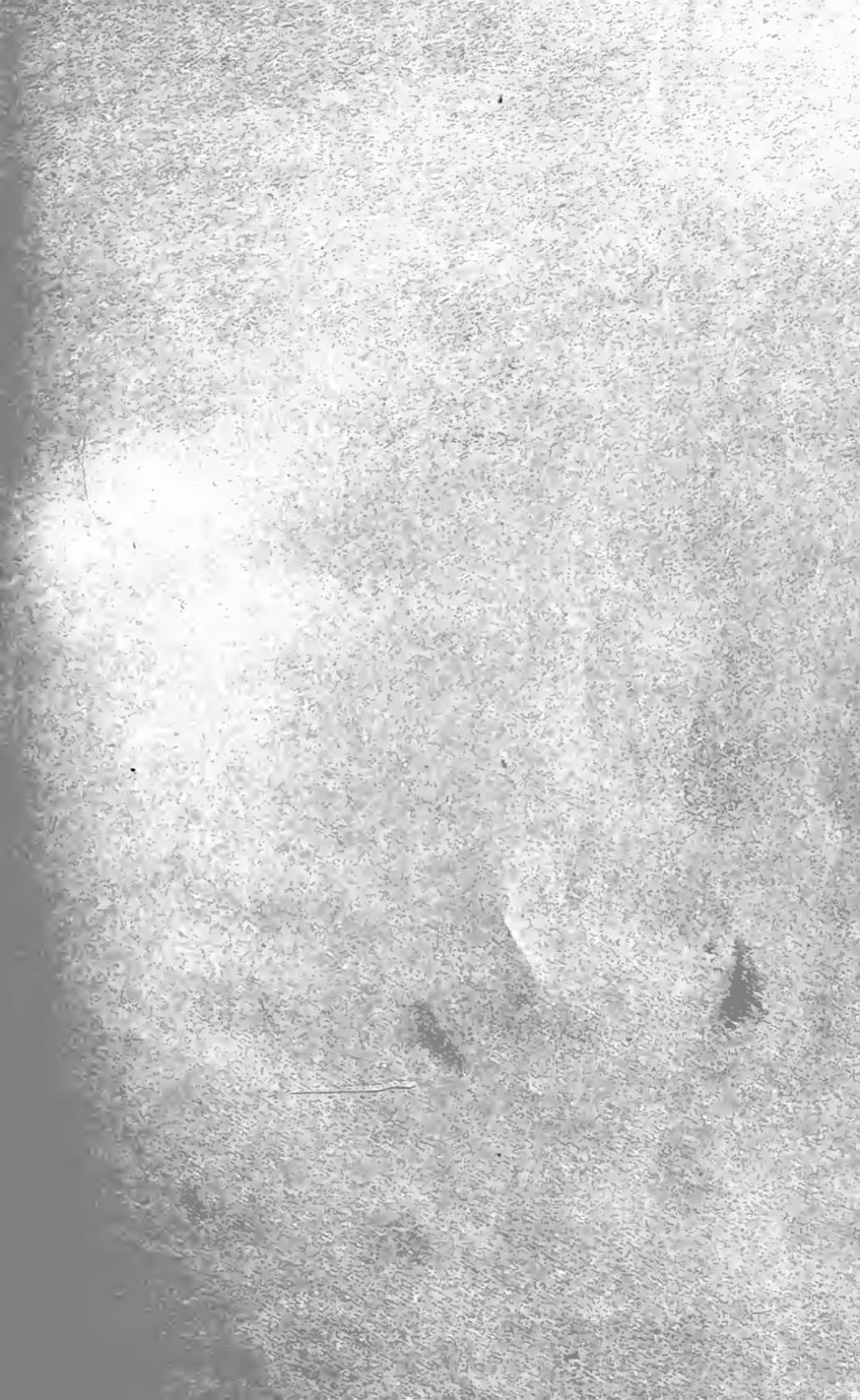




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THE THYROID GLAND

CLINICS OF
GEORGE W. CRILE
AND
ASSOCIATES

EDITED BY
AMY F. ROWLAND

WITH 106 ILLUSTRATIONS

PHILADELPHIA AND LONDON
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THE THYROID GLAND

INTRODUCTION

THE purpose of the series of clinical volumes of which this is the first is to present the present theoretic and practical viewpoints of my associates and myself—to present the Clinic at work. Both theory and practice, therefore, will be constantly subject to revision and possibly reversal of opinion. Since this is but an ephemeral publication, representing today's viewpoint in this Clinic, and does not purport to be a text-book or a monograph, but little reference will be made to the literature, excellent summaries of which are given by Crotti.¹

As we have chosen the thyroid gland as our theme for this volume, we wish first of all to express our sense of the obligation of medicine to Theodore Kocher in Europe for the secure foundation laid by him for surgery of the thyroid gland, to the Mayo Clinic, and to Marine, Lenhart, and Kimball for notable contributions in this field.

Our discussion in the following pages will be centered around the following principal points:

- (a) Endemic goiter is a geologic deficiency disease due to a lack of iodine in the organism.
- (b) By the proper administration of iodine to the pregnant mother, and to the child up to and through the period of adolescence, endemic goiter may be prevented; that is to say, the children of goitrous regions may be as goiter free as are the children of the seashore.

¹ Crotti, A., *Thyroid and Thymus*, 1918.

- (c) After the twenty-fifth year of age iodine exerts little or no beneficial effect on goiters.
- (d) By the improper use of iodine or thyroid products many cases of quiescent goiter, especially of the adenomatous type, are converted into exophthalmic goiter or hyperthyroidism.
- (e) Induced hyperthyroidism is essentially identical with spontaneous hyperthyroidism.
- (f) About 90 per cent. of all malignant tumors of the thyroid arise in the fetal adenomata. Therefore, iodine given the pregnant mother may prevent fetal adenomata, hence cancer of the thyroid, in the offspring.
- (g) Colloid goiters, colloid adenomata, and adenomata in patients with normal sensitization and normal metabolism may be considered as simple or quiescent goiters.
- (h) Hyperthyroidism may be associated with a colloid goiter (rare), colloid adenoma, adenoma, or hyperplasia. Hyperthyroidism presents no uniformly specific pathology of the thyroid gland.
- (i) With certain exceptions the increased sensitization of the organism due to hyperthyroidism is manifested by abnormal nervousness, tachycardia, tremors, increased basal metabolism, and loss in weight.
- (j) With certain exceptions increased sensitization due to hyperthyroidism is specifically exaggerated by the injection of adrenalin (Goetsch test).
- (k) Basal metabolism estimation provides a valuable, but not a specific test for the presence of hyperthyroidism. Basal metabolism estimations are of value in the differential diagnosis of borderline

cases, but are of little value in the determination of the operability or prognosis of cases of hyperthyroidism.

- (l) In a small group of cases goiter may cause myocarditis and hypertension without involving the nervous system.
- (m) We shall offer the general hypothesis that the body is an electrochemical mechanism in which the electric conductivity, hence oxidation, is controlled by the thyroid.
- (n) We shall show that the electric conductivity of certain active tissues and organs is increased by iodine. Therefore we may suppose that in all cases of hyperthyroidism or hyperiodism the same tissues would not be equally influenced, but that in some cases one and in others another tissue would show the greater alteration, thus producing such various types of disease as the exophthalmic type, "toxic adenoma," the myocardial and the cardiovascular types. Graves' disease, Gull's disease, Basedow's disease, exophthalmic goiter, toxic adenoma are, at best, loose and unsatisfactory terms.
- (o) We shall develop the following statements regarding the surgical treatment of hyperthyroidism:
 1. We now believe that the so-called hyperthyroidism is an intracellular acidosis which is overcome by restoring the normal acid-alkali balance. This is accomplished by the subcutaneous infusion of from 3000 to 5000 c.c. of water; by digitalizing the heart; by blood transfusion, and by rest.
 2. Any case up to the beginning of dissolution is

operable, or may be made operable by a short period of active treatment which will be described.

3. Preliminary ligations are made in about 40 per cent. of the cases.
4. The average reaction following ligation is practically the same as the reaction which follows admission to the hospital.
5. We no longer use hot-water injections, quinin and urea injections, *x*-ray or radium; but we add to surgical treatment a planned regimen of rest and diet just as if no operation had been performed.
6. In view of the surgical results we advise surgical treatment for all cases without regard to the degree of hyperthyroidism.

THE FUNCTION OF THE THYROID

GEORGE W. CRILE

THE brain drives the organisms of man and animals. Environment drives the brain. The driving power of the brain depends principally upon three organs: the adrenals, the liver, and the thyroid. The contribution of the thyroid is well illustrated by the two extremes of thyroid activity: myxedema and exophthalmic goiter. Without the thyroid the brain is dull and stupid. With excessive thyroid activity life is exquisitely tense, dramatic, and excessively responsive to every stimulus. Between these extremes the mass of humanity wends its normal way.

Coincident with conditions of special activity of the organism, as in emotion, in infection, in bearing offspring, in exophthalmic goiter, the volume of the thyroid gland is increased.

The peculiar function of the thyroid appears to be the splitting up of the iodine-containing molecules of any compound of iodine which enters the organism (Marine)—ferrous iodide, sodium iodide, potassium iodide, and the conversion of the iodine into the specific thyroid product—thyro-iodine or thyroxine (Kendall).

The crux of the thyroid problem, therefore, becomes this: *What is the fundamental function of iodine?* In attacking this question it is necessary to adopt a new hypothesis as to how the organism operates. We postulate that the organism of man and animals is an electrochemical mechanism which obeys physical laws; that the cells of the nervous

system are batteries; that the action current of stimulation is electricity; that, in accordance with Nernst's hypothesis and R. S. Lillie's researches, the nerves are biologically adapted to slowing the speed of transmission; that through oxidation electric energy is generated; that the nerve-cell as a battery is active only as long as a difference in potential between cell body and nucleus exists; that consciousness is the act of responding to the stimuli of the external and the

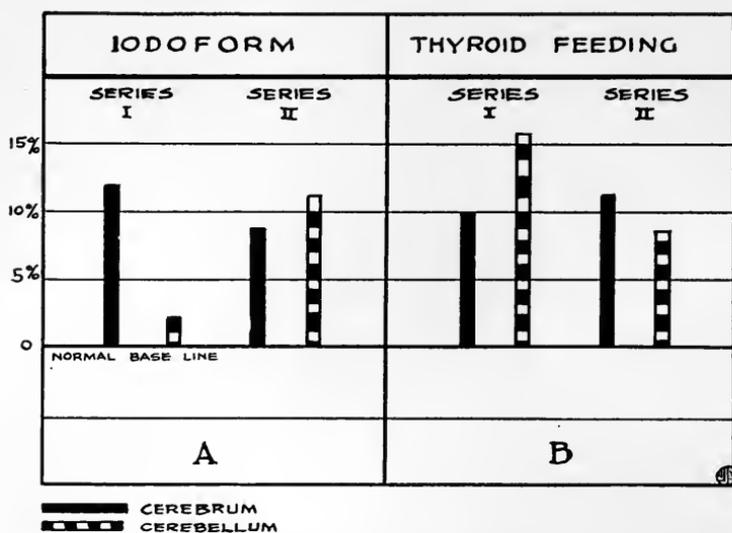


Fig. 1.—Increase in electric conductivity of the cerebrum and the cerebellum produced by iodoform and by thyroid feeding.

internal environment, and that sleep is the phase of recharging the batteries.

If we accept this hypothesis, that the organism is an electrochemical mechanism, in which increased functional activity is synonymous with increased electric conductivity, then, since iodine and increased thyroid activity alike have the power of speeding up the organism, it would follow that in iodism the electric conductivity of the brain would be increased. In the course of a research in our laboratory,

which I projected to test this point, Miss Hosmer and Miss Rowland found that the electric conductivity of the brains of animals in a state of acute iodism was increased (Fig. 1). The application of this finding to the phenomena of myxedema, on the one hand, and of exophthalmic goiter, on the other hand, would seem to indicate that in the former condition there is a state of chronic hypiodism; in the latter, chronic hyperiodism, or as C. H. Mayo designated it, hyperthyroidism.

The validity of the foregoing findings is strengthened by the work of Meyer in the Marine Laboratory in Florida, who found that iodine increased the electric conductivity of water, in which nerve was immersed, at the same rate that it increased the conductivity of the nerve itself.

In view of these findings it would appear that if iodine has the power of increasing both function and conductivity, then it should follow that in ordinary iodism the adrenalin sensitization test would be positive. In one clinical case of mild iodiform-poisoning a positive reaction to adrenalin was secured; but opportunities for such observations are necessarily, and fortunately, rare. It then occurred to us that since in most and perhaps all organs increased heat is coincident with increased function, the measurements of the actual temperature of the brain and other organs under varying degrees of activation might be of value. We therefore devised suitable copper-constantan thermocouples and installed sensitive galvanometers whereby temperature variations could be measured to one one-thousandth of a degree Centigrade.

Having found that the intravenous injection of adrenalin produced a measurable increase in the temperature of the brain, we proceeded to study the effect of the injection of adrenalin into iodized animals. Two rabbits out of four of

approximately the same weight and age, all of which had been kept for some time under identical conditions, were iodized by the intraperitoneal injection of iodoform; the other two were kept as controls. After the insertion of the thermocouple in the brain an identical dose of adrenalin per kilo weight was injected into each of these rabbits, the temperature reading being continuous before, during, and for a sufficient period after the injection. We found that the

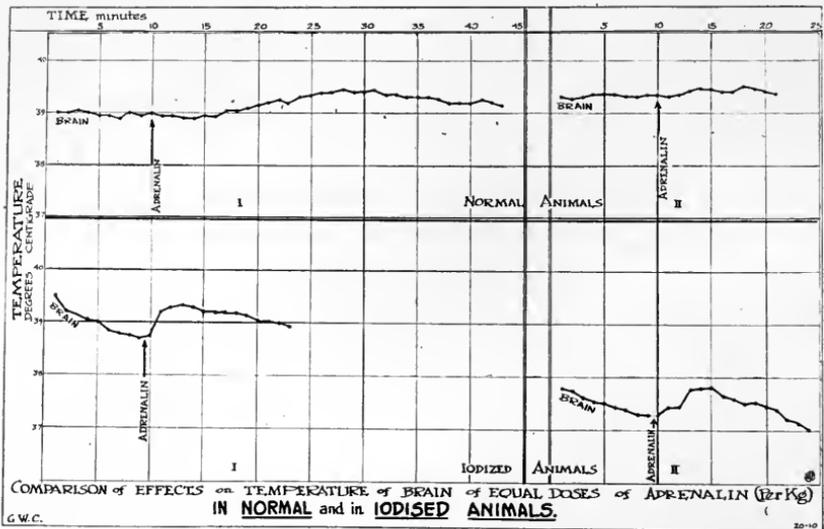


Fig. 2.—Comparison of the effects on the temperature of the brain of the injection of adrenalin in normal and in iodized animals.

adrenalin caused a greater and a more prompt increase in temperature in the brain of the iodized animals than in the controls. This finding may be offered as a physical interpretation of the sensitization of the organism to adrenalin in hyperthyroidism (Goetsch test) (Fig. 2).

It would appear that the study of the thyroid begins and ends with iodine. Marine states that simple goiters and the incidence of fetal adenomata result from a deficiency of iodine alone. On the other hand, goiters of the

exophthalmic type are due to hyperiodism—the hypersecretion of thyro-iodin by the thyroid. The excessive iodism causes abnormal permeability of the cell membranes. Increased permeability of the cells means increased activity. Increased activity of the cells—increased metabolism—is one of the results alike of iodism and of stimulation.



A PHYSICAL INTERPRETATION OF THE RÔLE OF THE ADRENALS IN EXOPHTHALMIC GOITER

GEORGE W. CRILE

THAT the adrenal glands are powerful activators of the brain, and that their aid is promptly elicited when increased metabolism—increased work—is required, is shown by the fact that adrenalin alone produces nearly all the symptoms produced by the various causes of increased energy transformation, such as emotion, exertion, injury, infection. That is, adrenalin causes increased metabolism, increased thyroid activity, increased blood-pressure, increased pulse, increased respiration, leukocytosis, increased sweating, dilation of the pupils, diversion of the blood to the surface, lowering of the threshold at the myoneural junction. But it is the thyroiodin (thyroxin) that sensitizes the tissues to adrenalin. Adrenalin increases hyperthyroidism; hyperthyroidism increases adrenalism; *i. e.*, hyperthyroidism, iodism, and adrenalism coexist, each augmenting the other.

Of no less significance are the facts that adrenalin causes hyperchromatism and later chromatolysis of the brain cells, just as do emotion, injury, exertion, infection; that it causes an immediate increase in the electric conductivity of the brain, and an immediate production of heat, as has been shown by thermocouple records; and that when the adrenals are removed the brain cells rapidly degenerate, the animal rapidly loses the power to fabricate heat, and muscular and mental action, and death usually follows.

We conclude, therefore, that the brain is dependent on

the adrenals, both for function and for survival. The adrenals may show enlargement in some chronic activations, such as infection, pregnancy, rutting season, exophthalmic goiter. The adrenals, therefore, must be included among the means by which the organism is activated.

In our measurements of the electric conductivity of animal tissues under varying conditions, we found that ad-

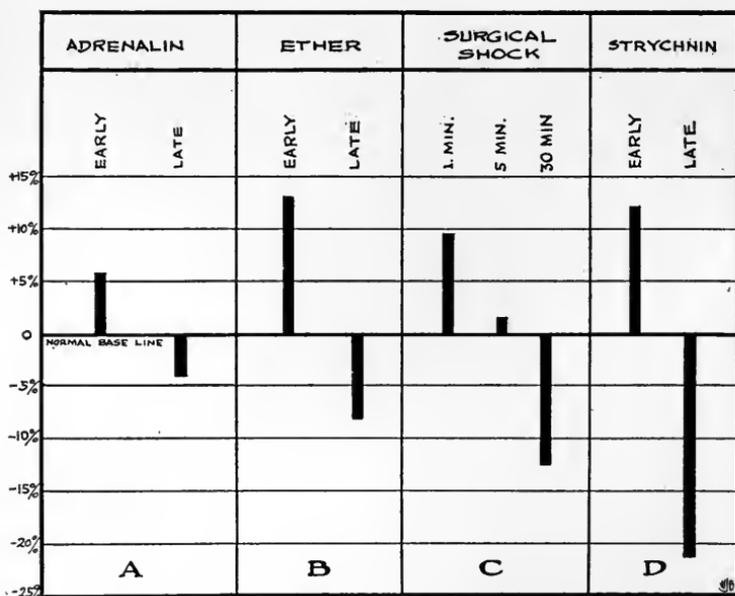


Fig. 3.—Early and late effects of various forms of stimulation on the electric conductivity of the cerebrum.

renalin first increases the conductivity of the brain, and that, as a result of the injection of excessive doses of adrenalin, the conductivity of the brain is decreased, as is the case in other forms of stimulation (Fig. 3, A). If conductivity is related to stimulation, then an increase or decrease in conductivity would be associated with an increase or decrease in function, *i. e.*, with activity or exhaustion. Our electric conductivity observations have indicated that the

first effect of the excitants of bodily activity, such as injury, fright, toxins, is to increase the conductivity of the brain, while in every type of exhaustion studied the conductivity of the brain was decreased when the state of exhaustion was established (Fig. 3).

If the activation of the brain is a phenomenon of electric energy, then since electric energy depends upon oxidation, and oxidation in part at least is controlled by adrenalin, it obviously follows that excessive adrenalin would ultimately cause fatigue and decreased conductivity. This may be the cause of the great fatigue which is uniformly seen in cases of advanced hyperthyroidism.

Both experimental and clinical phenomena seem to indicate that the body is driven by electricity, which is fabricated in the brain-cells with the aid of adrenalin. But we have seen no evidence that adrenalin covers more than the emergencies of moments and hours, or of days. Adrenalin is too evanescent, too volatile to establish and to maintain evenly an increased receptivity, increased sensitiveness to response, an increased metabolism, both basic and adaptive, day and night, for weeks and months. We assume that the brain has no power within itself to do this, and that, therefore, prolonged activation is accomplished through the aid of some other organ. If electricity is the driving force of the organism, and if electric power is increased by increasing the conductance of the tissues over which it passes, it would follow that there must be in the body an organ which is capable of supplying to the blood for weeks and months a substance that is known to increase electric conductance, the blood, in turn, supplying this substance to the nervous system. This is the rôle of the thyroid.



PARTIAL HYPERTHYROIDISM

GEORGE W. CRILE

IN true exophthalmic goiter the activity of every tissue and organ is speeded. May there be a less inclusive form of hyperthyroidism? In certain cases may some organs and tissues be more affected than other organs and tissues? For a long time it has been noted that, following the removal of colloid goiters, colloid adenomata and adenomata, especially those of large size, some patients have reported an improvement in general health beyond what one would anticipate would result from the mere removal of the enlarged gland. In some cases the improvement has seemed to pertain principally to the nervous system; in some cases to the heart; in some to the blood-pressure. At first it appeared that this improvement must be due to the following factors: psychic relief from worry due to the presence of the deforming tumors; mechanical relief from pressure; relief from interference with the respiratory exchange. Doubtless these factors are worthy of due consideration in certain cases.

But increasing experience has demonstrated that there is like improvement in cases in which there has been no psychic stress; no interference with the circulation in the venous trunks; no interference with the respiratory exchange. It appears, therefore, that the improvement in certain cases must be due to the diminution of thyroid activity following partial thyroidectomy.

As has been stated in the preceding section, the only

proved function of the thyroid gland is the fabrication of iodine into an organic compound which exercises a basic control over the bodily processes. In hyperplastic goiters this function is most active; and Marine and Allen Graham have shown that adenomata also perform the characteristic thyroid function. Clinical evidence of the functional activity of adenomata is found in the frequent development of symptoms identical with those which are characteristic of exophthalmic goiter, and in the disappearance of these symptoms after the removal of the adenoma.

A large gland showing no hyperplasia may secrete too much thyro-iodine or thyroxine, or one may suppose that in some cases some organ, such as the heart, is abnormally responsive to the normal thyroid secretion. In hyperthyroidism due to hyperactive adenomata either iodine or thyroid extract may cause an aggravation of the symptoms.

In view of these facts the following questions arise: Are the clinical symptoms of so-called *toxic* adenomata due to a physical degeneration of the adenoma and therefore to be compared with the clinical symptoms that result from the degeneration of fibroid tumors? Are they due to such changes as are produced by a chronic toxemia, from infection of the gall-bladder, the teeth, the tonsils, etc.? Or are they due to the thyro-iodine which is fabricated by the adenoma?

That the last of these queries suggests the true interpretation appears to be indicated not only by the identity of symptoms referred to above but also by the fact that the well-developed "toxicity" from the "toxic" goiter often produces a sensitization of the organism to adrenalin, identical with that present in cases of hyperplastic goiter which are associated with exophthalmos and the other characteristic symptoms of exophthalmic goiter. In fact, with the excep-

tion of exophthalmos, all the characteristic symptoms of true "exophthalmic goiter" may be present in cases of so-called "toxic adenomata," *i. e.*, increased basal metabolism, tachycardia, nervousness, tendency to fever, low thresholds, emaciation, although certain symptoms, such as increased appetite, may not be as marked as in exophthalmic goiter.

In toxemias from the toxins of degeneration of other tumors, such as fibroid of the uterus, and in chronic infections, as a rule, neither the appetite nor the basal metabolism is increased. Occasionally one sees cases of high blood-pressure, of myocarditis, or of neurasthenia in which the only evidence of the thyroid involvement is the presence of a goiter. In some of these cases good results have followed the excision of the thyroid gland. It would appear that adenomata may cause every grade of pathologic physiology progressively from myocarditis, increased blood-pressure, nervousness, and increased metabolism on up to true exophthalmic goiter. This progressive involvement of bodily processes, due to adenomata, is analogous to the progressive effects of various grades of infection from mild oral sepsis to chronic empyema of the gall-bladder, acute peritonitis, or acute osteomyelitis. It would seem, therefore, that the various types of goiter should logically be regarded as varying degrees of the same or similar processes, and that, certainly as far as treatment is concerned, no differentiation should be made between exophthalmic goiter with hyperplasia and the so-called "thyrotoxicosis" from adenomata, or some of the atypical forms of the disease; that the same regimen of management which has proved effective in the treatment of exophthalmic goiter will produce like results in the treatment of the so-called "toxic adenomata." It would seem that the

varying phenomena which have been called "toxic goiter" should be regarded as varying degrees of iodism or hyperthyroidism rather than a toxemia.

It is difficult to reach any conclusion on this point which is not fully in accord with the monumental work of Plummer. In any case, whatever one's opinion, the treatment and the clinical results are identical, so that the point of view matters but little after all.

DISEASES AND PATHOLOGY OF THE THYROID GLAND

ALLEN GRAHAM

IN considering the variations from the normal that occur in the human thyroid gland it is very important to bear in mind and differentiate between those changes that may in general be classed as physiologic and those that are distinctly pathologic. This is all the more necessary since the changes of both types may be closely associated in the same gland, and furthermore, a physiologic alteration may merge into one which is distinctly pathologic, the dividing line being not always distinct.

The consideration of the various types of changes in the thyroid gland will be facilitated and rendered more objective by the following classification, adapted from Marine, to whom I wish to express my indebtedness for much valuable information concerning the thyroid. This classification, although simple, at the same time includes all important variations from the normal.

1. Normal.
2. Hypertrophy.
3. Hyperplasia.
4. Colloid goiter.
5. Exhaustion, atrophy, fibrosis.
6. Adenoma, benign

| | | | | | |
|---|----------------------------|---|---|-------------|---------------|
| { | Type A. | Diffuse colloid adenomatous goiter. | | | |
| | Type B. Fetal ¹ | <table border="0" style="display: inline-table; vertical-align: middle;"><tr><td rowspan="3" style="font-size: 2em; padding-right: 5px;">{</td><td>Pure fetal.</td></tr><tr><td>Intermediate.</td></tr><tr><td>Colloid.</td></tr></table> | { | Pure fetal. | Intermediate. |
| { | Pure fetal. | | | | |
| | Intermediate. | | | | |
| | Colloid. | | | | |
7. Adenoma, malignant.
8. Carcinoma.
9. Sarcoma.
10. Inflammation.

¹ The divisions under "Fetal Adenoma" refer to the degrees of differentiation.

In order to save subsequent repetition we wish to dismiss with only a few words the host of accidental and complicating conditions that are so frequently present in tumorous thyroids, such as edema, myxomatous and hyaline degeneration, necrosis, scars, hemorrhage, calcification, ossification, or cysts. These conditions rarely occur in uncomplicated non-tumorous thyroids, and it is almost equally uncommon to find adenomata or tumors of any size without the presence of some or all of them. These complications are not peculiar to thyroids and have no other significance than has their occurrence in any other tissue of the body.

Thyroid cysts are of two kinds: First, simple colloid retention cysts, which bear no relation to tumors of the thyroid, distended thyroid follicles or a coalescence of follicles; and second, cysts resulting from hemorrhage into existing adenomata or other tumors, or their degeneration and necrosis. This second group includes a great majority of cysts of the thyroid.

As for *lymphoid tissue*, we have no very satisfactory explanation of its presence or significance, but it is frequently found in this locality and generally in those patients who show other evidence of lymphoid overgrowth, such as adenoids, hypertrophy of the tonsils, and enlargement of the superficial lymph-nodes. It occurs as diffuse lymphoid infiltration and well-organized lymphoid follicles with germinal centers.

No further reference to these accidents and complications will be made.

NORMAL THYROID (Fig. 4, A)

The normal thyroid is a uniform uncomplicated non-tumorous gland with two lateral lobes connected by an isthmus. The cut surface is uniformly lobulated through-

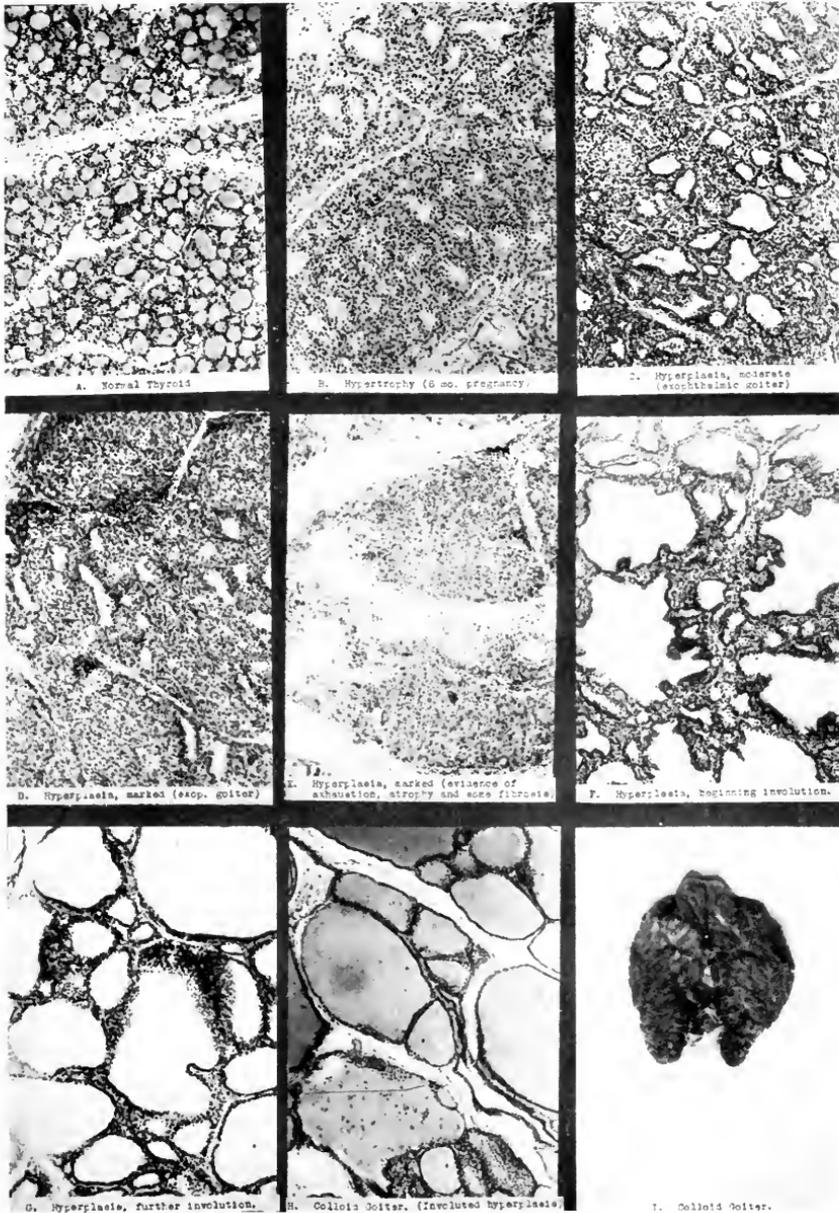


Fig. 4.—Hypertrophy and hyperplasia of the thyroid gland.

out; colloid material is present throughout; its weight varies between 25 and 40 grams; the iodine content averages about 3 mgm. per gram of the dried gland.

Histologic examination shows follicles of fairly uniform size and shape, which are well filled with deeply and uniformly staining colloid completely filling the acini and resting against a single layer of cuboidal epithelial cells.

HYPERTROPHY AND HYPERPLASIA (Fig. 4, B-H)

These terms are used in their strict pathologic sense and are considered together because they are frequently associated in the same gland, and when they so occur it is not always possible to distinguish one from the other. In this discussion no attempt will be made to draw fine distinctions nor to dissociate these commonly associated conditions.

Under such influences as induce thyroid enlargement in man, regardless of their nature or cause, the gland undergoes certain changes depending upon the intensity and duration of the exciting cause. Whatever the cause, so far as non-tumorous thyroids are concerned, there is a difference in the degree, but not in the character of the end-result.

In *developing* goiters, either simple or exophthalmic, the thyroid enlarges; the vascularity increases; the gland becomes softer; the iodine and colloid contents diminish; the follicles become larger, and may be variable in size and outline; the epithelial cells increase in size. These changes constitute simple hypertrophy.

If the exciting cause continues to operate, the changes listed above increase in degree; and to them may be added actual proliferation of the epithelium in the follicles, or the formation of new follicles, or both, and with this, infoldings, plications, and papillary projections of the wall into the

lumen of the follicles. These changes constitute hyperplasia. It is almost inconceivable that the thyroid can jump from its normal state into a well-marked hyperplasia without there having been some degree of simple hypertrophy, unless the hyperplasia is a manifestation of malignant new growth.

Should the exciting cause cease to operate after the gland has passed through the stages of hypertrophy and hyperplasia, the gland will tend to undergo involution toward recovery (Fig. 4, F-H). When the involution or recovery is complete the gland becomes a colloid goiter, according to our conception.

COLLOID GOITER (Fig. 4, H, I)

In the reversion from hyperplasia or hypertrophy to the colloid or resting state the gland generally decreases in size, becomes firmer, its vascularity decreases, the iodine and colloid contents increase, the follicles generally remain somewhat larger and not so uniform in size and shape as in the normal gland. The colloid is apt to show vacuoles and desquamated cells. The epithelial cells lining the follicles become cuboidal or even may be flatter than normal. The above applies to those glands that have undergone hypertrophy and hyperplasia for the first time. After involution they closely resemble the normal thyroid. In the case of glands that have passed through the cycle a number of times or of those in which the hyperplasia is of long standing, the appearance after involution will not so closely resemble the normal thyroid.

As far as is known, a colloid goiter has the same physiologic and biologic capabilities as the normal gland, and it reacts to a sufficiency or an insufficiency of iodine in the same way and almost if not quite to the same degree as

does the normal thyroid. The chief differences between a normal gland and a colloid goiter are the following: The colloid goiter has been hypertrophic or hyperplastic, or both, and has recovered; it is usually larger than the normal gland; the follicles show greater variations in size and shape; the lining cells are more apt to be flattened; the stroma is increased; and finally, we do not classify as strictly normal any thyroid in which there is an adenoma. We regard an adenoma in itself as an indication of previous thyroid enlargement.

EXHAUSTION, ATROPHY, AND FIBROSIS (Fig. 4, E)

After the gland has become hypertrophic, hyperplastic, or both, if the influences or causes that induce overgrowth continue to operate long enough or with sufficient intensity, the changes characteristic of hypertrophy and hyperplasia will progress to the point of breakdown or exhaustion of the thyroid parenchyma. At and beyond this point the epithelium is incapable of physiologic recovery. The percentage of gland tissue destroyed in this manner is, of course, variable, and depends upon the duration and intensity of the exciting cause or causes. Destruction of the entire gland is incompatible with life; a lesser degree of degeneration produces the clinical condition—myxedema.

Following this exhaustion and destruction of the parenchyma there is atrophy and fibrosis. Indeed, the fibrosis may have its origin in the repeated cycles of thyroid overgrowth and involution.

Under the preceding five headings we have considered only non-tumorous thyroid tissue; consideration of the tumorous conditions follows. Suffice it to say here that any kind of an adenoma may be present in a gland in any stage of hypertrophy, of hyperplasia, of colloid goiter, or of atrophy, but does not occur in normal glands.

ADENOMA, BENIGN

Clinically and pathologically there are two types of adenomatous thyroid which, for the sake of convenience, we shall designate as *Type A* and *Type B*.

Type A. Diffuse Colloid Adenomatous Goiter (Fig. 5, A).—It may be said at the outset that it is more difficult to explain satisfactorily the origin and nature of this type of goiter than of any other type of pathologic change of the thyroid gland. Two possibilities suggest themselves, neither of which is entirely satisfactory. Does this change originate in a fetal adenoma of possibly the more highly differentiated type? If so, it would be very difficult to explain the facts that this type of goiter is invariably present in both lateral lobes; that the individual nodules are made up of well-differentiated follicles rich in colloid; that the individual nodules do not make tumors of any considerable size; that the capsules are thin; that the goiter rarely if ever becomes malignant. In all these respects fetal adenoma presents a directly opposed picture. Does this type of goiter originate in old, long-standing colloid goiters? If so, it is difficult to understand why the change most frequently arises in the regions next the trachea and seems to proceed toward the outer capsule of the gland. On the other hand, the individual nodules are not densely encapsulated and histologically the follicles resemble those of the normal thyroid and of colloid goiter, except for one important difference, namely, that in the diffuse colloid adenomatous goiter, regardless of size, the individual masses are never lobulated structures.

Type B. Fetal adenoma, with its various stages of growth and differentiation (Fig. 5, B-I).

This type of adenoma has its origin in the so-called Wölfler's rests, embryonal remnants left over from the developmental period of the thyroid. This type is more

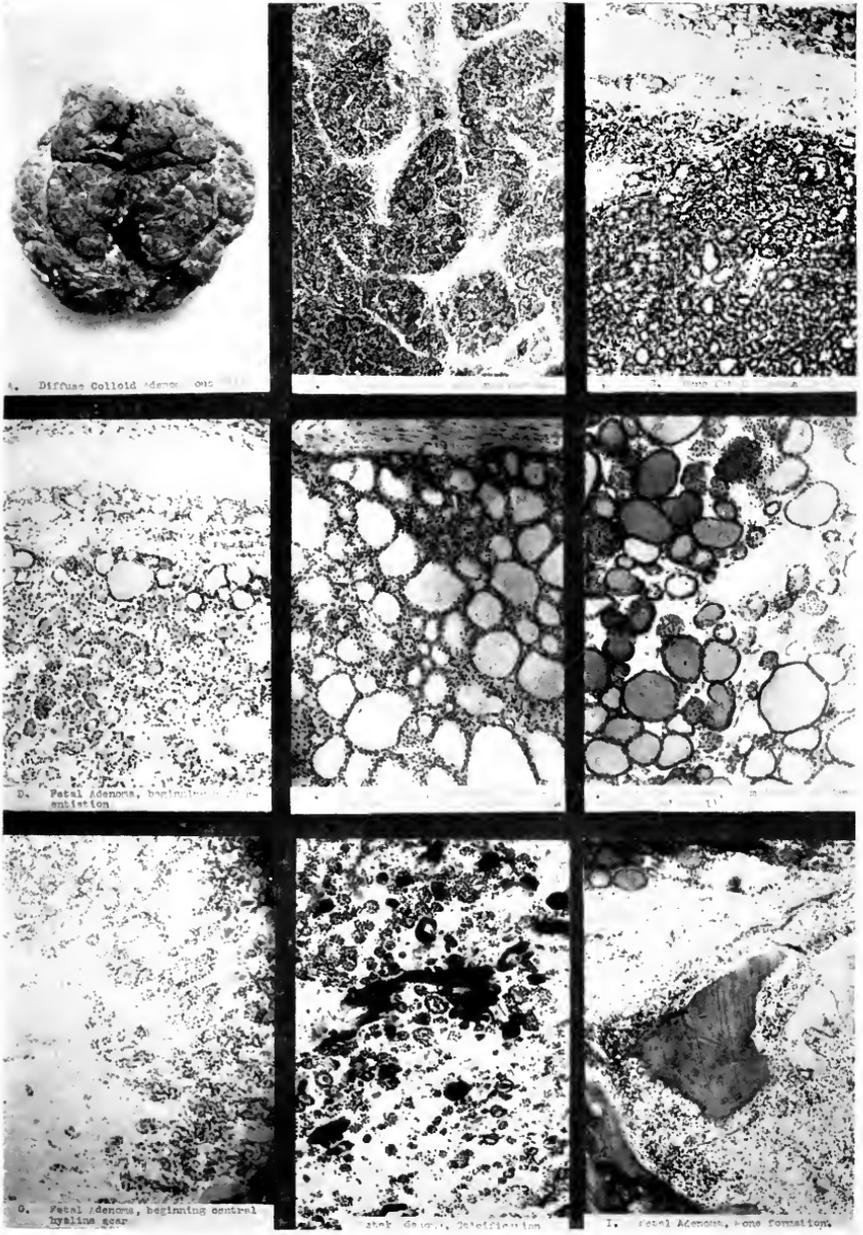


Fig. 5.—Fetal adenoma in various stages.

definitely a tumor than Type A. The fetal adenoma consists of a circumscribed, well-encapsulated mass of non-lobulated thyroid tissue made up of follicles, the histologic appearance of which, except for complications, depends upon the stage of growth and differentiation which they have attained at the time of examination. The Wöfler rests laid down in intra-uterine life may be present in one or both lobes and in any part of the lobe, as single or multiple small clumps of embryonal cells. In the early stages they have no capsule, are not arranged in follicles, contain no colloid or iodine. They may remain in this condition throughout life and never grow or differentiate, or they may start growing at any time of life. In their growth there is always the tendency to become more differentiated, that is, to develop definite well-formed follicles which increase in size, accumulate colloid and iodine, and are lined by a single layer of cuboidal epithelial cells, so that in an advanced stage a particular follicle may look just like a normal thyroid follicle of the same size. In the same gland there may be present a pure fetal adenoma showing little or no differentiation—a solid grayish opaque cellular mass with little or no colloid or iodine and having very small follicles, and next to it a fully differentiated fetal adenoma rich in colloid and iodine and having large follicles resembling those of the normal thyroid. The histologic and gross appearances of the two are very different, yet there seems no doubt that they represent different stages of the same process. Between these two extremes all gradations are frequently encountered in the surgical clinic.

