Grande from El Paso, Texas, prices for "black mollies," reputed to be the most popular pill sold on the United States black market, were 50 cents each in small quantities. A week ago the price was 25 cents. In large lots of 500 or more the price

this week was 25 cents. A month ago Government agents were buying them at wholesale for 9 cents each.

Mexican pharmacies that once sold the pills with no questions asked were exercising extreme caution this week. Clerks said that Mexican narcotics officers as well as those from the United States were trying to halt the illegal shipment of amphetamines from Mexico into the United States.

Since Jan. 15 Mexico has been enforcing a law that permits the sale of amphetamines only with a doctor's prescription.

Mexican government sources in Mexico City said that on that same date a new law took effect prohibiting the manufacture of amphetamines in that country, except in case of emergency, a step that could restrict the availability and further increase prices.

80 ARRESTS REPORTED

On Tuesday, United States Attorney General John N. Mitchell reported that the Bureau of Narcotics and Dangerous Drugs had arrested 80 persons who were smuggling amphetamines from Mexico into Texas or who were selling them illegally in 14 states from Colorado to Florida.

Mr. Mitchell said that the Strasenburgh Pharmaceutical division, of Rochester, N.Y., part of the Pennwalt Corporation, was being ordered to show cause why its license to export bulk amphetamine powder to Mexico should not be revoked.

The company's Biphetamine capsules, which contain 10 milligrams of amphetamine capsules, which contain 10 milligrams of amphetamine and 10 milligrams of dextro-amphetamine, have been sold in the United States for up to $1.50 each, the Bureau of Narcotics said. They are known on the United States black market as black mollies, black widows or black beauties.

The bureau estimated that more than 30 million of the pills had been smuggled from Mexico into Texas last year and then distributed throughout the South and Southeast.

The pills get their nicknames from the jet black gelatin capsules that hold the amphetamine powder.

Amphetamines taken by mouth case an airy feeling of euphoria for up to 24 hours and are popular with truck drivers and students seeking to stay awake. Amphetamines may also be injected into the blood stream to achieve an even higher euphoria.

In a telephone interview from Washington, Robert P. Rosthal, the deputy chief counsel for the Bureau of Narcotics, said that the mass arrests and the action taken Tuesday against Strasenburgh had virtually closed down black market activities in many southern states, at least for the time being. "We are getting reports that it is very difficult to make a buy," he said.

Paul Roberts, a 30-year-old Santa Monica, Calif., graduate student, make the purchase at the Iris Farmacia. The Bureau of Narcotics and Dangerous Drugs said that this pharmacy was one of the six main sources of amphetamines smuggled into the United States.

Paul Roberts, a 30-year-old Santa Monica, Calif., graduate student, agreed as a test case to try to make the purchase at the Iris Farmacis. The Bureau of Narcotics and Dangerous Drugs said that this pharmacy was one of the six main sources of amphetamines smuggled into the United States.

"Ah señor," the clerk said in Spanish, "they are now hard to come by. The authorities have been watching."

He told Mr. Roberts that a physician with a clinic next door to the pharmacy would write a prescription for 20 of the amphetamines for $4 and that the pills would cost 25 cents each under the prescription.

Mr. Roberts went to the next-door clinic but the physician was taking a siesta and declined to open up.

Accompanied by a friend, Mr. Robeerts returned to the pharmacy and related to the clerk that the clinic was closed. The clerk shrugged and said it would open soon.

"Oh, let's skip it," Mr. Roberts's companion said in English. "We'll buy them somewhere else."

"Well, if you are in such a hurry," the clerk said, still speaking in Spanish, "perhaps I can go ahead and sell you some."

Mr. Roberts offered $5 for 20 pills. The clerk asked $20, four times the price

he had quoted for pills with a prescription. After a moment of negotiation, Mr. Roberts agreed to pay $20 for 40 pills and the clerk handed him a glass vial of black capsules stamped with the imprint, RJS, which is the Strasenburgh symbol in Mexico.

There are five Iris pharmacies in Juarez—the main store where Mr. Roberts bought the pills and four branches.

At the Iris branch on the Avenue of the Americas, Mr. Roberts negotiated with a clerk for amphetamines while a photographer took photographs. The clerk said that pills would be available after 7 P.M. and told Mr. Roberts to return and to tell the night clerk that he had been sent by Dr. Jiminez, which the clerk said was a code word.

TROUBLES FOR BARTENDER

Last night, in a bar and joining a plush Juarez bordello, the bartender said he had not been able to get a steady supply of pills or marijuana for days because of the activities of narcotics agents.

A thin Mexican with a thin moustache, who appointed himself to protect a rental car in the bordello parking lot, offered to supply amphetamines or barbiturates for 25 cents each. But he did not deliver. He did steal the photographer's checkbook from under the car's front seat while he was watching it.

The 40 amphetamines that Mr. Roberts bought at the main Iris Farmacia were fast acting and long lasting. Their potency accounts in part for their popularity.

The Bureau of Narcotics said that these Strasenburgh pills were made by a patented process that was virtually impossible to counterfeit and that buyers were reasonably sure of getting "the real thing."

An agent of the bureau, Ernest Marquardt, said in a telephone interview from Dallas that the potency of the Strasenburgh pills had made them the most sought-after such pill on the United States black market.

For a time in Oklahoma City, he said, there was fierce competition between purveyors of "black mollies" and "minibennies" coming into the United States from Tiajuana on the Mexico-California border. The black mollies won.

Mr. Marquardt estimated that a million pills a month had been smuggled into El Paso from Juarez last year. He said that bureau agents had recently arrested one man with 60,000 pills and $82,000 in cash.

Mr. Rosthal, the Bureau of Narcotics and Dangerous Drugs deputy chief counsel, said that amphetamines bought in Mexico on prescription generally could not be brought into the United States.

If there is a genuine doctor-patient relationship, customs officers will allow a limited supply to be brought if they are bought under prescription by Mexican residents who are going to tour the United States, he said.

[From the New York Times, page 70, Oct. 10, 1971]

8. Drug Use Linked to Heart Attack

DOCTORS SUSPECT CONNECTION IN SEATTLE WOMAN'S CASE

(By Lawrence K. Altman, Special to The New York Times)

Seattle, Oct. 9—A 23-year-old woman is recuperating here from a heart attack that her doctors said they strongly suspected had resulted from an overdose of "speed," amphetamines, which she had injected into her veins.

The woman's case is a dramatic example of the serious consequences that can result from drug abuse. Hepatitis, or inflammation of the liver, and infections of the heart are said to be common, serious medical complications of drug abuse that can require long, expensive hospitalization.

Dr. David C. Dale, the chief medical resident physician at the University of Washington Hospital, said in an interview that the woman's heart attack had cost Federal and state taxpayers $1,000 for her care in the coronary care unit.

The woman is fortunate because she survived her medical complication of drug abuse. However, many addicts die from medical complications of their habit before they even reach a hospital for treatment. In other cases, doctors

are unaware that their patients have taken narcotics. Accordingly, the physicians said that it was not known how many other drug abusers had suffered heart attacks—called myocardial infarctions—from the drugs that they had improperly taken.

Effects of amphetamine

The doctors said that they suspect that the large amounts of amphetamine the woman took caused her heart to beat rapidly, to work extremely hard, and the coronary arteries to constrict—thus depriving the organ of its nourishment and thereby destroying a vital area of muscle. Though the cause differed, the result was similar to the damage older men and women suffer from heart attacks resulting from arteriosclerosis, or hardened arteries.