ADENOMA, MALIGNANT (Fig. 6, A-H)

This title is used in our classification to include the numerous thyroid tumors, regarding which at the time of

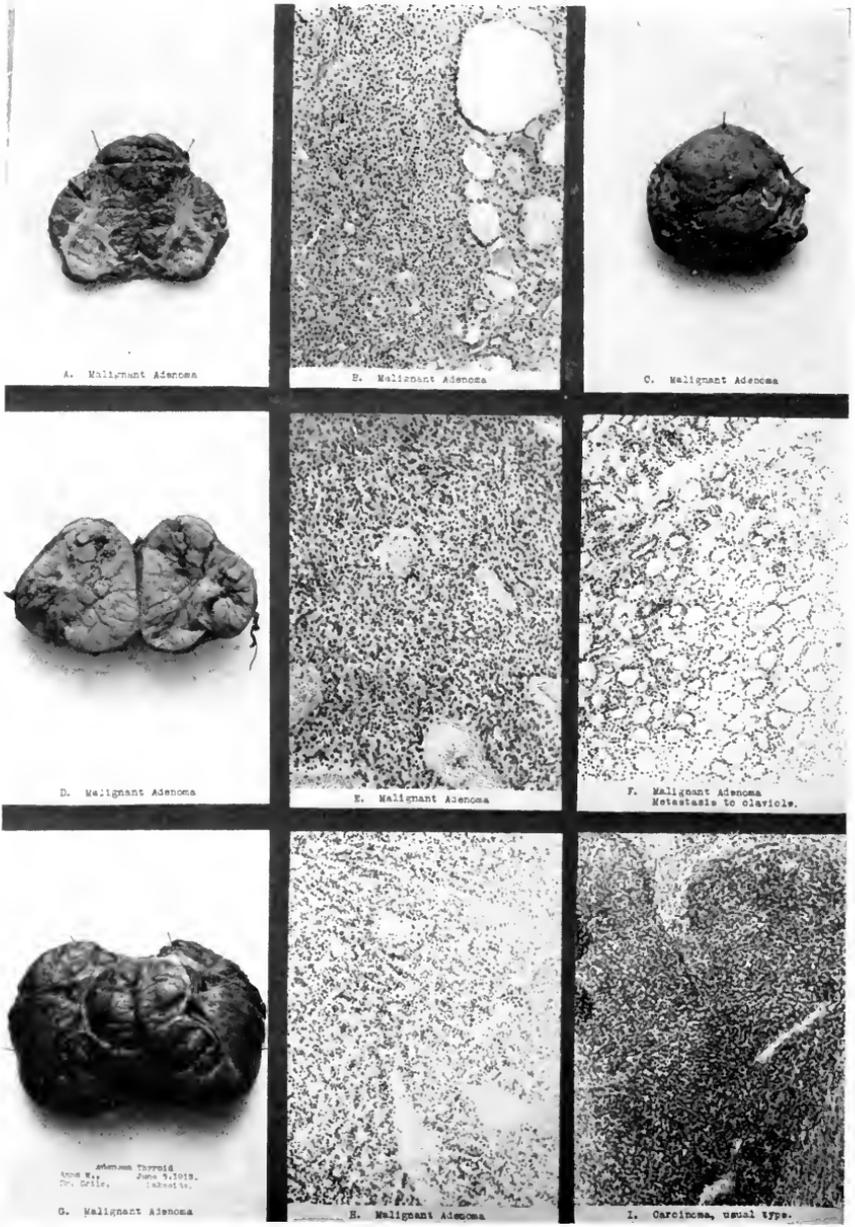


Fig. 6.—Malignant adenoma.

their removal in the clinic the pathologist cannot state definitely whether or not they are malignant. There is a firm and increasing conviction born of past experience and increasing yearly that these tumors represent a stage in progress from the certainly benign to the certainly malignant. They correspond to what more recently in the pathology of other tissues and organs has been called the precancerous or premalignant lesion. The subsequent history of many of these cases has proved the doubtful tumor to be malignant, while, on the other hand, some patients have lived for years with no evidence of recurrence or metastasis. The prognosis depends on whether these doubtful lesions are removed early or late in this premalignant stage and on whether or not the adenoma was completely removed without rupture. Practically all these tumors have their origin in fetal adenomata, as in this clinic there has been no instance in which this type of lesion had as its sole origin a diffuse colloid adenomatous goiter. Moreover, one may make a series as one wishes of the various steps, stages, and degrees whereby the innocent, certainly benign, pure fetal adenoma is transformed both grossly and microscopically to the undoubted cancer, with every evidence of malignancy. From our experience it appears that malignant adenomata arise most frequently from the less differentiated fetal adenomata, and that the more the fetal adenoma approaches maturity or full differentiation, the less likely is it to become malignant.

CARCINOMA (Fig. 6, I and 7, A)

From adenomata of the type we have just discussed it is but a step to malignancy with all the usual evidences thereof. Fully 95 per cent. of malignant growths in the thyroid are carcinomata, and fully 90 per cent. of these

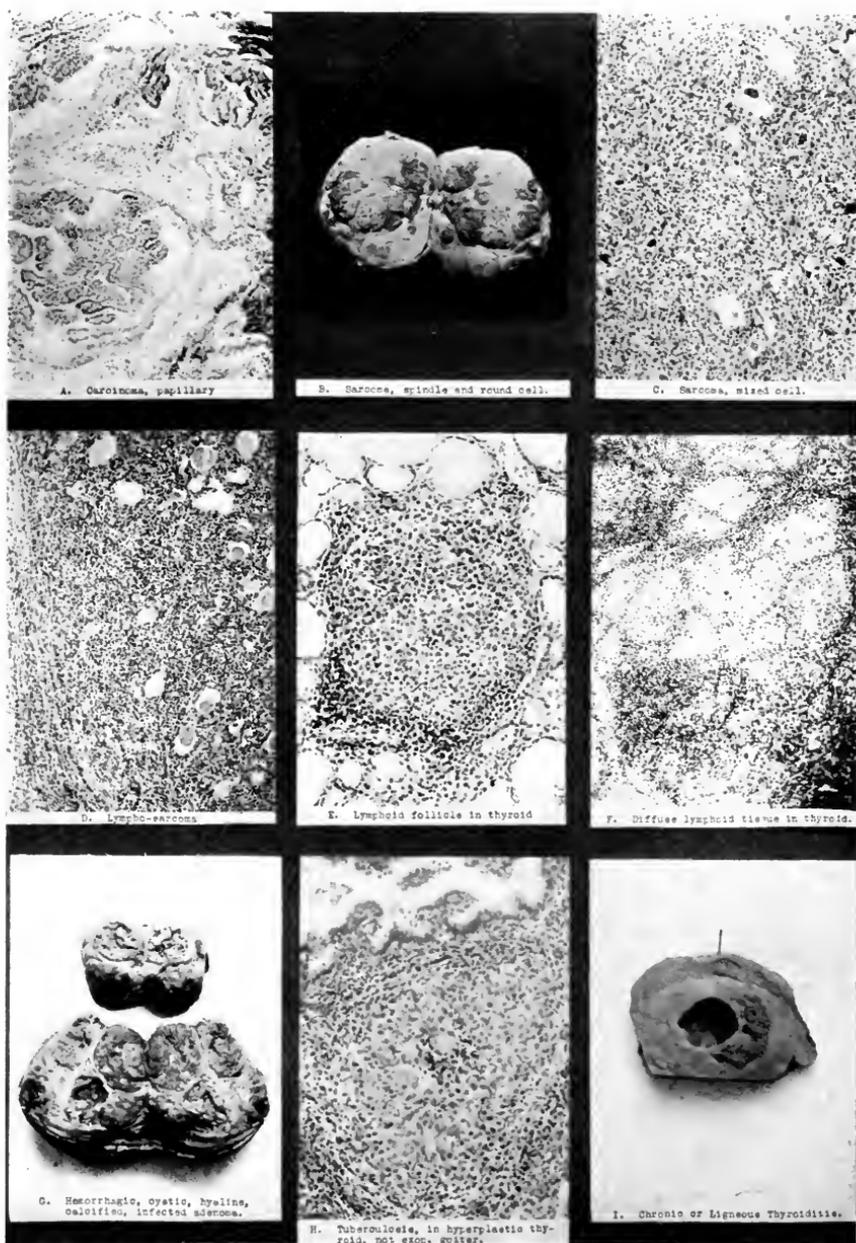


Fig. 7.—Various malignant types of thyroid disease.

develop from fetal adenomata, passing through the stage which we have denominated "malignant adenoma." Consequently, fetal adenoma, and especially malignant adenoma, becomes one of the most important surgical lesions of the thyroid. It is beyond the scope of this article to undertake a minute description of the gross and microscopic anatomy of these tumors.

Aside from this main group of thyroid malignancies there are a small number of carcinomata which are not dependent upon adenomata for their origin. In this group papillary carcinoma is most frequently encountered. This seems to originate in the papillomatous processes found in non-adenomatous as well as in adenomatous (not necessarily fetal) thyroids.

In addition to the above there are a few carcinomata which cannot be satisfactorily included in either classification whose exact origin and nature remains in doubt. It is interesting to note in this connection that occasionally a tumorous thyroid is encountered in regard to whose character pathologists will disagree as to whether it is a carcinoma, endothelioma, or sarcoma.

SARCOMA (Fig. 7, B-D)

Sarcomata represent less than 5 per cent. of the malignant tumors of the thyroid. Sarcomata of the thyroid do not differ from sarcomata in other organs or tissues, the most frequent types being the round and the spindle-cell sarcoma. Occasionally one meets with curious combinations of round, spindle-, and giant-cell tumors. Sometimes both a sarcoma and a carcinoma may be present in the same gland. Of course, primary lymphosarcomata are found whose origin is probably in the lymphoid tissue which is so commonly present in thyroids in this locality (Fig. 7, E, F).

INFLAMMATIONS

Any kind of infectious and inflammatory process may occur in the thyroid, particularly acute pyogenic abscess; more or less diffuse acute inflammatory reactions around adenomata, especially when they are hemorrhagic, degenerating or cystic; syphilis, and tuberculosis. Tuberculosis most commonly occurs in the form of miliary tubercles, although conglomerate and caseous areas are sometimes seen. The above-mentioned inflammatory lesions may occur in any type of thyroid (Fig. 7, G, H).

Of particular interest is a type of chronic inflammatory process that has been termed "ligneous thyroiditis" (Fig. 7, I). This generally occurs in adenomatous thyroids, and before operation is usually diagnosed as malignant on account of its firmness and immobility, due to adhesions to muscle and other cervical structures. In considering clinical cases showing such signs it is well to remember this "ligneous thyroiditis," as the patients in whom it occurs can be greatly and permanently benefited by operation and need not be doomed by the diagnosis of "inoperable malignant tumor."

CARDIAC DISTURBANCES ASSOCIATED WITH DISEASE OF THE THYROID GLAND

JOHN PHILLIPS

INTRODUCTION

AMONG the striking features associated with disease of the thyroid gland Parry, in his original description in 1815, emphasized the importance of cardiac disturbances. The first case of this character described by him was that of a married woman, aged thirty-seven, whom he saw in 1786. Six years previously she caught cold after childbirth and for a month suffered from acute rheumatic fever. Following this she had tachycardia and irregularity of the heart, with two or three nocturnal attacks of difficult breathing, accompanied by the spitting of a small quantity of blood. Three months after labor, while nursing her child, a lump the size of a walnut appeared on the right side of her neck. This continued to enlarge until the period when Parry saw her, when it had reached an enormous size, occupying both sides of the neck and projecting beyond the jaw. This proved to be an enlargement of the thyroid gland. The carotid arteries were greatly distended and the eyes protruded from their sockets. The patient subsequently developed general anasarca and died from cardiac failure. The primary etiologic factor of the cardiac lesion in this case in all probability was the acute rheumatic fever, but, unquestionably, the goiter played an important part in the later manifestations. Graves (1835), Basedow (1845), Stokes (1854), and Trousseau (1856) also mention the cardiac features of disease of the thyroid gland.

In colloid goiter or in cases of adenomatous enlargement

of the thyroid the contents of the superior mediastinum may be encroached upon, causing disturbances of the lungs and heart. Pressure on the trachea may prevent adequate filling of the lungs, this producing emphysema with deficient aëration of the blood and subsequent myocardial weakness. Pressure on the sympathetic ganglia on one or both sides of the neck may stimulate the accelerator nerves and cause a chronic tachycardia.

THE RELATION OF ADENOMATA TO CARDIAC DISTURBANCES

I would particularly like to call attention to marked cardiac disturbances which appear in middle life or later in patients who for many years have had an adenomatous enlargement of the thyroid gland. These cardiac manifestations may completely overshadow all the other toxic symptoms from the goiter, which, in fact, may be so slight as to make it appear that the goiter plays little or no part in the disease. In these cases the cardiac phenomena may resemble those of the ordinary case of toxic goiter, *i. e.*, continuous elevation of the pulse-rate with occasional attacks of intense tachycardia on awakening or brought on by emotion, excitement, exercise. These attacks usually differ from the ordinary attacks of paroxysmal tachycardia in that the slowing of the pulse-rate occurs gradually instead of abruptly, although occasionally there is a true paroxysmal tachycardia, as in the following case:

A woman aged forty came under observation in June, 1911, with symptoms of exhaustion, weakness, palpitation of the heart, and a loss of twenty pounds in weight. She had marked exophthalmos with a positive von Graefe's and Stellwag's sign in both eyes. Her thyroid was enlarged, the enlargement being greater on the right side than on the left, and in the right lobe could be felt a nodule the size of an

English walnut. A persistent fine tremor of the hands was present. The heart showed slight enlargement of the left ventricle and the apex-beat was very forcible and diffuse. The heart sounds were very loud, but were unaccompanied by murmurs. The cardiac rate varied from 140 to 160 beats per minute; the systolic blood-pressure was 140, the diastolic 60. Nothing of importance was disclosed in the remainder of the physical examination. As the result of prolonged rest in bed for three months, the use of warm baths, and the occasional administration of bromid to insure rest the patient gained fifteen pounds in weight and her average pulse-rate became 96 per minute. Since then, by living a life free from physical overstrain or mental worry, she has been able to attend to her household duties. In June, 1917, she had an attack of paroxysmal tachycardia lasting forty-five minutes, the heart abruptly increasing its rate to 180 per minute, and ceasing just as abruptly at the termination of the attack. She has had two similar attacks since then, one lasting thirty minutes and the other one hour.

Bamberger¹ in 1910 reported three cases of paroxysmal tachycardia associated with goiter and collected twenty-one cases from the literature. He mentions the fact that in some of the patients an irregularity of the heart was present.

One of my patients had auricular fibrillation at the time I first saw her and later had attacks of paroxysmal tachycardia. This patient, a woman aged forty-seven, was seen first in November, 1913. She complained that for the past four months she had had palpitation of the heart, vomiting, shortness of breath, and swelling of the feet. She had had a goiter for the past thirty years and recently had noticed that her hair was falling out, and that there was also a gradual disappearance of the hair from the

¹ Bamberger, Deutsche med. Wochenschrift, 1910, xxxv, 1403.

axillæ and pubes. Her eyes were prominent and she had a positive Stellwag's and von Graefe's sign. Her thyroid was enlarged and nodular, the right side being larger than the left. The cardiac sounds were irregular both in force and rhythm, the heart rate was 174, while that of the pulse was 120. The liver was enlarged to 6 cm. below the costal border and there was a small amount of free fluid in the abdominal cavity. There was quite marked edema of the lower extremities, while the hands showed no edema, but there was a fine tremor of the extended fingers. The urine showed a trace of albumin and a few hyaline and granular casts. The diagnosis was adenoma of the thyroid gland with toxic symptoms, chronic myocarditis, auricular fibrillation, and cardiac decompensation. With limitation of the total daily quantity of fluids, restriction of salt in the diet and the administration of bromids and digitalis, the edema disappeared, the pulse-rate dropped to 100 per minute and became regular, and the vomiting ceased. Throughout the next year, while the patient was under observation, there were periods of temporary improvement, but a lasting cardiac compensation was never fully established. During this time she had four attacks of paroxysmal tachycardia lasting from thirty minutes to thirty-six hours, the cardiac rate varying from 180 to 200. Both the onset and the termination of these attacks were abrupt. On December 21, 1914, Dr. Crile removed the left, median, and one-half of the right lobe of the thyroid. These showed numerous adenomatous masses with varying grades of degenerative changes. After the operation the patient gradually improved, cardiac compensation became well established, and when last heard from three years later she was able to do many of the lighter duties about her home. There was no return of the attacks of paroxysmal tachycardia.

The occurrence of other forms of cardiac disturbance in cases of goiter have been described, such as sinus arrhythmia, premature contractions, heart-block, auricular flutter, and attacks of angina. Krumbhaar,¹ in an electrocardiographic study of fifty-one cases of toxic goiter, found sinus arrhythmia in four cases; ventricular extrasystoles in three cases; auricular fibrillation in three cases; auricular flutter in one case; delayed conductivity in two cases. In two of the cases of auricular fibrillation and in the case of auricular flutter the disturbance remained constant for several years. In the other case of fibrillation the disturbance was transient, disappearing coincidentally with the improvement that followed medical treatment.

The following case illustrates the association of attacks of angina with the presence of a goiter showing comparatively mild symptoms: An unmarried woman, aged fifty-six, was seen first on June 15, 1912. She complained of feeling nervous and sleepless, of increased lacrimation, and that her ears felt "as if a lid had closed down." She had suffered a severe shock one year previously because of the sudden death of her brother. During the past year she had lost twenty pounds in weight. The eyes showed marked exophthalmos and on both sides there was a positive Stellwag's and von Graefe's sign. The median and right lobes of the thyroid were enlarged and a loud systolic murmur and venous hum were audible on auscultation over the thyroid. The heart was slightly enlarged to the left and the pulse-rate was 104; the systolic blood-pressure was 140, diastolic 80. There was a marked fine tremor of the outstretched fingers. As the result of rest in bed for a period of three weeks the patient's condition was considerably improved and the pulse-rate dropped to 80. She spent

¹ Krumbhaar, E. B., *Electrocardiographic Observations in Toxic Goiter*, Amer. Jour. Med. Sci., 1918, clv, 175.

two months at the seashore, and during the latter part of her stay there she began to have attacks of precordial pain, which was also referred to the left shoulder and down the inner side of the left arm. After she returned home she was seen during a number of these attacks, during which time her systolic blood-pressure averaged 180, her diastolic 100. She obtained considerable relief from the pain by taking nitroglycerin. As the anginal attacks kept recurring and she seemed to be making no progress toward recovery, on December 1, 1912, Dr. Crile removed the right lobe of the thyroid and ligated the left superior thyroid artery. Following the operation the patient had no return of the anginal attacks, in three months her weight had increased from 90 to 109 pounds, and her systolic blood-pressure had dropped to 140, the diastolic to 90, remaining at this level. At the present time, seven years later, she is enjoying good health and leading a busy life.

The blood-pressure in toxic goiter resembles that seen in cases of aortic regurgitation, viz., an increased systolic pressure with a low diastolic, the pulse pressure being increased above the normal limit. Studies of the variations in blood-pressure in goiter cases have been made by Taussig¹ and Plummer.² The latter author found that 27 per cent. of patients over forty years of age who had non-hyperplastic goiter had a systolic blood-pressure above 160. It is quite conceivable that a relatively slight overstimulation of the vasomotor mechanism from overactivity of the thyroid or from perverted secretion, if it persists over a long period of years, may lead to an elevation of blood-pressure or to permanent myocardial damage, which is manifested by auricular fibrillation, by paroxysmal tachycardia, or in some instances by cardiac decompensation.

¹ Taussig, A. E., *Tr. Assn. Amer. Phys.*, 1916, xxxi, 121.

² Plummer, H. S., *Tr. Assn. Amer. Phys.*, 1915, xxx, 450.

THE RELATION BETWEEN DISEASES OF THE THYROID GLAND AND LARYNGEAL FUNCTION

JUSTIN M. WAUGH

THE fact that in cases of thyroid disease the function of the larynx may be impaired to a greater or less degree is now generally recognized. In general, physicians have considered that this impairment of laryngeal function is always the result of surgical trauma of the recurrent laryngeal nerve. We wish, therefore, especially to call attention to cases in which the laryngeal impairment results from the growth of the goiter itself and is in no way dependent upon the surgical treatment. A systematic study of these cases has been undertaken at the Cleveland Clinic to the advantage alike of the surgeon and of the patient.

In the past the surgeon has not worked in sufficiently close co-operation with the laryngologist in either the pre-operative or postoperative study of patients with thyroid diseases. It follows that the surgeon has judged his results, as far as the larynx is concerned, entirely upon the patient's ability to use the voice without learning by actual observation of the movement and extent of excursion of the vocal cords whether or not they have been impaired.

In fact, many physicians think of the larynx only in its connection with voice production, which they regard as the one essential index to the integrity of the larynx rather than actual knowledge of its anatomic and physiologic condition. They forget that the most important function of the larynx is concerned with the respiration, and as this is one of the automatic processes of the body and its proper performance depends upon the operation of one of the most

delicately balanced mechanisms in the organism, any interference with this function, either by a pathologic growth of the thyroid or as the result of surgery, is obviously of greater importance than any interference with voice production.

The recurrent laryngeal nerves carry two distinct groups of fibers, one the abductor group which controls that function of the larynx which is associated with respiration, and the other the adductor group which supplies the voluntary muscles of the larynx and, therefore, is associated with the function of voice production. Careful investigations by both anatomists and pathologists show that about three times as many fibers are concerned in the performance of the adductor function of the larynx as in the abductor function. That the abductor function is much more easily impaired, either by pressure or by trauma, is beyond question, and in our opinion this cannot be wholly accounted for by the numerical relationship between the two bundles of fibers. Undoubtedly the abductor mechanism which is concerned with the automatic function of respiration is much more delicately arranged than the mechanism which is concerned with the voluntary function of voice production.

The exact cause of the weakening or destruction of the abductor fibers of the recurrent laryngeal nerve is not entirely known. Theoretically this condition is due either to a pressure neuritis resulting from the edema and swelling of the tissues, with later paresis or paralysis as the result of scar tissue formation in the operated area, or to section, ligation, or trauma during the operation. On account of the small postoperative mortality rate attending thyroidectomies exact pathologic data are not easily obtained.

We have been led to assume that the superior laryngeal

nerve is entirely a sensory nerve and that the motor function of the larynx is dependent entirely upon fibers received from the recurrent laryngeals. Whether this is a fact or not remains to be seen. It may be that in going over the experimental work upon which those conclusions are based we may find that the superior laryngeal nerve possesses a greater degree of motor function than has been heretofore supposed. It is a fact that after injury to the recurrent nerves the vocal cords lie at first in a semi-abducted position with the power of further abduction gone. But by repeated voluntary effort the patient, in attempting to speak, adducts the cords repeatedly, and apparently the cords come to assume a fixed position nearer to the median line than if this adductor power was not in force. In consequence, there is an ever-increasing dyspnea. These cords may finally assume a position so nearly approximate that on full inspiration the aperture does not appear to be wide enough to admit the edge of a ten-cent piece. At this stage these patients have but a narrow margin of safety.

In certain patients observation of the larynx is beset with certain difficulties. For example, it is difficult to secure satisfactory observations of patients with the curved or infantile type of epiglottitis. In some of these cases it is impossible to see the cords themselves or, at best, only a small portion of them. Usually, however, the movement of the arytenoid bodies can be sufficiently seen for the position and movement of the cords to be judged.

Occasionally it is difficult to make a laryngeal observation on a patient with hypertrophied tonsils, for in the presence of very large tonsils a very slight contraction of the throat is sufficient to prevent the use of the ordinary laryngeal mirror.

Patients with exophthalmic goiter in particular are

exceedingly nervous and their throat reflexes are very sensitive. The examination of a patient of this type requires a great deal of patience and persistence on the part of the laryngologist. Repeated séances with the patient may be required before a single correct observation can be made. Whether or not the throat of some of these cases shall be cocainized is a delicate question. We have found that by daily observations during a period of from one week to ten days, a very good view of the larynx will finally be secured even in the most difficult individual.

At the Cleveland Clinic all goiter cases are examined by the laryngologist before operation, and immediately after they leave the hospital with re-examinations at intervals of from thirty days to six months or whenever it is possible to secure an observation.

This experience has demonstrated the following facts which, we believe, should be emphasized, since they bear directly upon the safety of the patient:

1. Any laryngeal impairment which is the result of a pathologic condition of the thyroid gland is almost invariably *unilateral*. When a bilateral involvement exists previous to operation it is usually caused either by some lesion in the central nervous system, such as syphilis, or by a malignant condition of the thyroid which has passed beyond the limits of the gland itself and has damaged the recurrent laryngeal nerves.

2. The size of the goiter does not seem to bear any direct relation to the functional impairment of the laryngeal nerve. Furthermore, the impaired cord is not necessarily on the same side as the largest mass, as one would naturally expect, probably because twisting of the thyroid box and trachea by the unilateral growth produces pressure on the opposite side.

3. The degree of laryngeal involvement from non-operative causes varies from paresis to an actual paralysis.

4. The onset of the condition is so gradual that except for some fatigue following excessive use of the voice the patient is unaware of any lack of laryngeal function, for, coincidentally with the impairment of one cord, there develops a compensation by the opposite cord which is sufficient for the maintenance of the patient's voice and respiration.

In the first series of 185 cases examined before operation, the unilateral interference with the laryngeal function was found in 27, or 14.6 per cent. This percentage, however, is probably higher than will be the case when several thousand observations have been made. The occasional observer will find that his figures do not agree at all with those secured by the observation of a large number of cases. For instance, in a series of 100 goiter cases, taken in groups of twenty, in the order of their observation we found in one group six cases of abductor paralysis, in another two, in a third group nine, and so on. It follows that the occurrence of laryngeal involvement in any one of these groups of twenty would not agree with the percentage of occurrence in the total number of cases. Our experience to the present time leads us to believe that ultimately the occurrence of impaired laryngeal function in goiter cases prior to operation will be found to be in the neighborhood of 10 per cent.

The importance of this preoperative observation is self-evident. In the first place, the patient should be made aware of the fact that this damage, if present, is the result of the pathologic condition of the thyroid. Second, if the surgeon has been warned that this condition is present he will take unusual care in all manipulations of the side opposite to the damaged nerve, thereby preventing one of the most distressing postoperative sequelæ—bilateral abduc-

tor paralysis. Moreover, the preoperative laryngeal observation obviates the possibility of attributing to the surgeon any damage other than that which is the direct result of the surgical procedure.

As to the permanency of the laryngeal impairment which results from pressure by the thyroid in the process of its enlargement, we can say only that in certain of these cases the function of the vocal cord has been regained after thyroidectomy. We believe that in these cases the thyroid pressure has existed for only a short time. It has been stated by some writers that when the pressure has been present for as long as nine months, the resultant damage cannot be repaired. We believe, however, that this is a somewhat arbitrary statement which may be revised as knowledge of this condition and of its etiology is extended.

Nearly all writers make some reference to the assumption that laryngeal paralysis may result from toxemia. In our own experience we have never seen a case in which it has appeared that the laryngeal impairment has been the result of toxemia associated with disease of the thyroid. If these paralyzes were due to toxemia why should they be unilateral? And why should only the abductor fibers be involved? It seems much more probable that when laryngeal paralysis is associated with a diseased thyroid gland, whether the onset of the paralysis be before or after operation, it may be explained as the result of mechanical pressure or of trauma, rather than toxemia.

Thus far we have discussed the unilateral laryngeal paralysis which appears prior to operation as being due to the diseased condition of the thyroid itself. When any form of laryngeal paralysis *follows* a surgical procedure there is a complete loss of voice which lasts for from a few days to two or three months. If one of the laryngeal nerves has

been severed, the loss of voice is immediate and is accompanied by more or less dyspnea.

Many patients are able to speak immediately after operation, but later suffer a temporary loss of voice. In these cases the loss of voice is probably the result of the edema or swelling of the tissues in the operative area. In certain cases the pressure from the scar tissue may be sufficient to damage the vocal cord permanently. The loss of function on the part of one of the vocal cords is gradually compensated by an increased function on the part of the opposite cord, so that within a reasonable length of time the voice improves markedly, though the higher tones may be somewhat limited, and the voice may become husky as the result of fatigue. Many of these patients have a very good voice in the morning, but complain of slight hoarseness and distress if they have been compelled to use the voice a good deal during the day.

Bilateral abductor paralysis following surgery of the thyroid gland and due to any of the causes described above presents a distressing postoperative condition. Immediately after operation patients in whom this condition is present have little or no more difficulty than the patients with unilateral paralysis. As far as the voice alone is concerned it may be a little longer before it returns, but ultimately it approaches the normal, since the adductor power of the cords is not lost. The reason that these cases do not present more distressing symptoms immediately after operation undoubtedly is due to the enforced rest. These patients may leave the hospital apparently in almost as good a condition as patients with unilateral paralysis, but there follows a gradual onset of dyspnea, especially on exertion, which is very significant. The cords in these cases are at first fixed in a semi-abducted position; and the aperture between

the cords, instead of being widened during normal inspiration, remains unchanged or sometimes is even narrowed if the tensor muscles of the cord are affected, and the edge of the relaxed cord is sucked inward. When this is the case the patient when asleep develops a stridor which is very distressing to his family. It is very embarrassing for a patient in this condition to be away from home because he is unable to avoid this unpleasant, noisy breathing during sleep.

Another serious handicap to these patients is their inability to expel viscid secretions, in consequence of which a moderate cold or mild bronchitis becomes a serious menace, and should pneumonia develop, the patient is almost certainly doomed.

It follows that the margin of safety in these patients is diminished and at any moment it may be necessary to consign them to a tracheotomy life until some other measures are effected whereby to remedy the condition.

Until recently no direct surgical attempts have been made to relieve this condition. Chevalier Jackson, of Philadelphia, has performed cordectomy in three cases, operating by the direct laryngoscopic route. Jackson states that he believes that these patients regain a fair voice by the vicarious use of the false vocal cords. Whether or not this will be the operation of choice we are unable to say, but at present we believe that unless cordectomy by this method is performed by a laryngologist of extreme skill in direct laryngoscopic methods, it will prove disastrous to the patient.

In the first place there is danger that the cord may not be completely resected, with the result that granulation tissue and scar formation will practically reproduce the condition of stenosis. It is essential that the surgeon bear in mind the fact that the true vocal cord is not a plain

horizontal band, but rather the inner edge of a triangular body of tissue with its broad base toward the cartilage. Furthermore, if voice is to be secured by the use of the false cords, these must not be damaged.

The problem is to get a sufficiently wide aperture established so that respiration may go on with comfort, and to do this in such a way as to permit the patient to develop a speaking voice. It must be borne in mind that to accomplish this end work must be done in a tube of small caliber and that any procedure which tends to produce stenosis of the trachea is very undesirable. Various solutions have suggested themselves, most of which have their disadvantages. Thus we have considered the following procedures:

First, the possibility of creating two raw surfaces and anchoring the cords back to the lateral walls of the trachea with the hope of thereby widening the aperture between the cords and holding them in place by the development of adhesions between these two raw surfaces; second, the complete excision of both cords back to the perichondrium, permitting this area to granulate over; third, a submucous resection of both cords and closure of the area formerly represented by the base of the triangular shaped body of the cord by plastic closure of the mucous membrane.

Of these three methods the last one has seemed to be the most logical, even though it presents great difficulties.

The following case has recently been operated upon by this method: The patient, a woman sixty years of age, who had been operated upon in another state for adenoma of the thyroid, had developed bilateral abductor paralysis with gradually increasing symptoms of dyspnea and stridor. She had lost strength rapidly as the result of her disturbed sleep and her constant apprehension that she might choke to death. Her nervous state made her a very undesirable risk. Laryngeal examination showed bilateral abductor paralysis

with a very small opening between the cords, the edges of the cords being sucked in during inspiration. An immediate tracheotomy was done and the patient given a period of complete rest. She had a moderate degree of bronchitis which made tracheotomy life very difficult for her, and therefore it was decided to make a submucous resection of both cords at a favorable moment.

This was done under a combination of nitrous oxid-oxygen and ether delivered into the trachea through a tube fitting the tracheotomy wound snugly enough to make it fluid-tight. The larynx was split in the median line, an incision made through the mucous membrane below the level of the cords, and a light pack inserted down to the tracheotomy tube to prevent any fluid from entering the trachea. Working from below upward the wound was enlarged in the median line until both false and true cords were exposed. Incisions were then made running parallel with the edge of the true cord and the mucous membrane was dissected free in both the downward and the upward direction. The body of the cord was excised back to the lateral wall of the thyroid box and the free edges of the mucous membrane stitched together on either side with very fine linen. The larynx was then closed except for a small wick drain in the lower end of the wound just above the tracheotomy tube.

As far as respiration goes, we should be able to judge the result within ninety days. As for voice production our judgment should be deferred for many months. We hope that a decided forward step has been made in the solution of this very difficult problem.

Undoubtedly, we shall begin to find in the literature reports of cases managed along this or similar lines, and the prognoses of cases of bilateral-laryngeal paralysis will become materially improved.

DIFFERENTIAL DIAGNOSIS OF DISEASES OF THE THYROID GLAND

JOHN PHILLIPS

THE thyroid gland, consisting of two lateral lobes and an isthmus, surrounds the trachea like a horseshoe. The isthmus covers the second and third ring of the trachea and occasionally extends upward in front of the thyroid cartilage or even the cricoid. Special bands of connective tissue known as the cricothyroid or suspensory ligament pass upward from the isthmus and lateral lobes of the thyroid to form an attachment with the cricoid cartilage. This attachment is important because it is responsible for the movement upward and downward of the gland during deglutition. Sometimes the thyroid has also a pyramidal lobe which extends upward in the median line from the isthmus to the hyoid bone. This represents the remnant of the thyroglossal duct and may be the site of a struma or a cyst. Accessory thyroid glands are sometimes present, being situated in the neck in the neighborhood of the hyoid bone and below the thyroid, or in the mediastinum as low down as the arch of the aorta.

The posterior and inner surfaces of the lateral lobes of the thyroid lie in contact with the cricoid and thyroid cartilages, the trachea, esophagus, inferior laryngeal nerve, and the inferior constrictor of the pharynx. It is important to remember these relationships because when the gland is enlarged, pressure on these structures gives rise to definite symptoms. In front of the lateral lobes lie the superficial muscles of the neck—the sternohyoid, sternothyroid, omo-

hyoid, and a small portion of the sternomastoid muscle. To the outer side of and posterior to each lateral lobe and covered by the sternomastoid muscle lies the carotid sheath, containing the common carotid artery, the external jugular vein, and the vagus nerve. When this lobe is enlarged the carotid artery is displaced outward and backward. This outward displacement serves to differentiate thyroid enlargements from glandular swellings or tumors in this region, as the artery passes centrally through the inflammatory mass.

One of the two superior thyroid arteries enters the superior pole of each lateral lobe, one of the inferior thyroid arteries enters each inferior pole. In many cases of goiter these arteries are considerably increased in size, so that a distinct pulsation can be felt throughout the entire gland. The small ima arteries which arise usually from the aorta enter the lower portion of the isthmus, from which the corresponding veins pass to the innominate veins. The latter are of importance because they are sometimes the seat of air embolism. One of the recurrent laryngeal nerves passes to the inner side of each lateral lobe, a position which renders it liable to compression by a struma or to injury during the surgical removal of a goiter, with resultant paralysis of the abductor muscle of the corresponding vocal cord.

Various complicated pathologic classifications of diseases of the thyroid gland have been worked out by different observers, from among which I think the following headings are most convenient for the practical consideration of the clinician:

1. Simple goiter which includes the hyperplasias of the gland seen at puberty.
2. Colloid goiter.
3. Adenoma of the thyroid.

4. Exophthalmic goiter, hyperthyroidism.
5. Myxedema, hypothyroidism.
6. Tumors of the thyroid gland.
7. Inflammations of the thyroid.

SIMPLE GOITER

Under the term "simple goiter" are included the hyperplasias of the gland which are very frequently seen at puberty or in adolescence (Fig. 8). These occur more com-



Fig. 8.—Adolescent goiter.

monly in certain districts among which the region of the Great Lakes is one of the most important in this country. As a rule, in simple hyperplasia there is a diffuse enlargement of the entire gland affecting equally all its parts,

although in some instances one lateral lobe will be more enlarged than the other. In cases of simple goiter the size of the gland increases during menstruation and also during pregnancy. As a rule there are no symptoms present in these cases and treatment is usually sought because of the disfigurement of the neck (Fig. 9). The diagnosis of



Fig. 9.—Enormous diffuse simple goiter.

simple goiter is easy and its differentiation from other conditions presents no difficulty.

COLLOID GOITER

The only symptoms presented by colloid goiter are those due to the resultant compression of the surrounding



Fig. 10.—Colloid goiter.

structures. Like the simple goiter, a colloid goiter may present a uniform enlargement of the entire gland or one

lobe may be much more enlarged than the other (Figs. 10, 11). The muscles covering the growth may become greatly



Fig. 11.—Colloid goiter.

stretched and atrophied, and if the goiter is of great size the superficial muscles may not be sufficient to support it so



Fig. 12.—Pendulous goiter.

that it may descend from its own weight and become almost pendulous (Fig. 12). The larynx and trachea may be greatly compressed, the character of the resultant deformity of these structures depending upon the relative enlargement of the different portions of the gland. Thus, if the isthmus is enlarged, there will result an anteroposterior compression. If one lateral lobe is particularly enlarged, the trachea may be compressed and displaced to one side; or if both lateral lobes are greatly enlarged, the trachea may be flattened from side to side. If the enlargement in the two lobes is at different levels, the trachea may assume an S shape. As a result of this tracheal compression the patient may have great difficulty in breathing, with a resultant inspiratory stridor. The patient may have a persistent, irritating cough, which differs from the cough which results from compression of the recurrent laryngeal nerve, the latter occurring in paroxysms and being of a curious resounding character without any definite expectoration. If the esophagus is compressed there will be difficulty in deglutition, especially when the patient attempts to swallow solids. The blood-vessels may be very much displaced, particularly the common carotid, which is displaced outward. As the goiter enlarges it may descend into the superior mediastinum and give rise to trouble there as the result of compression of the mediastinal contents.

INTRATHORACIC GOITER

Sometimes an enlargement of the lower portion of either lateral lobe or the isthmus may descend within the thoracic cavity and form the complication called intrathoracic goiter (Fig. 13). Sometimes such a goiter develops from an accessory gland in the superior mediastinum (Fig. 14). The superior mediastinum is bounded in front by the



Fig. 13.—Intrathoracic goiter.



Fig. 14.—Substernal goiter with two metastatic abscesses in lungs.

manubrium sterni and the upper three ribs, posteriorly by the upper three dorsal vertebræ, in front of which lie the trachea and the esophagus, and below by the arch of the

aorta. Goiters which arise from the isthmus and lie in the median portion of the mediastinum compress the trachea and the esophagus, and may also displace the aorta downward. In cases of enlargement of the lateral lobe of the thyroid the trachea may be displaced and compressed from side to side, and if there is a double intrathoracic goiter involving both lobes the trachea may be twisted on itself, as well as compressed, thus resembling the deformity seen in scoliosis of the spine. There is always a great deal of interference with the venous trunks, in some instances even to the extent of causing almost complete occlusion of the superior vena cava as illustrated by the following case:

The patient, a male, sixty-two years of age, was seen first on March 7, 1921. He had always been well until ten years before, when his face began to swell, his lips and face became cyanosed, and the veins over his body, particularly over the chest and neck, were very much distended. He had never been very short of breath and never had any choking spells. He had noticed for at least ten years or more that he had a goiter, but had never been troubled with palpitation of the heart, and had only occasionally noticed a shaking of the hands.

Examination showed a well-marked cyanosis of the face and hands, particularly of the lips. The eyes showed a moderate exophthalmos, with some slight lagging of the upper lid on looking downward and increased widening of the palpebral fissure. There was no ocular palsy. There was an enlargement of the thyroid gland, particularly of the right lobe, which contained a hard, firm adenomatous nodule about the size of a hen's egg. There was also a similar nodule in the isthmus about the size of a hickory nut. The jugular veins were very much distended, and there was extreme distention of the veins over the chest

and anterolateral portions of the abdomen as shown by the accompanying picture (Fig. 15).

The examination of the chest showed diminished expansion of the base of the right lung. There was increased tactile fremitus at the apex of the right lung in front and



Fig. 15.—Venous thrombosis from obstruction due to intrathoracic goiter.

behind, while at the base of the right lung, from the angle of the scapula downward, the tactile fremitus was absent. The tactile fremitus over the left lung was normal. There was more or less impairment of resonance all over the right side of the chest with dulness over the base of the right lung from the level of the angle of the scapula downward.

There was also extensive impairment of resonance in the first, second, and third interspaces below the clavicle. Over this latter area the breath sounds were bronchial in character, and a few coarse râles could be heard. Over the base of the right lung posteriorly there was almost complete absence of breath sounds.

The heart was enlarged in both diameters, with a systolic murmur at the apex. The pulse was somewhat irregular, arrhythmic, rate 100; blood-pressure, systolic 126, diastolic 76. The liver edge could be easily felt and there was edema of the lower extremities. The Wassermann reaction was negative. The urine showed a trace of albumin and some granular casts. The blood count showed red blood cells 4,290,000, white blood cells 6400, and hemoglobin 80 per cent. The differential count showed polymorphonuclear neutrophils 60 per cent., small lymphocytes 32 per cent., large lymphocytes 2.5 per cent., and transitionals 5.5 per cent. The blood chemistry showed blood urea 29 mgm. per 100 c.c., blood-sugar 112 mgm. per 100 c.c., and blood chlorids 580 mgm. per 100 c.c.

Fluoroscopic examination of the chest revealed a homogeneous shadow occupying the entire upper lobe of the right lung. The aortic arch was prominent. The trachea was not displaced. The mass was definitely connected with the mediastinum and pulsated, but not with the expansile pulsations characteristic of aneurysm. On deep respiration and deglutition the shadow did not separate from the aortic shadow.

The oblique view was of no aid in determining the character of the mass. The entire lower lobe of the lung was consolidated, having an irregular upper border with a dense base, the picture indicating fluid in the base with an inflammatory process above. The middle lobe of the lung

was free from involvement. The heart was apparently normal in shape and position, but somewhat increased in size. From the fluoroscopic findings the diagnosis was probable aneurysm. Plates of the chest were made which confirmed the fluoroscopic findings, with the exception that a rather indistinct regular shadow could be seen within the homogeneous mass. This was interpreted as a probable saccular aneurysm with luetic involvement of the rest of the lung.

In addition to this, the diagnosis included adenoma of the thyroid, chronic myocarditis with beginning decompensation, and hydrothorax with infiltration at the base of the right lung.

The patient was advised to rest, and fifteen minims of tincture of digitalis with five grains of sodium iodid three times a day were prescribed. We expected him to return in two weeks for further observation, but he did not return until September 12, 1921. He had been taking the iodid regularly, and had lost forty pounds in weight; the edema of the extremities had disappeared and his cyanosis was somewhat decreased. His pulse-rate, however, had increased to 120. He showed a marked tremor of the hands, his skin was very moist, and he had been troubled with diarrhea.

Examination of the chest showed that there was some diminution in the area of dulness below the clavicle on the right side. The signs of fluid at the base of the right lung had disappeared. *x*-Ray examination of the chest at this time, plates giving anterior, posterior, and oblique views being taken, showed quite a contrast to the picture taken at the first examination. All the inflammatory involvement of the upper lobe had disappeared, except for a dense, thickened pleura between the upper and the middle lobes extending to the periphery of the lung. The shadow which

was seen within the mass at the first examination, in these plates, appears distinct and clear, and in the oblique view



Fig. 16.—Radiograph of patient shown in Fig. 15, showing well-defined outline of intrathoracic goiter.

is seen to be continuous with a goiter shadow in the neck, and separated from the aorta (Figs. 16, 17).

There is very little doubt that the development of the

symptoms of hyperthyroidism was due to the long-continued administration of sodium iodid, because in the preceding month, since the iodid had been discontinued, the patient



Fig. 17.—Radiograph of patient shown in Fig. 15, oblique view.

had begun to gain in weight, the tremor of the hands was less, and he was not so conscious of the palpitation of the heart.

Upon the sudden death of this patient, shortly after his last visit, there was found at autopsy a marked hyperplasia of both lobes of the thyroid gland and of the isthmus, with an intrathoracic goiter about the size of a small orange, extending from the lower pole of the right lateral lobe. This was covered by a thick capsule, which was adherent to the posterior and inner portion of the right apex of the lung, to the right vagus nerve, and to the right subclavian and innominate veins. The right innominate vein was almost completely obliterated by fibrosis, doubtless resulting from the organization of a thrombus.

These autopsy findings justified our previous conclusion that the enlargement of the veins of the trunk and neck were the result of obstruction of the venous return to the heart through the superior vena cava (Fig. 18).

The outstanding subjective symptoms of intrathoracic goiter are, therefore, as one would expect, the mechanical result of the position and degree of enlargement in the individual case.

Dyspnea, which is usually continuous and associated with an inspiratory stridor, is present in most cases. In some instances there may be choking spells which are very serious. These are more likely to occur when the intrathoracic goiter is not very large and is situated in the median line, so that it may slip in and out of the superior strait of the mediastinum.

Coughing is another troublesome symptom. This is due either to the irritation of the trachea resulting from compression, or in some instances to irritation of the recurrent laryngeal nerve. Hoarseness from the same causes is also present. Sometimes these patients complain of wheezing, which also is due to compression of the windpipe. Dysphagia, especially difficulty in swallowing solid food, is a not infrequent symptom.



Fig. 18.—Autopsy specimen from case of intrathoracic goiter described in text.

Cardiac disturbance is sometimes present in cases of intrathoracic goiter as the result of compression and resultant irritation of the sympathetic and vagus nerves. This may manifest itself in tachycardia, bradycardia, and various cardiac arrhythmias. Sometimes there may be attacks of paroxysmal tachycardia.

On physical examination, one of the most striking features of intrathoracic goiter is the distention of the veins in the upper part of the thorax. These veins may be quite large, and extend outward over the shoulders as shown in the case described above. Their enlargement is more marked on one side than on the other, depending upon whether the goiter arises from the right or left lateral lobe. On palpation, when the patient swallows, sometimes the upper part of the intrathoracic goiter can be felt to ascend into the superior strait. Displacement of the trachea to the right or left may also be noted. Percussion often discloses a retrosternal dulness or dulness on either side of the sternal border.

Fluoroscopic examination is of great assistance in the diagnosis of intrathoracic goiter. The tumor shows a convexity laterally, and if the goiter is nodular the surface may be uneven. The tumor may pulsate because of its close proximity to the aorta. For this reason it may often be difficult to differentiate between an intrathoracic goiter and aneurysm. Under the fluoroscope, however, it will be seen that except in malignant cases the intrathoracic goiter changes its position during inspiration and expiration, and also during the act of swallowing, so that an angle is formed between the tumor and the ascending aorta, whereas the shadow of an aneurysm remains continuous with the aorta.

ADENOMA OF THE THYROID

Adenomata of the thyroid are manifested by an enlargement of the gland that is nodular in character (Figs. 19,



Fig. 19.—Multiple adenomata of the thyroid.



Fig. 20.—Adenoma of the thyroid.

20). They may be single or multiple, and vary greatly in size. They can be readily differentiated on palpation by the fact that usually they are harder in consistency than the other portions of the gland. In some instances, however,

they become cystic, and then are quite soft in consistency. Occasionally calcification occurs. Adenomata of the thyroid are much more likely to cause asymmetric enlargements of the thyroid than any other condition. Sometimes hemorrhage may occur in them as the result of severe exertion. One such case I saw five years ago in a boy sixteen years of age, who, while wrestling with some other boys at the place where he was employed, developed a sudden acute swelling of the neck which caused considerable difficulty in breathing because of its compression of the trachea. This, however, subsided in the course of ten days, and most of the swelling entirely disappeared.

In the majority of cases the general symptoms of adenomata of the thyroid differ in no way from the symptoms of colloid goiter. In other words, as a rule the only symptoms are those resulting from the compression of the surrounding structures. This is not always true, however, because sometimes hyperthyroidism may develop in patients with adenomata. One interesting feature of the cases of adenomata with hyperthyroidism is that the toxic symptoms, as a rule, do not develop until after the adenomata have been present for a number of years, and they are more likely to be accompanied by cardiac disturbances in the form of arhythmia and myocardial changes than the ordinary case of hyperthyroidism. This characteristic probably is the result of the long-continued toxemia.

EXOPHTHALMIC GOITER OR HYPERTHYROIDISM

Other names applied to this condition are toxic goiter, thyrotoxicosis, Basedow's disease, Parry's disease, Graves' disease. Sir William Osler has stated that if the name of any one physician is applied to the disease, the credit should go to Parry.

The cardinal symptoms of exophthalmic goiter are: (1) the presence of an enlarged thyroid or struma; (2) exophthalmos; (3) tremor; (4) tachycardia (Fig. 21).

Changes in the Thyroid Gland.—The thyroid may show a symmetric enlargement, although in some cases there may not be very much increase in the size of the gland. However, physical examination of the thyroid does not



Fig. 21.—Typical case of exophthalmic goiter.

always give us a true estimate of the size of the gland, as at operation, some of the cases in which the gland appeared quite small, show quite marked enlargement. Sometimes the gland is firm and presents a granular feeling to the palpating hand on account of the irregularity due to the hyperplasia; at other times it feels soft, almost cystic. The superior thyroid artery can often be felt to pulsate

much more vigorously than in the normal gland. In fact, the whole gland may show an expansile pulsation almost like that of an aneurysm. Frequently, as a result of the increased vascularity, a systolic murmur can be heard. Occasionally also a thrill can be felt on palpation.

Eye Signs.—The eye signs present some of the most characteristic features of this disease. There is a noticeable staring expression and exophthalmos, usually bilateral, but occasionally unilateral, is present in a large proportion of the cases. The degree of exophthalmos varies a great deal, sometimes being so extreme that the eyeball is displaced from the socket. Riesman has described one rare instance in which a murmur was plainly audible over the ball of the eye. There is a lagging of the upper lid on looking downward (von Graefe's sign). The slit between the two eyelids is widened so that even the sclera will show between the lid and the iris (Dalrymple's sign). There is infrequent winking (Stellwag's sign), and the power of convergence is often decreased (Moebius' sign). There may be epiphora or the tears may be diminished. In occasional cases paresis of some of the external ocular muscles has been described. Sometimes, too, there is quite a marked pigmentation of the eyelids.

Vascular Symptoms.—Tachycardia is such a common symptom that the presence of Graves' disease should be suspected in any case in which there is a persistently rapid pulse. The rate may vary from 90 to 100 in the milder cases to from 160 to 180 in the more severe cases. The volume of the pulse is large, and there is a marked throbbing of all the accessible arteries. The patient also complains of a subjective sensation of throbbing. This is particularly marked when he puts his head on the pillow at night. Various forms of cardiac arhythmias are present, and in the

late stages of exophthalmic goiter there may be well-defined signs of myocardial degeneration and cardiac decompensation. The heart may show some enlargement, and a systolic murmur may be heard over the precordium. The blood-pressure may show very little change except that the systolic pressure may be slightly increased, and the diastolic may be lower than normal. In other words, the pulse-pressure is increased. The cardiac manifestations have been described at length in another section of this volume.

Blood Changes.—The most characteristic change in the blood-picture in hyperthyroidism is the presence of a moderate degree of lymphocytosis.

Vasomotor and Tropic Symptoms.—One common subjective symptom is the sensation of warmth and there is a tendency to flushing of the skin. The skin, as a rule, is very moist and has a soft feeling. There is very free perspiration of the extremities and from the armpits. Dermatographia is nearly always present and the pilomotor reflex is increased. Very often there is pigmentation of the skin. This may occur on various parts of the body, but is most marked on the face. Occasionally well-defined areas of vitiligo or leukoderma are seen on the neck or other parts of the body or extremities (Fig. 22). The hair is scanty on the body and the hair on the scalp has a tendency to fall out. Very often the nails show signs of degeneration. Pruritus may be a persistent and unpleasant symptom.

Respiratory Symptoms.—The respirations are increased in rate and are superficial and irregular. The excursion of the chest shows a diminished amplitude. The patient complains of shortness of breath and at frequent intervals will take a very deep inspiration to overcome the feeling of air hunger. The voice is often hoarse and the patient is often troubled with a cough. These last two symptoms may be

due either to a compression of the trachea or to interference with the recurrent laryngeal nerve.

Digestive Disturbances.—In the early stages the appetite, as a rule, is increased. In fact, the excessive appetite



Fig. 22.—Lack of pigmentation of skin sometimes associated with hyperthyroidism.

presents a strong contrast to the great loss in weight. In the later stages, however, there may be persistent nausea, vomiting, and belching of gas. Very frequently, too, diarrhea is a troublesome symptom.

Urinary and Genital Symptoms.—Frequency of urination and the passage of large quantities of urine are not uncommon symptoms. There is a diminished tolerance to carbohydrates, so that often sugar will appear in the urine. Sometimes there is a sexual hyperexcitability, but usually there is a diminution both of libido and of potentia.

Metabolic Disturbances.—In a severe case the patient loses weight very fast. This is due to the rapid oxidation of the tissues and the burning up of his own tissue protein. Therefore the basal metabolism as shown by the calorimeter is greatly increased. Estimation of the basal metabolism is, therefore, a valuable diagnostic measure in cases of hyperthyroidism. There is also an increased sensitiveness in these patients to the injection of adrenalin. This sensitiveness is manifested by increase in the rate of the heart-beat, by increased blood-pressure, and by hyperexcitability after an injection of five to seven minims of adrenalin (Goetsch test). Cases of toxic goiter often have a slight elevation of temperature.

Nervous and Mental Disturbances.—Patients with exophthalmic goiter are extremely nervous and apprehensive. In many instances they seem to be in the state of constant fear. Very often they are irritable and given to fits of temper. They are very restless and, as a rule, the mental processes are not as keen as when they are in normal health. Sometimes they are quite forgetful. In severe cases the mental symptoms may take the form of an active delirium. In others there may be great depression amounting to melancholia. A fine tremor of the hands varying in rate from seven to ten per second is a striking feature.

Muscular Symptoms.—These patients complain of great weakness and extreme exhaustion after any severe or prolonged effort. Sometimes they complain of a sudden giving

way of the knees. At times, too, they have muscular cramps of the extremities.

DIFFERENTIAL DIAGNOSIS OF HYPERTHYROIDISM

Neurasthenia.—In the differential diagnosis of cases of hyperthyroidism we must take into consideration the fact that it is very difficult to differentiate some forms of nervous exhaustion or simple neurasthenia from the mild cases of hyperthyroidism. In a case of neurasthenia, however, the pulse slows down to normal as soon as the patient is put at rest and the basal metabolism is not increased.

Neurocirculatory Asthenia.—Another condition which has given rise to a great deal of difficulty in differential diagnosis is neurocirculatory asthenia (irritable heart), which was seen so frequently among soldiers during the last war. This condition, which was first described during the Civil War by Da Costa, simulates hyperthyroidism very closely. It occurs after infections or in individuals who have shown evidence of physical inferiority from the time of birth. These individuals are delicate as babies and very often present evidence of rickets. As they become older they are unable to take part in the games with other children, and when they reach the age of taking up some trade they always choose some line of work which requires very little physical exertion. These patients complain of dizziness when standing in an upright position; they also complain of palpitation of the heart and throbbing of the vessels; they often complain of pain in the precordium and of tenderness of the pectoral muscles. They perspire very freely, and very often faint when they stand for a long time. Many of these cases have digestive disturbances and a large proportion of them have visceroptosis. The cardiac rate, as stated above, is very much increased. They

have tremor of the fingers and cyanosis of the hands, very free perspiration, and very marked dermatographia.

In fact, in many instances the absence of ocular symptoms and the absence of goiter are the only points of differentiation between neurocirculatory asthenia and hyperthyroidism. Many observers think that there is a very close relationship between these conditions, and I am inclined to believe that this is true. In the majority of cases, however, basal metabolism estimations in these patients have not shown an increase in rate.

Pulmonary Tuberculosis.—Another condition which must be kept in mind in the differential diagnosis of hyperthyroidism is pulmonary tuberculosis. Many cases of early pulmonary tuberculosis do not show any very definite evidence in the lungs and may complain only of exhaustion and an increased pulse-rate. It is, therefore, always important in making a diagnosis of what appears to be a mild case of hyperthyroidism to be on the lookout for pulmonary tuberculosis.

Paroxysmal Tachycardia.—Cases of paroxysmal tachycardia, because of their nervousness, anxiety, and increased pulse-rate may be confused with hyperthyroidism when seen for the first time. A careful history, however, will show that, except for some shortness of breath, the patient has been in normal health, and that the onset of tachycardia has been very sudden and the return to the normal cardiac rate equally sudden. However, one must bear in mind the fact that hyperthyroidism is often complicated by attacks of paroxysmal tachycardia.

MYXEDEMA

Myxedema may be congenital in origin, in which case it is due to the absence of the thyroid gland (thyreo-aplasia);

or it may occur late in life as the result of a deficiency of thyroid secretion or as the result of the removal of too much of the gland at operation.

In cases of **congenital myxedema** the child fails to develop mentally or physically. The head is brachycephalic in type and the fontanels remain open. The child has a dull,



Fig. 23.—Congenital myxedema. Typical case. Child aged seven years.

heavy appearance, the tissues are very thick and dry, the hair is scanty and dry, there is a sacculation under the eyelids, the face is swollen, the nose broad and flat, the lips are thick, and the tongue is enlarged, protruding between the lips (Fig. 23). The voice is husky and coarse. The abdomen is protuberant and there is a tendency to umbilical hernia. The child develops very slowly mentally, so that

at the age of ten he may not be any further advanced than a child of two. The extremities are short and the hands are thick and pudgy. The bones ossify very slowly, so that the ossification of the bones in a child of twelve may not be any farther advanced than in a child of five. In the supraclavicular regions there are large pads of fat. The temperature is persistently subnormal.

This condition must be differentiated from **Mongolian idiocy**. In cases of Mongolian idiocy the tissues are not thickened as much as in myxedema; the tongue is not as much enlarged and does not protrude so far between the lips; and there is a curious slanting of the eyes downward and inward toward the nose, which is absent in myxedema. In Mongolian idiocy the anteroposterior diameter of the skull is very much decreased; the eyes are set closely together, the palpebral fissure is narrow, and there is frequently epicanthus; the hands of the Mongolian idiot are short and thick, and the little finger is so short that often it does not reach to the last interphalangeal joint of the ring finger. Congenital heart disease is much more common in the Mongolian idiot than in cases of myxedema. Relaxation of the ligaments of the joints is a striking feature, so that the extremities can be put in almost any position with ease. But the most important feature in the differentiation between congenital myxedema and Mongolian idiocy is the presence or absence of the slanting eyes described above.

Achondroplasia is another condition which is occasionally mistaken for cases of congenital myxedema. The characteristic feature of this disease is the shortness of the arms and legs, as compared with the length of the body. In cases of achondroplasia, moreover, the intelligence is normal and the thyroid gland can be easily palpated.

In adult cases of **myxedema**, which are found more frequently in women than in men in the proportion of four to one, the most striking symptoms are a feeling of chilliness, a tendency to drowsiness, increase in weight, dryness of the skin, loss of hair, and change in the voice. The subcutaneous tissues are very thick and the patient's weight is increased. The facial features are greatly altered. The lines of expression of the face are gone, the eyes are dull and heavy, there is sacculation under the eyes, the nostrils are broad and thick, the lips are thickened, and the voice is husky. Pads of fat are present in the supraclavicular region. Although there appears to be a swelling of the subcutaneous tissue, it will not pit on pressure. The temperature is subnormal, and the basal metabolism rate is from 20 to 40 per cent. below normal. There is an increased tolerance to carbohydrates. The memory is defective; the patients are often irritable and suspicious; and in some instances they pass into a condition of dementia. The thyroid is diminished in size and may become completely atrophied. These patients show a tendency to arteriosclerosis with arterial hypertension and myocardial degeneration. With the dryness of the skin there is almost complete absence of perspiration and the sensation of touch is impaired. Patients with myxedema often complain of rheumatic pains in various parts of the body. The hands and feet are thick and clumsy, the fingers are enlarged and lose their dexterity. To this condition of the hands Gull has aptly applied the term "spade hands." Menstruation is often suppressed and there is a diminution in the sexual desires of both sexes. The blood shows a diminution in the number of red corpuscles and a correspondingly greater reduction in the hemoglobin. The white cells show a leukopenia and a hyperlymphocytosis.

Because of the anemia cases of myxedema have sometimes been incorrectly diagnosed as **pernicious anemia**. In the latter condition, however, there is no infiltration of the subcutaneous tissue, and the blood findings serve to establish the differentiation. In pernicious anemia the color index is high, the anemia is more marked, the presence of nucleated red corpuscles and the characteristic changes in size, shape, and staining properties of the red cells make the diagnosis easy. Moreover, in pernicious anemia pathologic changes in the central nervous system, with the characteristic symptoms and physical signs, are found in 70 per cent. of the cases.

The infiltration of the tissues in myxedema has led this condition to be incorrectly diagnosed as *nephritis*. In the latter disease the tissues pit on pressure, and if there is much edema fluid accumulates in the serous sacs. The urinary findings together with functional kidney tests will render the diagnosis clear.

Hypopituitarism.—Cases of hypopituitarism are sometimes incorrectly diagnosed as myxedema. I have seen two instances of this error in diagnosis within the past six months. One of these cases, a young man twenty-two years of age, is shown in Fig. 24. In hypopituitarism the skin is soft, the body practically hairless. In the male the distribution of the pubic hair when present resembles that of the female, the sexual organs are imperfectly developed, and the configuration of the body and the development of the breasts resemble those of the female. The voice is high pitched. The fingers are long and tapering. In cases of hypopituitarism various grades of enlargement of the sella turcica are seen and bitemporal hemianopsia may be present.



Fig. 24.—Typical case of infantilism due to hypopituitarism. Note lack of hair on axilla and on pubes, characteristic form of hand, female contour. Patient aged twenty-two.

TUMORS OF THE THYROID

Tumors of the thyroid may be benign or malignant, and usually develop in a pre-existing goiter. Of the benign tumors, the most common are the adenomata, which we have described above; such growths as fibromata, lipomata, and echinococcus cysts being so rare as not to warrant much consideration. Occasionally adenomata may become malignant. The most important malignant tumors are the carcinomata. They are found much more frequently than the sarcomata. Malignant tumors of the thyroid invade the

capsule so that it becomes adherent to the surrounding structures. The trachea and the esophagus may be invaded and compressed. The carotid artery may be displaced and the carotid sheath may become adherent to the tumor mass. The walls of the veins are less resistant than the walls of the arteries to the invasion of the tumor, so that thrombosis often occurs. There may be pressure on the recurrent laryngeal, vagus and sympathetic nerves, and the upper roots of the brachial plexus. Metastases may occur in any



Fig. 25.—External appearance of malignant goiter.

organ. In one case that I saw some years ago at autopsy metastases from a carcinoma of the thyroid were found in the pituitary gland and in the lungs.

A malignant tumor of the thyroid should always be suspected when a goiter begins to enlarge quite rapidly, and especially if it is painful and is adherent to the surrounding skin (Figs. 25, 26). Sometimes the pain is quite severe and may be referred to the shoulder because of pressure on the brachial plexus. Interference with deglutition and difficulty

in breathing are caused by the pressure on the esophagus and trachea. The voice is hoarse and there may be aphonia. The veins of the neck may be greatly congested and edema of the face and cyanosis may be present. The skin is reddened and in rare cases may become ulcerated. If the sympathetic nerve in the neck is compressed there may be a



Fig. 26.—External appearance of malignant goiter.

slight exophthalmos, miosis, and loss of pupil reaction. In the late stages of the disease ulceration into the trachea and esophagus, with resulting hemorrhage, may occur. The patient shows rapid emaciation and cachexia, and a remittent fever is not uncommon. Death occurs from exhaustion or from pneumonia.

INFLAMMATION OF THE THYROID GLAND (THYROIDITIS OR STRUMITIS)

An inflammatory condition of the thyroid gland may occur during the course of an acute disease, such as typhoid fever or influenza, or it may be more chronic in character as the result of a tuberculous or syphilitic infection. In the

acute cases the onset of the disease is sudden and is ushered in by chills and fever. There is intense pain in the neck which is referred to the occiput, the ear, or down the arm. A sense of constriction of the neck and difficulty in breathing is complained of in the majority of cases. Very soon the thyroid is swollen, hot, and tender. The tenderness and pain in the gland is increased by swallowing or by movements of the head and neck. Sometimes there is an accompanying tracheitis with hoarseness and cough, and occasionally aphonia. In these cases alarming suffocative attacks may occur. If suppuration occurs the skin over the gland becomes reddened. I saw one such case a year ago in a man forty-five years of age who had typhoid fever. He had always had a goiter and the right lobe of the thyroid contained a cystadenoma about the size of a hen's egg. During the fourth week of the disease this became painful and tender, increased considerably in size, and the skin became reddened. On the tenth day after the onset of the strumitis an incision was made and six ounces of pus evacuated. The inflammation quickly subsided and the patient made a good recovery.

A rare form of thyroiditis, which has been termed "woody thyroiditis," was first described in 1896 by Riedel. The gland is hard and firm, resembling a malignant tumor, and the most striking symptoms are pain and dyspnea. Bacteriologically the cause of the condition has not been determined. It may cause all the symptoms and physical signs from pressure on the surrounding structures that have been described under colloid goiter. Though rare, it is important to remember that such a condition exists because it is not infrequently mistaken for malignant tumor.

ADRENALIN SENSITIZATION TEST FOR HYPERTHYROIDISM

ROBERT S. DINSMORE

THE adrenalin sensitization test¹ is based on the observation that in cases of hyperthyroidism there is a constitutional hypersensitiveness to the injection of adrenalin chlorid. Dr. Goetsch used the test to establish a differential diagnosis between hyperthyroidism and early tuberculosis in patients presenting the syndrome of loss of weight and strength, fatigue, and slight elevation of temperature, in whom the physical signs and *x*-ray findings for tuberculosis were negative.

The test is not made until the patient has been in the hospital for at least twenty-four hours and has become thoroughly accustomed to his new surroundings. It is essential that the normal readings be obtained while the patient is quiet and calm. Six minims of adrenalin chlorid, 1 : 1000, are injected subcutaneously with a tuberculin syringe. In cases of severe exophthalmic goiter the Goetsch test is not only unnecessary, but is unsafe as well. As a rule patients with a blood-pressure above 160 are not subjected to the test.

Observations are made at five-minute intervals and include the following:

1. Blood-pressure.
2. Pulse-rate.
3. Respiration rate.

¹ Goetsch, E., N. Y. State Med. Jour., 1918, xviii, 259.

4. Nervousness.
5. Tremor of fingers.
6. Hyperhydrosis.
7. Size of pupils.
8. Pallor or flushing of skin.

If, before the adrenalin is injected, the patient becomes excited or frightened, it is advisable to discontinue the test at once. The observations and readings are continued for from forty minutes to one hour or longer if the reaction persists. At the completion of the test the patient is asked for his subjective symptoms, which are also recorded on the chart. The results of the reaction are recorded as either negative, slight, positive, or marked.

We have made Goetsch tests on 251 patients. In 213 of these, 89 per cent., there were positive reactions of varying degrees. In the remaining 11 per cent. the reaction was negative.

The average increase in blood-pressure in the entire group was eighteen. Some of the patients showed no increase in blood-pressure, but increased tremor, nervousness, and hyperhydrosis. The highest increase in blood-pressure was in a patient with a blood-pressure of 168 mm., which, following an injection of four minims of adrenalin, was increased to 260 mm., an increase of 92 mm. Another patient showed an increase of 74 mm., the blood-pressure rising from 138 to 212.

Pallor was noted only in severe reactions, occurring in about 11 per cent. of the cases. Sweating was more frequent. Pallor is probably the most difficult objective symptom to interpret, and little reliance can be placed upon it as a positive symptom. Tremor occurred in 204, or 81 per cent., of the patients tested. Nervousness as an objective symptom occurred less frequently, only 147 of

the cases, or 58 per cent., displaying an increased objective nervousness. If the subjective nervousness of which the patients complain so frequently at the completion of the test were included the percentage would be slightly higher.

Comparing the results of basal metabolism measurements with the results of the Goetsch test, we find them in accord in about 80 per cent. of the cases. Among a group of patients with metabolism more than 20 per cent. above the normal the Goetsch test was positive in 85 per cent. We had hoped that the Goetsch test and metabolism would give us a means whereby to estimate the operability of our patients. While it is true that a large percentage of patients with a very greatly increased metabolism and a marked reaction to adrenalin would probably show marked postoperative reaction, the following observations show that one cannot, with accuracy, predict the severity of the postoperative reaction.

- Case I. Metabolism increase, 75 per cent.;
Goetsch test positive;
Postoperative reaction slight.
- Case II. Metabolism increase, 19 per cent.;
Goetsch test negative;
Postoperative reaction moderately severe.
- Case III. Metabolism increase, 82 per cent.;
Goetsch test positive;
Postoperative reaction, none.

A total of sixty-five Goetsch tests have been made in patients with adenomata. In forty-one of these the test was entirely negative, and it was definitely positive in only eight. In only one of the sixty-five cases was there a severe postoperative reaction with dementia. In all the other cases there was no, or a very slight, postoperative reaction. In these patients the basal metabolism was normal.

Practically no difference can be noted between the post-operative reaction in patients with a slight positive reaction to adrenalin and that in those with a negative reaction.

SUBJECTIVE SYMPTOMS

Among the interesting aspects of the Goetsch test are the subjective symptoms of the patients. Some of these should certainly be discounted. Some patients become frightened, restless, and cry immediately after the hypodermic injection. This response can always, however, be easily differentiated from the reaction to the adrenalin.

Among the more common complaints are pain in the chest and neck, various cardiac symptoms, nervousness, and a feeling of warmth or of cold. Some patients exhibit a distinct reaction with no complaint. The verbal expressions of the patients best describe their subjective symptoms:

"Body shaking," "I feel hot," "My feet are sweating," "My back is hot," "Heart pounded," "Nervous and trembly," "Throbbing in ears" (one case only), "Choked up sensation in neck," "Heart beating better," "Heart thumping," "Heart beating hard," "Heart jumping," "Short of breath," "One of my normal attacks," "Chilly," "That medicine you gave me has effected my heart," "Headache," "I feel a thud in my heart," "Like overloading the stomach," "Pressure against eyes," "Shaky," "Like a current of electricity through the body," "Choking," "Weak and trembly," "Backache," "Heart missing a beat," "I feel weak and my heart is beating so fast," "Pinching sensation in left side," "My heart is beating much stronger and shakes my body," "I feel so nervous," "My heart is beating faster," "My heart is pounding," "Feel as if my heart was all over me," "Every beat goes to the end of my toes," "Something is making my heart thump," "I feel better."

CONCLUSIONS

1. The Goetsch test has been of distinct value to us in the differentiation of borderline cases of hyperthyroidism.

2. Eighty-nine per cent. of the patients with clinical symptoms of hyperthyroidism give a positive reaction to adrenalin.

3. In about 85 per cent. of the cases the results of the Goetsch test are in agreement with the metabolism estimations. (Basal metabolism estimations themselves are distinctly less than 100 per cent. accurate.)

4. The results of the reaction to adrenalin cannot be used as a basis for estimating the operability or postoperative reaction of a patient. In this respect the Goetsch test can never supplant clinical experience with large numbers of patients with hyperthyroidism.

A SERUM TEST FOR EXOPHTHALMIC GOITER

FRANK D'HOUBLER

THE test described below was devised by Dr. Kurt Kottman, of Berne, Switzerland, who, after trying it in a number of cases, believes that it is a valuable diagnostic means for the detection of either hyper- or hypothyroidism.¹ The writer is greatly indebted to Dr. Kottman for his personal demonstration of the technic of this method.

TECHNIC

Blood is withdrawn from a patient by the same method as that employed for a Wassermann test. In order to secure reliable end-results care must be observed that the patient has not tasted food within twelve hours or used medicine containing bromin within two months of the withdrawal of the blood, and the test must be performed soon after the blood has been taken.

The blood is centrifuged, and to 1 c.c. of the clear serum are added 0.5 c.c. of potassium iodid solution ($\frac{1}{2}$ per cent.) and 0.6 c.c. silver nitrate solution ($\frac{1}{2}$ per cent.). This part of the test is performed in a dark room with a red light. The resulting whitish opaque fluid is thoroughly mixed by drawing it up into a pipet and allowing it to flow back into the containing tube. This mixing must be done very carefully so as not to produce bubbles or foam. The small glass test-tubes used in determining Wassermann reactions are suitable for the test. The blood-serum from a normal individual is used as a control.

¹ Kottman, Karl, Schweiz. Med. Wochensch., 1920, 1, 644.

The tubes containing the serum-potassium-iodid-silver nitrate mixture (from now on to be regarded as colloidal suspension of silver iodid) are exposed for fifteen minutes to a 500 candle-power light at a distance of 25 cm. Then, under a red light, 1 c.c. of hydrochinon ($\frac{1}{4}$ per cent.) solution is added to each tube. The sera from hypothyroid cases is the first to assume a reddish-brown tinge, which soon turns to a deeper shade. Normal sera show color and the deepening of color more slowly than the hypothyroid sera. In the sera from hyperthyroid cases color appearance and development are manifested most slowly.

The time relations between hypothyroid, normal, and hyperthyroid reactions depend in part upon the amount of light exposure. In our own experience the light used exceeds 500 candle-power and has to be removed to 120 cm. and the time is reduced to twelve minutes. By this arrangement the normal reaction appears within five minutes, while the hyperthyroid reaction usually shows color only after thirty minutes or more. In less strongly positive cases the time difference is less, but sufficient for sharp differentiation. Any one employing the test will do well to vary the distance of the light to find what is best with the lamp he is using. The technic is readily mastered and the differences in the reactions are so clear cut that the determination of the result is extremely easy.

THEORY

The theory on which this test is based is in accordance with the principles of colloidal chemistry. One colloid is able to influence the state of another colloid, and often through protective action makes possible a colloidal suspension of a substance which in water would not be stable. The human serum is a colloid and is able to cause the diffi-

cultly soluble silver iodid, resulting from the potassium iodid and silver nitrate, to remain in colloidal suspension. This explains the opaque whitish color of the primary mixture. To be brief, this protective quality varies in different sera, and is stronger in hyperthyroid serum than in normal serum; and in hypothyroid serum is weaker than in normal serum. In other words, the fineness of suspension of the silver iodid is greatest under the influence of serum from a case of hyperthyroidism and least under the influence of serum from a case of hypothyroidism, while the normal serum effects an intermediary reaction. Further, a substance, such as silver iodid, which is sensitive to light, is less sensitive in a fine colloidal suspension than in a coarse suspension.

It is now evident why, after the addition of hydrochinon, we find different reaction times in the various tubes containing different sera. The hydrochinon is simply a developer. The light has caused a reduction of silver iodid to subiodid and the hydrochinon completes the reduction to metallic silver.