When Dr. Stephen R. Shaul, a medical resident at the hospital, saw the woman in the emergency room at 2 o'clock one recent morning, he said that at first he had been skeptical that her severe chest pains were due to a heart attack. But when Dr. Shaul saw the tell-tale squiggles on her electrocardiogram, or heart tracing, indicating a heart attack he said the diagnosis was clear to him and to the hospital cardiologists. Later, when laboratory technicians reported the results of her blood tests, they further helped to confirm the diagnosis.

The woman told her doctors that she had dissolved eight methadrine (amphetamine) tablets in water and then injected the solution into her needle-scarred veins late the previous afternoon. The dose was the largest that she had taken, she said, in expectation of her "biggest kick." The woman told her doctors that it was the third time she had shot "speed" that day and that she had, in the past, used other drugs including heroin and LSD.

Immediately thereafter, Dr. Dale said that she had a headache, chills and sweating, followed by a severe crushing pain in her chest and her arms.

INFECTION DISCOUNTED

Her physicians said that they had discounted the possibility that the woman's heart attack was due to an infection of a valve or the inside wall of her heart because no bacteria grew from several cultures of her blood. Infection of the heart, called bacterial endocarditis, is considered an important complication of drug abuse. Sometimes treatment necessitates open heart surgery, costing several thousand dollars, often at public expense.

While the woman addict was being treated in the coronary care unit, she told Dr. Dale and her nurses that she "was afraid to let her mother know she was ill because my mother will bawl me out."

Once her pain disappeared on the second day of her stay, she became bored and upset with the restraints that, due to the seriousness of her heart damage, the doctors had imposed on her physical activities.

Five days after the woman entered, Dr. Dale said, "She signed out of the hospital against medical advice.

She returned to the heart clinic for follow-up care last week. Depending on her future medical course, the doctors said they might do more extensive tests to determine if another cause existed for her heart attack.

Meanwhile, until evidence is found to the contrary, the doctors said her heart attack was due to "speed."

[From the New York Times, page 14, Aug. 8, 1971]

9. British Doctors Curb "Pep Pills"

(By Lawrence K. Altman)

Many physicians in England and Scotland have voluntarily stopped prescribing amphetamines and thereby have helped curb abuses of the drugs that are considered among the most potent stimulants of the brain, a medical journal has reported.

Doctors in such large cities as Glasgow and in smaller ones like Ipswich have made "a gratifying reduction in the amount of amphetamine" drugs prescribed, the British Medical Journal said in an editorial.

American physicians in some areas are trying similar measures.

Last June, doctors and pharmacists in Huntington, L.I., acted to restrict the use of amphetamines. Some doctors elsewhere on Long Island and in Utah have taken similar steps to limit that portion of the abuse problem that results from legal prescriptions for the drugs.

Many Americans treat themselves with amphetamines that they have obtained from other patients who have gotten the pills on a doctor's prescription. Others are said to obtain the drug easily from illegal sources.

Value is called limited

The world epidemic of abuse of amphetamine and other drugs, the British journal said in its current issue, has made many British doctors aware that revisions were necessary in prescribing amphetamines because they were "drugs with a limited use in modern therapeutics."

"Bennies" (for Benzedrine), "dexies" (for dextroamphetamine) and "ups," or "pep pills" are commonly used terms that students and truck drivers, among others, use when they swallow the pills to stay awake. Some people abuse amphetamines by injecting the drug as "speed" or "splash" to gain the false sense that sleep and food are not needed.

Use of amphetamines for depressed moods, like the "housewife blues" and obesity are the major abuses noted. In many such cases, doctors have said, psychiatric care may be needed to treat the underlying, basic problems.

Doctors generally agree that amphetamines are useful in a rare condition called narcolepsy in which the patient has uncontrollable paroxysms of sleep. Some doctors also advise amphetamine treatment for hyperkinesis, a condition of overactivity in children.

The British journal credited Dr. Frank O. Wells for providing the impetus for much of the success in voluntarily curbing amphetamine prescriptions in Britain. In 1967, Dr. Wells began monitoring the extent of drug abuse in the Ipswich area and by 1969 he had found that amphetamine abuse was rising steadily there. As a result, the local physicians and druggists agreed not prescribe amphetamines.

Some pills destroyed

"The manufacturers had been persuaded to take unopened packs back, while opened ones were destroyed," Dr. Wells said.

Two months later, the journal said that "there was no evidence whatsoever of amphetamine abuse in the Ipswich area."

Publicity about the Ipswich scheme led doctors in other areas to start similar voluntary bans.

"Even in a city as large as Glasgow there has been little more difficulty in implementing the band than at Ipswich," the journal said.

Because British physicians in 1970 prescribed more than 36 million doses of amphetamines, weighing eight tons, the British Medical Association held a meeting last month to which representatives from 48 medium-size towns in England came.

At the meeting, Sir. George Godber, Britain's chief medical officer, said that "there was almost nothing that amphetamines could do which was not done better by other drugs."

Another physician, Dr. T. R. Cullinan of Ashford, urged strong national action to tackle the problem because:

"We made this mess, we must clear it up, and the public must see us clearing it up."

The success to date, the journal noted, has made many doctors ask "themselves whether other potential drugs of dependence [addicting] at present being prescribed without much thought could not also be exposed to similar careful scrutiny."

[From the Congressional Record—Extensions of Remarks, page E1319, Feb. 18, 1972]

10. Forged Rx's Are Passports to Perilous Drugs

(Hon. Seymour Halpern of New York, in the House of Representatives, Wednesday, February 16, 1971)

Mr. Halpern. Mr. Speaker, I would like to draw the attention of this body to a problem that has reached critical proportions. This is the sale of dangerous drugs on the basis of forged, illegal prescriptions.

The New York Daily News of February 14 vividly points out the ease with which one can obtain such dangerous drugs as benzedrine, nembutal, and desbutal. With the cooperation of the Manhattan District Attorney's Office, investigative reporters for this newspaper were not only able to obtain 1,000 prescription blanks under false pretenses, but also used them to buy amphetamine and barbiturate drugs.

The drug traffic which is ransacking our streets today will never be wholly eliminated unless such practices as those outlined in this article are brought to a halt. I would like to submit this valuable article for the RECORD and in doing so, commend the New York Daily News for its attitude of public concern and its exposition of an area which is sorely in need of tighter regulation.

The article follows:

FORGED RX'S ARE PASSPORTS TO PERILOUS DRUGS

(By Richard Oliver)

"The system for dispensing dangerous drugs to the public is so loose, so shoddy that anyone with a little knowledge, a lot of nerve and a ball point pen can buy amphetamines and barbiturates through forged prescriptions.

"The News demonstrated this on a single day last week when reporters from this newspaper presented bogus prescriptions and purchased dangerous, supposedly controlled, drugs with no difficulty at 16 pharmacies in various parts of Manhattan.

"The investigation was conducted with the permission and active cooperation of Manhattan District Attorney Frank Hogan. State Attorney General Louis Lefkowitz also was apprised of the probe.

ALL TURNED OVER

"All the drugs and receipts, along with nearly 1,000 unused prescription blanks, were turned over to Hogan's office for investigation into possible violations of federal and state laws.

"This inquiry is being conducted with the cooperation also of Sal Rubino, president of the State Pharmaceutical Society, who met with Hogan's aides last week.

To the credit of the profession, it should be noted that a substantial number of pharmacists would not or could not fill the phony prescriptions. Thirty-two said they did not have the requested drug in stock, while 14 demanded a federal narcotics registry number, which purposely was omitted from all the phony prescriptions.

MANY HAVE SUSPECTED

As Rubino said it is quite possible that some of those who said they were out of the drugs did so because of the missing number or because they suspected the prescriptions were bogus.