PRACTICAL APPLICATION

We have tested fifty-eight clearly defined cases of exophthalmic goiter, trying to avoid patients who had been taking bromids. Of these, fifty-seven gave positive results and, strangely enough, one severe case reacted as a case of hypothyroidism. Of fifteen borderline cases (some with normal metabolism), fourteen were positive and one reacted normally. Three goiter cases, without definite exophthalmic goiter symptoms and signs, were tested. Two of these reacted as mildly hypothyroid cases and one gave a normal reaction. Twenty "normal" individuals have been tested with consistent results. These were mostly patients tested before operation, and included among them were cases of hernia and gastric ulcer and other non-thyroid conditions.



THE RÔLE PLAYED BY THE RADIOLOGIST IN THE DIAGNOSIS OF GOITER

BERNARD H. NICHOLS

THE type of goiter in which the radiologist becomes of the greatest assistance in diagnosis is the so-called intra-

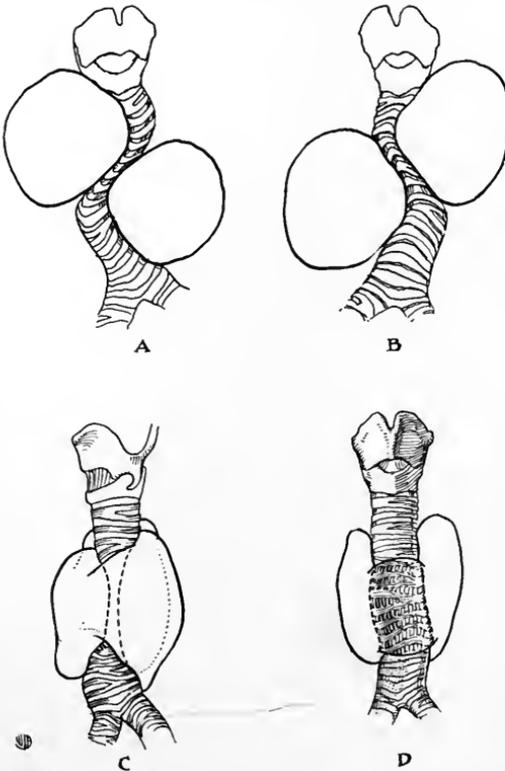


Fig. 27.—Schematic drawings illustrating different types of compression of trachea produced by goiter.

thoracic or substernal type, which includes those goiters which lie wholly or partially within the thoracic cavity. There

are goiters whose pole may project into the upper portion of the thorax, but for so short a distance as to give rise to no resultant symptoms. These should not be classified as intrathoracic in character in reporting the findings of a radiographic examination of the chest. Kocher refers to goiters of this type as "struma profunda," or deep goiter.

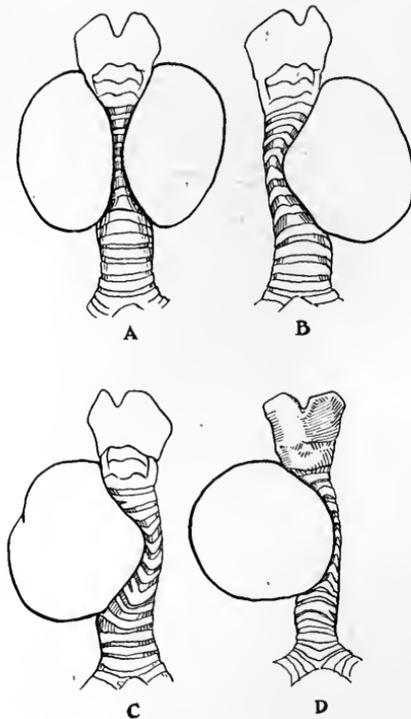


Fig. 28.—Schematic drawings illustrating different types of compression of trachea produced by goiter.

A consideration of the development of intrathoracic goiter may be of considerable aid in the diagnosis. Intrathoracic goiter may develop from the isthmus or one of the lower poles of the thyroid or from an intrathoracic accessory lobe; but the larger percentage of cases undoubtedly develop from a pre-existing goiter which gradually extends

into the thoracic cavity. The origin of an intrathoracic goiter can usually be determined by the position of the

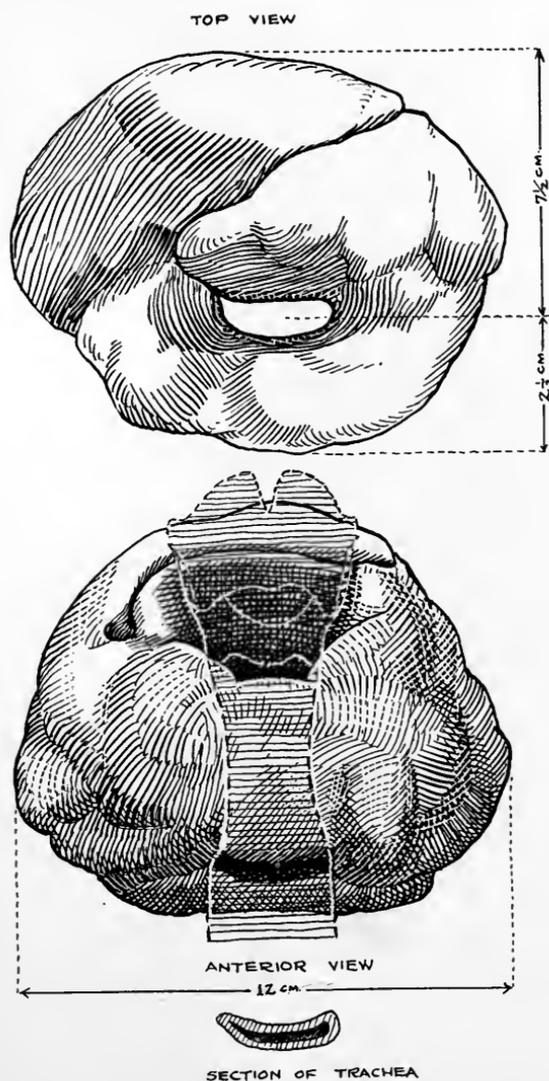


Fig. 29.—Encircling goiter with posterior compression of the trachea.

trachea as it appears in the radiograph. For example, development from the right lobe alone will usually displace

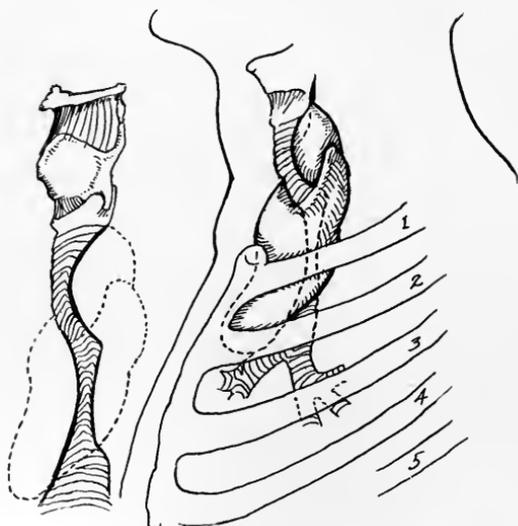


Fig. 30.—Partially intrathoracic median spiral goiter with anterior pressure on trachea.

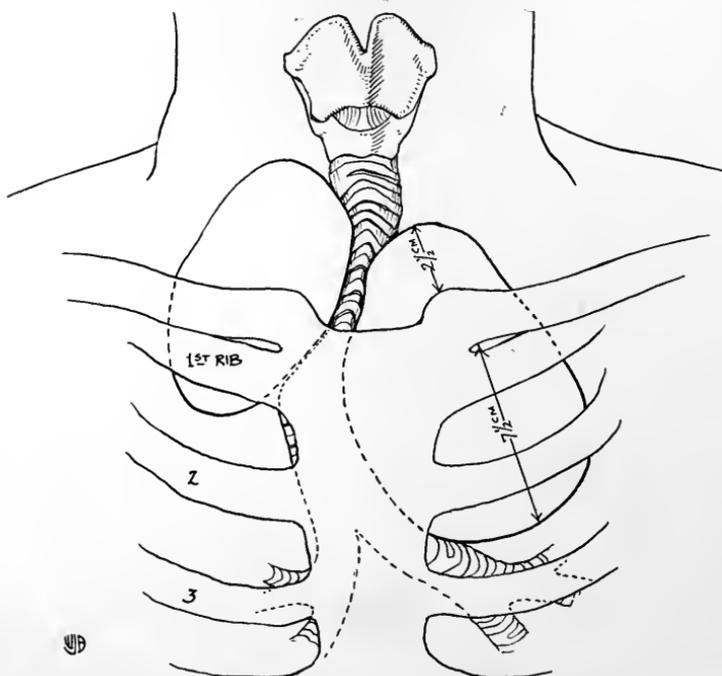


Fig. 31.—Intrathoracic bilateral goiter with bilateral pressure on trachea.

the trachea to the left of the median line; while, if the growth is from the left lobe, the opposite condition will be present. If the growth extends from both lobes, but is more extensive on one side than on the other, there results an irregular compression of the trachea somewhat simulating the letter S. If both lobes have developed about equally

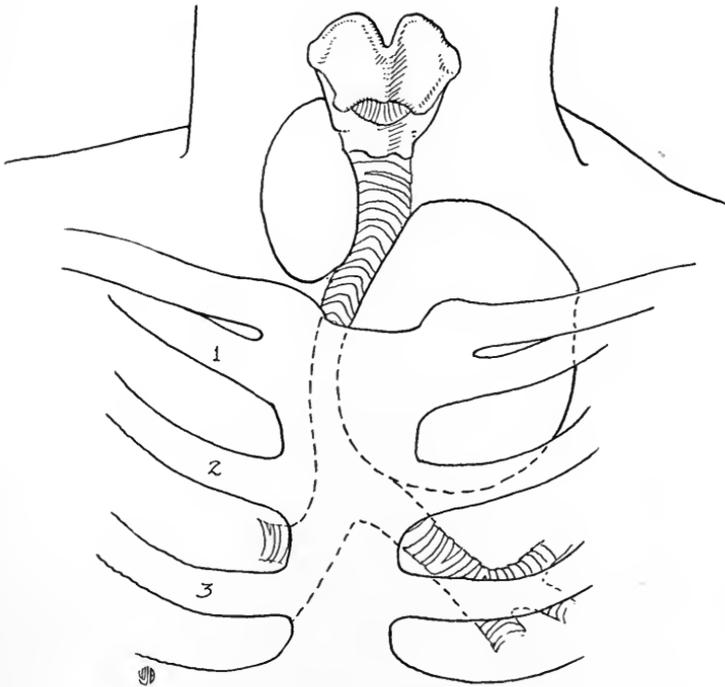


Fig. 32.—Partially intrathoracic goiter.

there results a double compression of the trachea producing the so-called "saber-sheath" trachea. If the enlargement originates in the isthmus, the trachea may be compressed and the shadow obliterated (Figs. 27-32).

Since the trachea is an air-filled organ located in the mediastinum where the surrounding structures are of greater density than air, the tracheal position is usually

easily identified on a radiograph, and any displacement or abnormality in shape at once attracts attention.

METHODS OF EXAMINATION

The examination of the chest for intrathoracic goiter should be made both by radiograph and by fluoroscope, as



Fig. 33.—Differential diagnosis of intrathoracic goiter. Radiograph showing compression of trachea by goiter and aortitis.

each of these methods contributes important points to the diagnosis.

Stereoscopic anteroposterior radiographs should be

made, the plate being placed against the anterior chest wall, with the patient in either a standing or reclining position. The second oblique position is often of value, for from this position it is possible to study the retrocardiac



Fig. 34.—Differential diagnosis of intrathoracic goiter. Radiograph of intrathoracic goiter showing displacement of trachea toward the left.

space in the case of a goiter developed from the isthmus and to determine whether or not the trachea is compressed.

The importance of the radiograph lies in the fact that it tends to bring out the sharpness and regularity of outline of the shadow as well as the position and deformity of the trachea. It also acts as a permanent record and guides the

surgeon at the time of operation in determining the location and extent of the tumor.

For the fluoroscopic examination the patient is best examined in the upright position. The patient should first face the screen and then be rotated to the most advan-



Fig. 35.—Differential diagnosis of intrathoracic goiter. Radiograph of intrathoracic goiter.

tageous position for a good view of the mediastinum. This may prove to be either the first or second oblique position, or the reverse position with the patient's back to the screen. In this manner we may determine many points in the diagnosis which are not elicited by radiographs. The most

important of these are the behavior of the mediastinal shadow during the normal heart and vascular activities, during deglutition and during deep inspiration and expiration; the size and position of the heart; the excursion and position of the diaphragm on either side; the appearance of



Fig. 36.—Differential diagnosis of intrathoracic goiter. Radiograph of intrathoracic goiter showing saber-sheath trachea.

the retro-cardiac space; and the size, shape, and position of the esophagus after the ingestion of a barium mixture.

The abnormalities which may be found in the upper thoracic cavity become of diagnostic interest to us in connection with the study of intrathoracic goiters, as many of

these give definite clinical symptoms, which require the radiologic findings for their differential diagnosis.

An **intrathoracic goiter** shadow usually lies high in the mediastinum and appears as a continuation of the supra-clavicular shadow. The outline is regular in cases which



Fig. 37.—Differential diagnosis of intrathoracic goiter. Radiograph of intrathoracic goiter.

are not nodular or malignant in character and is usually silhouetted over the pneumonic cavity of the lung on one or both sides of the mediastinum (Figs. 33-38).

The fluoroscopic image of an intrathoracic goiter usually appears as a dense shadow in the upper mediastinum, and

in the case of an extension from the supraclavicular goiter it broadens out above to join the tumor in the neck. The outline is regular and may be seen to move up and down during deglutition or on deep inspiration or expiration. If



Fig. 38.—Differential diagnosis of intrathoracic goiter. Radiograph of intrathoracic goiter with marked displacement of trachea.

there is pressure on the vessels the tumor may have the appearance of pulsating. This appearance, however, is due to a transmitted impulse and is not expansile in character.

From stereoscopic plates of the chest in the postero-anterior position we may study the outline of the tumor to

a better advantage and may also determine the presence of any compression or displacement of the trachea.

A goiter does not usually cast as dense a shadow as the heart and great vessels, thus the latter may often be dis-



Fig. 39.—Differential diagnosis of intrathoracic goiter. Radiograph of aortic aneurysm.

cerned through the goiter shadow. The shadow of the vessels may be seen to continue down directly from a supraclavicular goiter.

The nodular carcinomatous type of intrathoracic goiter

offers the greatest difficulty in diagnosis, and the clinical symptoms, as well as the physical examination, may be necessary in addition to the fluoroscopic examination to confirm the diagnosis.

In all mediastinal work we get the best results from very



Fig. 40.—Differential diagnosis of intrathoracic goiter. Radiograph of aortic aneurysm.

rapid exposure with duplitzed films, and feel that nowhere is it so important to use a short exposure as in radiographing the mediastinum.

Every roentgenologist is familiar with the excursion of the mediastinal shadow during the pulsation of the heart

and adjacent vessels which moves the bronchi and supporting tissues to a varied extent in different individuals, so that from a three- or four-second plate of the chest one may often make an erroneous diagnosis of peribronchial thickening at the hilus or entertain a suspicion of mediastinitis.



Fig. 41.—Differential diagnosis of intrathoracic goiter. Radiograph of aortic aneurysm with trachea displaced to right.

Thoracic aneurysm is perhaps one of the most important pathologic conditions in the upper thorax with which we have to deal in the differential diagnosis of intrathoracic goiter. The aneurysm, as seen on the radiograph, is a clean-cut shadow, regular in outline, and may appear as a distinct bulging or expansion of the aorta or great vessels

of the thorax. From the radiograph we may study the cardiac displacement and also the displacement of the trachea, but the most valuable information is obtained by fluoroscopic examination.

The diagnostic sign of aneurysm is a distinct expansile pulsation which does not allow the tumor to recede to its normal size between pulsations.

There is a distinct angle between the aortic shadow and that of an intrathoracic goiter. This angle is seen to change during deglutition and deep inspiration, due to the rising and falling of the intrathoracic goiter. This is almost diagnostic of thoracic goiter and distinguishes it from aneurysm.¹ By careful radiographic and fluoroscopic examination little difficulty should be experienced in determining the presence of an aneurysm (Figs. 39-41).

A **dilated or elongated aorta** has often to be considered, and the transverse position of the heart, which is so aptly described by Thomas, is well established in the study of these cases (Figs. 42, 43). Fluoroscopic examinations demonstrate an expansile pulsation of these tumefactions which recede during pulsation to the size of the normal vessel.²

A **thymus tumor** is usually lower in the chest and overshadows the heart. The mass is triangular in shape and an oblique fluoroscopic study discloses it well anterior in the chest (Figs. 44, 45). The majority of thymus tumors occur in children, but occasionally a persistent thymus is encountered which offers a grave complication in goiter cases. For this condition deep radiotherapy is indicated, by means of which very striking results in the reduction of the thymus may be secured.

¹ Crotti, Andre, J. A. M. A., 1913, lx, 117.

² Thomas, George F., Am. J. Roentgenol., 1914, iii, 126.



Fig. 42.—Differential diagnosis of intrathoracic goiter. Radiograph of supraclavicular goiter and enlarged aorta with transverse heart.



Fig. 43.—Differential diagnosis of intrathoracic goiter. Radiograph of elongated aorta with transverse heart.

Dorsal vertebral tuberculosis with an abscess may give a confusing shadow. Uncertainty may easily be overcome by a study of the spine by means of anteroposterior and oblique or lateral radiographs, which will show distinctly



Fig. 44.—Differential diagnosis of intrathoracic goiter. Radiograph of enlarged thymus gland.

the destruction of the vertebræ, with the accompanying kyphosis.

Hodgkin's disease is usually manifested in the mediastinum by multiple glandular enlargements. The enlarged glands show an irregular or indistinct outline, which should not be confused with intrathoracic goiter. It is often

impossible to differentiate this condition from lymphosarcoma or carcinoma. However, the presence of enlarged glands in other parts of the body, with the blood-picture, easily establishes the diagnosis of Hodgkin's disease.



Fig. 45.—Differential diagnosis of intrathoracic goiter. Radiograph of enlarged thymus gland.

In doubtful cases a resection of one of the superficial glands may be made, a microscopic study of which will definitely determine the diagnosis.

Lung abscess at the hilus may sometimes simulate intrathoracic goiter. By careful radiographic examination

we may discover a fluid level in the abscess cavity surrounded by an irregular inflammatory area. This, with the clinical history, determines the pathologic condition.

Osseous tumor of a rib, enchondroma of the chest wall, or tumor of the vertebral spine is usually well defined, and the origin of each is easily determined from stereoscopic radiographs of the chest.



Fig. 46.—Differential diagnosis of intrathoracic goiter. Radiograph of apical pneumonia.

Pneumonia, primarily in the apex of a lung, may give a dense shadow extending to the mediastinum, but the history of the case and the clinical symptoms are so evident that there should be no difficulty in the diagnosis (Fig. 46).

A **malignant growth in the lung** may be sarcoma or



Fig. 47.—Differential diagnosis of intrathoracic goiter. Radiograph of right pneumothorax showing trachea, heart, and aorta displaced to the left and old fibrous tuberculosis of the left lung.

carcinoma, either primary or metastatic in character (Fig. 48).

A primary malignant growth of the lung almost always develops from the hilus and extends toward the periphery. However, it may arise in the parenchyma. The normal



Fig. 48.—Differential diagnosis of intrathoracic goiter. Radiograph of sarcoma of right lung.

mediastinal shadow is displaced to the opposite side and the condition is associated with pleural effusion.

Metastatic carcinoma shows the typical multiple areas with fuzzy outlines, as has been described by Moore and Carman.¹

¹ Moore, A. B., and Carman, R. D., *A. J. Roentgenol.*, 1916, vol. iii, 126.

There is, however, another type of malignancy with which we are more concerned, described by Holmes and Ruggles.¹ This type is found in the hilus and simulates many inflammatory conditions; but presents a more definite dense localized mass and tends to extend upward with an accompanying mediastinitis (Fig. 49). These masses



Fig. 49.—Differential diagnosis of intrathoracic goiter. Radiograph of mediastinal tumor (lymphosarcoma).

often become well defined and of greater size at the sterno-clavicular junctions and may simulate goiter, but they are not so regular in outline and the lower border cannot be made out as in the rounded tumor of goiter.

¹ Holmes, George W., and Ruggles, Howard E., *Roentgen Interpretation*, 1919, p. 145.



Fig. 50.—Differential diagnosis of intrathoracic goiter. Radiograph of esophageal diverticulum.

An **esophageal diverticulum** may be discovered by fluoroscopic examination or by radiographs when it contains food or fluid. If a diverticulum be suspected the patient is given a barium mixture and then radiographed in the antero-posterior and oblique positions. The plates will show a



Fig. 51.—Differential diagnosis of intrathoracic goiter. Radiograph of esophageal diverticulum.

dilated pouch which is connected to the esophagus and has a smooth rounded lower end with no opening leading therefrom.

These shadows are typical in appearance and offer little difficulty in diagnosis (Figs. 50-53).



Fig. 52.—Differential diagnosis of intrathoracic goiter. Radiograph of esophageal diverticulum.

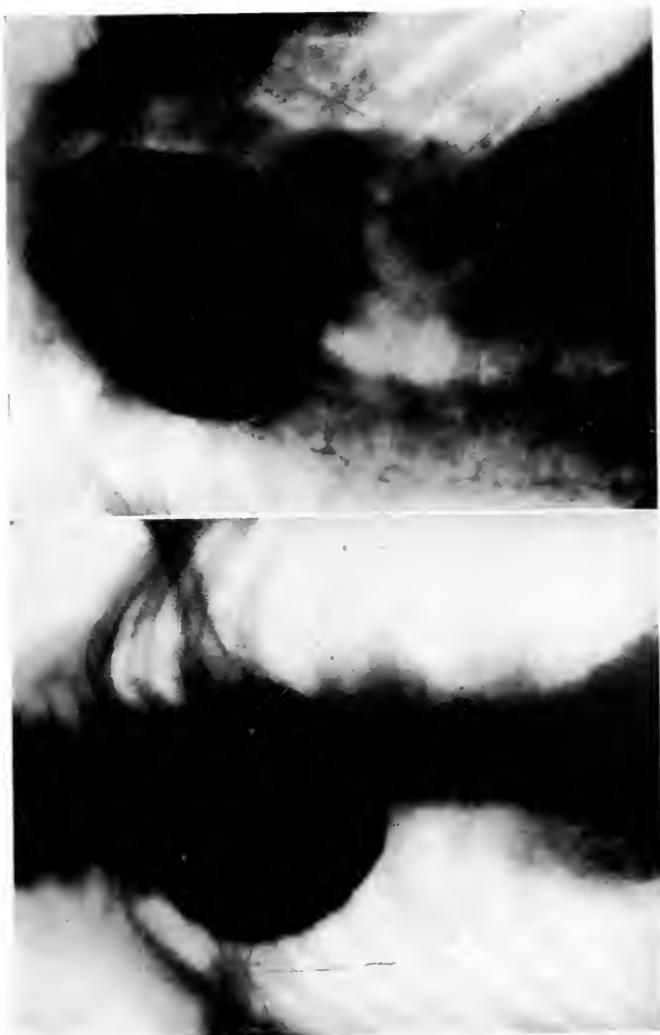


Fig. 53.—Differential diagnosis of intrathoracic goiter. Radiograph of esophageal diverticulum:
a, Anteroposterior view. *b*, Oblique view.

Carcinoma of the esophagus may be determined by filling the esophagus with a thick barium mixture, which will show a dilatation above with a narrowing below (Figs. 54, 55).



Fig. 54.—Differential diagnosis of intrathoracic goiter. Radiograph of carcinoma of the esophagus.

The dilatation above the carcinoma is usually not so pronounced as in cardiospasm, and the lower end of the barium shadow is irregular, tapering to a narrow channel, which also is irregular in outline.



Fig. 55.—Differential diagnosis of intrathoracic goiter. Radiograph of carcinoma of the esophagus.

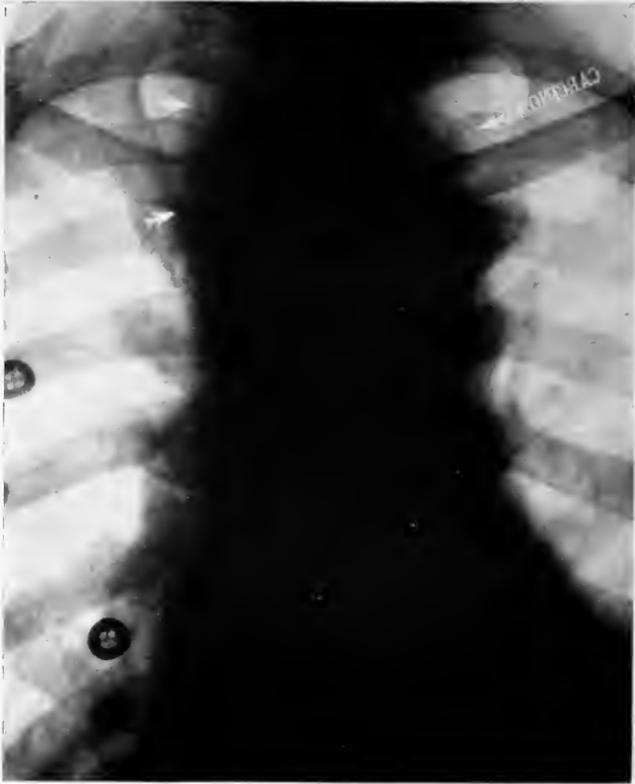


Fig. 56.—Differential diagnosis of intrathoracic goiter. Radiograph of metastatic carcinoma of the mediastinal glands.

SUMMARY

1. A careful radiologic examination should be made in all cases in which the clinical symptoms and the history of the case lead one to suspect intrathoracic goiter or thymus disease.
2. Radiographs should be made in every case by rapid exposure to eliminate pulsating movements in the mediastinum.
3. The movement of the goiter shadow with deep inspiration and expiration and during deglutition is almost pathognomonic.
4. Careful study of the spine, ribs, and chest wall for pathology associated therewith should be a routine procedure.



THE VALUE OF BASAL METABOLISM STUDIES IN EXOPHTHALMIC GOITER

CHESTER D. CHRISTIE

THE study of metabolism dates back to the early part of the seventeenth century, when experiments on the "insensible perspiration" were recorded by Sanctorius. Following Sanctorius there were numerous contributions to the subject of metabolism by such distinguished investigators as John Mayow, Lavoisier, Laplace, and Liebig. It remained, however, for the whole subject of metabolism to be established on a firm scientific basis by the work of Pettenkofer and Voit. The observations of these two men on the metabolism of animals and normal men, measured by means of a respiration calorimeter, represent the real beginning of our present-day conception of the science of nutrition.

We are indebted to subsequent workers, prominent among whom have been Rubner, Lusk, and Benedict, for the elaboration of the subject of nutrition to its present state of scientific development in so far as it bears on the vital physiology of normal men and animals. To these investigators the credit is largely due for the construction of that branch of physiology which in all probability is most intimately concerned with the future health and happiness of the race.

It is surprising that with such an enormous accumulation of scientific data regarding the normal nutrition of men, much of which has been secured by modern workers, it is but recently that observations on nutrition under

abnormal conditions have been attempted. With the exception of certain scattered and desultory attempts the field of pathologic metabolism has been left essentially clear for modern workers. Boothby, D. Du Bois, and E. F. Du Bois were the pioneers in the application of basal metabolism studies to the clinic. Their work has been just as fundamental and quite as far reaching in the development and application of basal metabolism studies to the clinic as was that of Pettenkofer and Voit in their application of basal metabolism observations to the study of normal vital processes.

DEFINITION

By metabolism is meant the changes which are constantly taking place in the cells of the organism whereby new cells are constructed and old cells are destroyed. Metabolism is expressed in terms of the energy liberated by the physicochemical or the electro-physico-chemical union which takes place in the tissues after food which has been taken by mouth and broken down into the end-products of digestion has been absorbed and has met in the blood with the oxygen which is taken in by the lungs. Metabolism is a process of oxidation and reduction within the cells of the body, as a result of which nourishment is supplied and heat generated. The term covers much which it would seem is utterly hidden from us, as, for instance: how each cell receives its proper proportion of nourishment and heat; what happens to liver cells to make them act individually and collectively as they do; what takes place in the kidney to make its cells react to external stimuli and to one another in a fashion different from that in which the cells of the liver react; and how these individual cells, with totally different functions, keep just the right amount of water and salt, and maintain their acid-base equilibrium,

and at the same time not only carry on their own special functions, but contribute their part to the neighboring cells. In a rather crude sense the human body may be looked upon as a great test-tube in which millions of different kinds of reactions are going on at the same time, each reaction independent in a sense, but all of them interdependent; and all these reactions are included in the one term—"metabolism."

Metabolism, then, is the very basis of life, the unseen and unheard force which runs along on lines determined within the species, making possible birth, growth, and development of bodily or mental characteristics. It is through this complex operation which we term metabolism that the organism is supplied with energy to do the day's work. By means of metabolism we are supplied with an increased power if we are called upon to perform a muscular feat; and, on the other hand, if we are inclined to lie down and rest, the mechanism of metabolism is equally willing to reduce its activity to the minimum and to rest with us. Metabolism is to the individual what civilization is to the interaction of individuals. Metabolism is the architect, the merchant, the doctor, and, in addition, it is the power plant which makes transportation possible, the repair department which reconstructs worn parts. In youth, when the organism is fresh and vital, the processes of metabolism produce a surplus of energy; conversely, when the organism has nearly run its course, these processes become less liberal in their production. Thus, by its infinite adaptability, metabolism makes possible the playful activity of youth as well as the slow and faltering movements of old age.

Numerous attempts, some of them successful, have been made to devise a simple method for the measurement

of the basal metabolism by indirect calorimetry. This method for the estimation of metabolism demands some means by which the individual may be connected by a mouthpiece with a spirometer containing oxygen, the nose being clamped so that the amount of oxygen consumed by the individual can be measured for a given length of time. From the amount of oxygen used the rate of elimination can be estimated. From time to time numerous investigators have used methods based on this principle for the collection of clinical data. The information accumulated has been buried here and there in the literature. It is disconnected, and in the majority of cases the obvious technical objections and the lack of established standards make it necessary to disregard the findings. Many of these earlier observations have been reviewed by Du Bois,¹ but few have proved to be of value.*

NORMAL FACTORS WHICH AFFECT THE METABOLIC RATE

Age.—In applying the data to the determination of normal standards account has to be taken of the fact that the metabolic rate varies widely between the extremes of age, and that this age variation is different in the two sexes. Du Bois³ has worked out graphically the normal basal metabolism in the male from infancy to the age of eighty-three years. In the female the average normal rate for each age is about 8 per cent. lower than in the male. It is lowest in the newborn babe and reaches its maximum at about the fifth year, from which age it gradually declines throughout the life of the individual. For the average adult male the normal metabolic rate is considered to be 39.7 calories per hour per square meter of body surface;

* The earlier types of apparatus for the measurement of metabolism by indirect calorimetry have been described by Carpenter.²

and for the average adult female 36.9 calories per hour per square meter of body surface.

Digestion.—The metabolic rate may be increased 15 per cent. above the normal when active digestion is taking place. This increase is most marked after the ingestion of cold food or a diet rich in protein, fat, or alcohol.

Exercise.—Any movement of the voluntary musculature of the body causes some increase in metabolism. Therefore if the exercise be violent enough the metabolic rate may be increased to the limit of which the individual is capable. The increase of metabolism caused by the uncommon use of the musculature in a boat-race must be very great indeed.

Excitement.—If an individual whose metabolism is being measured becomes unduly excited or apprehensive, a mild increase will be noted. Excitement plays an important rôle when metabolism estimates are being made for the first time. It is because of this factor that we advocate two determinations on successive mornings before conclusions are drawn.

Menstruation.—Recently Snell, Ford, and Rowntree⁴ have made a preliminary report showing that in some instances during the menstrual period the metabolic rate in girls may be increased to 15 per cent. above normal. I have made the same observation.

The assurance of true basal conditions demands the elimination of all such factors as those just mentioned. If basal conditions are assured, then one may safely conclude that in any case in which a variation from the normal metabolism rate has been established some pathologic condition is present.

ABNORMAL CONDITIONS WHICH CAUSE AN INCREASE IN BASAL METABOLISM

Fevers.—It has long been recognized that fever causes an increase in basal metabolism. Coleman and Du Bois,⁵ in their extensive studies on the basal metabolism of patients with typhoid fever, found that during the course of the fever the average basal metabolic rate was increased about 40 per cent., and that it might rise to even 50 per cent. above the normal. It is not known whether or not this increased metabolism is wholly dependent upon the fever. Doubtless the increase in protein destruction which always accompanies a fever is an important element in the heightened metabolism. During a chill the metabolism may rise to a very high level above the normal.

Anemia and Leukemia.—Cases of severe anemia show an increase in basal metabolism. The increase always bears an inverse relation to the hemoglobin. Mild cases of secondary anemia and chlorosis have not been shown to have a definite increase in the basal metabolism. Cases of leukemia show an increase which has been demonstrated as more or less constant throughout long periods of observation. All the cases of leukemia in our series have shown a definite increase up to 50 per cent. above the normal basal metabolic rate.

Diabetes Mellitus.—Patients with severe diabetes have shown an increase in the basal metabolic rate which is especially evident during the period of hyperglycemia and acidosis. This increase is but slight, usually not more than 15 per cent. above the normal, and disappears with the return to a normal sugar level in the blood and with the disappearance of acidosis. In fact, during periods when there is no sugar in the urine the metabolism may fall well below the normal limit.

Cardiac Dyspnea and Asthma.—In cases of well-marked cardiac decompensation the basal metabolism may be increased to 50 per cent. above the normal. It is always well to bear this fact in mind, particularly when studies are being made on goiter patients in whom decompensation is present or threatened. It is possible to fall into this error, and more drastic treatment might be employed when digitalis would suffice.

In cases of asthma there is likewise an increase in metabolism, as we have found repeatedly in our series. We have made a few observations on these patients both during an attack and immediately after the arrest of the attack by the use of adrenalin injections. The results of these observations will be recorded elsewhere. In the case of both cardiac dyspnea and asthma it is my impression that the increased metabolism is due simply to the increased work occasioned by the difficult breathing.

Pituitary Disorders.—An increase in the basal metabolism has been observed in cases of acromegalia. We have had but one patient with this syndrome, and in that instance the metabolism was increased to almost 50 per cent. above the normal. Recently Snell, Ford, and Rowntree⁶ have observed a moderately increased metabolism in two cases of diabetes insipidus during the phase of extreme polyuria. In these cases the metabolism became normal when the great increase in water transportation had been lessened by the use of pituitrin injection.

BASAL METABOLISM IN EXOPHTHALMIC GOITER

The first metabolic studies on exophthalmic goiter patients were made by Friedrich Müller⁷ in 1893. Müller found that his patients with exophthalmic goiter not only were eating more food than they required to meet their

caloric needs, but, in addition, they were excreting more nitrogen in their urine than they were taking in their food. This meant that these patients were not utilizing all the increased protein of their own bodies in an effort to supply the unnatural demand. In other words, these patients were not in a state of nitrogenous equilibrium and, therefore, were actually in a state of starvation even though they were eating and utilizing far more food than a normal person of the same weight and height. This metabolism observation by Müller offered the first explanation of the two most evident and paradoxical manifestations of patients afflicted with exophthalmic goiter, *i. e.*, the enormous food consumption and the marked weight loss.

A short time after the observations of Müller, Magnus-Levy⁸ was able to demonstrate with a respiration calorimeter that the metabolism of patients with exophthalmic goiter was increased, and that the basal metabolism of patients with myxedema was decreased. Magnus-Levy was the first investigator to use basal metabolism studies to control the treatment of his patients.

After these basic observations were made by Müller and Magnus-Levy, practically no attention was paid to the question of basal metabolism in exophthalmic goiter until Du Bois⁹ undertook a similar study, but one more elaborate and better controlled than those previously made. The findings of Du Bois, like those of the earlier observers, emphasized the fact that the most characteristic manifestation of exophthalmic goiter is an increase in the basal metabolism to a higher degree than is ever reached in other conditions; and that, moreover, the increased metabolism is the most constant manifestation of the disease. The observations and conclusions of Du Bois have been confirmed by Means and Aub,¹⁰ Boothby and Sandiford,¹¹ McCaskey,¹² and Christie.¹³

During the last few years we have made in our laboratory a total of 826 basal metabolism measurements on 472 patients. Among these patients 202, or just slightly less than 43 per cent., showed an increase in metabolism to more than 15 per cent. above the normal; and we believe that in each instance this increase was due to an exophthalmic goiter. The degree of the increase in the basal metabolic rate in the 202 patients may be summarized as follows:

| | |
|---|-----|
| Number showing an increase of from 15 to 55 per cent. above the normal metabolic rate..... | 121 |
| Number showing an increase of from 55 to 85 per cent. above the normal metabolic rate..... | 60 |
| Number showing an increase of more than 85 per cent. above the normal metabolic rate..... | 21 |
| | 202 |

The highest basal metabolic rate we have observed in any of our patients was 170 per cent. above the normal. Four other determinations were made on this patient, and in none of them did we find the rate lower than 110 per cent. above normal.

Some patients who for a long period of time have had comparatively mild exophthalmic symptoms, with very marked cardiac and eye signs, may show a very slightly increased metabolism—from 15 to 25 per cent. above the normal. In this group, however, metabolism measurements are not a very accurate index to the degree of disability. This may be due to the fact that the metabolic rate had previously been higher, and that much of the disability manifested by the patients at the time the measurements were made was no longer entirely due to the active exophthalmic goiter, but rather to the devastating effects of the chronic disease upon the patient's entire system. With most cases, however, the degree of the increase in the

metabolic rate does give a fairly accurate index of the severity of the disease.

The Value of Basal Metabolism Measurements in the Diagnosis of Exophthalmic Goiter.—I feel that the greatest service of basal metabolism measurements to the clinic is the aid which they furnish for the diagnosis of disease referable to the thyroid gland. When intelligently interpreted the results are of very distinct value, and supply the clinic with an additional method of precision which is quite as useful in its field as any method which we now possess.

Obviously an established case of exophthalmic goiter offers very little difficulty from a diagnostic point of view. It is in the borderline cases that we have found metabolism measurements of the greatest service. In cases in which the classical symptoms of the disease are present but the classical signs are not sufficiently obvious to warrant a definite diagnosis, repeated careful basal metabolism measurements are of inestimable value in establishing an accurate diagnosis.

Often patients are encountered who do not have the classical signs of the disease. The eye signs are very frequently absent and are often equivocal. Enlargement of the thyroid is not always present, but is far more constant than the eye signs. The uniformly enlarged, hyperplastic and vascular gland, with palpable thrills and audible murmurs, is a very constant factor in the disease. Certain patients with thyroid disease may not have any demonstrable pathology in relation to the thyroid, but they are in the great minority. Other patients may have the classical symptoms of the disease and an elevation in the metabolic rate with only an innocent-feeling adenoma in the thyroid. The one most constant sign of exophthalmic goiter which we have found is the uniform enlargement of the heart.

Of course, this is purely a compensating factor for the great increase in the amount of blood which the heart is called upon to transport because of the increased metabolism. If the metabolism is greatly increased, it is obvious that the heart will be much larger than if the metabolism is only slightly increased. Therefore, if the metabolism be only slightly increased, it follows that the relatively slight increase in the size of the heart will be harder to discover by physical examination. From my own experience I should consider the relative value of the various signs of exophthalmic goiter in the following order: 1. Positive anamnesis. 2. Uniform dilatation of the heart with rapid rate, provided other factors which might cause these heart signs have been eliminated. 3. Increased basal metabolism established by careful and repeated measurements. 4. Presence of signs directly referable to the thyroid gland. 5. Presence of characteristic eye signs. 6. Tremor, sweating hands, and pigmented skin.

It seems certain that an increase in basal metabolism represents the fundamental and basic symptom of exophthalmic goiter, just as a hyperglycemia represents the basic symptom of diabetes mellitus. There is no other condition in which such an increase in metabolism persists seven days out of the week and thirty days out of the month, as is the case in exophthalmic goiter. An increase in metabolism may be produced by exercise; but the exercise would soon be discontinued if the increased metabolism equaled or approached the increase found in some patients with exophthalmic goiter. Moreover, exercise causes an active increase in metabolism, while, in the case of exophthalmic goiter, the increase in metabolism is passive. It seems probable that, if we could activate the metabolism of a normal individual to the same degree that is found in exophthalmic

goiter, and could continue that activation, persistently, for a long period, all the classical signs and symptoms of the disease would be produced. All of the signs and symptoms are accentuated in proportion to the increase in metabolism, and subside as the metabolism again approaches the normal. This is particularly true with regard to the size of the heart.

I have seen active exophthalmic goiter mistaken for aortitis in two or three cases. In each of these instances basal metabolism estimates were of distinct service. After my attention was called to these mistaken diagnoses I began observing more closely the aortas in patients with exophthalmic goiter. I observed that there was an increase in the transverse percussion dulness over the root of the aorta in many of these patients; and that, in addition, there was a palpable systolic impulse and diastolic impact over the aortic area. On several occasions I have been able to demonstrate a "tracheal tug." The size and the position of the heart simply added to the confusion. If the increase in the size of the heart is due to dilatation, caused by the greater demand for the increased transportation of blood resulting from the heightened metabolism—and this seems to be the obvious explanation—then it would appear that a dilatation of the aorta must follow as a matter of course. On this theory, and bearing in mind the results of many examinations of the aorta in patients with exophthalmic goiter, I routinely have 6-foot x-ray plates made of their hearts and aortas. These have given us splendid confirmation of the fact that in many cases of exophthalmic goiter there is present a very definite widening of the root of the aorta. This dilatation of the aorta recedes as the metabolism is reduced. It is probable that it is not confined to the root of the aorta, but that the vessels of the whole vascular

system of the patient with active exophthalmic goiter are increased in their cross diameter.

Value of Basal Metabolism Measurements in the Control of Treatment.—Basal metabolism estimates during the course of the treatment of patients with exophthalmic goiter provide a very accurate index to the progress of the disease. They supply, as it were, a yard stick wherewith to measure the intensity of the disease at any given time. The history and the physical examination may both give rise to misleading information regarding the clinical condition of the patient. From the history, in particular, one is apt to obtain misleading information regarding the clinical condition of the patient, since much depends on his mental attitude. If the patient be inclined to optimism it tends to mitigate personal feelings; or, conversely, if the patient be pessimistically inclined, his personal feelings may be exaggerated. In either case the personal history of the patient with exophthalmic goiter may be wrongly interpreted. Basal metabolism measurements will obviate some of this difficulty. As was pointed out earlier in this paper, the physical examination of the patient, although invaluable, will not detect slight grades of change in the patient's condition with the same precision as do basal metabolism measurements.

The treatment of exophthalmic goiter is finally determined by the changes in the basic symptom of the disease—the variations in metabolism—just as the treatment of diabetes mellitus is determined by changes in the basic symptom of that disease—the variations in hyperglycemia. Therefore any rational treatment of exophthalmic goiter must depend upon agents which are known to reduce the metabolism.

The Treatment of Exophthalmic Goiter.—Numerous

agents have been employed from time to time in the treatment of exophthalmic goiter. It seems clear that if any agent is to be successful it must be efficacious in reducing the heightened metabolism which is known to exist in the disease. There are several procedures which are known to accomplish this purpose, the most important probably being *rest in bed*. This rest should include not only physical but mental rest, as exercise and mental excitement are both factors which increase the metabolic rate.

The question of *food* is also an important factor. If the metabolism of a patient is increased 100 per cent. above normal, it is obvious that the patient needs to eat just twice as much food if the body weight is to be maintained. It has long been known that certain food-stuffs activate metabolism out of all proportion to others. As was mentioned earlier in this article, those foods are protein, fat, and alcohol. It is apparent that these food-stuffs should be avoided in the treatment of exophthalmic goiter, and the patients should be maintained as nearly as possible on the one food which is known not to activate metabolism, namely, carbohydrate. The appetite of these patients should be encouraged by every means possible so that they will avoid great loss in weight. It seems rational to employ the duodenal tube for forced feeding if the amount of food which they are able to eat is not sufficient to supply their caloric needs.

It is our custom on the medical service of this hospital to treat exophthalmic goiter patients with adequate rest and diet, as was outlined above, and, in addition, we employ the *x-ray*. Patients are given maximum exposure to the *x-rays* over the thyroid gland about every three weeks. Any other treatment is used merely symptomatically.

In Table I is listed a group of patients upon whom the

foregoing procedures have been employed. In selecting this particular group from our series I have been guided by the fact that they have been observed for the longest period. I do not know how closely they have adhered to the rest régime, for most of them have been here under continuous observation for only short periods. The number and frequency of *x*-ray treatments have also been variable, three treatments being the least that any patient had had, and seven the maximum.

TABLE I

PATIENTS WITH EXOPHTHALMIC GOITER TREATED BY REST AND *x*-RAY ALONE FOR PERIODS RANGING FROM THREE MONTHS TO ONE AND A HALF YEARS.

| Case No. | On admission. | | One month after treatment. | | Three to six months afterward. | |
|----------|---------------------|-------------|----------------------------|-------------|--------------------------------|------------------------|
| | B. M. R., per cent. | Pulse-rate. | B. M. R., per cent. | Pulse-rate. | B. M. R., per cent. | Pulse-rate. |
| 79,867 | 29 | 110 | 38 | 90 | 8 | 90 |
| 74,357 | 33 | 150 | 48 | 110 | 42 | 130 (patient operated) |
| 72,768 | 42 | 110 | 24 | 110 | 55 | 120 (patient operated) |
| 80,623 | 54 | 120 | 9 | 95 | 23 | 95 |
| 76,872 | 78 | 110 | 66 | 95 | 27 | 80 |
| 71,956 | 77 | 130 | 52 | 110 | | |
| 77,700 | 61 | 105 | 15 | 180 | | |
| 83,335 | 59 | 110 | 48 | 100 | (Doing own work) | (patient operated) |
| 75,552 | 65 | 110 | 42 | 92 | | |
| 81,680 | 25 | 90 | 13 | 90 | 26 | 90 |
| 77,439 | 61 | 105 | 11 | 75 | 22 | 75 |
| 76,731 | 48 | 130 | 25 | 115 | 50 | 110 (patient operated) |
| 81,185 | 34 | 110 | 40 | 85 | 44 | 40 (patient operated) |
| 76,967 | 18 | 90 | 12 | 80 | 4 | 75 |

In all of these patients who were treated by *x*-ray and rest alone there were times when the metabolism reached lower figures, and in many there were higher values recorded. In most of the cases in which there were pretty violent recurrences it was due to some acute infection like influenza or tonsillitis.

Through the kindness of Dr. Crile and his staff I have been allowed to make many observations on their exophthalmic patients, both before there was any surgical intervention and in many phases of the postoperative care.

In Table II I have tabulated a group of patients who have been treated by the *surgical procedures* which are employed in this hospital. In choosing this particular group from the large series upon which I have made observations I have again been guided by the fact that they are all patients who were treated more than a year and a half ago, and I am more or less familiar with their subsequent course. Where there were several metabolism measurements made near the same time I have endeavored to strike a rough average. The pulse-rates which are recorded also represent the approximate mean at the time the basal metabolism measurements were made.

This table represents the effect of surgical treatment alone on the metabolism and pulse-rate:

TABLE II

| Case No. | Before. | | Approximately two months after ligation | | Two weeks to two months after operation. | |
|----------|---------------------|--------|---|--------|--|---------------------|
| | B. M. R., per cent. | Pulse. | B. M. R., per cent. | Pulse. | B. M. R., per cent. | Pulse. |
| 76,731 | 50 | 110 | 15 | 85 | 16 | 85 (2 weeks after) |
| 81,185 | 44 | 112 | 38 | 105 | 26 | 96 (3 weeks after) |
| 72,768 | 24 | 108 | 35 | 110 | 10 | 70 (2 weeks after) |
| 76,477 | 76 | 110 | 65 | 120 | 35 | 92 (3 weeks after) |
| 76,875 | 93 | 110 | 65 | 100 | 18 | 75 (2 weeks after) |
| 73,579 | 44 | 120 | 58 | 120 | 36 | 90 (16 days after) |
| 74,732 | | 120 | 104 | 135 | 30 | 96 (2 months after) |
| 82,409 | 95 | | 90 | | 24 | 85 (1 year after) |
| 83,335 | 44 | 110 | 33 | 100 | | 115 (3 weeks after) |
| 74,357 | 67 | 150 | | | 37 | 92 (1 year after) |
| 73,758 | 44 | 85 | | | 12 | 70 (1 month after) |

I should not wish to leave the impression that a mere tabulation of the metabolic rate and the pulse-rate in exophthalmic goiter, as shown in Tables I and II, represents in its entirety the condition of the patients. As has been constantly emphasized in this article, there are many other clinical factors to be taken into consideration in determining the result of treatment. For, after all, it must be remembered that basal metabolism measurements, while important

in controlling the treatment of the condition, should not supersede careful clinical observation.

The tabulations serve to emphasize the fact that rest and exposure to the x-ray, ligation, and thyroidectomy are all very potent factors in reducing heightened metabolism, the basic symptom of exophthalmic goiter, and therefore favorably affect the course of the disease.

It will be found that the pulse-rate represents a fairly accurate index to the metabolic rate. In exophthalmic goiter, as well as in other conditions in which there is a known increase in the metabolic rate, the increase in pulse-rate represents a fairly accurate index in lieu of actual metabolism measurements.

CONDITIONS WHICH GIVE RISE TO A DECREASE IN BASAL METABOLISM

The conditions which cause a decrease in the basal metabolic rate are myxedema, cretinism, and general chronic asthenic conditions.

Myxedema.—Most of the adult cases of myxedema which we have encountered have followed thyroidectomy. We have, however, encountered myxedema in patients on whom thyroidectomy has not been performed. In our series we have considered ten cases as instances of the adult type of myxedema. Among these the lowest metabolic rate was 39 per cent. below normal.

Cretinism.—We have encountered but one case of what we believed to be a juvenile type of cretinism. In this instance the basal metabolic rate dropped as low as 20 per cent. below the normal level. This patient was markedly improved by the oral administration of thyroid extract.

Chronic Asthenic Conditions.—A low metabolic rate is frequently encountered in elderly individuals, particu-

larly in women who have a very generalized arteriosclerosis. A low metabolic rate may occur in senile diabetics who are sugar free; in cases of chronic tuberculosis in which there is no fever, and in old people with chronic bronchitis and emphysema without "air hunger." It is unusual to find the metabolic rate more than 15 per cent. below the normal in this class of patient. The metabolic rate is not elevated in these patients by the administration of thyroid extract nor is the course of the condition favorably affected.

I desire to express my thanks to Mr. E. J. Warnick, upon whom the task of much of the routine technical work involved in these studies has fallen. His careful technic and kindness to the patients have contributed much to the value of our efforts. I also wish to express thanks to our chemical assistant, Miss Ruth A. Trump, for her everwilling assistance.

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THE PREVENTION OF SIMPLE GOITER IN MAN *

O. P. KIMBALL

To understand why anyone should undertake a goiter survey of a whole community for the purpose of establishing a principle of prevention by a simple and practical method it is necessary to study the literature of goiter with this idea in view. For the literature, while rich in statements regarding the distribution of goiter, the pathology of the thyroid gland, methods of medical and surgical treatment, hereditary tendencies and etiology, has little indeed to offer regarding the *prevention* of goiter.

A survey for merely determining the incidence of goiter in the different localities and cities of this portion of the Great Lakes basin would have been unnecessary. There is an abundance of scientific data giving in general the geographic distribution of endemic goiter throughout the world. Surveys of various communities in Europe have been made, and the scientific data of the last century has so emphasized the sociologic and economic importance of endemic goiter, cretinism, and deaf-mutism that national commissions have been appointed by some of the countries of Europe to study this problem for the purpose of finding some method of relief.

For ten years preceding the beginning of our work in Akron, Marine and Lenhart, working in the Department of Experimental Medicine of the Western Reserve University, had been showing the ease with which endemic

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goiter could be prevented. The results of laboratory experiments and demonstration in animals, however convincing, must be applied to man for final proof of their prophylactic or therapeutic value. The prevention of goiter in man was yet to be proved. Therefore, with Dr. David Marine, I undertook to establish in man the applicability of the work of Marine and Lenhart as summed up in their statement that "simple goiter is the easiest of all known diseases to prevent."

DEFINITION AND HISTORY OF ENDEMIC GOITER

The term "goiter" means hypertrophy of the thyroid gland. The term as used in this paper refers only to what is known as *simple* or *endemic goiter*, and does not include the so-called exophthalmic goiter.

The incidence of simple goiter has been so high and so continuous for generations, in certain districts of the world, where all kinds of domestic animals as well as humans are involved, that it has come to be considered as characteristic of or endemic in those districts.

The study of the history of this disease is like studying the history of the human race. The Arthorva Veda, an ancient Hindu collection of incantations dating from 2000 B. C., contains extensive forms of exorcisms for goiter. Cæsar mentions the frequent occurrence of big neck as one of the peculiar characteristics of the Gauls. The origin of the term "cretin" shows the familiarity of the early Romans with this disease. They originated this expression of contempt by calling the myxedematous idiots Christians. The Swiss physician, Paracelsus (1493-1541), was the first to emphasize the relationship between goiter and cretinism, and the earliest positive information concerning the latter disease dates from this author. In 1793

appeared Fodere's essay on Goiter and Cretinism in the Maurienne and Aosta Valley; and in 1800 his Treatise on Goiter and Cretinism. During the last century there have been numerous publications on Endemic Goiter and Cretinism, one of the most exhaustive of which is by A. Hirsch in his study of *The Historical and Geographical Relations of Goiter*.

About the middle of the last century the governments of the European countries began to see the economic and sociologic importance of this problem. In 1848 the Sardinian Government appointed a commission to study the cause of endemic goiter and find some method of relief. In 1864 the French Government appointed a similar commission, which reported in 1874 that at least one-half million people in France were suffering from goiter and that there were over 120,000 cretins and cretinoid idiots. This commission seemed to establish as a scientific fact the popular idea that goiter is a water-borne disease. In 1908 Switzerland created a goiter commission, and since then Italy has created a similar commission to study the cause and prevention of endemic goiter.

DISTRIBUTION

The extent to which goiter prevails throughout the world is seldom appreciated. Few countries are free from endemic districts and we find the so-called sporadic cases of goiter in every section and among every nationality in the world. But there are localities where the incidence of goiter is so extremely high that they have been known for years as endemic goiter districts. The best known of these districts is in southern Europe, or more specifically the Alps mountain region, comprising southeastern France, southern Germany, all of Switzerland, northern Italy, and

southern Austria. In Asia practically all of the Himalaya district is an endemic goiter belt, with a very high incidence in northern India and parts of southern and western China and eastern Mongolia. In South America goiter is endemic throughout most of the Andes region, with probably the highest incidence of both goiter and cretinism on the Peruvian plateau and in parts of western Brazil. In North America goiter is endemic in the whole of the Great Lakes' basin, in the basin of the St. Lawrence, and in the north-west Pacific region.

In each of these large endemic regions there are localities in which the incidence of goiter is much higher than in the surrounding territory, and in such districts all of the domestic animals are affected. In some of these smaller districts the incidence of goiter has been determined with sufficient accuracy to be mentioned here. For example, as we have stated above, in 1874 the goiter commission of France estimated that in that country there were half a million goitrous people and 120,000 cretins and cretinoid idiots; statistics furnished by Kocher show that 80 to 90 per cent. of the school children of Berne were goitrous; in his recent reports Klinger states that in some of the schools of Zurich, where he is carrying out methods of goiter prevention, 100 per cent. of the children are goitrous. In southern Bavaria, according to the statistics of Schittenhelm and Weichardt, who base their conclusions on examinations of school children, the incidence of goiter is as high as from 77 to 89 per cent. of the total population. In Switzerland and certain provinces of Italy, France, and Austria the problem of endemic goiter, cretinism, and deaf-mutism has been recognized as of sufficient economic importance to demand investigation by their respective governments.

We are told that on the Gobi-desert and the Plateau

of Thibet the incidence of goiter is very high, and that among the various tribes of southeastern Mongolia one-third of the population is goitrous.

McCarrison carried out some of his researches and made several surveys in Himalayan India. He states that in some of the villages of this section it is difficult to find a man, woman, or child who is not suffering from the deformity. He estimates that not less than 20 per cent. of the total population of Gilgit in northern India suffer from goiter, and that among a population of 70,000 he found 200 cretins.

The frequency of goiter in North America has been known in a general way for more than a century. In 1800 Barton wrote an excellent monograph on the occurrence of goiter among the American Indians living along the shores of Lakes Ontario and Erie. Other goiter centers among the Indians of the Rocky Mountain States have been described by Munson. Adami pointed out the frequency of goiter in the St. Lawrence Valley, and speaks of French Canadian villages in this district in which there was scarcely a family without one or more goitrous members. Osler has emphasized the frequency of goiter in Ontario. Marine finds the disease widely disseminated all along the Great Lakes, where it occurs not only in humans but also in animals, especially dogs and sheep. In a report to the Commission of Conservation of Canada in 1918 Shepherd states that the incidence of goiter is very high in British Columbia and Alberta, and that in some localities of these large states most of the domestic animals are affected.

INCIDENCE OF GOITER IN THE UNITED STATES

Efforts to determine the incidence of goiter in different sections of the United States have been made, but no

accurate survey of a whole community had been reported previous to our work in Akron. In 1913 Clark examined 13,836 school children in eleven counties of West Virginia and found 1234 cases of goiter—9 per cent. of the number examined. In Virginia the same worker examined 6432 school children and found 817 cases of goiter, or 12 per cent. of the number examined. In Huntington 50 per cent. of the girl students were found to be affected. In the Virginia survey less than 0.1 per cent. of the goiters found were among boys.

The report of Hall of 3339 students at the University of Washington is indicative of the incidence of goiter in the Northwestern States. This writer found enlarged thyroids in 18 per cent. of 2086 men whose average age was twenty years and five months, and in 31 per cent. of the 1253 women examined whose average age was nineteen years and three months.

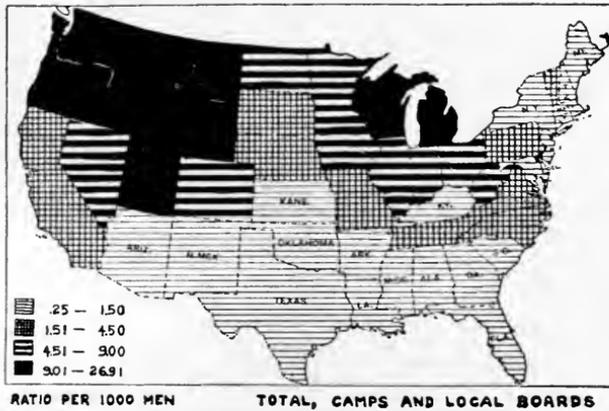
In Chicago Olson examined 606 women and 193 men, with ages ranging from eighteen to sixty years. Among the women 18 per cent. had well-developed goiters and 7 per cent. of the men were affected.

During 1917 and 1918, when so many of our young men were in camp, an opportunity was offered to determine the incidence of goiter among young men and to compare the incidence of goiter in different sections of the country. Thus, from Camp Lewis, Washington, Kerr reported the examination of 21,182 recruits, with the finding of 1276 large or well-formed goiters. The percentage of unquestionable goiters compared to the number of recruits from each state was as follows:

| | Per cent. | | Per cent. |
|-------------------|-----------|-------------------|-----------|
| Washington..... | 11.0 | Minnesota..... | 5.1 |
| Oregon..... | 8.6 | Wyoming..... | 3.7 |
| Idaho..... | 7.3 | South Dakota..... | 2.0 |
| North Dakota..... | 6.6 | Nevada..... | 1.1 |
| Utah..... | 5.5 | Colorado..... | 0.5 |

Brendel and Helm, studying the same problem at Camp McDowell, California, conclude that goiter is endemic in

GOITER, SIMPLE



GOITER, EXOPHTHALMIC

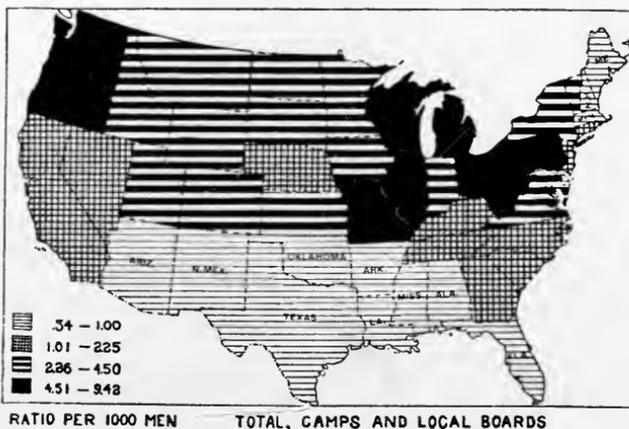


Fig. 57.—Comparative incidence of goiter, simple and exophthalmic, in the various regions of the United States. (Love, Albert G., and Davenport, Charles B.: Defects Found in Drafted Men, 1920, p. 86. Reproduced by permission of the Surgeon-general.)

Washington and Oregon. Smith, at Jefferson Barracks, Missouri, reports that in the examination of 65,507 men

there were found 1074 cases of simple goiter, or an incidence of 1.63 per cent. of the total number examined. These recruits represented fifteen different central and western states (Fig. 57). These findings only emphasize in a general way the fact that goiter may be considered as distinctly endemic in certain sections of the United States.

THE PHYSIOLOGY OF THE THYROID

In order to appreciate the principle of goiter prevention one must review briefly the biochemistry and function of the thyroid gland.

Early in the sixteenth century Paracelsus emphasized the relation between endemic goiter and cretinism. In 1825 Parry's descriptions of cases of goiter or enlargement of the thyroid gland in connection with enlargement of the heart with palpitation and exophthalmos were published. In 1835 appeared Graves' description of the clinical complex of exophthalmic goiter, with enlargement of the thyroid as one of the cardinal symptoms. Basedow's description of the same syndrome appeared in 1840. But none of these observers interpreted their findings in terms of the function of the thyroid. The first important observations of the functions of the thyroid were published in 1874 by Sir William Gull. At this time the clinical complex of myxedema (Gull's disease) was described in detail, and this clinical picture was interpreted as in some way associated with a lack of function of the thyroid.

Gull's observations and interpretation of the etiology of myxedema were confirmed in 1880 and 1881 by Kocher and Reverdin, who had observed the results of the total removal of goitrous thyroids. Kocher gave to the clinical syndrome resulting from complete thyroidectomy the name of cachexia strumipriva; Reverdin called it operative

myxedema. In 1877 Ord designated the disease as myxedema, because he thought he had recognized a mucoid change in the subcutaneous tissue. Sir Victor Horsley verified the findings of these observers by his researches on experimental myxedema in monkeys. As a result of these observations Murray and McKenzie in 1891 gave glycerinated thyroid extract to a myxedematous patient and obtained definite therapeutic results.

The early Greeks treated goiter by the internal administration of the ash of burned sea sponges, not knowing that the substance was rich in iodids. Iodin was first knowingly used in the treatment of goiter by Coindet in 1820. From that time iodine was used very extensively and stood alone in goiter therapy for seventy-five years before the discovery by Baumann in 1895 that iodine was a normal constituent of the thyroid gland. Our knowledge of the chemistry of the thyroid progressed rapidly after Baumann's discovery. In 1901 Oswald showed that the iodine is bound with the globulin and is contained for the most part in the colloid.

In 1907 Marine emphasized the fact that iodine is necessary for the normal function of the thyroid, and also that in active hyperplasia of the thyroid the iodine store is reduced. The later experiments of Marine and Lenhart have established the following facts relative to the importance of iodine in the chemistry, function, and histologic anatomy of the thyroid:

(1) Iodine is a constituent of the normal thyroid of all animals with the ductless thyroid. As shown by their experiments on the rapidity of absorption of iodine by the thyroid, and its elaboration into the active hormone, and by alkaline hydrolysis as introduced by Kendall, iodine exists in the thyroid in an *active* and *inactive* form. That is, the

elaboration of the hormone goes on slowly from the inactive iodine collected from the blood. The excess of physiologically active iodine is for the most part stored in the "colloid" or globulin of the alveoli, and it is believed the colloid serves merely as the vehicle or means of storing the excess of this remarkably active substance in a harmless manner. The store of iodine then normally consists of inactive iodine for the most part in the cells, and of active iodine for the most part in the colloid or thyroglobulin.

(2) This store of iodine shows wide variations in any series of animals. These variations reach their maximum in the so-called goiter districts and their minimum in non-goitrous districts.

(3) Further, these variations in iodine store have been shown to have an intimate relation with the histology of the gland. Thus, in all species of animals with the ductless thyroid the iodine store is decreased in the hyperplasias. This decrease is proportional to the degree of hyperplasia. In mammals—*e. g.*, dog, sheep, ox, pig, rabbit, cat, and man—it has been shown that normal thyroids have the highest percentage of iodine, averaging 0.2 per cent., with extremes of 0.1 and 0.5 per cent.

(4) It has been further shown that as soon as the store of iodine falls below 0.1 per cent. active hypertrophic and hyperplastic changes in the thyroid begin. In other words, no functional hyperplasia and, therefore, no goiter can develop, at least in the mammals above mentioned, if the iodine store in their thyroids is maintained above 0.1 per cent.

(5) This iodine store may be rapidly and markedly increased by the administration of exceedingly small quantities of iodine in any known form and through a great variety of means, as inhalation, enteral and parenteral

administration, cutaneous application, etc., and, as indicated above, marked histologic changes are at the same time brought about in hyperplastic glands, viz., the arrest of the hypertrophy and the involution or return of the thyroid cells to their resting form.

The active iodine compound found in the thyroid, beginning with its discovery by Baumann in 1896, and the successive attempts to isolate it, has been known as iodothyryn, iodo-thyroglobulin (Baumann and Roos), thyroïdin (Oswald), and thyroxin (Kendall). In 1915 Kendall succeeded in isolating this iodine-containing hormone in crystalline form and has determined its structural formula. He believes it to be tri-iodo-indol-propionic acid.

In 1895 Magnus-Levy indicated that the thyroid in some way controlled the rate of oxidation in the tissues. He showed that in myxedema the rate of metabolism was much lowered and that by feeding thyroid the rate could be raised. Also he was the first to demonstrate that as regards metabolism exophthalmic goiter was the opposite to myxedema. This work has been confirmed from many sources as regards experimental and spontaneous myxedema. And as regards exophthalmic goiter, it has so developed that at present the rate of metabolism is the best available basis for classification.

In a recent publication on "The Physiology of the Thyroid," Marine states that "The thyroid has to do in some important way with internal respiration or the utilization of oxygen by the tissues. Indeed, this is the only known function of the thyroid."

THE PREVENTION OF GOITER

Before 1896 Halsted had shown that if a portion of the thyroid is removed or destroyed the remainder under-

goes hyperplasia. Marine and Lenhart found that this compensating hyperplasia could be prevented if the remainder of the thyroid was kept saturated with iodine. This was true in dogs as long as at least one-sixth of the gland was left, but if more than five-sixths was removed a compensatory hyperplasia followed even though iodine was given. This important observation pointed directly to iodine as the means for the prevention of thyroid hyperplasia (goiter).

One of the first practical applications of the principle of prevention of goiter and myxedema accidentally followed the discovery of salt in Michigan, and its more extensive use (as crude salt) in the sheep industry of this state at a time when the industry was being crippled by endemic goiter. This crude salt was afterward found to be rich in iodine. The first definite application of the use of iodine in the prevention of goiter on a large scale in animals was the prevention of goiter in brook trout. This disease had been the cause of much trouble and expense. The so-called thyroid carcinoma in brook trout had become so serious at the state fish hatchery at Shady Grove, Pennsylvania, that the question of abandoning the industry was being discussed. An investigation of the causation and a study of methods of prevention was undertaken by Marine and Lenhart in conjunction with the Pennsylvania State Fish Commission during the years 1909, 1910, and 1911. Their conclusions as to the etiologic factors producing goiter and the practical method of its prevention were definite and convincing. The important factors which in this instance caused endemic goiter were: (1) overfeeding with an artificial food; (2) overcrowding. These investigators showed that goiter could be prevented in young fish, under the same environmental conditions which pro-

duced goiter, by adding a very small amount of iodine to the food or water, or it could be prevented by changing the diet and remedying the overcrowding. The results of this practical research have been far reaching.

In addition to the experimental work above mentioned the treatment of goiter with iodine at the Dispensary at Lakeside Hospital had been followed for the past ten years. Also the maternity dispensary of Lakeside Hospital had not only been using iodine in the treatment of goiter, but had been using it as a prophylactic measure during pregnancy. To most of the men in touch with the goiter clinic at Lakeside or the School of Medicine the prevention of goiter was no longer an experiment, but an accomplished fact.

Therefore, at the beginning of our work in Akron the possibility of goiter prevention had been clearly demonstrated by animal experimentation, but only a very limited application of methods of prevention had been made in man. No subject in preventive medicine had a sounder or more scientific basis for its practical application to man on a large scale than the prevention of endemic goiter. Yet there was considerable criticism and opposition which had to be overcome. This criticism centered about the possible untoward effects of iodine, especially the danger of producing exophthalmic goiter.

ETIOLOGY OF ENDEMIC GOITER

Before any one can fully comprehend the fundamental principles underlying the method of prevention which we have used he must have some conception of the factors causing the disease. There have been many theories as to the cause of goiter, most of which are only of historic value and will not be taken up here. At present there are

a few who consider goiter as a primary disease or idiopathic enlargement of the thyroid gland.

McCarrison considers it a water-borne infectious disease the exciting factor of which is a contagium vivum and suggests that it belongs to the colon group of bacteria. Shepherd also in his report in 1918 on the occurrence of goiter in Canada concludes that it is a water-borne infectious disease, directly comparable to typhoid.

However, most of the scientific investigators of this country look upon goiter as a deficiency disease; Marine has been emphasizing this point since 1907. As has been pointed out:

1. Iodin is essential to the normal thyroid activity.
2. From a purely biochemical standpoint any substitution for iodine destroys the physiologic activity of the thyroid hormone.
3. From the histologic point of view glandular hyperplasia of the thyroid is due to a deficiency of iodine.
4. The physiologic action produced by thyroid extract is always proportional to the iodine content.
5. In animal experimentation, if the iodine content is maintained at or above $\frac{1}{10}$ of 1 per cent., no anatomic changes toward goiter formation can take place.

These facts, with our results in preventing goiter in school girls by simply keeping the thyroid saturated with iodine, make the infectious theory at once untenable.

These facts lead to the conclusion that the immediate or exciting cause of endemic goiter (hypertrophy of the thyroid gland) is a lack of iodine in the organism. This lack of iodine may be relative or absolute. The remote or fundamental cause of goiter is quite unknown.

PRACTICAL APPLICATION OF THE PRINCIPLE OF GOITER PREVENTION

In the practical application of the principle of prevention we chose the public schools for two reasons: (1) The children are in the adolescent age, the most important period in the development of goiter. (2) The public school group furnishes the best census of goiter in any community, and makes it possible to carry out, through the school organization, the most expedient, economic, and practical plan of prophylaxis and education.

In October, 1916, we explained the principle of the prevention of goiter to the Superintendent of Schools of Akron, Dr. H. V. Hotchkiss. He promised the full support of all the school authorities if the local Medical Society would sanction the work. After this idea had been explained to the Summit County Medical Association this body, in a regular session, voted to send the following message to the school board: "The idea of prevention of goiter, as outlined, can do no harm and may do good. We are in favor of seeing it carried out." The school board authorized the superintendent to call upon Dr. Marine and myself to make a survey of goiter among the school children of Akron and carry out any plan of prevention we saw fit.

In April, 1917, an examination for thyroid enlargement was made of all the girls from the fifth to the twelfth grades, inclusive. The boys were not examined because of the relative infrequency of goiter in boys. The result of each examination was recorded on a special individual card which on one side had space for the pupil's *name, school, age, grade*, and the tabulations of four thyroid examinations. On the back of this card was space for the record of eight series of prophylactic treatments, which

were recorded by the teacher giving the treatment. This goiter card was attached to the school record of each pupil and was transferred with the pupil whenever transfer to another school was made. In no other way could we have kept track of so many cases over so long a time.

The details regarding this examination and the plan for carrying out the treatment were then published. Only the resultant figures will be given here. 3872 girls were examined, with the following results:

| | |
|----------------------------------|-------------------------|
| Normal thyroids, | 1688, or 43.6 per cent. |
| Slightly enlarged thyroids, | 1931, or 49.9 per cent. |
| Moderately enlarged thyroids, | 246, or 6.3 per cent. |
| Markedly enlarged thyroids, | 7, or 0.2 per cent. |
| Among these there were adenomas, | 39, or 1.0 per cent. |

In April, 1917, the first prophylactic treatment was administered to more than 1000 girls who had elected to take it. No girl was urged, and no one was permitted to take it unless she had a written permit from a parent.

In November, 1917, a second examination of all girls from the fifth to twelfth grades inclusive was made, in all, 4415 cases, 1772 of which were new records. Of the 2643 old records, 764 had taken the prophylaxis during the preceding six months and 1879 had not. As was published then, there was not a single case in which a normal thyroid increased if the pupil was taking iodine, while among those not taking iodine 26 per cent. of those marked normal at the first examination showed definite enlargement—some already having developed moderately large goiters. Even more than a prophylactic action was shown by the results—just one-third of the “small goiters” had disappeared, and one-third of the “moderate goiters” had decreased 2 cm. or more.

In November, 1918, a third examination of 4277 girls

was made. In October, 1919, 5520 individual examinations were recorded, and during the entire period 9967 different girls were reported.

EFFECT OF PROPHYLACTIC TREATMENT

The prophylactic treatment as carried out for the past three years in the Akron schools consists of the administration of 2 gm. of sodium iodid, given in 0.2 gm. doses daily, for ten consecutive school days, repeated each spring and autumn. The general data of the pupils not taking the treatment are given in Table I, and of those taking the treatment in Table II. Only pupils who have had two or more consecutive examinations have been included in these tabulations. A considerable number of pupils, both of those who have been taking the treatment and of those who have not been taking the treatment, have been omitted because they missed one examination, although otherwise their records were complete; 2305 pupils are included in the tabulation of those not taking treatment, and 2190 in the tabulation of those taking treatment.

Furthermore, properly to interpret the results it was necessary to take into consideration the length of time each pupil had been under observation. As the prophylactic treatment was given at intervals of six months, we have used this interval as the unit, and grouped the pupils according to the periods each had been under observation—*i. e.*, six, twelve, eighteen, twenty-four, or thirty months. The results of only three groups, those with normal, slightly enlarged, and moderately enlarged thyroids, are included, because the fourth group, those with markedly enlarged thyroids, is too small. A comparison of the two tables brings out striking differences between those not taking and those taking iodine. These differences are manifested

both in *prevention of enlargement*—prophylactic effect, and in a *decrease* in the size of existing enlargements—therapeutic effect.

Prevention.—The preventive value of the treatment is shown in the column marked “unchanged” and “increased.” Taking the totals for the periods of six months each, the following results were obtained. Of those that were normal at the first examination and did not take iodine, 347, or 27.6 per cent., had enlarged thyroids, while of those that were normal at the first examination and took iodine as outlined, 2, or 0.2 per cent., had enlarged thyroids. These two instances of enlargement were investigated.

The first pupil, aged sixteen, had her thyroid examined and classified as normal on May 2, 1917, October 17, 1918, and December 3, 1918. At the examination on October 15, 1919, it was classified as slightly enlarged. This girl had taken 2 gm. of sodium iodide during each of the five possible periods—May, 1917, November, 1917, May, 1918, December, 1918, and May, 1919. A special examination was made on January 13, 1920, when the enlargement of the thyroid was verified. That this enlargement was acquired rather than congenital was shown by the absence of a pyramidal process of the thyroglossal tract. The tonsils were markedly enlarged and abnormally hyperemic. On direct questioning we were informed that the pupil was subject to recurrent attacks of tonsillitis. There was also slight enlargement of the lymphoid tissue at the base of the tongue and in the nasopharynx, and the general impression was that of a neurotic individual with general lymphoid hyperplasia.

The second girl, aged fifteen, had her thyroid first examined and classified as normal on November 27, 1918.

At the examination on October 16, 1919, it was classified as slightly enlarged. This girl had taken 2 gm. of sodium iodid during each of the two available periods, November, 1918 and May, 1919. A special examination was made January 13, 1920, when the thyroid enlargement was verified. Careful inspection revealed the presence of Hutchinson teeth, depressed nasal arch, and interstitial keratitis. We considered the case as one of neglected congenital syphilis.

Of the cases classed as having slightly enlarged thyroids at the first examination and *not taking* the prescribed iodin, 127, or 13.3 per cent., underwent further enlargement, while among those *taking* the prescribed treatment, only three, or 0.3 per cent., underwent further enlargement. Two of these three were re-examined on January 13, 1920, and the previous finding verified. One of these was another case of chronic infection of the tonsils with recurrent attacks of tonsillitis during the last year. In the second girl superficial inspection failed to show any pathologic condition to account for the enlargement. The third girl was not present for examination. These five cases were the only instances that showed enlargement of the thyroid out of 2190 pupils. Of the 2305 cases *not taking* iodin, 495 showed thyroid enlargement. Of the group with small goiters, *taking* iodin, 659, or 57.8 per cent., returned to normal, while of the same group, *not taking* iodin *at school*, 134, or 13.9 per cent., returned to normal. However, we know that there is an error in the last figure, for many cases not taking iodin under the school jurisdiction were taking it in some form from their physician. No attempt has been made to detect or estimate this error.