"Nevertheless, the investigation did show conclusively that it was no difficult to find pharmacies that will fill authentic-looking prescriptions for dangerous drugs even if the required federal number is missing.

"Drug abuse experts regard the forged prescription problem as epidemic. Dr. Richard Koeppel of the city's Addiction Services Agency described as "frequent" the use of stolen prescriptions, and said that in many cases youths print or have printed prescription blanks, purchase "ups" or "downs" over the counter and then peddle them on the streets to youthful drug abusers at fantastic profits.

PROMPTED BY TIP

"In fact, The News investigation was prompted by a tip from an anonymous letter writer who actually enclosed a phony prescription blank. Hogan's office subsequently approved the newspaper's probe.

"Two weeks ago, a reporter opened the Yellow Pages and chose a professional printer at random. Using an assumed name, that of a physician, the reporter ordered 1,000 prescription blanks.

"The first printer apparently smelled a rat and demanded the physician's federal narcotics registry number. A second printer, again chosen at random from the telephone book, took the order, no questions asked.

"A typewritten sample was sent to the printer on Jan. 31 by a youthful messenger who left a $5 deposit. Four days later, another messenger picked up the blanks. Total cost: $13.38.

BOGUS M.D.

"The blanks bore the name of a "doctor" D. M. Sugob, which, spelled backward, reads Bogus M.D. The address on the blanks was 36 W. 34th St., which is the office of the Federation Against Drug Addiction, Inc. A telephone number was established as a control to determine whether pharmacists called to check up on Dr. Sugob.

"With the advice of Chief Assistant District Attorney Alfred Scotti and Assistant DA John Fine, five dangerous drugs popular with drug abusers were selected for the survey:

"Bamadex (Lederle), a dextroamphetamine; used for obesity, as a short-term regimen of weight reduction; improperly used, the drug has produced extreme psychological dependence. On the streets and in schoolyards it is known as an up.

"Desbutal (Abbott), methamphetamine hydrochloride and sodium pentobarbital, which, according to the manufacturer, 'should be used with extreme caution and only for limited periods of time in weight reduction programs.' This is an up.

ANOTHER UP

"Benzedrine (Smith Kline & French), amphetamine sulfate, a powerful drug which, incidentally, many druggists refuse to stock to be used "only for limited periods" in weight reduction. An up.

"Nembutal (Abbott), sodium pentobarbital; produces sedation or hypnosis; may be habit forming. Known as a down.

"Seconal Sodium (Lilly), sodium secobarbital, a quick and short-acting sedative and hypnotic; may be habit forming. A down.

"Under federal law in effect since October, prescriptions calling for controlled drugs, including the above, are required to carry a special number issued to physicians by the U.S. Bureau of Narcotics and Dangerous Drugs. Without the number these drugs may not be legally sold.

IT'S A SAFEGUARD

"A spokesman for the bureau here said the regulation was put into effect in part to attack the forged prescription problem. 'Prescription pads are not tightly controlled,' he said. 'This is an additional safeguard to assure that the prescription is proper.'

"In The News investigation, by design, no such numbers appeared on the prescriptions and no such numbers were given out to those pharmacists who took the trouble to reach Dr. Sugob, whose answering service reported him 'out of the office' when anyone called.

"A total of 25 prescriptions were made out by a reporter, a relatively easy process since anyone can obtain Rx signs and symbols in most dictionaries and almanacs.

"For instance, this information appears at page 1670 of the "Random House Dictionary of the English Language" (unabridged, ed., 1971), and, for that matter, on page 55 of 'The World Almanac and Book of Facts 1971.'

"Five reporters, each with five Rx's, went to different sections of Manhattan, where pharmacies were selected at random. The results:

"Jean Perry, who covered Harlem and northern Manhattan, purchased four drugs. In all, she visited 13 pharmacies, eight which were out or said they were out of the particular drug requested, and one which demanded the missing federal number.

"Preston Layton, who covered the upper West Side, returned with all five prescriptions filled. He visited 10 stores, five of which said they did not have the requested drugs.

"Meriemil Rodriguez, who was assigned to the upper East Side, had three prescriptions filled. She went to 15 pharmacies, eight which said they didn't have the drug called for, and four which demanded numbers.

"Fred Loetterle, who covered lower Manhattan, came back with two drugs. He visited 15 pharmacies, nine which said they did not have the drugs requested, and four which demanded numbers.

"Another reporter, who covered midtown, had two of five prescriptions filled of a total of nine stores visited. Five requested numbers, two said they didn't have the drug.

"An interesting sidelight to the probe came as a result of a serious medical mistake made by the reporter, alias Dr. Sugob, in filling out the Rx's calling for Bamadex, a strong stimulant that should be taken in the morning, according to the manufacturer.

"By accident, the prescriptions were made out to call for one at bedtime—an absurd direction, akin to say, taking sleeping pills upon awakening—which an alert pharmacist should have spotted easily.

"Four of five Bamadex prescriptions were filled. Of the four, one pharmacist marked the label 'one capsule as directed,' and told the customer to check with his doctor; two caught the error but filled the Rx's anyway; one made no mention of it."

[From the Times-Picayune, Apr. 2, 1972]

11. Surgery Unveils Method to Curb Obesity

'intestinal shunt' said safe, effective

(By Bill Stockton, AP Science Writer)

Los Angeles (AP)—Surgery to lose weight?

It sounds like a fat worrier's dream.

And it is for certain people, says the surgeon who pioneered the operation 25 years ago but kept it under experimental wraps until recently, fearing possible abuse.

But now there is no doubt the "jejuno-ileal intestinal shunt" operation, when performed and monitored by a qualified team of specialists, is safe and effective, Dr. J. Howard Payne clinical professor surgery at the University of Southern California, said in an interview.

Accurate figures on how many of the operations are being performed aren't available, but Payne said he knows of several surgeons across the country now doing several operations a week. And their number seems to be growing.

The surgical technique is being hailed as a dramatic new treatment for the chronically obese who make no progress with fasting or diet pills.

"The technique has been proven and we think the point has been reached where this will become more prevalent," Payne said. "We've had enough experience to know where the hazards are."

But alas, the fat worrier only 15 or 20 pounds overweight will just have to continue dieting, Payne said. He ticked off the requirements research has pinpointed for the prospective patient.

First, he must be at least 100 pounds overweight.

The obesity must be assuming life-threatening proportions, causing the onset of such maladies as heart trouble, diabetes, gout, hypertension or high cholesterol.

Most importantly, the patient must have a bright, optimistic outlook and desire the surgery to preserve his health, Payne said. Prospective patients without such an attitude have been refused.

Other doctors have objected to the surgical technique because it makes major changes in the body's digestive machinery. They feared it might seriously upset body metabolism—causing nutritional problems worse than obesity.

But Payne said careful followup studies of the 180 patients he and his colleagues have treated have shown no untoward effects.

The danger of heart failure during surgery is always a concern with the older obese person, Payne said, so no patient over 50 is accepted.

The jujuno-ileal intestinal shunt received new attention recently when Al Hirt, the famed jazz trumpeter, received it to bring his weight down from 333 pounds. Less than a month after he entered a Richmond, Va., hospital, 26 pounds had dropped away.

'Preventive step'

"I had reached the point where this operation was preventive medicine for me," Hirt said. "I hope I'll get to see my grandchildren now."

The operation can change your life, said Wayne Monroe of Alhambra, Calif., who underwent surgery in December 1970.