In the practical application of the preventive treatment one must keep in mind the three periods when simple

thyroid enlargements most commonly occur, viz.: (1) fetal period; (2) adolescence, and (3) pregnancy.

1. The prevention of goiter in the mother and the fetus is as simple as the prevention of goiter which develops during adolescence. Practically, it would seem that the prevention of goiter during these periods, *i. e.*, 1 and 3, is properly the responsibility of individual members of the medical profession supplemented by education of the public.

2. The prevention of goiter in the adolescent period, on the other hand, should be a public health measure under state, county, or municipal control. The existing systems of organization of the schools, both public and private, are sufficient to handle all the details without additional aid or expense. Education of the pupils could be combined with the actual administration of iodine so that after leaving school they could continue the treatment if necessary. In industrial medicine physicians could render an important service in this direction. As thyroid enlargement is approximately six times as frequent in girls as in boys, each community must decide whether it will include both sexes in prophylactic measures; as it must also decide regarding the ages when the use of iodine should begin and end. In this climate probably the maximum of prevention, coupled with the minimum of effort, would be obtained by the administration of iodine between the ages of eleven and seventeen years. As applied to our schools this would mean beginning with the fifth grade.

METHOD AND FORM OF ADMINISTRATION

As has been shown, iodine is taken up by the thyroid gland when given by mouth, by inhalation, or by external application. And it makes very little difference from a

scientific point of view what form of iodine is used; the thyroid gland will take up iodine from the most stable compound, *i. e.*, mercuric iodide. Weith reports favorable therapeutic results from the inhalation of iodine secured by the suspension in the schoolroom of a wide-mouthed bottle containing 10 per cent. of tincture of iodine.

It has been suggested by Sloan that in these mildly goitrous districts a mixture of small amounts of sodium iodide in common table salt could be made which would suffice for all iodine therapy. However, we feel that the most satisfactory method is the individual oral administration of definite small amounts of some salt of iodine, either in solution or tablet form. For private use the well known U. S. P. preparations, syrup of ferrous iodide and syrup of hydriodic acid, are excellent. As described above, as a public health measure we used 2 gm. of sodium iodide over a period of two weeks and repeated twice yearly. This dosage has prevented enlargement of the thyroid in more than 99 per cent. of the children in this mildly goitrous district.

When one recalls the small amount of iodine required to saturate the normal thyroid and the specific affinity of this gland for iodine, it is perfectly obvious that only very small amounts are needed. The normal thyroid contains about 5 mgm. of iodine per gram of dried gland; 25 to 30 mgm. is the total storage capacity. From this it is clear that a few milligrams of iodine daily over a longer period (a month or more) would produce optimum thyroid effects.

The prevention of thyroid enlargement in individuals with other diseases or in those residing in extremely goitrous districts, as in some glacial valleys of Alaska and British Columbia, and in certain districts of the Alps and Himalayas,

might require larger amounts of iodine than those indicated above as sufficient for normal individuals.

POSSIBLE ILL EFFECTS

As was stated above, there was some anxiety among medical men as to the possible ill effects of giving iodine promiscuously. Some men anticipated many cases of exophthalmic goiter, while others looked for an outbreak of iodine rash. The actual results were better than we had hoped for. In all the cases taking the prescribed 2 gm. of sodium iodide twice yearly there was not a single instance of exophthalmic goiter nor any evidence of a nervous irritability simulating it. In all, there were eleven cases of iodine rash, and six of these cases were so mild that the girls did not even stop the treatment; five cases, however, caused sufficient difficulty for the treatment to be stopped, when the rash cleared up promptly.

Both of these possibilities were considered and mentioned in each school. In all, there were over 3000 different girls taking the prophylactic treatment, many of whom took it for three years, and among these the sum total of the ill effects was a mild rash in less than 0.4 of 1 per cent.

THE POSSIBILITY OF THE ELIMINATION OF ENDEMIC GOITER THROUGHOUT THE WORLD

Following the publication of the results of our first year's work in Akron the public schools of Kent and Ravenna adopted the same procedure, and in 1919 the village of Berea began the prevention of goiter through the schools on the same plan. In the spring of 1920 we completed a survey of goiter among the school children of Warren, Ohio, including all boys and girls from the fifth to the twelfth

grades, inclusive. As the incidence of thyroid enlargement was low—24.4 per cent. in girls and 9.5 per cent. in boys—we advised the school physician and nurse that we considered it sufficient in this vicinity to provide each school with a stock solution of sodium iodid and treat each goiter as soon as it was detected. This method has been in operation in Warren for one year and is just now being started in Niles. This same method of treatment is being practised in some of the large factories of Cleveland where many young women are employed, and it is being provided in the different factories of the National Lamp Works in eight different cities of the United States.

It is interesting to note that in the spring of 1918, Prof. R. Klinger, of Zurich, Switzerland, undertook to carry out the same treatment in the schools there. This was soon started with a different method of administration, but practically the same amounts of iodine as we used in Akron. In January, 1921, Klinger published the results of the first sixteen months' treatment, reporting extraordinary results, even though he was working in some schools in which the children were 100 per cent. goitrous. Klinger's results certainly supply striking confirmation of the results we obtained in Akron. It is even more gratifying to know that recently this same plan for the prevention of goiter has been recommended to the goiter commission of Switzerland to be carried out as a public health measure throughout the whole state, the most noted endemic goiter nation in the world.

The same imagination which developed the practical application of the principle of the prevention of goiter can now see, a few generations hence, the closing of the chapters on endemic goiter and cretinism in every civilized nation in the world.

TABLE I.—RECORD OF PUPILS NOT TAKING PROPHYLACTIC TREATMENT

| Time under observation, months. | Normal. | | | | Slightly enlarged. | | | | | | Moderately enlarged. | | | | | |
|---------------------------------|-------------|------|-------------|------|--------------------|------|-------------|------|-------------|------|----------------------|------|-------------|------|-------------|------|
| | Un-altered. | | In-creased. | | Un-altered. | | In-creased. | | De-creased. | | Un-altered. | | In-creased. | | De-creased. | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 6 | 47 | 50.0 | 47 | 50.0 | 93 | 69.4 | 36 | 26.9 | 5 | 3.7 | 16 | 69.6 | 7 | 30.4 | 0 | 0.0 |
| 12 | 420 | 75.5 | 136 | 24.5 | 251 | 70.3 | 35 | 9.8 | 71 | 19.9 | 17 | 65.4 | 8 | 30.8 | 1 | 3.8 |
| 18 | 103 | 65.2 | 55 | 34.8 | 108 | 74.5 | 18 | 12.3 | 19 | 13.1 | 11 | 57.9 | 3 | 15.8 | 5 | 26.3 |
| 24 | 135 | 76.7 | 41 | 23.3 | 106 | 79.7 | 8 | 6.0 | 19 | 14.3 | 9 | 60.0 | 3 | 20.0 | 3 | 20.0 |
| 30 | 205 | 75.1 | 68 | 24.9 | 140 | 73.7 | 30 | 15.8 | 20 | 10.5 | 4 | 66.7 | 0 | 0.0 | 2 | 33.3 |

TABLE II.—RECORD OF PUPILS TAKING PROPHYLACTIC TREATMENT

| Time under observation, months. | Normal. | | | | Slightly enlarged. | | | | | | Moderately enlarged. | | | | | |
|---------------------------------|-------------|-------|-------------|-----|--------------------|------|-------------|-----|-------------|------|----------------------|------|-------------|-----|-------------|------|
| | Un-altered. | | In-creased. | | Un-altered. | | In-creased. | | De-creased. | | Un-altered. | | In-creased. | | De-creased. | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 6 | 17 | 94.4 | 1 | 5.6 | 54 | 69.2 | 1 | 1.3 | 23 | 29.5 | 9 | 81.8 | 0 | 0.0 | 2 | 18.2 |
| 12 | 344 | 99.7 | 1 | 0.3 | 187 | 45.5 | 0 | 0.0 | 224 | 54.5 | 10 | 23.8 | 0 | 0.0 | 32 | 76.2 |
| 18 | 73 | 100.0 | 0 | 0.0 | 72 | 52.3 | 1 | 0.7 | 64 | 46.7 | 7 | 28.0 | 0 | 0.0 | 18 | 72.0 |
| 24 | 184 | 100.0 | 0 | 0.0 | 72 | 37.9 | 1 | 0.5 | 117 | 61.6 | 2 | 7.7 | 0 | 0.0 | 24 | 92.3 |
| 30 | 288 | 100.0 | 0 | 0.0 | 92 | 28.5 | 0 | 0.0 | 231 | 71.5 | 1 | 2.6 | 0 | 0.0 | 38 | 97.4 |

TABLE III.—SUMMARY—RECORDS OF PUPILS TAKING AND NOT TAKING PROPHYLACTIC TREATMENT

| | Taking. | | Not taking. | |
|----------------------|---------|-----------|-------------|-----------|
| | Totals. | Per cent. | Totals. | Per cent. |
| Normal: | | | | |
| Unchanged..... | 906 | 99.8 | 910 | 72.4 |
| Increased..... | 2 | 0.2 | 347 | 27.6 |
| Slightly enlarged: | | | | |
| Unchanged..... | 477 | 41.9 | 698 | 72.8 |
| Increased..... | 3 | 0.3 | 127 | 13.3 |
| Decreased..... | 659 | 57.8 | 134 | 13.9 |
| Moderately enlarged: | | | | |
| Unchanged..... | 29 | 20.3 | 57 | 64.0 |
| Increased..... | 0 | 0.0 | 21 | 23.6 |
| Decreased..... | 114 | 79.7 | 11 | 12.4 |
| Total..... | 2190 | | 2305 | |

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SURGERY VS. X-RAY IN THE TREATMENT OF HYPERTHYROIDISM¹

GEORGE W. CRILE

HYPERTHYROIDISM (C. H. Mayo) seems a more fitting name for a disease whose chief characteristic is a super-normal activation of the thyroid gland than *exophthalmic goiter*, a term which signifies but one of the features of this complex syndrome.

That great student of the thyroid gland, Marine, has stated that in the literature the cure of hyperthyroidism has been credited to each of 239 drugs and other methods of treatment. From among all the opinions in favor of one or another of these many therapeutic measures, the verdict in favor of physiologic rest, by itself alone, or combined with other methods, is practically unanimous; and only two other methods of treatment have emerged as worthy of particular consideration—surgery and the *x*-rays.

To those who have not noted the increasing importance which is assigned by many physicians and surgeons as well as by roentgenologists to the use of the *x*-rays in the treatment of hyperthyroidism, a study of the literature is illuminating. A brief survey reveals 105 papers, in which the favorable action of the *x*-ray on hyperthyroidism is reported. Ludin¹ made a collection of 208 articles on this subject.

The general conclusions of the majority of these writers may be summarized briefly as follows:

¹ Reprinted from J. A. M. A., 1921, lxxvii, 1324.

² Ludin, Centralb. f. d. Grenz. d. Med. u. Chir., 1915, xviii, 205-235.

1. "It is utterly impossible to draw conclusions from any collection of statistics on this subject, because the cases reported show such a variation and such indefinite technic that the reduction of the statistics would give us nothing accurate by which we could judge future results."¹

2. All writers agree that the pulse-rate is nearly always reduced promptly; that usually the tremor and nervous symptoms are relieved at once; that the body weight usually begins to increase immediately.

3. There is a divergence of opinion regarding the effect upon the gland itself, as the experience of different writers appears to have varied widely.

Seymour expresses the opinion of most advocates of the *x*-ray treatment of hyperthyroidism in his summary of its advantages:²

"1. There are no fatalities.

"2. There is no resulting scar, as after operation.

"3. It does not interfere with the patient's occupation.

"4. It is painless and causes very little inconvenience to the patient.

"5. If unsuccessful, an operation may be done with less work because of the favorable action of the *x*-ray on the thymus gland."

Means and Aub, in a more recent report from the Massachusetts General Hospital,³ conclude that "The chance of cure in exophthalmic goiter is as good with the Roentgen ray as with surgery in groups of equal toxicity; and that this being true the former method is preferable, for the danger of a fatal outcome is less." These authors believe that surgery should be employed only after the *x*-ray and other methods have failed.

¹ Pfahler, G. E., and Zulick, J. D., *A. J. Roentgenol.*, 1916, iii, 63-72.

² Seymour, Malcolm, *Boston M. and S. J.*, 1916, clxxv, 568-569.

³ Means, J. H., and Aub, J. C., *Archiv. Int. Med.*, 1919, xxiv, 645-677.

On the other hand, we find Hildebrand¹ concluding from his personal experience with thirteen cases that in none had he observed any real lasting effect; and that when the cases finally came to operation the muscles, gland capsule, and the gland had become so adherent that the difficulty and hazard of the operation were increased; moreover, there were signs of necrosis in the superficial layers of the gland. He reports also that fatal cases of acute swelling of the gland, "thyroidismus," have resulted from *x*-ray treatment.

In discussing a paper by Boggs² Waters made the following comments:

"Before attempting the treatment of exophthalmic goiter or hyperthyroidism with *x*-rays it is vitally necessary:

"1. That it be known what histologic change takes place in the gland;

"2. That the superficial and deep structures of the skin be not injured by the *x*-rays;

"3. That the effect upon the vagus, sympathetic ganglion, and parathyroids be definitely known;

"4. That it be known what effect upon the thyroid gland is desired, that is, stimulating or inhibiting.

"Therefore, until these points are proved the work is being done not only unscientifically, but with extreme danger."

In 1916, Berkman reported from the Mayo Clinic³ that although in their experience the results of *x*-ray treatment were good, they were temporary; that the results were delayed and required many repetitions of treatment; that practically no dependable beneficial results were obtained in less than a month; and that in the more serious cases

¹ Hildebrand, Otto, *Archiv. Klin. Chir.*, 1919, cxi, 1-70.

² Boggs, Russell H., *A. J. Roentgenol.*, 1919, vi, 613-619.

³ Berkman, D. M., *St. Paul Med. Jour.*, 1916, xviii, 300-303.

“the excitement and mobilization incident to *x*-ray treatment usually offset whatever early benefits may be received.”

In a recent article C. H. Mayo¹ writes:

“With *x*-ray treatment remissions may occur just as remissions occur without treatment or with several other methods of treatment. Our experience has been failure or but temporary benefit. It is possible that the ray treatment may destroy the gland and produce hypothyroidism. It is difficult to regulate the dosage, and its use adds to the difficulties of operation.”

Most writers agree as to the beneficial effect of the *x*-rays in adolescent hyperthyroidism; and many consider that this beneficial effect is due principally to the action of the *x*-rays upon the hyperplastic thymus, which, according to some reporters, is present in 90 per cent. of the cases of exophthalmic goiter. In our own experience we have never had a single case of hyperthyroidism in which we had reason to consider an enlarged thymus a complicating factor. At the Mayo Clinic a study of 100 necropsies of fatal cases of exophthalmic goiter was made to determine the possible relation between the thymus in adults and exophthalmic goiter.² The investigators concluded that a hypertrophic thymus is present in all exophthalmic goiter cases under forty years of age, and in half of those over forty years of age. “Hypertrophy of the thymus is inversely proportional to the age of the patient and directly proportional to the duration of the disease.”

As to the cause and effect of the enlarged thymus, however, these reporters make the following comment:

“Our records in general show that the most severe acute cardiac damage is seen in those violent intoxications

¹ Mayo, C. H., Surg., Gyn., and Obst., 1921, xxxii, 209-213.

² Blackford, J. M., and Freligh, W. P., Collected Papers of the Mayo Clinic, 1916, viii, 507-512.

in which the onset occurs after the age of forty; that is, in the 'menopause' group. These, as a rule, have a small thymus or no thymus. In every case of cardiac damage in which a thymus was found there was definite parenchymatous hypertrophy in the thyroid with no demonstrable thymus. . . . The findings indicate that a thymic hypertrophy and lymphatic hyperplasia should be considered as a result rather than as a cause of the intoxication in hyperplastic or non-hyperplastic goiter. Hypertrophy of the thymus probably depends on the presence of vestigial tissue at the onset of disease which may regenerate under toxic stimulation."

Several writers, notably Means and Aub,¹ base their judgment as to the efficiency of the x-ray treatment of hyperthyroidism on its effect on the basal metabolism. In Lakeside Hospital Dr. Christie has made a series of comparative studies of the effects of the x-rays, of ligation, and of thyroidectomy on the basal metabolism. He has found that bilateral partial thyroidectomy reduces the metabolism more markedly and more promptly than either the x-rays or ligation; and that the x-rays reduce the metabolism more than ligation. Since ligation is employed only as a preliminary step to thyroidectomy, it need not be considered in this discussion. On the other hand, since Dr. Christie's findings appear to show that thyroidectomy exerts the greater immediate curative effect, it becomes necessary to determine whether or not there are other considerations which should prohibit the employment of thyroidectomy in preference to the x-rays. To determine this it is necessary to compare thyroidectomy and x-ray treatment as to (a) the resultant discomfort; (b) the resultant period of disability; (c) the immediate mortality,

¹ *Loc. cit.*

and (d) the end-results. It is significant to note that many cases that came to operation have had x-ray treatment (Figs. 58, 59).

Discomfort.—In Lakeside Hospital in all severe cases of hyperthyroidism the operation is performed in the patient's



Fig. 58.—Burn due to treatment of goiter with x-rays.

room, without moving the patient from bed; the patient is protected from worry, anxiety, and fear by tactful management; no discomfort follows the preliminary ligation; and there is relatively little discomfort after the thy-

roidectomy. It follows that this plan of surgical management produces no greater subjective disturbance of the patient—probably less in the severe case—than results from transportation to and from the x-ray treatment room.

Period of Disability.—In a recent series of 500 thyroidectomies the average stay in the hospital before ligation was four and three-fourths days, after ligation, from three to five days. The average stay in the hospital before



Fig. 59.—Burn due to the x-ray treatment of the thyroid gland after partial thyroidectomy.

thyroidectomy was four and one-half days, after thyroidectomy, thirteen days. The total hospital period, therefore, averaged twenty-five and one-fourth days—broken by the period at home between the ligation and the thyroidectomy.

In the Massachusetts General Hospital series reported by Means and Aub¹ no data are given from which one may

¹ *Loc. cit.*

judge the length of stay in the hospital required for each *x*-ray treatment or group of treatments. Nevertheless, it is obvious that the total loss of time and the inconvenience necessitated by repeated visits to the hospital exceed that occasioned by surgical treatment alone.

Mortality.—Among our last 500 thyroidectomies there were 5 deaths, a mortality rate of 1 per cent.; among the last 500 ligations there were 2 deaths, a mortality rate of 0.4 per cent. Our records show a series of 331 consecutive thyroidectomies and 145 consecutive ligations—that is, 476 consecutive thyroid operations without a death. And among thyroid operations for exophthalmic goiter the records show a series of 227 consecutive thyroidectomies and 180 consecutive ligations, that is, 407 consecutive thyroid operations for hyperthyroidism without a death. These series are not made up of selected cases. No patient was rejected, although the series included patients in every stage of hyperthyroidism, some with edema of the extremities and ascites.

As we have stated above, we have found in the literature no statistics which give a basis for comparison, although it is obvious that the immediate mortality of *x*-ray treatment is hardly to be considered; although, from among the cases treated by *x*-ray, a goodly number, probably several per cent., die while taking the treatments.

Our statistics, however, show that the operative risk in cases of hyperthyroidism, under the type of surgical management indicated above, may be largely disregarded.

End-results.—It is too early to report on the end-results of our recent series, as at least three years should elapse before the end-results may be considered as stabilized; but it is conceded that surgical reduction is altogether the most curative method.

CONCLUSION

From a study of the evidence offered by those who advocate the *x*-ray treatment of hyperthyroidism and a consideration of our own experience we believe that the surgical treatment of hyperthyroidism combined with physiologic rest yields the most favorable results. Heretofore the only valid objection to surgical treatment has been the mortality; but surgery now undertakes every case; the mortality is practically eliminated; much time is saved and a more certain cure is achieved.



PREOPERATIVE MANAGEMENT OF EXOPHTHALMIC GOITER

W. R. GOFF AND E. O. RUSHING

THE preoperative treatment of patients having exophthalmic goiter is very important because they are so exquisitely sensitive and nervous that even the slightest disturbing element in their treatment may seriously impair their already lowered thresholds.

INTRODUCTION OF THE PATIENT TO HOSPITAL ACTIVITIES

It must be remembered that most patients have never before been in contact with hospital life. Therefore it is necessary to eliminate every possible source of anxiety and worry which may be occasioned by the hospital routine. In fact, the treatment begins before the patient arrives at the hospital, for care is taken to make sure that the patient's room is ready on his arrival so that he may be immediately conducted to it, for waiting is poorly tolerated. The nurses and attendants are instructed to receive their patients with the greatest consideration and to win their confidence as quickly as possible.

The patient is weighed and put to bed, and is not allowed to get out of bed again until after the operation. One or two relatives or friends may remain with him during the remainder of the day of arrival, but after this but one visitor is admitted at a time, to remain for thirty minutes only. No formal history is taken or examinations made on the day of admission. The ward physician makes a social call and only in an indirect way enters into conversation con-

cerning the illness. Nothing is said concerning the operation. We recently saw a crisis develop in one case because when the patient asked to wear her own nightgown the nurse told her she should put on the operating-room clothes.

PRELIMINARY EXAMINATIONS, TESTS, AND THERAPY

On the second day a thorough history is taken, and if the patient is not tired by this, the routine physical examination is made. The utmost care is taken to prevent the patient from becoming overtired and, upon the first evidence of fatigue, all activities cease, to be resumed later.

Special attention is given to the heart because acute myocardial failure is frequently encountered in exophthalmic goiter cases. If any sign of myocarditis is present a course of treatment is begun at once—20 minims or less of the tincture of digitalis every four hours for from eight to twelve doses. If this is not sufficient for the maximum restoration of the myocardium, a second preoperative course of digitalis may be given after a few days of complete rest.

The renal function is tested routinely by the Mosenthal method. This method is preferred because it is reliable, it does not interfere with other tests, and it does not disturb the patient as do some of the other nephritic tests which depend upon the secretion of dyes injected with a needle.

The test is made as follows: At 8 A. M. the patient voids, the specimen being discarded. Breakfast is then given, lunch at 12, and dinner at 6 P. M. Moderate amounts of fluids are taken at mealtime only. Specimens of urine are collected at 10 A. M., 12 noon, at 2, 4, 6, and 8 P. M. From 8 P. M. to 8 A. M. the specimens are collected in one container, the amount and specific gravity of each urination being first ascertained. Normally the 10 A. M. and the

2, 4, and 8 P. M. specimens will be large in amount and low in specific gravity; the 12 noon and 6 P. M. specimens will be smaller in amount and high in specific gravity; the night specimen will be larger in amount, but high in specific gravity. If nephritis is present, however, the specimens will tend to be the same in amount and in specific gravity. If nephritis is suspected, the phenolsulphonephthalein test is made by intramuscular injection. If the excretion is low, operation is deferred until the output is raised to a safe level by treatment, which consists of rest in bed, the administration of large quantities of water by the mouth, subcutaneous infusions of novocain— $\frac{1}{32}$ per cent. (Bartlett)—the administration of glucose and sodium bicarbonate per rectum in a 10 per cent. solution and the elimination of the amount of food intake, particularly of protein and salt, to a minimum. Frequently the patient is restricted to a milk diet. If there is a retention of fluids with edema, together with renal insufficiency, hot packs are used as in the treatment of advanced nephritis. With this treatment the systolic blood-pressure is frequently reduced from 30 to 40 points.

Exophthalmic goiter patients frequently suffer from insomnia. To avoid this thirty grains of sodium bromid are given every evening at eight o'clock. Usually after one or two nights in the hospital the patients relax and sleep well.

In order to prevent any systemic disturbance which may result from the sudden diminution of the thyroid secretion by thyroidectomy two grains of thyroid extract are given on the evening before and on the morning of operation.

The cycles of vomiting, tachycardia, restlessness, delirium, etc., usually called hyperthyroidism, are now believed

to be due to an intracellular acidosis which can ordinarily be cleared up by active treatment consisting of measures which restore the internal respiration. This treatment comprises the digitalization of the heart by the administration of 20 minims or less of the tincture of digitalis every four hours until eight to twelve doses have been given, blood transfusion, and subcutaneous infusion of from 3000 to 5000 c.c. of normal saline solution every twenty-four hours.

PREOPERATIVE ROUTINE

Because of the nervousness of these patients and their poor tolerance for suspense they are usually not told when the operation is to be performed; in fact, if possible, the subject of operation is altogether avoided, and stress is laid upon treatment. In order to prevent the patient from knowing exactly when the operation is to take place the following routine is carried out daily for several days beforehand.

The operating-room clothes are put on usually the day after admission. Some kind of explanation has to be given for each move to satisfy the curiosity of the patient. He is told the pneumonia jacket and leggings are kept on to insure an even temperature of the body, etc.

- A hypodermic injection of sterile water is given every morning about eight and breakfast is deferred.

At nine each morning, before the patient's breakfast is served, the anesthetist takes a nitrous oxid-oxygen machine to the bedside and, after explaining to the patient that she is going to give him some oxygen for his heart, the mask is held lightly over the face, and a small amount of nitrous oxid and oxygen is given, never allowing the patient to become unconscious. This procedure is usually explained by the ward physician the night before during his social

call. In some cases several mornings are required to get the inhalations started, because if the patient becomes at all disturbed, the maneuver is suspended, to be tried again the next morning.

On the morning of the operation a hypodermic injection of morphin, gr. $\frac{1}{6}$, and atropin, gr. $\frac{1}{150}$, is substituted for the sterile water. The patient is not disturbed by nurses or visitors after the hypodermic injection has been given, and at the usual time the anesthetist gives the inhalation. This time the patient is allowed to pass into the analgesic or anesthetic stage, and in this condition is operated upon in his bed, if the severity of the case demands it, or is transferred to the operating room.



THE RÔLE OF THE NURSE IN THE PREOPERATIVE AND POSTOPERATIVE CARE OF THE PATIENT WITH EXOPHTHALMIC GOITER

ABBIE R. PORTER

SINCE patients with exophthalmic goiter are in a very abnormal mental state—frightened and apprehensive—the nurse's first duty is to gain their confidence, and to reassure them in every possible way. The general preoperative routine to which all patients are subjected upon admission to the hospital must be applied also to exophthalmic goiter patients, but in such a way that it is scarcely obvious to them. As a rule patients are weighed, measured, etc., as soon as they reach the hospital. The goiter patient, however, is put to bed at once; and some time during the first day, as opportunity presents itself, the weight, measurement, temperature, pulse, respiration, and blood-pressure, both diastolic and systolic, are taken.

As soon as these patients have been seen by the doctor they are placed on a special preoperative routine, which consists chiefly of rest and quiet in bed. An ice-bag is placed over the heart and is kept there constantly. Each night the patient is given a sponge bath if restless, and thirty grains of sodium bromid if required to insure a good night's rest. The regular house diet is given with especial restrictions—tea, coffee, red meats, highly seasoned and glandular foods, such as sweetbreads, oysters, etc., being eliminated.

At 7.30 on the morning of the second day after admission a sponge-bath is given. The operating clothes are put

on and a hypodermic injection of sterile water is given between 7.30 and 8.30 A. M. The hour is thus varied because on the morning of the day of operation a hypodermic injection of morphin and atropin will be given between these hours, an hour before the operation is to be performed. Before the injection is given the shades are drawn, and afterward the patient is left absolutely alone. If any questions are asked, it is explained that the injection is part of the treatment.

The best rule for the nurse to follow during the first few days is to say as little as possible; first, in order to avoid the possibility of contradicting anything which may have been said at the doctor's office previous to the patient's admission to the hospital; and, second, because it is always wiser to study a patient's temperament, especially that of an exophthalmic goiter patient, before talking much. The first few days should, therefore, be spent in observing the patient, noting just where to break away from the regular routine, just what to concede.

Seemingly trivial things annoy these patients. They are often greatly annoyed and irritated by the operating clothes, and in such cases it is best not to put them on until the patient is anesthetized. One attractive and seemingly tractable young girl absolutely refused to take her inhalation. Baffled by this unexpected action, the nurse studied her patient in order if possible to discover the difficulty, and later in the day found that this girl's special pride was her hair, and the fact that it was not arranged in a certain way so annoyed her that she became quite unreasonable. The next morning her hair was becomingly dressed, and she took the inhalation without resistance. It is therefore evident that each case must be studied individually and treated accordingly.

Each morning between eight and nine o'clock an inhalation from the nitrous oxid anesthetic apparatus is given by the anesthetist. This, like the hypodermic injection, is explained as part of the treatment. Breakfast is served between nine and half-past ten, according to the time at which the inhalation was given. The nurse must watch the effect of the first inhalation carefully in order to report any

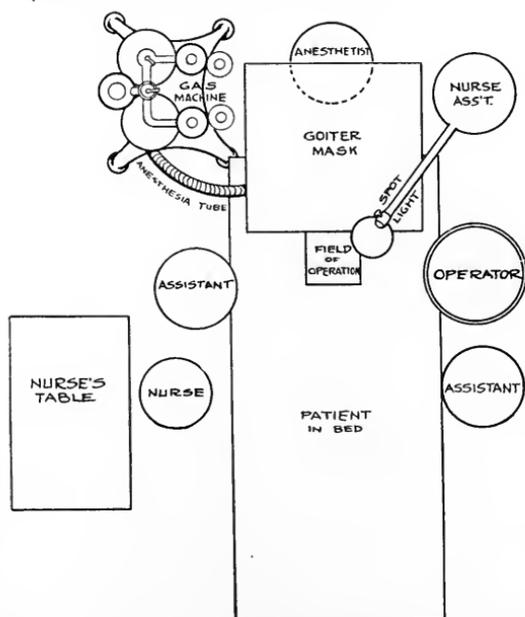


Fig. 60.—Operation in patient's room. Schematic drawing showing arrangement of room and position of operating staff.

increase in the pulse-rate, restlessness, or other significant symptoms to the resident or the surgeon.

During the preoperative period the exophthalmic patient is sent in a wheel-bed to the hospital porch for one hour each morning and afternoon. Care is taken to keep these patients from the other patients in order that they may not become excited. For the same reason visitors are restricted to one only for one-half hour twice a day.

On the morning of the operation the routine described above is followed, but morphin or atropin are substituted for the hypodermic injection of sterile water. The inhala-

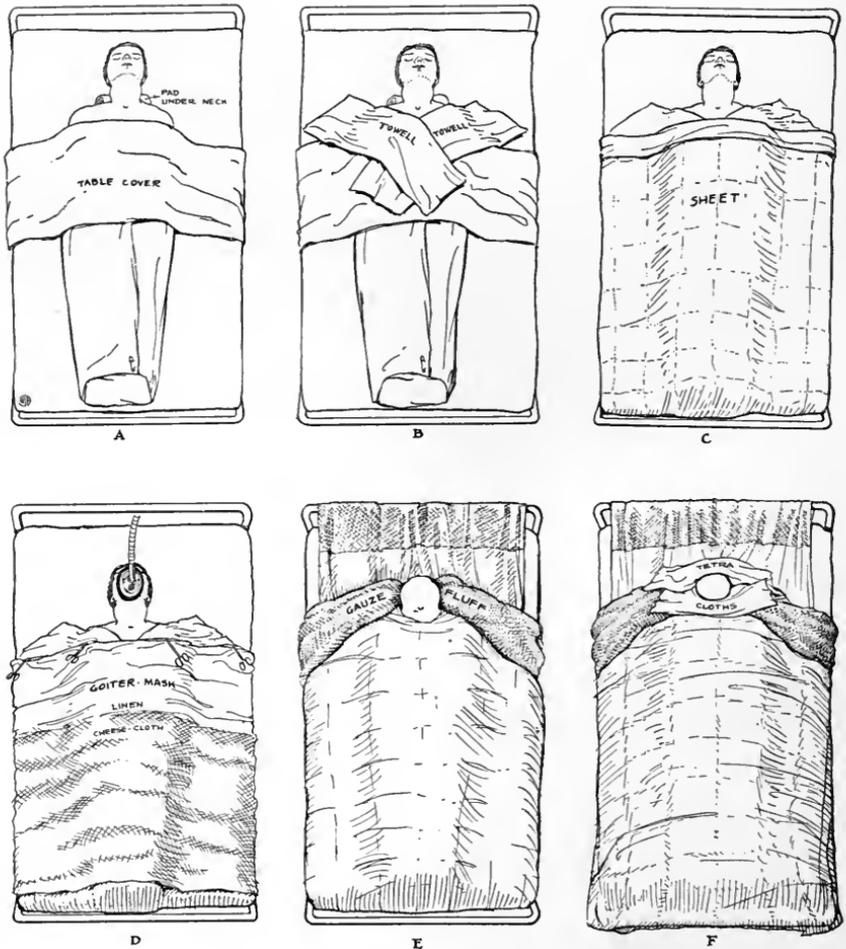


Fig. 61.—Operation in patient's room. Position of patient and arrangement of aseptic coverings.

tion is given as on the previous days, but a sufficient amount of nitrous oxid is added to the oxygen to produce analgesia. If the operation is to be performed in the patient's room

all the essential articles are placed on a wheel-bed or cart in the hall outside. This is brought into the room just as soon as the anesthetist indicates the patient is ready, as are also the sterile trays which have been sent from the operating room (Figs. 60-62).

Just before the close of the operation the patient's nurse should be in the room in order to remove everything which was not in the room before the operation, and to



Fig. 62.—Operation in patient's room. Patient ready for operation.

have the shades drawn so that when the anesthetic mask is removed the room will appear just as the patient remembers it. An ice compress is then placed over the patient's forehead and eyes; she is propped up with four or five pillows, and is left with one nurse. The postoperative care then begins.

Sponging of the hands and face and a general sponge bath for restlessness are given as occasion demands. The temperature, pulse, and respiration are watched carefully,

the temperature being taken every two hours. Any rise in temperature is immediately reported to the resident. Six or more ice-packs are placed around the patient if a temperature of 101° F. or over is reached. If the temperature rises to 103° F. the patient is put in an *ice-pack* as is described elsewhere in this volume, and the pulse and respiration are taken and recorded every fifteen minutes. Any increase or irregularity in pulse or respiration is reported at once. At all times an emergency tracheotomy tray is kept ready for use, but not in the patient's room. Any increase in the amount of drainage on the dressing is noted and reported. The blood-pressure is taken every four hours.

As soon as water is tolerated, it is urged. Inhalations of the fumes of tincture of benzoin compositus in boiling water are given as indicated, beginning the night following the operation, to relieve mucus and the cough which at times follow thyroidectomy. On the day following operation soft diet is given.

During the postoperative period visitors are restricted as before operation. The patient is kept in bed each morning until 10.30, after which he is permitted to go to the solarium on a wheel-bed or in a wheel-chair, according to the progress of convalescence. Between two and five o'clock he remains in his room, and he is required to retire at nine. During convalescence water is urged, and milk is given as extra nourishment, routinely. Just before dismissal from the hospital the patient is weighed and the neck measured.

THE RÔLE OF THE OPERATING-ROOM NURSE IN OPERATIONS ON THE THYROID GLAND

BLANCHE E. SNYDER

THE first duty of the operating-room nurse is so to prepare the operating rooms that everything will be in readiness when the operative schedule begins. This means that in the early morning the room must be cleaned and thor-

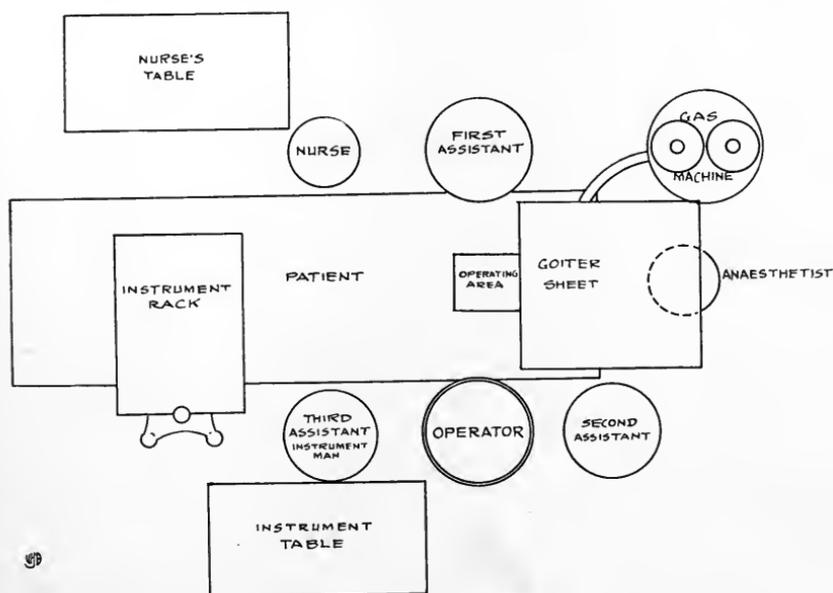
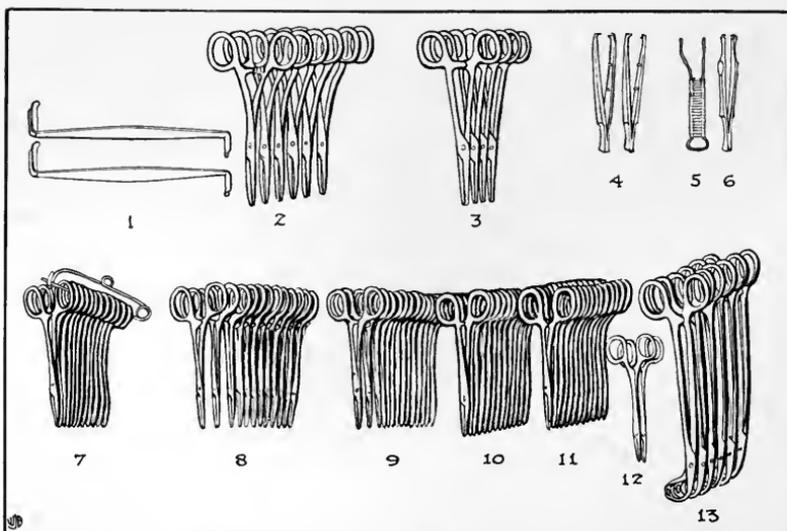


Fig. 63.—Schematic drawing showing positions of operating table, instrument tables, operator, and assistants for thyroidectomy.

oughly dusted; that the supplies, sufficient to carry through the morning's work without interruption, must be assembled; that the nurses' table and the instrument table must be properly set up, ready to be uncovered (Figs. 63-65).

The hot-water bed covering the operating table should be filled with warm water and covered with a sheet (Fig. 66); and the hand straps, knee straps, and goiter attachment put in place. The artificial light must always be in readiness within easy reach (Fig. 67).