Monroe, 34, weighed 464 pounds then, had been a "fatty" all his life. Now he's dropped to 245 pounds and hopes light dieting will take off another 20 pounds.

"It's like being reborn again," he said. "People ask me how old I am and I tell them I'm 1 year old.

"It's completely changed my life both mentally and physically. There are so many things I can do. The mental outlook is just tremendous."

The surgery is simple, Payne said. Doctors join 14 inches of the upper small intestine to four inches of the lower portion of the small intestine, bypassing more than 17 feet of the digestive organ.

The effect is to short circuit the body's food factory.

Continues eating

The patient continues eating as before, but most of the food's nutrients are excreted. Only enough small intestine remains to absorb a fraction of the food into the blood.

As a result, the body is forced to begin tapping its enormous stores of fat.

But therein lies the operation's greatest danger. The liver is the organ that converts fat to nutrients the body can use.

In the middle-aged chronically obese, however, the liver is stuffed with fatty deposits. The strain of converting additional fat can overload the liver and cause a malfunction.

The solution, Payne said, is to operate early on the patient doomed to a life of obesity. The surgery has been performed successfully on teen-agers.

Payne and his colleagues said they kept the surgical technique under experimental wraps for almost a quarter-century because they feared medical charlatans might seize upon it before it had been properly tested.

[From the New York Times, Mar. 26, 1972]

12. Needle Infections Rise in Drug Abuse

(By Lawrence K. Altman)

The spreading epidemic of drug abuse in the country has brought with it an increase in infectious diseases caused by the use of contaminated needles and syringes among persons who inject themselves with heroin, amphetamines and many other drugs.

Accordingly, American doctors are treating more cases of heart, liver and other infections among "skin-poppers" and "mainliners."

Experts in infectious disease and pathologists said in interviews that many such patients often require lengthy hospitalizations and treatment with costly medications and technologic devices.

Also, skilled teams of cardiac surgeons to do open-heart operations with heart-lung machines are needed to minimize the death rate among some addicts whose drug abuse has led to heart damage.

Repeated needle punctures break the skin's protective barrier and open the way for infections that can damage not only the skin and muscles but also organs like the heart and brain.

"The fact is that we have more drug abusers using contaminated equipment," said Dr. Louis Weinstein of Tufts Medical School in Boston, one of the country's leading infectious disease experts.

"As they pass needles and syringes around, they spread the bugs," he added. "The reason is nothing more complicated than just that."

Statistics about such cases are not available because no national reporting system exists and because doctors seldom list "drug abuse" on death certificates.

Dr. Donald B. Louria of the New Jersey School of Medicine said that for 20 years infections have been an important problem among drug addicts in large cities like Jersey City.

"But where suburban youngsters are beginning to use heroin, or 'speed,' obviously there will be a big increase in infections," he said.

Several doctors observed that thousands of drug abusers—even persons who injected drugs just one time—had spent weeks, even months, at basic costs of $100 a day in Bellevue, Harlem and similar municipal hospitals throughout the country for treatment of hepatitis, tetanus, malaria, and infections of the skin, bone, brain and other areas.

In some municipal hospitals, one of every 10 patients is said to be a drug abuser with a serious infection.

Patients, parents and families, subscribers of private health insurance policies like Blue Cross-Blue Shield, and taxpayers spend millions of dollars each year for care of such patients.

To heighten awareness of how devastating infections can be among drug abusers, the American Medical Association, in an editorial in its journal, recently told doctors:

"Any physician may encounter an addict for reasons other than a craving for the narcotic."

The sophisticated medical treatments discovered in recent decades have helped to save some infected drug abusers from premature deaths. Yet last year, 24 young adults in New York City died from heart infections called bacterial endocarditis that resulted from skin punctures.

As a case in point, Dr. Michael M. Baden, deputy medical examiner of New York City, cited the recent death of a 24-year-old girl from an upper middle class family here who had mainlined drugs like morphine and methadone but not heroin for the last few months.

Boils developed where contaminated needles had repeatedly pierced her skin. Staphylococcal bacteria traveled through her veins and lodged on the tricuspid valve, one of the four sets of leaflets that are critical for normal cardiac function.

The golden-colored staph bacteria "chewed up" a portion of the valve. Clots of blood, which formed on the damaged valve, became infected.

Small fragments of the infected clots, called septic emboli, broke off the tricuspid valve and were carried from the right heart ventricle into the lungs where they destroyed air sacs and led to formation of scores of tiny abscesses that caused a high fever and difficult breathing. Despite treatment with tens of millions of units of antibiotics, she died.

Because even with antibiotic therapy, endocarditis can kill swiftly, some doctors are now treating such patients more vigorously. At Bellevue Hospital, Dr. Fred T. Valentine, said:

"If any patient comes in with fungia endocaritis—the nastiest type to treat—often we must do open-heart surgery."

Despite the rising incidence, some doctors are amazed that the toll is not higher. As Dr. Tazewell Banks of the (Washington) D. C. General Hospital concluded:

"It's surprising everyone on heroin [or injecting drugs] doesn't get staph infections with such unsanitary conditions."

[From the New York Times, Thursday, June 3, 1971]

13. Physician Draws Jail in Drug Case

Doctor convicted of abusing amphetamine also fined

(By Will Lissner)

A 65-year-old physician convicted of running an amphetamine "supermarket" in his office at 40 Central Park South was sentenced by a Federal Judge yesterday to five years in jail and ordered to pay a $10,000 fine.

In the first conviction of a recent drive against doctors offering "speed shots" to all applicants without examination, Judge Constance Baker Motley in the United States District Court, Southern District, rejected a plea for leniency.

Dr. Alois Peter Warren of 515 East 89th Street, the defendant, pleaded that he had injected combinations of the amphetamine and vitamins for bursitis and a variety of ills. According to medical testimony during the trial,

amphetamine has no therapeutic value in treating bursitis or the other ailments for which Dr. Warren was accused of administering the drug.

Educated in Prague

Judge Motley told the Polish-born defendant, a graduate of the University of Prague medical school who came to the United States in 1947, that the evidence was that his activities were "not a form of legitimate medical practice, "but were carried on "for the purpose of making money without any regard for the health, mental health or well being of the persons involved."

"We are dealing here with what can only be described as a menace to the community and to the health and safety of the people of this district," said Judge Motley.

Noting that one of the witnesses had come here from Texas and had testified that he had been taking the shots for a long period, Judge Motley said "this is also a national health hazard."

Big profit cited

In the trial, concluded May 28, a narcotic agent testified that Dr. Warren had sold him a large quantity of liquid amphetamine and 260 hypodermic syringes, which together cost the physician $105, for $2,400.

Former patients told of becoming physiologically dependent on the drug, used in the treatment of over-active or hyperkinetic children and of pathological sleepiness, narcolepsy.

The physician has a son in college.

His wife, stunned, watched as the judge delivered the sentence and considered a lengthy plea by the defense counsel, Sidney O. Raphael, for a stay pending appeal. "There is no substantial question on which to base an appeal," Judge Motley ruled.

The assistant United States Attorney, Walter J. Higgins Jr., argued that the facts established a design to violate the laws restricting the dispensing of dangerous drugs.

[From the Evening Star, page A–3, Mar. 13, 1972]

14. U.S. Peps Up Its Drive to Curb Pep Pills

(By Miriam Ottenberg, Star Staff Writer)

The millions of American users of "pep pills" are going to find them much harder to get from both legitimate and black market sources.

The Bureau of Narcotics and Dangerous Drugs has backed up its recently announced 83 percent cutback in amphetamine production and 80 percent cutback in methamphetamine production with half a dozen moves to curb the illicit traffic.

That's on top of the controls imposed on the amphetamines last year, particularly the one hardest—the ban on refilling hitting the drug users the amphetamine prescriptions.

The synthetic stimulants, known to users as "pep pills," "bennies" (short for benzedrene) and "speed," are abused particularly by straying teen-agers, drug dependent housewives and obese people who use them while trying to lose weight.

Because continued misuse may result in psychosis, physical exhaustion, paranoia, hallucinations and even violent behavior, the government has become increasingly involved in curbing it.

Here are the steps now being taken at home and abroad to get the pills off the legitimate and illegitimate markets:

1. On Feb. 12, amphetamine production was cut from about 935,615,500 dosage units or pills in 1971 to 269,800,000 for 1972, compared to an industry request for a 1972 quota of over 3-billion dosage units.

Methamphetamine production was cut from 492,625,600 dosage units in 1971 to 116,300,000 in 1972, compared to an industry request for a 1972 quota of over 1 billion dosage units. The average dosage unit is 10 milligrams.

2. Since the demand remains, the bureau suspects there will be increasing pressure to manufacture amphetamines clandestinely. But the illicit producers have to have certain basic chemical materials before they can go into production and the bureau wants to stop them before they're well started.

"We have a liaison program with chemical supply houses which closely monitor to whom they're selling the precursor materials," on a voluntary basis, said Kenneth A. Durrin, BNDD assistant director for compliance.

3. The Bureau is working with the Mexican government to shut off the sources of diversion that agents identified during Operation Blackjack. In that investigation, 59 persons were arrested in connection with the illegal sale of approximately 1 million dosage units of bifetamina, an amphetamine product of the Strasenburgh Co., then the largest amphetamine exporter in the United States.

U.S. agents are now working under cover with Mexican federal police to make illegal sale cases. The United States government also is sending experts to Mexico to work with Mexican authorities on auditing and inspecting Mexican amphetamine producers to determine whether excess amphetamine is being distributed in Mexico.

4. In addition to working with Mexico to prevent its future use as an illegal amphetamine source, bureau offices around the world have been ordered to monitor the movement of amphetamine material overseas to determine any trends indicating new pipelines into the United States.

5. In the past, legitimate U.S. firms who wanted to make some illegitimate money could divert their amphetamine to the black market by ostensibly shipping a consignment of the drug to a foreign consignee but actually shipping some other product.

Now that loophole has been closed. Senders now have to have a permit and a corresponding permit for the country of destination. Since the foreign government has to check the permit, a fictitious corporation at the other end is no longer feasible.

6. Agents are examining the drug-dispensing records of the so-called "fat doctors," those who make considerable fortunes simply by peddling amphetamine to the obese.

Some cases have been made but Durrin said that as long as the Food and Drug Administration finds amphetamines effective for coping with short-term obesity and as long as the doctor has a valid state license and has not been convicted of a major drug violation or falsified his application for a drug registration, the bureau can't interfere with his dispensing of amphetamines.

FDA has already said amphetamines are not effective against long-term obesity. The agency is slated to decide by July 1 whether it still considers amphetamines effective against short-term obesity. Meanwhile, a number of medical societies have urged their doctors to voluntarily curb the prescription of amphetamines.

What's going to happen to those dependent on amphetamines? Durrin does not think they will turn to heroin because it's a depressant and what they want is a stimulant.

"What we're hoping," he said, "is that people can satisfy their life-style some other way and escape from their psychological dependence on amphetamines."

[From Time, page 44, Jan. 31, 1972]

15. Speed and Strokes

The elderly are most often victims of strokes—the circulation stoppages in the brain that can cause paralysis and death. Yet for five years doctors at the University of Southern California Medical Center have been noticing an increase in young stroke victims and looking for an explanation. Now they have found one. Reporting in the journal *Radiology*, a U.S.C. research team has disclosed evidence that methamphetamine, or "speed," one of the most widely used of the current "pop" drugs, can cause deterioration of the small blood vessels of the brain.

DYE PATH

A link between amphetamines and circulatory problems was first suggested in 1970 by Dr. B. Philip Citron. He observed the signs of widespread small-vessel deterioration in 14 young drug abusers, most of whom mainlined speed. Four of them died as a result. Observation of nearly 100 other patients since then has strengthened Citron's initial theory.

A controlled experiment by a second research team has provided still more proof. Dr. Calvin Rumbaugh of the hospital's radiology department had already examined 19 patients by cerebral angiography, an X-ray technique in which a dye is injected into the brain's arteries to enable doctors to follow its path through the smaller blood vessels. The tests showed most of the patients to be suffering from occlusion, or blockage, of the small arteries. To determine whether speed could cause such damage, Rumbaugh and his team injected five rhesus monkeys with methamphetamine every other day for two weeks. Then the scientists killed and autopsied the five, plus two animals that had received no drugs but had otherwise been kept under identical conditions. Neither of the drug-free monkeys showed any sign of brain damage. But all five of the others, which had received speed doses comparable to those taken by many thrill-seeking youngsters, had irreversible brain damage in the areas around the small blood vessels—similar to the damage found in humans who die from strokes.

(E) Glossary of Terms and Drug Bibliography Relating to the Use and Abuse of Amphetamine Diet Pills

1. Drug Abuse Research and Education Presents Glossary of Slang Terms Associated With Today's Youth and Their Drugs of Abuse (pages 1–12)

Apapulco Gold—A form of marijuana.
Acid—LSD, lysergic acid diethylamide.
Acid head—LSD user.
Amping; over amping—See "O.D."
(Where Its)—Where (drug) action is taking place.
Babysit—To guide a person through his drug experience.
Backwards—Term applied to tranquilizers.
Bag—A container of drugs.
(Finding Your) Bag—See "Doing Your Thing."
Balloon—Rubber toy balloon used for storing or delivering narcotics, usually capped heroin in bulk form but occasionally papered or capped.
Barbs—Barbiturates.
Bennies; Beans—Amphetamines (benzadrine).
Bindle—A small paper jacket of heroin, morphine, cocaine or methedrine.
Blast; Blow—To smoke a marijuana cigarette.
Blow Your Mind—To get high or on drugs.
Blue Bands—(Pentobarbital Sodium).
Blue Cheer—Type of LSD.
Blue Birds; Blue Devils; Blue Heaven; Blues—Amobarbital capsules (Amytal; Amobarbital Sodium).
Bogart (from Humphrey Bogart)—To "Bogart a joint" is either to salivate on or to retain (and not pass around) a marijuana cigarette.
Bombed—Intoxicated on drugs.
Boo—Cannabis.
Booster—Consumption or injection of additional dosage to continue or prolong a "trip."
Bottle Dealer—A person who sells drugs in 1000 tablet or capsule bottles.
Bread—Money.
Brick—Kilo of marijuana in compressed brick form.
Bridge—See "Crutch"—usually alligator clamp or like device used to hold marijuana cigarette while smoking same.
Bummer; Bum Trip—A "bad trip"—See "freak trip," "freak out."
Burn—To accept money and give no drug in return, or to give a substance in lieu of the drug; also, to burn the skin when injecting.
Burned—Used to describe the acquisition of bad drugs, diluted drugs, or no drugs at all.
Button—Peyote buttons (containing the psychedelic, mescaline).
Buy—To purchase drugs.
Can—One ounce of marijuana. Term derived from tobacco can in which marijuana was commonly sold in the past. Now, it is more frequently sold in small plastic or paper bags.
Candy—Barbiturates.