The trays and tables which hold the sterile supplies for the operation in the patient's room or on the wards



INSTRUMENT TABLE

Fig. 64.—Arrangement of instruments on instrument table for thyroidec-
tomy: 1, 1 pair of Crile retractors. 2, 6 Ochsner clamps. 3, 4 muscle clamps.
4, 2 mouse-tooth dressing forceps. 5, Skin clips. 6, Skin clips forceps. 7,
12 hemostats. 8, 12 hemostats. 9, 12 hemostats. 10, 12 hemostats. 11, 12
hemostats. 12, 2 Alice hemostats. 13, 6 tetra-clamps.

and in the operating room are set up by two graduate "scrub-up" nurses with the assistance of pupil nurses. As soon as the trays are arranged, they are sent to the wards. Operating gowns, clothes, and extra supplies are also sent to the wards at this time. This makes it possible to carry through the entire operative schedule on the wards without returning to the operating room.

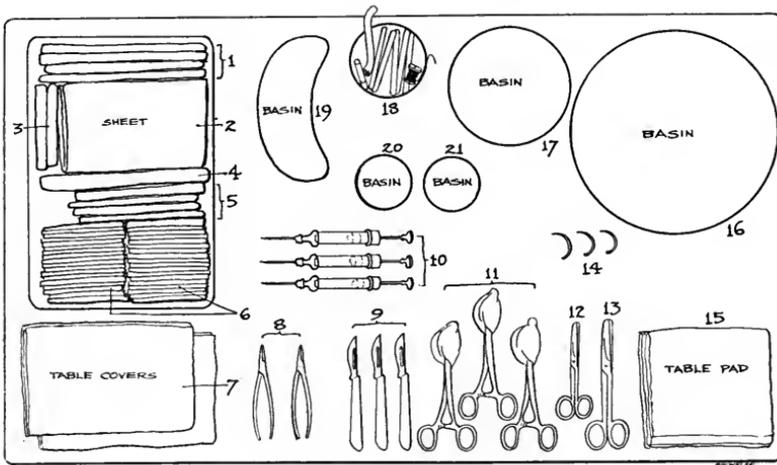


Fig. 65.—Arrangement of instruments and supplies on nurses' table for thyroidectomy: 1, 4 gauze dressings. 2, Plain sheet. 3, 2 tetra cloths. 4, Goiter mask. 5, 4 towels. 6, 36 gauze sponges. 7, 2 table covers. 8, Crile needle-holders. 9, Parker detachable-blade knives. 10, Luer syringes for novocain injection. 11, Kelly forceps with cotton pledgets for scrubbing field of operation. 12, Nurses' scissors. 13, Straight shears. 14, Kelly oblique needles No. 2. 15, Table pad folded into 9-inch square for threaded sutures. 16, Solution basin for sutures. 17, Specimen basin. 18, Suture material basin containing reel of black silk, flexible rubber drain, 5 tubes Luken's plain catgut No. 1. 19, Curved basin for catgut tubes. 20, Novocain 1 : 200 solution. 21, Picric acid 5 per cent. in alcohol.

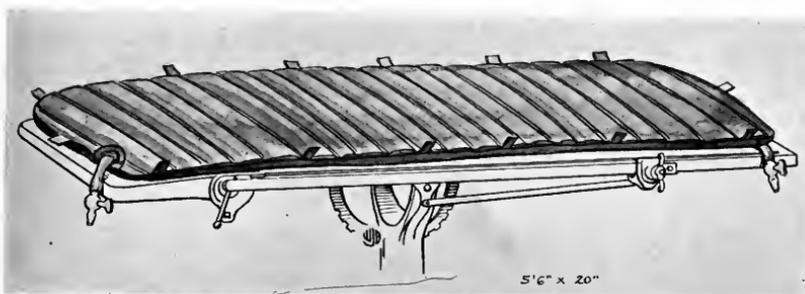


Fig. 66.—Hot-water mattress on operating table.

In thyroid operations in which the anesthetic is started in the patient's room the operating nurse must have an operating room wheeled stretcher waiting outside the

patient's room, so that the patient may be taken to the

operating room as soon as the anesthetist has him ready. The ward surgeon must previously have been notified, so that he will be on the ward ready to accompany his patient to the operating pavilion, for patients to whom the anesthetic is administered in their rooms are always accompanied to and from the operating room by the ward surgeon.

When the patient arrives in the operating room and has been transferred to the operating table the nurse must at once see that the goiter attachment is in the proper position, that is, a 3-inch elevation should be under the patient's shoulders. The gown and flannel jacket are then turned down and the hand and knee straps tied, after which the nurse is ready to "pour scrubs"—ether and a 5 per cent. solution of picric acid in alcohol. The most important part played by the operating-room nurse begins at this time. She must watch the "scrub-up nurse" very carefully, keeping her table well supplied with novocain, sponges, catgut, etc., so as to eliminate delay during the operation—a sufficient supply of these articles is always placed in the operating room early in the morning. The operating-room nurse is also responsible for having

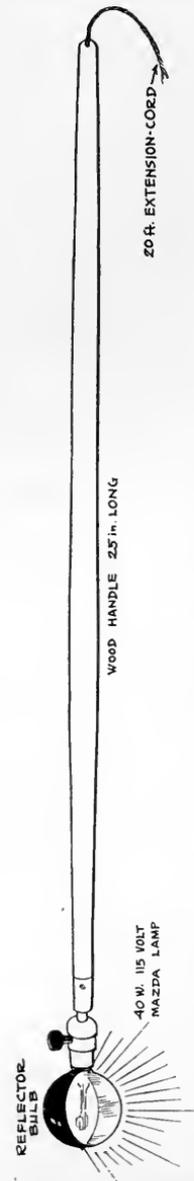


Fig. 67.—Extension reflector for illumination of field.

tracheotomy tubes sterilized and at hand, so that, in emergency, they may be given to the "instrument man" (surgical

intern) without any delay whatsoever. It is hard to make the pupil nurses understand the necessity for this, as a tracheotomy is so rarely required. The nurse must also watch the instrument table carefully, adding more instruments, particularly hemostats, as the operation progresses. The number of hemostats used varies considerably in different thyroid operations, the average number being about six dozen.

As the extent of the operation will depend entirely upon the condition of the patient, and as, therefore, the patient may be sent back to his bed at any moment—after the excision of one or of both lobes—with the wound dressed open with flavin gauze, the nurse must always be ready with her dressings.

After one patient leaves the operating room the nurse in charge must be prompt in preparing the room for the following operation so that there may be no delay in getting it started. This is particularly important in cases in which the patient comes to the operating room under anesthesia, as every minute's delay means an unnecessary prolongation of the anesthesia. It is almost equally important, however, when the patient is brought to the operating room without being anesthetized, for it is then essential that the anesthetic be started at once before the patient has time to become unnecessarily excited by viewing the operating room.

When the thyroidectomy is to be performed in the patient's room the co-operation of the ward nurses is essential, and is always gladly given. They prepare and have waiting outside the patient's room the drop light, ether, picric acid solution, alcohol, ice compresses, and small bedside tables on which the sterile dressings are placed. Thus but a moment is required for these articles to be

taken inside the patient's room after the anesthetic is started.

The operating-room orderlies follow up all operations on the ward, and return the trays to the operating room promptly after each operation. In this way, by the time that the ward work has been completed, all operating-room supplies have been returned and have been washed and resterilized by pupil nurses, so that when the doctors and nurses return to the operating room after having performed from four to eight operations in the patients' rooms everything is in readiness to continue the morning's work in the operating room itself.

The graduate "scrub-up nurses" play a very important part in connection with thyroidectomies, as they are expected not only to anticipate the wishes of the operator but also those of his assistants. In this clinic a spirit of entire co-operation has been developed among the surgeon, the assistants, and the "scrub-up nurses." This co-operation is of vital importance to the operating-room nurse, whose prime duty it is to assist in every way possible in shortening the duration of the operation, particularly in extremely severe cases of exophthalmic goiter when the operation is performed without moving the patient from bed.

THE ADMINISTRATION OF NITROUS OXID-OXYGEN ANALGESIA IN OPERATIONS ON THE THYROID GLAND

AGATHA HODGINS

For all goiter operations nitrous oxid-oxygen analgesia is the anesthetic method of choice, whatever the physical condition of the patient. The more serious the risk, the greater is the necessity for using analgesia.

PLAIN GOITERS

For the removal of the usual colloid goiter, if the patient's general condition is good, and there is no reason for modifying the routine surgical procedure, the patient is brought to the operating room and the anesthetic is administered there in the usual way. In these cases, especially if the gland is large, the anesthetist must bear in mind the possibility of compression or collapse of the trachea, with consequent interference with the respiratory exchange. Should this happen, the immediate administration of oxygen under pressure will overcome the condition.

Since the dissection may be difficult the anesthetist must make sure that the air passages are clear. If there is any tendency to obstruction the flat air-way is inserted. This appliance in no way affects the condition of the patient, while it does assure the anesthetist that no obstruction can occur as a result of the tongue's dropping back over the pharynx. With this precaution, if obstruction does occur, it will be below the larynx, in which case, unless the obstruction is complete, the anesthetist can keep the patient safe with oxygen given under pressure.

Nasal tubes are useful in these cases, but as their introduction necessitates deepening the anesthetic while the tubes are inserted, it has been our experience that this procedure is usually unwise. However, when the tubes are inserted, a very smooth, even type of respiration is insured. With the mouth closed, the lungs can be very quickly insufflated with oxygen through the upper air passages. A valve for regulating the pressure is, of course, attached to the gas machine. The ease with which nitrous oxid-oxygen anesthesia can be deepened or diminished also contributes to the comfort and safety of the patient. Some patients are carried to full surgical anesthesia during a difficult part of the operation, after which they are brought back to analgesia.

EXOPHTHALMIC GOITER

For operations on exophthalmic goiter patients we employ a different technic. These patients are hypersensitive to any external stimuli, their sense of fear is exaggerated, and they make a marked response to even slight physical injury. These patients, therefore, must be approached with great caution. On several consecutive days before the day of operation they are given inhalations of oxygen, with perhaps a very small amount of nitrous oxid, in order that the preoperative apprehension of the patient may be minimized. This procedure is also valuable to the anesthetist, as it gives her a very good idea of the patient's reaction to the anesthetic; in other words, she gets an idea of the patient's mental control. It is necessary that these patients be handled both tactfully and sympathetically by the anesthetist. For this reason it is very important that an anesthetist be taught the proper method of approach to a patient. The preoperative inhalations are made to

appear as very ordinary procedures. No mention is made of going to sleep or of anesthesia. The anesthetist usually speaks casually about giving the patient a little oxygen to see how he will adjust himself to breathing into the face mask, assuring him that it will be a very comfortable and easy thing to do. On the morning of the ligation the anesthetist enters the patient's room in the usual way to give the inhalation. This time, however, the patient is told that the doctor is coming in to look at his neck and that he will perhaps put some medicine on the skin.

The state of analgesia is then approached, and the mental control of the patient is assured by the anesthetist. The anesthetist follows the line of least resistance with these patients and tries to secure their co-operation by means of suggestion rather than command. Fortunately, in most patients analgesia establishes more or less indifference to the environment, a condition to the advantage of the anesthetist in securing mental control of the patient. As the preparation of the patient for operation proceeds everything that is done is explained in a matter-of-fact manner. We have found that, unless there is an utter lack of self-control, patients respond very well indeed to the suggestion that they can co-operate with the anesthetist.

The pressure sense is exaggerated under analgesia. Therefore when there is any evidence that the face mask is causing discomfort it is taken off and the gas is allowed to flow over the patient's face without actual contact. Cloths chilled with ice should be at hand, as they are very refreshing when placed over the eyes and forehead.

It must be remembered in connection with the administration of analgesia that it is necessary for the anesthetist to interpret the respiration of the patient and the expression of his eyes in order to judge accurately the exact stage

of analgesia at any moment. It has been our experience that for the first five minutes patients vary to about the same degree as during the induction of anesthesia. The first subjective feeling which the patient experiences is usually one of warmth and exhilaration. During this stage the respiratory rate may be a little increased, and the anesthetist needs to instruct the patient to breathe more slowly, to relax his muscles, and to take things quietly.

After this phase the secondary stage of analgesia develops. In this stage the indifference to surroundings becomes more or less apparent. A "don't care" state of mind is evidenced. The respiratory rate is slow, sometimes slower than normal, partly due, perhaps, to the pre-anesthetic dose of morphin. The expression of the eyes supplies a valuable guide. There is usually a quiet, sleepy expression and the movement of the eyeball itself is very slow. The anesthetist, however, should be able to maintain direct contact with the patient, asking him to open his eyes and to look at her. Sometimes the patient is disinclined to do this, and insisting upon this point may produce discomfort and fretfulness. The face assumes the tranquillity of sleep. As the stage of analgesia proceeds, after ten minutes, huskiness of the voice may become apparent. In some patients slow response and inco-ordination of thought is marked. The pressure sense is exaggerated, so that the patient may complain of pressure during the operation. The respiratory and pulse-rates are usually unchanged. However, in a very apprehensive patient, there may be an increase in the pulse and respiratory rate when pressure is being exerted by the surgeon or when pain is felt.

It must be remembered that the next anesthetic stage after that of indifference is that of intoxication, which is

always marked by an increase in the rate of respiration; the tranquil expression of the eyes vanishes and they assume an active expression. At this stage it is difficult for the anesthetist to be guided in gaining mental control of the patient by looking at his eyes.

When a marked exhilaration is manifested at the beginning of analgesia the anesthetist must bear in mind that such patients very rapidly approach the stage of intoxication, which may interfere with control. These patients are also very near the dream stage. If the hallucinations or sensations are unpleasant, the patient shows evidence of mental stress. It is nearly always a simple matter to bring the patient back to the stage of indifference by saying that the anesthetist wants him to talk to her. By watching the rate of respiratory decrease and the return of the eyes to an expression of tranquillity, it is possible again to approach the true analgesic state.

Patients who by reason of the severity of their illness are apprehensive sometimes have the impression that the duration of time is much prolonged. If at any time during the analgesia the patient should drift into oblivion, his sense of the duration of time is, of course, immediately shortened. It must also be borne in mind that with the perfect nerve-blocking of local anesthesia this drifting into light sleep may occur. When this happens it is a perfect state for the patient. The pulse-rate is normal, the color is good, the respiration is tranquil, and the patient is apparently undisturbed mentally. Dreams, if they occur, are usually of a pleasant or interesting nature.

The anesthetist must, of course, realize that it devolves upon her to guide the patient through the analgesic stage and to interpret to him comfortably the happenings of the operation. This, of course, requires study and an adapta-

bility which is not always easily attained. It is also necessary that there be perfect co-operation between the surgeon and his anesthetist. At the end of the operation the anesthetist explains to the patient that she wants him to have a sleep. She also impresses on him how much his co-operation has been appreciated and in what a splendid condition he is.

SPECIAL NOTES

At the present time most of our severe exophthalmic goiter cases are operated upon in the patient's room under *analgesia plus local anesthesia*. During the course of a thyroidectomy the perfect blocking with local anesthesia is a more necessary factor in the maintenance of good analgesia than is the case with ligation. It may develop that the enucleation of the gland is a more difficult procedure than the surgeon had anticipated. If this happens, the anesthetist should be warned by the surgeon. However, she will know by the increased activity of the respiration, pained expression of the face, increase in the pulse-rate, and the activity of the eyes that the patient is not comfortable. If the situation is not promptly met by the surgeon it may be necessary for the anesthetist to explain to the patient that she knows he is not comfortable, and that she is going to let him have a little sleep for a few minutes. The increased activity of the respiration, which results from breaking through the veneer of analgesia, will make it necessary for the anesthetist to increase the dosage of nitrous oxid in order to control the phenomena thus developed. As soon as comfort is re-established the rate of respiration becomes slower, the eyes again become tranquil, and the troubled expression of the face disappears. The anesthetist must then bring the patient back quickly to analgesia, as otherwise the patient will drift over into

the second or dream stage of anesthesia, which is the most uncomfortable state for the patient and the most difficult for the anesthetist to control. In some patients the invasion of pain will cause a temporary feeling of faintness. With these patients the anesthetist simply says that she will give something to relieve the faint feeling, a statement which she can make with assurance, since we have found that an increased amount of oxygen will usually meet the situation. A feeling of faintness may develop also if the operation is prolonged. The application of cold cloths to the lips and eyes with the inhalation of oxygen gives relief. Sometimes smelling salts also are helpful.

One of the outstanding thoughts in the anesthetist's mind in taking a patient through a thyroidectomy under analgesia is the possibility that obstruction of the trachea may occur. It is well, therefore, to be prepared to give the patient oxygen under positive pressure, should such an emergency develop. If the oxygen brings the patient back to light analgesia, unless the return to this stage is comfortable to the patient, he is "put to sleep" for a few minutes to relieve the distress which the work on the trachea may have occasioned. After this phase of the operation is passed the patient is brought back slowly to analgesia, and it is necessary for the anesthetist to control the patient mentally as he comes back from oblivion to the stage of indifference. In other words, as soon as the respiratory phenomena and the expression of the face indicate that the patient is coming back to analgesia, the anesthetist must again control him by suggestion.

It is of the utmost importance, of course, that any untoward or serious occurrence during an operation under analgesia be kept from the patient's knowledge. There should be no whispering during an operation, as whispering

always arouses suspicion and anxiety on the part of the patient. Unnecessary noise and the clinking of instruments must be avoided. The exaggeration of the sense of sound under analgesia is very marked in some patients. Others are apparently indifferent to sounds. If the surgical procedures should involve injury or pressure on the laryngeal nerve there will result stertor and disturbance of respiration with attendant restlessness. Therefore, unless the patient is an unusually good subject for analgesia and the anesthetist has established perfect control from the beginning, it is advisable to put the patient into the stage of light anesthesia. *Deep anesthesia should be avoided.*

In milder cases of exophthalmic goiter, when it is felt that it is not necessary to perform the operation in the patient's room, the patient is anesthetized in bed, lifted from the bed to the wheeled stretcher, and taken to the operating room under light anesthesia. When the patient has been placed comfortably on the operating table he is, if possible, brought back to the stage of analgesia. When the patient does not come back to the stage of analgesia with comfort, light anesthesia is maintained throughout the operation. Toward the end of the operation the anesthesia is moderated to analgesia, the patient is lifted from the operating table to the stretcher, taken back to the ward under very light analgesia, and put comfortably in his bed. These patients have no memory of proceedings before and for some time after the point of oblivion is reached.

In cases of adenomata in which there is no cardiac impairment or other special necessity for the protection of the patient, the patient is taken to the operating room and put under analgesia there. This necessitates a quick grasp of the situation by the anesthetist. It is somewhat

harder to get the mental control of the patient in the operating room than it is in the patient's bedroom. As everything around the patient indicates operative procedure, the anesthetist has a more difficult task.

In some patients the respiration is hyperactivated. This activation of the respiration makes it rather difficult to establish true analgesia. If there is considerable hyperactivation, both mental and respiratory, it is sometimes best to put the patient under anesthesia and then bring him back slowly to analgesia. This is usually a more effective procedure than to try to exert mental control over a patient who is already hyperactive, but whose condition is not endangered by anesthesia. Usually these patients tolerate the operative procedure very well, and it is simply a question of carrying them through the operation with mental comfort and without tiring the respiration.

In anesthesia in contrast with analgesia it must be remembered that in these patients as well as with exophthalmic goiter patients nausea may develop, and therefore, whenever possible, it is best to avoid deep anesthesia. Light anesthesia is better and analgesia is best. With true analgesia there is no nausea. It is only when a patient approaches the second or intoxication stage or has passed well into that stage that nausea occurs, for our experience with nitrous oxid-oxygen anesthesia seems to indicate that nausea is in part at least the result of suboxidation. Other factors which may produce nausea are fear and the preliminary dose of morphin. The sign of approaching nausea is usually an indication for oxygen.

The hyperactivity shown at the beginning of the anesthesia may be repeated at the end of the operation. If this is marked, the patient is treated as in exophthalmic goiter and is taken back to his room under light analgesia.

This is done also when there has been a mechanical obstruction of the trachea with the consequent necessity for pure oxygen after the operation.

SUMMARY

1. The proper administration of analgesia requires prolonged special training on the part of the anesthetist.
2. Analgesia therefore offers the greatest measure of protection to the patient.
3. The surgeon and anesthetist must co-operate closely.
4. All forms of inhalation anesthesia interfere with the internal respiration. In exophthalmic goiter the internal respiration is near the point of failure. Analgesia does not interfere with the internal respiration.

THE TECHNIC OF OPERATIONS ON THE THYROID GLAND*

G. W. CRILE AND W. E. LOWER

THE TYPICAL LIGATION

ALL ligations are performed under analgesia and local anesthesia in the patient's room without removing the patient from his bed. The superior thyroid artery is ligated



Fig. 68.—Ligation of superior thyroid artery. Infiltration of skin.

in preference to the inferior artery for the reason that the latter lies deeper and its ligation apparently is less effective, probably because the nerve supply to the thyroid runs along the wall of the superior artery. The field, including the skin, subcutaneous tissue, muscles, etc., is completely

* Reprinted from *Surg., Gyn., and Obst.*, 1922, xxxiv, 258-264.

infiltrated with 1:200 novocain (Figs. 68, 69). Immediately after the novocain is injected firm pressure is made

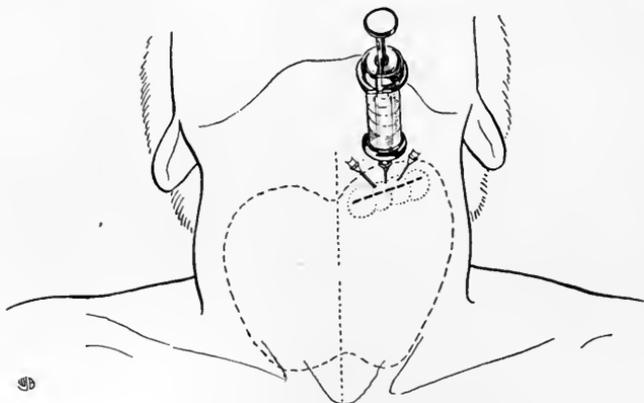


Fig. 69.—Ligation of superior thyroid artery. Deep infiltration for complete protection of field of operation.

over the injected area, as this diffuses the anesthetic and increases its efficiency. The skin is divided parallel to the

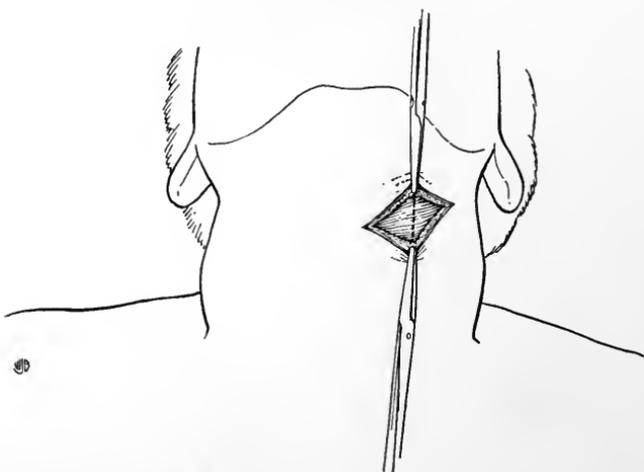


Fig. 70.—Ligation of superior thyroid artery. Line of incision through fascia.

skin folds, and should be symmetrical on the two sides, if both sides are ligated. The fascia is then divided, exposing

the preglandular muscles (Fig. 70). The muscles are not severed, but the fibers are separated with narrow-bladed

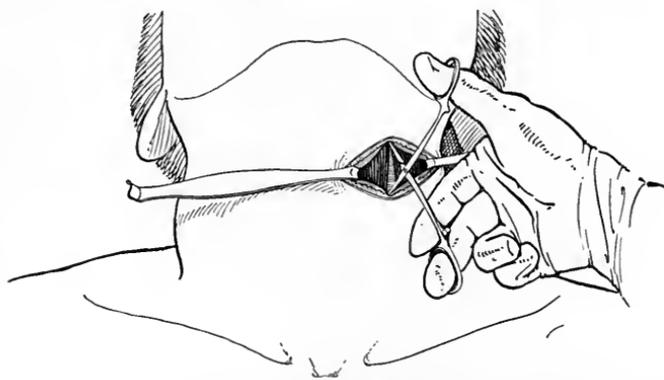


Fig. 71.—Ligation of superior thyroid artery. Separation of fibers of preglandular muscles with narrow-bladed hemostats.

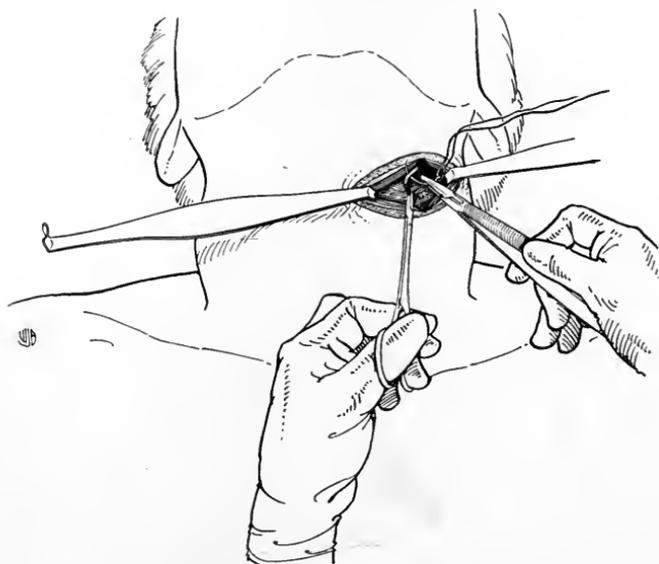


Fig. 72.—Ligation of superior thyroid artery. Passage of suture under artery which is elevated with forceps.

hemostatic forceps (Fig. 71) and the divided muscles are held apart to expose the upper pole of the gland by means of special retractors having different sized blades. This

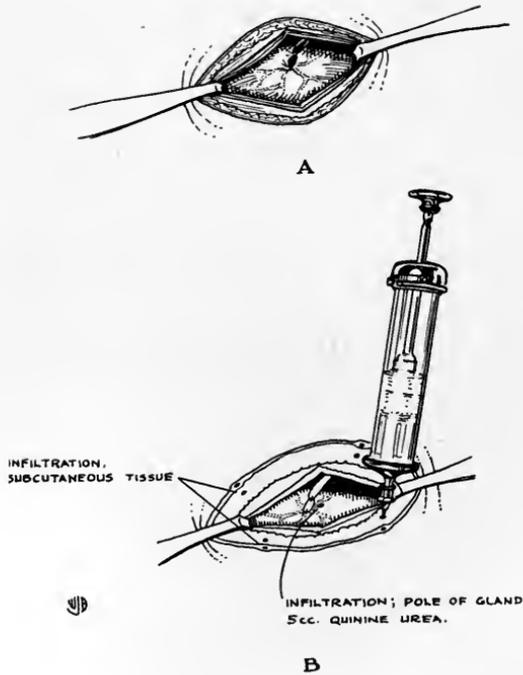


Fig. 73.—Ligation of superior thyroid artery: *A*, Sutures of artery and of superior pole. *B*, Infiltration of pole and of subcutaneous tissues with quinine and urea hydrochlorid.

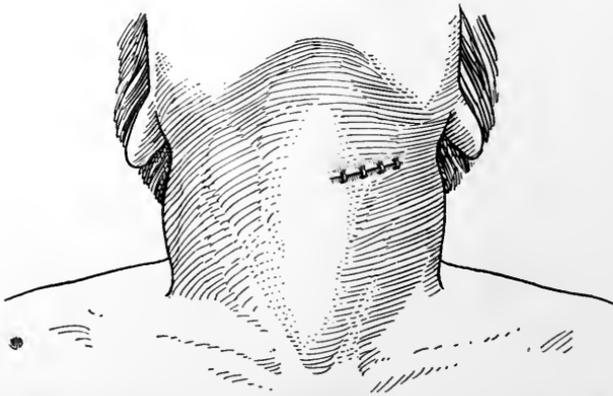


Fig. 74.—Ligation of superior thyroid artery. Closure of skin incision with clips.

retraction gives an almost uniform exposure of the artery, which is then picked up and held by a forceps while a full curved needle armed with silk is carried around it (Fig. 72).

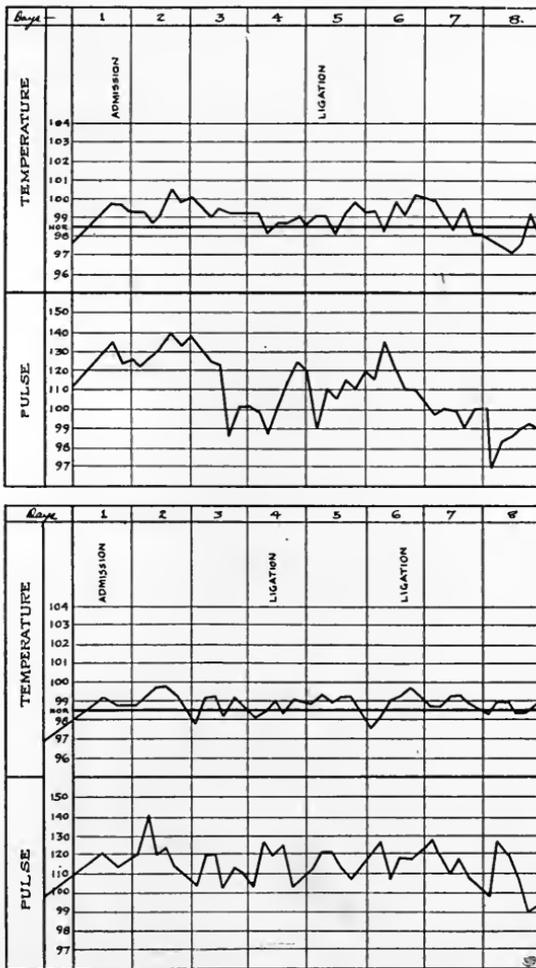


Fig. 75.—Typical charts showing that reaction to ligation is no greater than reaction to entrance to hospital.

A second ligature is passed around the superior pole to make sure that the main artery and not only a branch is included (Fig. 73, A).

The tissue involved in the ligature is infiltrated by injection with 1 : 600 quinin and urea hydrochlorid (Fig. 73, B), as are the subcutaneous margins which are to be grasped in the barbs of the skin clips, the injection being made from below outward so that the skin border becomes white and edematous. No deep sutures are used. The skin incision is closed with clips (Fig. 74) which are removed on the third day, for, if left longer, they may cause slight punctated scars.

Usually the artery of but one side is tied at one séance, for, if it is a grave risk, the double ligature would increase the hazard too much; and even in apparently safe cases the single ligation may disclose a hazardous situation. Moreover, if there is doubt as to whether the patient might safely endure a thyroidectomy, a single ligation will give the cue; and if the indication is favorable the thyroidectomy may follow the tell-tale ligation in three days. Our rule is: If there is any doubt as to the advisability of the thyroidectomy, make a single ligation. There will be at most only a three days' loss of time; and occasionally the single ligation may mean the saving of a life (Fig. 75).

THE TYPICAL RESECTION OF THE THYROID GLAND

Posture.—The patient is placed on the table in an inclined position, feet downward, and the base of the neck is sufficiently elevated by a small pillow to produce an advantageous elevation of the chin (Fig. 76).

Position of the Scar—the Platysma.—A collar incision, at about the level of the middle and lower thirds of the neck, paralleling the natural folds of the skin, is the favored position for the scar. If the goiter is large, especially if the patient has a short fat neck, the incision must be made correspondingly high above the clavicle, as otherwise the

scar will fall down upon the sternum, well below the clavicle, and be conspicuously displayed.

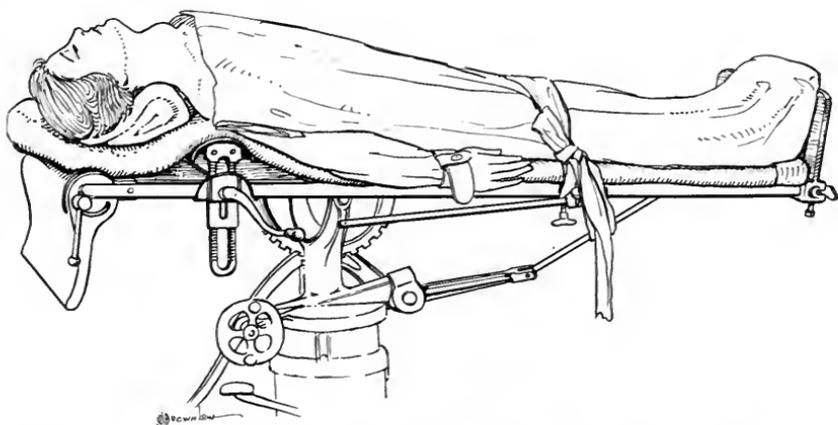


Fig. 76.—Typical thyroidectomy. Position of patient on operating-table.



Fig. 77.—Operator and assistants ready to operate on patient who is being brought to stage of analgesia.

The skin and subcutaneous tissue along the line of incision is infiltrated with 1 : 200 novocain (Fig. 78), after

which the incision is made without holding the skin, by a free but *not rapid* sweep of the knife, keeping the eyes



Fig. 78.—Typical thyroidectomy. Distribution of novocain after infiltration by pressure.

on a natural fold, or failing that, upon the line of junction of the neck and chest (Fig. 79). The most common error



Fig. 79.—Typical thyroidectomy. Line of incision through area infiltrated with novocain.

is to make the incision too low, especially if the goiter protrudes prominently in the front of the neck. The short-

coming of the so-called necklace incision is that an ordinary ribbon or band will not cover it as in the case of the higher incision. In addition, if the incision is made in the manner just described, a covering will rarely be required. Under

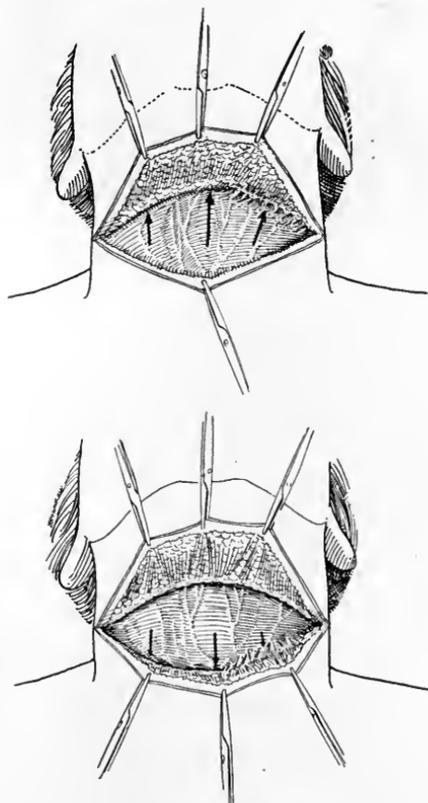


Fig. 80.—Typical thyroidectomy. Division and reflection of skin.

no circumstances should the incision be made in a vertical direction.

The platysma muscle is divided and reflected with the skin (Fig. 80). Formerly, in perhaps 1000 cases, we made a separate dissection and suture of the platysma, but further experience showed that this is unnecessary, for if the platysma is attached to the skin, it will be approxi-

mated with the skin if clips are used, and if the platysma remains with the preglandular muscles it will be approximated with them. In either case it will function normally. In other words, no special attention is paid to it.

Preglandular Muscles.—Shall the preglandular muscles be split vertically and their margins drawn back by retractors, or shall the preglandular muscles be divided transversely, thus completely exposing the thyroid, giving the

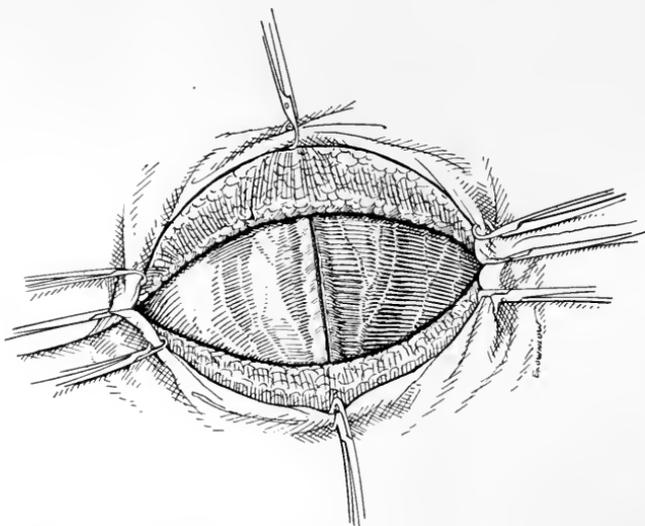


Fig. 81.—Typical thyroidectomy. Infiltration of preglandular muscles before transverse incision.

opportunity of making the operation of resection under the eye without the need of retractors to pull back the muscles? In the case of small goiters the median vertical division will answer; but in the great majority we have found it best to divide the muscles transversely. The transversely divided muscles become so soundly healed that no later disability occurs. The preglandular muscles, on one or both sides as required, are therefore divided between transversely applied special clamps after the line of incision and

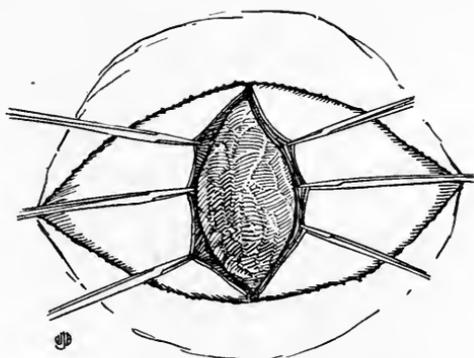


Fig. 82.—Typical thyroidectomy. Vertical incision along infiltrated line in preglandular muscles. Skin-flaps protected by sterile cloths.

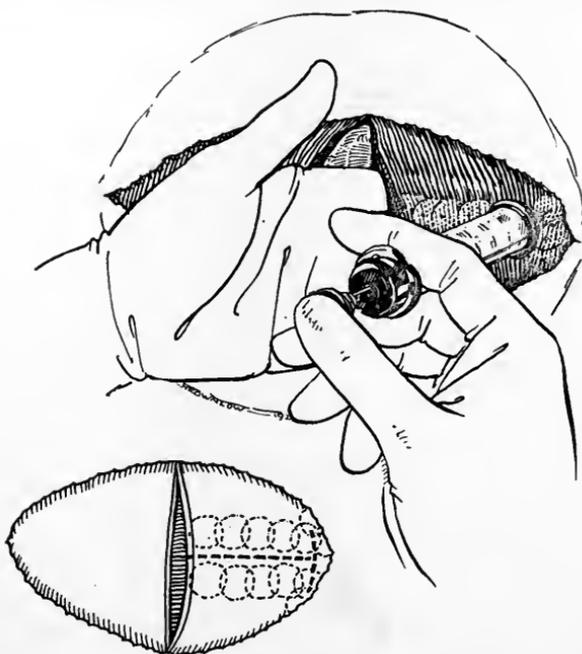


Fig. 83.—Typical thyroidectomy. Vertical division of preglandular muscles exposing gland.

the areas to be grasped in the clamps have been completely infiltrated with novocain. These muscle clamps are especially designed for this purpose. They grasp and hold, but do not crush the muscle (Figs. 81-84).