Cap—Capsule containing a drug; commonly a number 5 capsule.
Cargo—Load of supply of narcotics or drugs.
Carrying—In possession of a drug.
Cartwheel—Amphetamine tablet (round, white, double scored).
Cents—C.C.'s—cubic centimeter.
Chalk—Methamphetamine.
Chicken Powder—Amphetamine powder for injection.
Chip; Chippy; Chipper—To play around with a drug; to use drugs sporadically.
Christmas Tree—Tuinal.
Clean—To remove stems and seeds from marijuana; also, refers to an addict who is free from needle injection marks; also, not holding or possessing any narcotics.
Cocktail—A regular cigarette into one end of which a partially smoked marijuana cigarette is inserted so as to waste none of the drug.
Coke—Cocaine.
Cold Turkey—Trying to break the habit. "Kicking it cold turkey" is breaking the habit of addictive drug use at home, in prison, etc., without the aid of any medication or medical care.
Come Down—To come off of drugs.
Connect—To buy drugs.
Connection—Refers to the peddler of source of supply for the user.
Contact High—A feeling of being on drugs or "high" from merely being in contact with someone or something reminding one of drugs.
Cooker—Bottle cap for heating drug powder with water.
Cool—See "groovy."
Co-Pilots—Amphetamines.
Cop, To Cop—To get drugs.
Cope—To handle oneself effectively while under the influence of drugs.
Crash—To end a drug experience, particularly from an amphetamine like methedrine.
Crash Pad—Temporary residence, usually for a night or two, usually communal, often used to end a drug experience.
Crazy—Exciting, in the know, enjoyable.
Crutch—Device used to hold marijuana cigarette when it has burned to the point where it will burn the fingers—usually a half of a paper match book. Also, a container for a hypodermic needle.
Crystal—Methedrine (methamphetamine), "speed," or other amphetamine.
Crystals—Amphetamine powder for injection.
Cube—Sugar cube impregnated with LSD.
Cut—To dilute a powder with milk, sugar, baking powder, etc.
"D"—LSD.
Dealer—A drug peddler.
Dexies—Dextroamphetamine sulfate or Amphetamine tablets, a mixture of barbiturate and amphetamine.
DMT—Dimethyltryptamine, a psychedelic, nicknamed "the businessman's LSD."
Dime or Dime Bag—Ten dollars' worth of drugs.
Deuce Bag—A two-dollar container of a drug.
Doing—May be any "happening"; but specifically the taking of a drug.
Doing Your Thing—Doing what seems best to you; finding your "bag."
Dope—Any drug.
Doper—Drug user.
Dotting—Placing LSD on a sugar cube.
Double Cross—Amphetamine tablets (double scored).
Downer—A depressant drug such as a barbiturate or tranquilizer; also a "bum trip"; also, to come off of drugs.
Dreamer—One who takes opiates or morphine.
Fat—Describing someone who has a good supply of drugs.
Fine Stuff—Drugs of unusually good quality, only slightly adulterated.
Fit; Outfit—Equipment for injecting drugs.
Fix—To inject drugs or one dose of a particular drug—also "Outfit."
Flash—The intense feeling the user has just after "fixing"; to throw up after "fixing."

Flashback—Reoccurrence of the drug reaction, from LSD weeks to months later without taking the drug again.

Flush—The initial feeling the user gets when injecting a drug like methamphetamine.

Footballs—Amphetamines (oval shaped).

Forwards—Pep pills, especially amphetamines.

Frantic—Nervous, jittery drug user.

Freak—One who has flipped, i.e., one who uses drugs to the point of loss of reality; especially used as "speed freak" referring to a heavy methedrine user.

Freak Out—To lose all contact with reality; to have a drug party.

Freak Trip—Adverse drug reaction, especially with LSD.

Fuzz—The law.

Garbage—Poor quality drugs.

Geeze—Injection of drugs.

Go—To participate freely in the drug scene.

Good Go—A good or reliable dealer in drugs.

Goof Balls—Barbiturates; any barbiturate tablet or capsule, may be combined with an amphetamine.

Goofer—One who uses pills.

Goofed Up—Under the influence of barbiturates.

Going Up—Taking drugs for their effects; said of smoking cannabis or injecting "speed," etc.

Giggle-Smoke—Cannabis, or cannabis smoke.

Grass—Marijuana in the raw state, such as leaves, stems, seeds.

Grasshopper—Marijuana user.

Grass Brownies—Cookies containing cannabis.

Groovy—Good; "out of sight."

Griffo—Cannabis.

Guide—One who "babysits" with a novice when he goes up on a psychedelic substance.

Gun—See "Outfit."

H.—Heroin.

Habit—Physically or psychologically dependent on drugs; addiction to drugs.

Hallucinogens—See psychedelics.

Hand-to-Hand—Delivery of narcotics person-to-person.

Hash, Hashish—Resin from the Cannabis Indica plant which contains a very high tetrahydrocannabinol content.

Hashbury—Haight-Ashbury, District of San Francisco.

Head—Chronic user of a drug or drugs.

Hearts—Amphetamines, specifically dextroamphetamine and benzedrine sulfate; also dexedrine (orange colored, heart shaped tablets).

Heat—A Police Officer—the law.

Heavy—Significant, weighty; highly emotional.

High—Under the influence of a drug, usually a stimulant. A drug user who is "up."

Hit—One dose of a particular drug.

Hog—A drug user who takes all of a drug he can get his hands on.

Holding—Possessing narcotics.

Hooked—Addicted; a confirmed addict.

Horning (Snorting, Sniffing)—Sniffing narcotics through nasal passages.

Hype—One who uses intravenous drugs, specifically heroin or "speed."

Hype Outfit—Equipment for injecting drugs.

Ice Cream Habit—Sporadic use of drugs.

J or Jay—"Joint" or marijuana cigarette.

Jar Dealer—A person who sells drugs in 1000 tablet or capsule bottles.

Joint—A marijuana cigarette.

Jolt—An injection of narcotics.

Joy Pop—Intermittent (rather than continuous) injection of one dose of a drug; also one who is "joy popping" only takes an injection now and then.

Jug—1000 tablet or capsule bottle.

Junk—Heroin.

Kee—Kilo.

Keg—25,000 Amphetamine capsules or tablets, or more.

Kick, Kicking—To stop using drugs (see "cold turkey").

Kicks—A drug experience.
Kilo—2.2 pounds.
Kit—Same as "Outfit" or narcotic paraphernalia.
"L"—LSD.
Lab—Equipment used to manufacture drugs illegally.
Laid Out—Being informed on.
Lame—Not very smart, dumb, or green, not street wise.
Lean—A non-drug user.
Lid—See "Can."
Loaded—High on drugs; under the influence of drugs.
Magic Mushroom—The Mexican species of mushroom, containing psilocybin, a psychedelic.
Main-Line—Veins of body, usually arms; also intravenous injection.
Main-Liner—One who injects narcotics directly into the veins, intravenously.
Make It—To buy narcotics; to leave the scene, area.
Man (The)—The law; or a connection (drug supplier).
Manicure—Prepare marijuana for use in cigarettes—removing seeds and stems.
Mary Jane—Marijuana—an old term, rarely used.
Matchbox—A small amount of cannabis sufficient to make between five to eight cigarettes; about a fifth of a lid.
MDA—A hallucinogen, methyl-3, 4-methylenedioxyphenethylamine.
Mellow Yellow—Refers to smoking banana skins, a hoax as they contain no mind altering drugs.
Mickey; Mickey Finn—Chloral Hydrate.
Mind Blower—Pure, unadulterated drugs.
Mohasky; Mu; Muggles—Cannabis.
Mota—Marijuana.
Mule—A person who delivers or carries a drug for dealer.
Narcotic—Refers to the natural and synthetic derivatives of opium (morphine, heroin, codeine); not a synonym for drugs.
Nark—Narcotics Agent.
Needle—Hypodermic needle.
Nickle Buy—A $5.00 (five dollar) purchase.
Number—A joint.
O.D.—Overdose of drugs, usually heroin.
Ope—Opium.
Out of It—Not in contact, not part of the drug scene.
Out of Sight—Good; groovy; a positive descriptive term.
Outfit; Fit—Equipment for injection by hypodermic method; a "hype" outfit—eyedropper and needle, spoon pacifier, etc.
Owsley's Acid—LSD purportedly illegally manufactured by Augustus Owsley Stanley III, also infers that it is good quality LSD.
Oz—Ounce—Refers to ounce of narcotics, usually heroin or meth.
Panama Red—A potent type of South American cannabis.
Panic—Refers to condition when the drug supply has been cut off (usually caused by the arrest of a big peddler); a scarcity of drugs.
Paper—A container of drugs.
Peace Pill; P.C.P.—Refers to the drug phencyclidine, originally an anesthetic for dogs.
Per—A prescription.
Pez—Pez candies impregnated with LSD.
Piece—A pistol, revolver.
Pig—See "Hog."
Pill Head; Pill Freak; Pilly—Amphetamine or barbiturate user.
Poke—A puff on a "joint."
Point—Hypodermic needle.
Pop—A subcutaneous injection, usually referred to as "skin poppin."
Popper—Amyl Nitrate in ampule form, inhaled.
Pot; Pothead—Marijuana (user).
Pot Likker—Cannabis tea, usually made with regular tea boiled with cannabis leaves.
Powder—Amphetamine powder.
Psychedelic—Means a drug whose actions primarily effect the mind; i.e., "mind-manifesting" (LSD, marijuana, etc.).

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Pusher—Drug peddler to users; one who seeks more business from regular customers.

Put Down—Stop taking (drugs).

Quarter—Quarter of an ounce of either heroin or meth, usually 4 to 8 grams.

Rainbows—Tuinal (Amobarbital Sodium and Secobarbital Sodium).

Red; Reds; Red Birds; Red Devils—Seconal (Secobarbital Sodium).

Reds & Blues—Tuinal (Amobarbital Sodium and Secobarbital Sodium).

Reefer—Marijuana cigarette.

Register—To wait until blood comes into the "hypodermic" before injecting a drug intravenously.

Righteous—Good quality drugs.

Rip Off—To forcibly rob a peddler of his drugs or money.

Roach—Small butt of marijuana cigarette.

Roll, Roll Deck—A tin foil wrapped roll of tablets.

Roll Dealer—A person who sells tablets in rolls.

Run—To take drugs continuously for at least three days.

Rush—See "Flash."

Score, Scoring—Make a drug purchase.

Script—Drug prescription.

Shooting Gallery—Place where users can purchase drugs and inject them. Place where an injection of drug can be used and/or bought.

Shoot Up—To inject drugs.

Shot—An injection of a drug.

Skin popping—Intradermal or subcutaneous injection.

Sleepers—A depressant type drug such as barbiturates.

Smack—Heroin.

Smashed—Intoxicated, "stoned," high."

Sniffing; Snorting (Horning)—Using narcotics by sniffing through nasal passages, usually heroin or cocaine.

Snitch—Informer, stoolie.

Snow—Cocaine.

Snowbird—Cocaine user.

Source—Where narcotics are obtained; supplier, such as pusher, dealer, connection.

Space Out; Spaced—In a daze, particularly a daze resulting from a trip due to use of drugs.

Spatz—Capsules.

Speed—Methedrine (methamphetamine) or crystal; now broadened use in some areas to mean any amphetamine or any stimulant.

Speed Freaks—See "Freak."

Speedball—A powerful shot of a drug, usually heroin and cocaine combined.

Spike—Hypodermic needle.

Split—To leave, flee, break up with.

Splash—Speed.

Spoon—A quantity of heroin, theoretically measured on a teaspoon (usually between 1 and 2 grams), 16 spoons per ounce.

Square—A person who does not know what's happening—a nonuser.

Stanley's Stuff—LSD purportedly manufactured by Augustus Owsley Stanley III. See "Owsley's Acid."

Stash—Place where narcotic or "outfit" is hidden; also, refers to one's own supply of drugs.

Stoned—Under the influence of drugs.

Stoolie—Informer, see "Snitch."

STP—Serenity, Tranquility, Peace—a drug mixture of methdrine and psychedelic compounds (4-Methyl 2, 5 Dimethoxy Alpha Methyl Phenethylamine), DOM-hallucinogenic drug.

Straight (Teen Meaning)—(1) Under the influence of narcotics; (2) Applied to a peddler—gives a good deal.

Strung Out—Heavily addicted or hooked.

Stuff—General term for drugs and narcotics.

Syndicate Acid—STP.

Taste—A small sample of a narcotic.

TD Caps—Time disintegrating capsules.

Tea—Cannabis, marijuana.

Toke Up—To light a marijuana cigarette.

Torn Up—Intoxicated, stoned.
Tracks—A series of puncture wounds in the veins, caused by continued narcotic injections.
Travel Agent—A pusher of hallucinogenic drugs.
Trey—A $3.00 (three dollar) purchase.
Trigger—To smoke a marijuana cigarette immediately after taking LSD.
Trip—The hallucinations and/or feelings experienced by a person after taking a drug, particularly LSD.
Turn On—To use drugs, or to introduce another person to the use of drugs.
"Turn On, Tune In, Drop Out"—Take LSD, learn about the "real" world and drop out of the non-drugged world.
Upper—Amphetamine.
Up Tight—Angry; anxious; (may rarely also be used to mean good, as in the words to a song "Everythings up tight, out of sight").
User—One who uses drugs.
Vibes, Vibrations—Feelings coming from another; may be "good" or "bad" vibes.
Wasted—High or drunk.
Wedges—Small tablets of wedge (almost triangular) shape.
Weed—Marijuana.
Weed Head—Marijuana smoker.
Weekend Habit—Irregular drug habit.
Weird—On drug.
West Coast Turn-Arounds—Amphetamine tablets or capsules.
Wheels—Car, automobile.
Whites—Amphetamine tablets.
Wig Out; Wigging—See "Blow Your Mind."
Works—Equipment for injecting drugs.
Yellow Jackets, Yellows—Nembutal (Pentebarbital Sodium).

[By D.A.R.E. (Drug Abuse Research and Education), Los Angeles, Calif.]

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2. Engage Volume 4, No. 1, October 1971, Pages 59–61, Published by the Board of Christian Social Concerns of the United Methodist Church

GLOSSARY OF TERMS SPECIFYING UPPER AND DOWNERS [1]

Abscess.—Infected injection site.
Amphetamines.—Bennies, Co-Pilots, Dexies, Dynamites, Eye-Openers, Hearts, Lid Proppers, Marathons, Peaches, Pep Pills, Roses, Truck Drivers, Wake-Ups, Cartwheels, Footballs, Greenies, Crystal, Meth, Crank, Crink, Cris, Christian, Speed, Bombidos, Bottles, Amped, Jugs, Cross Tops.
Baggie.—Used as package for various powders and grass.
Ball.—Absorption of stimulants and cocaine via the genitalia.
Balloon.—Used as package for heroin.
Bang.—Injection of drugs.
Barbiturate.—Barbs, Candies, Peanuts, Pills, Purple Hearts, Sleeping Pills, Softballs, Blues, Blue Birds, Blue Bullets, Blue Devils, Blue Dolls, Blue Heavens, Double Trouble, Blue Tips, Rainbows, Reds and Blues, Nimbies, Yellows, Yellow Bullets, Yellow Jackets, Pinks, Reds, Red Birds, Red Bullets, Red Devils, Seccies, Seggies, Phennies.
Barbs.—Barbiturate drugs.
Bent.—High or intoxicated from a drug.
Bindle.—Packet of narcotics.
Blow.—To inhale heroin or cocaine through the nose.
Bombita.—Amphetamine injection, sometimes taken with heroin.
Boot.—To prolong the injection by advancing the plunger slowly.
Bottles.—Injectable methamphetamines.
Browns.—Long acting amphetamines.
Bum Out.—Refers to downer experience.

[1] The glossary is designed to acquaint readers with the street jargon relating to drugs. The list is incomplete, for the terms above refer prmarily to stimulants and depressants. The use of the words varies from town to town and from one day to the next. However, knowledge of the slang helps facilitate communication on this subject.

Candy.—Cocaine.
Candy Man.—Seller of drugs.
Chipping.—Taking narcotics occasionally.
Christian.—Methamphetamine.
Cocaine.—Bernice, C, Candy, Carry Nation, Cecil, Chalk, Coke Coconuts, Corrine, Dust, Flake, Frisky Powder, Sniff, Snow, White Powder.
Cokie.—Cocaine addict.
Cold Turkey.—Sudden withdrawal of drugs (from the gooseflesh, which resembles the skin of a cold plucked turkey) without benefit of medication.
Cook.—To heat the drug mixture to dissolve.
Cop.—To buy.
Crash.—To recover from a high to a normal state; also, to sleep or sleep off effects of drug.
Crystal.—Methamphetamine.
Cut.—Dilute drugs by adding milk sugar or another inert substance.
Deck.—Packet of narcotics.
Downers.—Sedatives, alcohol, tranquilizers, and narcotics.
Dried Out.—Detoxified, withdrawn from a drug.
Dummy.—Equipment for injection.
Dynamite.—term used to indicate quality—if it's dynamite you know it's really good stuff.
Edge.—Unpleasant effects of stimulants "edgy"—nervousness.
Fix.—Injection of narcotics.
Flash.—A feeling of excitement or pleasure; a quick jolt felt in the abdomen as the injected drug enters the blood stream.
Freak.—A person may be termed a "downer freak" or "upper freak" if they limit themselves to one of those drug experiences.
Garbage.—Weak, heavily diluted heroin.
Gee.—Intravenous injection.
H.—Heroin.
Habit.—Being physically dependent upon a drug.
Hard Narcotics.—Opiates, such as heroin and morphine.
Hard Stuff.—Heroin.
Head.—One who refers all drug effects to how it affects thinking, delusions, hallucinations.
Heroin.—Boy, Caballo, Corga, Doojee, H, Hairy, Harry, Horse, JeeGee, Joy Powder, JoJee, Junk, Smack, Schmack, Schmeck, Shit, Scott, Scag, Skot, Tecata, White Stuff, Dope.
Hit.—A single dose of a drug.
Honeymoon Stage.—Period when a heroin user is not yet dependent on the drug.
Hophead.—A drug dependent person.
Horse.—Heroin.
Hot Shot.—An injection of an impure drug or one of too high a dose.
Hustle.—From the perspective of an outsider or street person, everybody has a "hustle", i.e., their particular variety of behaviors designed to get what they want or need.
Icecream Man.—A seller of opium.
Jolly Beans.—Pep pills.
Jones.—habit or addiction; heroin habit.
Joy-Pop.—Inject narcotics irregularly.
Jugs.—Injectable methamphetamines.
Juice.—Hard liquor.
Juicer.—One who prefers alcohol.
Junkie—Heroin addict; a seller of drugs.
Kick.—A feeling of excitement or pleasure.
L.A.—Long-acting amphetamines.
Layout.—Equipment for injecting drug; or outfit.
Lemonade.—Poor quality heroin.
M.—Morphine.
Machine.—Syringe, needle, bottle cap, and cotton swab for injections.
Mainline.—Vein; to inject into a vein.
Meth.—Methamphetamine.

Methadone.—Dolly.

Methamphetamines.—Crank, Crink, Cris, Christian, Meth, Bombidos, Bottles, Jugs, Crystals, Speed, Amped.

Meth Freak.—A frequent user of methamphetamine.

Meth Head.—A frequent user of methamphetamine.

Meth Monster.—A frequent user of methamphetamine.

Mixing.—Using uppers and downers one after the other.

Morphine.—Dope, Hard Stuff, Hocus, Mary Ann, Miss Emma, MoJo Morpho, White Stuff.

O.D.—an overdose.

On the Nod—Sleepy from narcotics.

Over Amped.—Extremely high dose of stimulant.

Pill Head.—Heavy user of pills, barbiturates or amphetamines or both.

Pill Popper.—Persons who use pills.

Purple Hearts.—A combination of dextroamphetamine and amobarbital (from the shape and color).

Quill.—A matchbook cover for sniffing methamphetamine, cocaine, or heroin.

Rainbows.—Amobarital and Secobarbital combination in a blue and red capsule.

Reds or Red Devils.—Secobarbital capsules.

Ripped.—Synonymous with being under the effects of drug.

Rip Off.—Some one who will take advantage of you; Stealer; synonymous with Barb Freak or Downer Freak; to steal.

Run.—A period of addiction, as in "I had a year run."

Rush.—The feeling when an infected drug enters the blood stream.

Scoop.—A makeshift object from which to sniff cocaine or heroin (matchbook).

Shooting Gallery.—Place where addicts inject.

Skin Pop.—To inject drugs under the skin.

Snort.—Inhale drugs.

Snow.—Cocaine.

Speedball.—An injection of a stimulant and a depressant, originally heroin and cocaine.

Speed Freak.—Persons who use amphetamines frequently.

Spoon.—A measure of heroin, or coke, cocaine (1/16 ounce).

Strung Out.—Addicted.

Stuff.—Narcotics, usually heroin.

Switching.—Changing preference from one drug, or a person or sexual behavior, etc., to another.

Tracks.—Scars along veins after many injections.

Tree.—Tuinals, a moderately long-losting rapidly effective sedative.

Turnabouts.—Long-acting amphetamines.

Turps.—Elixir of Terpin Hydrate with Codeine, a cough syrup.

Uppers.—Stimulants, cocaine, and psychedelics.

Wasted.—The drug effect has taken over ego functions or even autonomous body functions.

Works.—Syringe, needle, bottle cap, and cotton swap for injections.

Yellow Jacket.—Barbiturate in a yellow capsule.

Yen Sleep.—A drowsy, restless state during the withdrawal period.

Zapped or zonked.—The effects of a drug—could be either upper or downer.

[Drug Education Bibliography, The National Coordinating Council on Drug Education, 1971, pages 25–27]

3. Stimulants

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"Kids are very different today,
I hear every mother say:
Mother needs something today to calm her down.
And though she's not really ill,
There's a little yellow pill—

"She goes running for the shelter
Of her mother's little helper,
And to help her on her way,
Gets her through her busy day—

"Things are different today,
I hear every mother say:
Cooking fresh meat for her husband's just a drag.
So she buys an instant cake
And she burns a frozen steak.

"And she goes running for the shelter
Of her mother's little helper,
And to get her on her way,
Gets her through her busy day. . . .

"Doctor, please,
Some more of these;
Outside the door,
She took four more. . . ."

—*The Rolling Stones (1966)*