The advantages of the muscle clamps are of the first order, for they completely control bleeding, their handles serve as retractors, and they cause almost no tissue injury. By means of the four muscle clamps holding the divided muscles the structures overlying the goiter are unfolded. After the neck has been opened the skin and platysma myoides are protected by a sterile cloth. If more room is required than is provided by the transverse division of muscles, then, in addition, vertical incisions are made in the muscle at the outer end of the transverse muscular division.

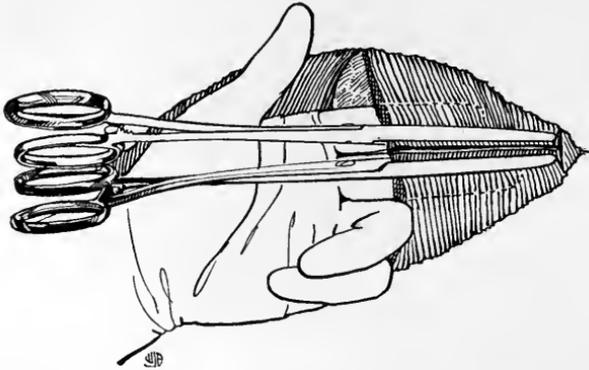


Fig. 84.—Typical thyroidectomy. Transverse division of preglandular muscles between clamps.

Blocking of the Gland with Novocain.—The capsule and the entire portion of the gland which is to be removed are infiltrated freely with 1 : 200 novocain (Fig. 85). In exophthalmic goiter, in particular, the infiltration of the gland with novocain is of prime importance because there is evidence that the thyroid discharges its secretion quickly in response to nerve stimuli. Novocain blocks the sympathetic nerve impulses just as it blocks the impulses of the nerves of common sensation. Care must be taken not to include the recurrent nerves in the infiltration. The superior pole in particular is well infiltrated. If care is exercised

there is no danger of puncturing vessels nor of novocain intoxication. We have not seen a single instance of intoxication in our series.

Superior Thyroid Artery.—In thyroidectomy the superior thyroid arteries are isolated and ligated to prevent their retraction and the resultant difficulty of catching and tying them. If catgut is used it should be made secure by

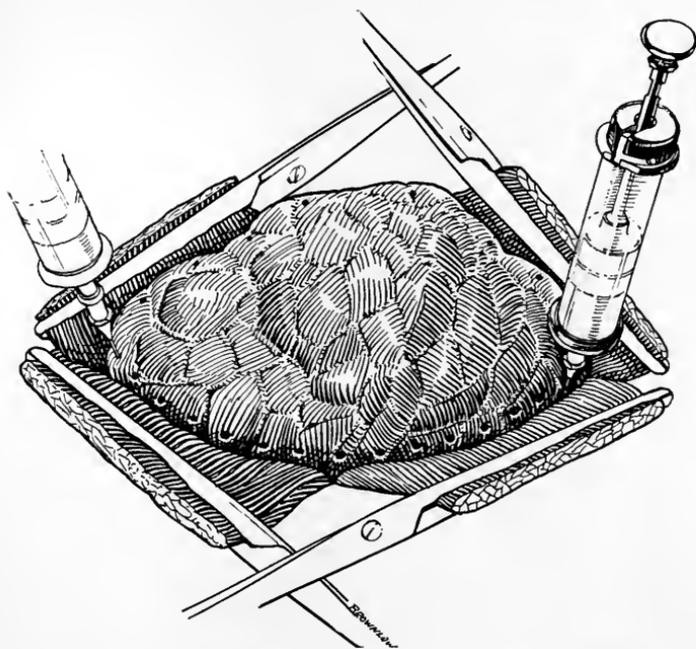


Fig. 85.—Typical thyroidectomy. Infiltration of gland with novocain.

passing it around the artery with a needle. If a free tie is made with catgut then in the case of vomiting or coughing the ligature may slip off. If a free tie is to be made, the ligature should be silk.

Resection of the Gland.—In the resection of the gland itself, as in the preliminary steps, the points of prime importance are the maintenance of a clear field and the absolute surgical control of every phase of the operation.

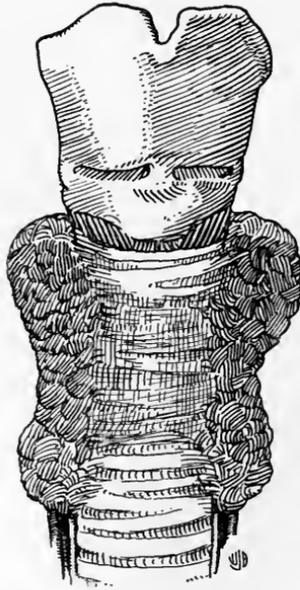


Fig. 86.—Typical thyroidectomy. Posterior portion of gland which is left after thyroidectomy. Note thin layer of tissue covering trachea.

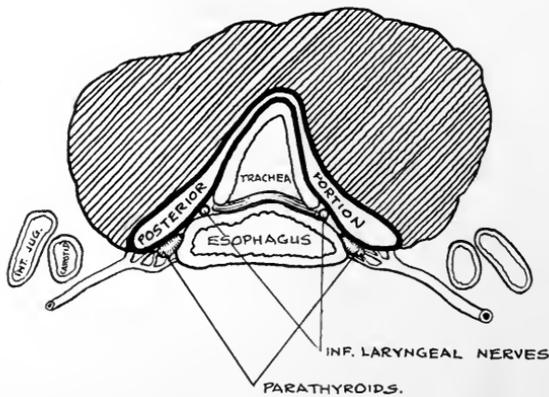


Fig. 87.—Typical thyroidectomy. Schematic drawing in which shaded area represents portion of gland that is removed.

A margin of thyroid tissue is left along each lateral border from the upper to the lower margin of the gland (Figs. 86, 87). To leave this margin it is necessary to carry the

division through the most vascular part of the gland. Hemorrhage is prevented by first grasping the tissue in Halsted forceps, then dividing it. Many forceps are required. The forceps are tied off afterward with catgut on a needle. The remainder of the lobes and the isthmus are removed, usually in a block. The division of tissue is made with a sharp knife in a field so clear that the parathyroids and the recurrent nerves would be seen clearly, although in practice they should never be seen, for if they are exposed the edema, and later the scar, may interfere with their function, this interference being expressed by tetany and hoarseness.

The Trachea.—The line of cleavage across the trachea and the larynx is developed in such a way that an undisturbed covering remains to protect these structures (Fig. 86). Under no circumstance is the surface of the trachea or larynx touched by a forceps. A connective-tissue covering of the trachea and larynx is always left, for if the sensory nerves on the surface of the trachea or larynx are disturbed the impulses are registered in the brain as coming from the inside of the trachea; therefore coughing and mucus are produced. After the front of the trachea and larynx have been crossed, then, as a rule, all the vessels held by the forceps (light Halsted's) are tied and a warm, moist gauze sponge is laid on the field.

Unusual Cases.—Occasionally in a hazardous case of exophthalmic goiter the operation is stopped and the wound dressed with flavine or sterile gauze. The next morning, if conditions are favorable, the operation is completed, and if the condition of the patient is favorable at the close of this shorter operation the entire wound is closed. However, if the condition the next morning does not warrant resection of the second lobe, the wound is closed under

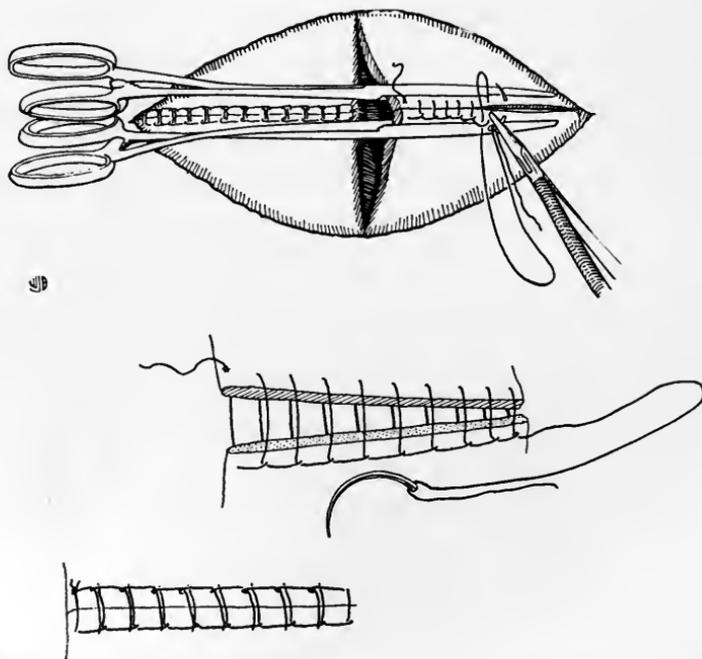


Fig. 88.—Typical thyroidectomy. Suture of preglandular muscles with buttonhole stitch.

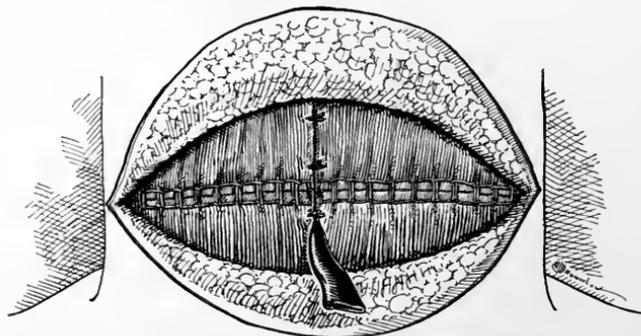


Fig. 89.—Typical thyroidectomy. Vertical closure of preglandular muscles. analgesia and local anesthesia and the patient sent home for a period of controlled rest, the second lobe being removed at a later date. If, after the second lobe is resected on the

morning after the first operation, the patient's condition is in doubt, a flavine dressing is again applied and the wound finally closed in the afternoon of the same day or the following morning, according to indications.

To return to the usual and typical case of bilateral partial thyroidectomy—after the right lobe and isthmus

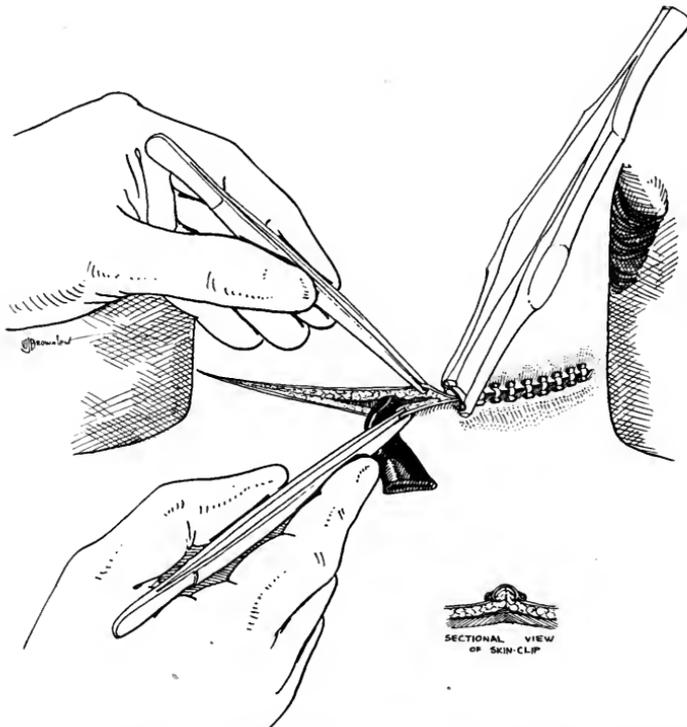


Fig. 90.—Typical thyroidectomy. Closure of skin incision with clips.

are completely separated, and the attachments of the left lobe to the trachea and of the upper pole to the larynx are divided so as to clear the trachea and larynx, the left lobe will be so greatly mobilized that the forceps grasping the vessels may be used to displace the lobe so as to bring the line of proposed division of the lateral thyroid tissue clearly under the guidance of the eye. The lateral lobe is then

divided bloodlessly and without bringing into vision the parathyroid or the recurrent nerve. If at any point the patient is disturbed, additional novocain is at once infiltrated. The entire field is inspected to determine whether or not too much thyroid tissue has been left, and whether or not any vessels have been overlooked. If these points are satisfactory, the anesthetist raises the head of the



Fig. 91.—Typical thyroidectomy. Appearance of incision after closure.

patient, and the divided pregladular muscles are brought in apposition by means of the handles of the compressing forceps. The muscles are united carefully by means of a buttonhole stitch made with a curved needle and catgut (Fig. 88). When both sides are thus closed, the wound is finally inspected for bleeding. Then the vertical incision

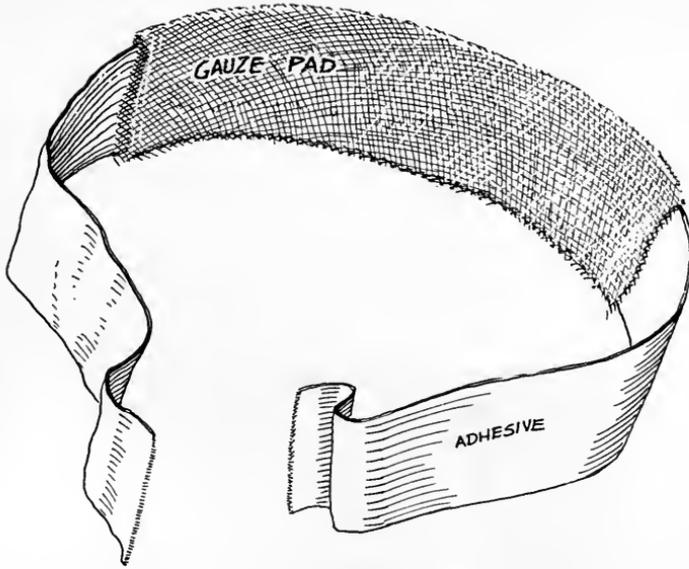


Fig. 92.—Postoperative dressing. Gauze pad used to protect back of neck from adhesive plaster.



Fig. 93.—Postoperative dressing, completely applied.

is united by suture, a small drain is inserted, and the skin is closed with clips (Figs. 89-91). The drain is removed the following day.

SPECIAL COMMENTS

How Much Gland Shall Be Left?—The amount of gland to be left varies according to the type of goiter. A block of hyperplastic gland (exophthalmic), $\frac{1}{2}$ inch square and 1 inch long, would probably have as much functional value as a piece of colloid gland ten times as large, for the reason that the hyperplastic gland consists almost entirely of large columnar cells, while the colloid goiter is made up mainly of colloid material and a single layer of cubical cells. The amount to be left should, in general, be the functional equivalent of a normal gland. This would mean that in hyperthyroidism only a small portion of the gland would be left; but in the case of a large colloid goiter a bulk larger than that of a normal thyroid is required because the colloid goiter is not as active as the normal gland.

In our earlier operations we usually erred by leaving too much of the gland. It was only by trial and error that we finally realized that in cases of hyperthyroidism a very small amount of gland is sufficient. It should be noted, however, that the recurrence of symptoms may be due to the presence of some focus of infection.

What Part of the Gland Not to Leave.—In our earlier series we followed Kocher's advice and removed the larger lobe, leaving intact the smaller lobe, expecting that the readjustment of the trachea, larynx, and the smaller lobe would be satisfactory to the patient. For cosmetic reasons this proved very unsatisfactory to the average American patient and we were sometimes obliged to resect the remaining lobe. Then we resected both lobes, leaving the posterior capsule (C. H. Mayo) and only a portion of the

upper and of the lower poles on each side, believing that thus the parathyroids would be well protected and the gland well distributed. Though this was better than unilateral thyroidectomy, the poles would too often display



Fig. 94.—Enlargement of median lobe after operation.



Fig. 95.—Enlargement of the upper portion of the median lobe after operation.

themselves as lumps. This plan was not entirely satisfactory.

In our first series, unless it was enlarged, the *median lobe was left*. We soon found, however, that occasionally after operation this quiescent lobe increased markedly in size, giving the appearance of an Adam's apple, which in the case of women, in particular, proved unpopular. As a matter of precaution this lobe is now routinely removed (Figs. 94, 95).

Line of Division of the Preglandular Muscles.—We have dealt with the preglandular muscles in many different ways. A long vertical median incision, depending on lateral traction for exposure of the gland, was soon abandoned except for adenomata occupying a median position or for small goiters. For laterally developed lobes and in exophthalmic goiter the single median vertical division of the preglandular muscles is too often unsatisfactory.

We have tried the high division of the muscle, employed by C. H. Mayo. For the majority of cases this gives adequate exposure, but in some goiters it does not always give adequate opportunity for the dissection of the lower pole.

It is for these reasons that, when more than a vertical incision is required, we have adopted the transverse division described above.

Tying the four arteries outside the capsule occasionally results in parathyroid deficiency because of the limitation of their blood-supply. In about 100 cases I made a bloodless, sharp knife separation of the true capsule from the surrounding tissues, whereby the parathyroid and the recurrent nerves were plainly exposed and were, therefore, left anatomically safe. From the anatomic and dissectional point of view this is a perfect technic; but it has one defect which condemns it: occasionally, although the voice was little or not at all disturbed for some days after the operation, a hoarseness appeared later and persisted in spite of every form of treatment. This was presumably due to involvement of the recurrent nerve in the new scar tissue.

Catching of masses of thyroid tissue by large forceps and then ligating them by needle and catgut *en masse* was tried as a means of minimizing the number of ligatures and cutting down the time of operation. From these two standpoints this maneuver proved a great success; but the

pulling together of such a mass of tissue occasionally interfered with the voice. This method was, therefore, abandoned and the more detailed method of catching the individual branches of the main vessels with small forceps was adopted.

Turning Out Gland with Finger.—In our earlier series after the gland was freely exposed the forefinger was slipped behind or below or above it, and the deeply lying gland rolled out into view, thus greatly simplifying the operation. This did well in most cases, but in the case of a *bilateral*, deeply burrowing gland, especially if it is wedged tightly in behind the larynx so that considerable force is necessary to dislodge it, the mere traction and pressure and stretching—that is to say, the mechanical abuse of the recurrent nerves—even though they are not torn, may block the passage of nerve impulses; and hence may cause an immediate bilateral paralysis of the vocal cords, which will interfere with or completely block the intake of air, necessitating an immediate tracheotomy. Or, in the case of a partial paralysis, respiratory distress may occur after the operation, necessitating the reopening of the wound, even a tracheotomy. The actual number of such *contretemps* may be few; but one such case seems the equivalent of many in the impression it makes, more especially if, following the tracheotomy, bronchopneumonia and later death ensue in an otherwise sound and curable patient.

There is another objection to this otherwise highly desirable maneuver—the turning out of a large thyroid from its burrow with the finger, which applies especially to cases in which the lower pole extends into the chest. In such a case everything may be progressing well, the projecting lobe is rolled out carefully, but just as the maneuver is completed a large vein, greatly stretched,

tears, and a full stream of venous blood fills the hole vacated by the ousted lobe. The entire field is at once stained and blood soaked. The particular vessel is not seen. Promiscuous grasping with forceps in this black pool is a gamble. Packing the entire cavity with gauze will quickly arrest the hemorrhage, but meanwhile the mechanical process of gauze packing has torn neighboring, equally thin-walled veins, which are waiting their opportunity to bleed when the gauze is removed. Everyone gets out of this hole in his own way, and his own way is usually different in each case. The best method is *prevention* by a controlled technic, which implies grasping every vessel in advance of its rupture and the primary separation of the upper attachment of the lobe so that the thyroid will rise spontaneously with but slight *pull from above*, not *push from below*.

Catching and Tying Bleeding Vessels on the Surface of the Trachea.—If the dissection is carried directly on the trachea or larynx, and vessels are so divided that they can be caught only by picking up and tying the peritracheal fascia with the vessel, thus including the sensory nerves which enter the wall of the trachea, the brain interprets this as if there were a foreign body in the trachea. There will be irritation, coughing, increased mucus. If there is increased mucus and coughing a local tracheitis will occasionally develop. A local tracheitis, in turn, will occasionally terminate in bronchitis. Bronchitis occasionally develops into bronchopneumonia. Bronchopneumonia may terminate in death. Thus an innocent ligature may cause death.

Contact with the trachea and the larynx may be wholly avoided by a sharp, bloodless dissection above the line of cleavage, and hence at a sufficient distance from the trachea and larynx to tie the vessels, without including the sensory

nerves of the trachea, leaving on the trachea an undisturbed biologic coat. This is a most important point.

Interference with the Mechanism of Swallowing.—In cases in which a growth is thrust backward on each side behind the larynx, and between it and the esophagus and the pharynx, if the enthrusting, encircling portion of the gland is dislodged with the finger, in some instances there will result interference with the innervation of swallowing; and the consequent difficulty in swallowing may persist for several days. As a result fluids and even solids may enter the respiratory tract, causing paroxysms of coughing and even bronchopneumonia. A like interference with swallowing may result when the superior thyroid artery escapes and retreats above, just as the inferior artery may retract below. The interference with swallowing is due to the physical injury of the nerves in the catch-as-catch-can process of grasping the vessel. The dissection may be led into this territory without appreciation of the risk. Caution and prevention is the only sure method.

Respiratory Obstruction During Operation.—With the nitrous oxid-oxygen apparatus oxygen under pressure may be given at once in case of tracheal obstruction. We have seen a collapsed trachea dilated at will with a change in pressure by means of the gas-oxygen apparatus. But if for any reason tracheotomy is needed, a transverse small opening between the rings with a knife should be made *early* rather than *late*. Just as soon as the obstruction is removed, if conditions are favorable, the trachea may be closed with a French curved round needle, and the wound closed as usual.

Maintenance of a Clear Field.—For every reason the field should be kept clear from the start to the finish. No division of tissue should be made through blood, especially

if scissors are being used. We prefer the knife because the division is more definitive and the chance for error much less.

Blood in the Trachea.—If, in an emergency, the trachea be opened the inhalation of blood must be avoided whatever may be the cost in effort and precaution. This is assured by the control of the local field by hemostats, and by the sheer skill of the first and the second assistants. Inhaled blood is very likely to cause death from bronchopneumonia.

After all these statements regarding the possible sources of error it would seem that a thyroidectomy could not be made satisfactorily; that the possibilities of danger are innumerable and beset the operator on all sides. But these difficulties cease to be pitfalls the moment the possibility of their occurrence and the manner of their avoidance have been fixed in the mind of the operator and in the minds of his staff. There has been no tracheotomy in our last 1080 operations. By bearing in mind the precautions indicated above we now rarely see any, even the minor, mishaps.

Delayed Closure.—As stated in the section on Technic, in any serious case the wound is left wide open—completely so, the divided muscles and tissues down to the trachea and larynx and the depths of the wound under the clavicle—and the open wound is dressed with 1:5000 flavine gauze (Fig. 96). The advantages of this procedure are:

1. It shortens the time of operation. It may cut off the fatal last minute.

2. There is practically no postoperative pain or discomfort, thus it lessens by so much the postoperative drive.

3. *And most important:* Leaving the wound open pre-

vents the absorption of wound secretion. Aseptic wound secretion has always been known to cause some post-operative increase in temperature in normal non-sensitized individuals, but in the hypersensitized exophthalmic goiter patients this reaction may be multiplied many times and become a raging destroying fever.

These wounds are closed under analgesia and local anesthesia without removing the patient from bed, as soon



Fig. 96.—Interrupted operation. Wound packed with flavine gauze.

as it seems safe, usually in the afternoon of the same day—sometimes the next morning—occasionally on the second day after operation (Figs. 97, 98).

As for infection, the wounds closed on the same day run a course almost identical with those in which primary closure has been made. There is a slight tendency after the first six hours to increased contamination. Among 485 wounds left open on account of their gravity the mortality was 3.9 per cent.

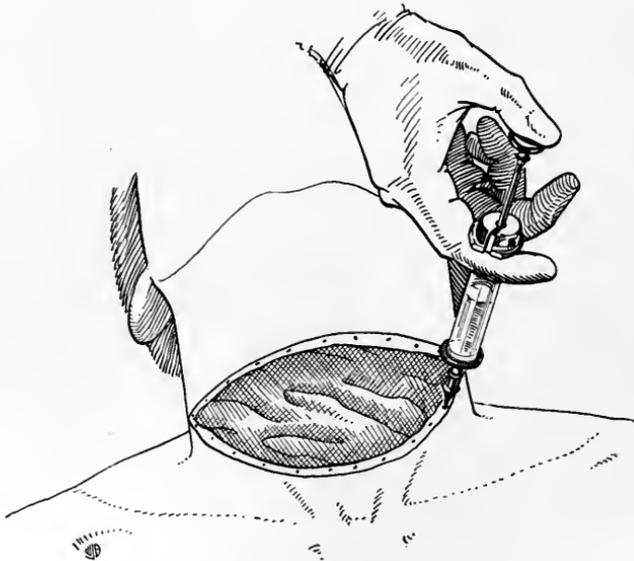


Fig. 97.—Interrupted operation. Deep infiltration of subcutaneous tissues before removal of flavine gauze.

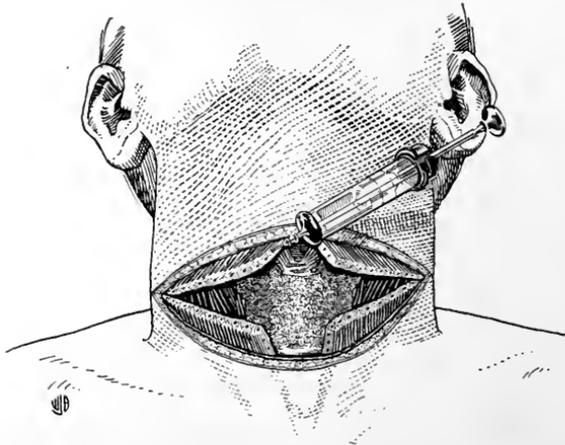


Fig. 98.—Interrupted operation. Infiltration of muscle-flaps with novocain before suture after delayed operation with interim packing with flavine gauze.

When to Stop the Operation.—If there is any doubt of the outcome *at any point*, that is the moment to stop the

operation, tie off the vessels, and dress the open wound with flavine or plain sterile gauze. Whether mistaken or not, the operation can usually be resumed and completed on the following morning.

Deception of the Patient.—Patients are not deceived as to the time of operation. If we have their consent and confidence, we go ahead so carefully that they are not aware of the day and the hour of operation. But, if a patient demands to know the proposed day and hour, he is told. If, in consequence of this information, his condition becomes unsatisfactory, operation is deferred. This is only an occasional experience. After the strain of one delay the patient usually is willing to take a passive rôle.

***x*-Ray Treatment vs. Thyroidectomy.**—*x*-Ray treatment does reduce the activity of the thyroid. It is a simple, painless procedure. Then why not use *x*-ray to the exclusion of other procedures? Because of the following disadvantages:

(a) The dose required to produce a given effect is at best a guess.

(b) Relapses are common.

(c) The delay in unsuccessful cases leads to serious damage to certain organs—the myocardium, liver, nervous system, etc.

(d) In case of operation later the scar tissue and adhesions caused by the *x*-ray are a handicap. The dilemma in the use of the *x*-ray is: Myxedema or relapse. If the dose is sufficient to kill all the thyroid cells, myxedema results; if the dose does not kill the cells, they recover and there is relapse.

Indications for Ligation.—In this clinic ligation is employed only as a preliminary to thyroidectomy. Double ligation rarely cures, but as is the case after *x*-ray treat-

ment, there is a tendency to relapse. And when relapse occurs, we have lost the nicest step in the graded operation.

x-Ray might be used instead of ligation as a part of a graded operation, except for the uncertainty of the extent to which it has destroyed the thyroid tissue.

To What is the Good Effect of Ligation Due?—Certainly not to the diminution of the blood-supply, for no matter how soon or how late after ligation the thyroidectomy is performed, the local blood-supply is found to be diminished but little, if at all. In fact, it often seems as if the blood-supply after ligation is richer because of all the developed collateral branches. I am of the opinion that the greater part of the benefit from ligation is the result of a break in the nerve supply of the thyroid, since the principal sympathetic nerves run in the walls of the superior thyroid arteries.

What is the Indication for Thyroidectomy?—*Diagnosis of hyperthyroidism is the indication for thyroidectomy.* We believe this because if we wait to try out the rest cure, in case rest fails to cure, and this is true in too many instances, the patient has sustained serious additional damage, perhaps permanent damage, to the myocardium, to the liver, to the nervous system; his life has been shortened; the difficulty of the operation has been increased; and much time has been lost.

It is only within recent years that we have been able to put hyperthyroidism in the class with appendicitis as to operability, but now the mortality of thyroidectomy is almost as low as the mortality of appendectomy. In view of the comparatively short stay in the hospital, the slight risk, the inconsequential scar, we are prepared to accept the dictum "*operate on diagnosis.*"

CERTAIN POSTOPERATIVE COMPLICATIONS OF OPERATIONS ON THE THYROID GLAND*

G. W. CRILE AND W. E. LOWER

Attachment of the Scar to the Trachea.—In certain rare instances the scar becomes attached to the trachea at the point of drainage. An objectionable consequence of this scar is its rise and fall during swallowing, coupled, in some instances, with a slight pulling sensation. The complaint of the patient, however, is nearly always directed against the appearance rather than against the pulling sensation. After tracheotomy the scar is sometimes attached closely to the line of healing of the opening in the trachea. In any case such a scar is easily relieved by excision of the scar tissue down to the normal tissue, the separated fascia and muscle being approximated so that a normal superimposed tissue intervenes between the trachea and the skin. The skin is closed with skin-clips. The operation is slight; the discomfort, negligible; the result is invariably good.

Unevenness of the Neck after Thyroidectomy Due to Permanent Absorption or Displacement of Tissue Made by the Long-continued Pressure of the Growth.—After the removal of a large deforming goiter which has left inequalities in the contour of the neck the occasional patient develops an uncontrollable longing for the perfect neck of her girlhood days; rather of the girlhood days of her friends, for her own neck was always full, uneven, deformed. After years of skilful shading, draping, and posing, as skilful as the revealing and concealing adaptations of animals

* Reprinted from *Am. J. Surg.*, 1921, xxxv, 317-318.

in struggle and survival, it is not unnatural that in these patients the sensibilities are so heightened, and the hope for a perfect neck is so intense, that special consideration is demanded. In such a case after every attempt has failed to persuade the patient that she has already made a good bargain with fate, we have reopened the neck, and have reflected back the skin rather widely so as to give an opportunity for sliding fascia or muscle and transplanting fat from elevation to depression. In short, we have modeled a new neck which in its lines and depressions approximates as nearly as possible the neck of youth.

Postoperative Hoarseness.—In the occasional case hoarseness persists. This is usually overcome spontaneously and very rarely remains permanent. In our earlier series hoarseness was much more common, and in every instance its cause could be traced. The most common cause was grasping or making traction on the nerves in the control of bleeding. The vessels in apposition to the recurrent nerves or the parathyroid would occasionally escape and retract, carrying their bleeding ends behind the position of the parathyroid, the blood meanwhile flowing freely, hiding the vessel. The securing of the bleeding end is aptly likened to catching a squid. No squid was ever more beclouded nor more elusive than the bleeding superior or inferior thyroid artery. In the pursuit it is best to expose the spurting end and secure it alone.

Another cause of hoarseness was the rough tearing out of the goiter with the finger from the side and from behind, or the use of the large Kocher barbed forceps which gathered in the tissue in the neighborhood. Still another cause was the complete exposure of the recurrent nerve during the operation, leaving it in contact with the process of healing and cicatrization of the wound.

Aphonia.—Occasionally a patient returns from the operating room serene, but voiceless; or after some days of clear voice, she becomes abruptly aphonic. With these psychic voice failures the surgeon gives himself no concern. In due course the voice returns unheralded and as abruptly as it disappeared.

Singing and Thyroidectomy.—A singer with a gradually enlarging goiter apparently is in a dilemma. If the goiter is left alone there is the ever-present possibility that the strain on the vocal cords will be increased and the voice altered. In any case the stage appearance is affected. On the other hand, there is the fear that the removal of the goiter will change the physical environment of the larynx sufficiently to alter the quality of the voice, and the possibility of temporary huskiness or hoarseness, after even the best planned operation, is increased in the case of a highly developed voice, and, of even more importance, in the case of a highly developed temperament. The surgeon's burden of responsibility is increased by the consciousness that if the artist later loses prestige from any cause, even including the inevitable effect of increasing years, the blame will probably be placed upon the operation. However, by the avoidance of each of the dangerous maneuvers described above we now seldom note any essential alteration in the voice, even immediately after the operation. In fact, it has been our experience that even the singing voice is more often improved than injured; a certain tendency to flatness is replaced by resonance; certainly the flat, speaking voice, so commonly resulting from the pressure of the massive goiters is greatly improved. Taken as a whole, we believe that the average effect on the voice is an improvement.

Intermittent Respiratory Block.—An inspiratory block

occurring principally at night at irregular intervals is an occasional sequel. This is due to adductor paralysis, as a result of which the vocal cords are floated out by the current of expired air, but block the incoming current of air in somewhat the same manner as the aortic valves block the blood from returning to the heart, or as the gates of a lock block the flow of water. The effect of this distressing complication is due in part to the sensation of suffocation and its resultant fear as well as to the actual want of air.

False Alarms.—For some time after thyroidectomy the patient's low thresholds lead to needless worries from mistaking an enlarged lymphatic gland for goiter; from mistaking pharyngitis or laryngitis for some feared "inward" trouble; from interpreting worry and sleeplessness, resulting from normal causes, as an "inward goiter." Any local pain, stiffness, pull, hoarseness, depression, or inequality may cause uneasiness or apprehension. Usually a word of reassurance, given, however, only after a careful re-examination, is sufficient.

Postoperative Infection.—Because of the large, loose, partially occupied space in the neck following the removal of large thyroids; and in particular because of the facility for the pooling of wound secretion under the clavicle and because of the necessity for drainage, infection is occasionally seen. We have found that on the first appearance of infection it is best to open the neck widely and promptly and sterilize the entire field of operation by hot packs and Dakin's fluid, and making an early secondary closure in accordance with the method which was so extensively and successfully practised in the war. The point of prime importance is immediate and wide opening and exposure of the entire wound to treatment.

The Prevention of Postoperative Enlargement of the Remaining Thyroid Tissue After the Removal of Colloid Goiters or of Colloid Adenomata.—After the removal of large, plain goiters, especially in obese women, the portion of the gland which is left often retains sufficient growth-energy to rebuild a goiter of large size within a few years. These patients are disappointed, and their confidence in reoperation is not easily established—nor should it be. Basing our practice on the easy control of endemic goiter by the administration of iodine, we now give iodine for not less than one year after thyroidectomy to all goiter patients except cases of exophthalmic goiter or of toxic adenomata. Thus far the redevelopment of plain goiters seems to have been effectively prevented by this measure.

Thyroid Deficiency.—In perhaps 1 out of 500 cases the thyroidectomy is followed by symptoms of thyroid deficiency. This complication is easily controlled not by iodine, but by the intermittent administration of thyroid extract. In course of time, for some unknown reason, the symptoms of deficiency permanently disappear.

Parathyroid Deficiency.—Parathyroid deficiency is more frequently encountered than thyroid deficiency, and its management is more difficult. This complication has two phases, the first appearing immediately after operation, the second after the patient returns home.

The immediate symptoms of parathyroid deficiency are the characteristic signs of tetany beginning with slight stiffness or merely tingling sensations in the fingers and progressing to intermittent tonic spasms. The causes are several—the removal of the parathyroids at the operation, wound infection, or interference with the blood-supply of the parathyroids, any of which may result in a suspension of function. Our pathologist, therefore, is charged with

the duty of searching every specimen to ascertain whether or not the parathyroid has been removed. The pathologist has found three in the last 269 operations. As a result of the earlier reports we first changed our technic so as to see the parathyroids and thus assure their retention. This technic had several serious defects: first, in exposing the parathyroids there was the danger of blocking their blood-supply in the course of operation itself; second, in the course of healing, either the gland itself or its blood-supply might be strangled by the enveloping scar; if infection occurred the blood-supply of the exposed parathyroids or the parathyroids themselves might be affected. In one case we have reason to believe that infection precipitated an acute tetany. Another danger which threatens the parathyroid in the course of operation is its possible inclusion with a mass of thyroid tissue in heavy barbed forceps or within a suture passed around the gland by a needle. These measures must be regarded as a menace and avoided as a routine.

TREATMENT OF INOPERABLE CANCER OF THE THYROID BY DECOMPRESSION

GEORGE W. CRILE

IN our series of operations on the thyroid 1.8 per cent. have been for cancer. In addition to these cases of frank cancer there is also a group of cases in which neither by clinical nor microscopical criteria can the diagnosis be made with certainty. The end-results of the surgical treatment of the cases in which thyroidectomy was possible will be made at a later time.

The special problem, however, in a consideration of the surgical treatment of cancer of the thyroid gland is not concerned with the cases in which the growth can be removed, but rather with the inoperable cases in which the patient is suffering great distress from obstruction and partial asphyxiation. We believe that this problem has been partially solved satisfactorily by the application of the following operative procedure: Under analgesia and local anesthesia, through a median collar incision, the preglandular muscles are divided for the entire distance across the tumor. On exposure of the preglandular muscles it is at once noted that there is a tenseness which is not usually seen in cases of ordinary goiter. This tenseness is due to the fact that the preglandular muscles are holding in restraint a growing carcinoma, thus reflecting the pressure back upon the trachea. As the muscles are divided the gland itself protrudes freely, thus relieving the back pressure, and in consequence relieving the patient from the distressing symptoms. Nothing more is done excepting to close the skin, leaving the muscles

retracted, for this is merely a decompression operation designed only to give temporary relief.

A very pleasant surprise occurred in one of these cases: The patient, a woman sixty years of age, presented herself with a hard, deeply situated, fixed, infiltrating growth of moderate size extending across the median line. She stated that she had first noted the beginning of this growth one



Fig. 99.—Patient five months after decompression operation for carcinoma of the thyroid.

year before, that for the first six months it had increased in size rather rapidly, but for the last few months there had been little change in the external appearance. During the preceding month, however, her voice had become hoarse and she had suffered occasional spells of choking.

At operation, upon division of the preglanular muscles, it was found that the entire thyroid gland was invaded and

that the adjacent tissues were infiltrated with extensions from the carcinoma. The operation was, therefore, confined to the decompression procedure described above.

During the five months since her operation this patient has been under *x*-ray treatment by Dr. B. H. Nichols. The cancerous goiter cannot be palpated. She has been entirely relieved from her choking spells and from the local discomfort. An acute myxedema has developed, the result of the extensive involvement of the thyroid tissue in the cancer, her basal metabolism being reduced to -14 , and she is therefore receiving thyroid extract to supply this deficiency (Fig. 99).

While it is still too early to make any prediction as to the end-result in this or in similar cases, nevertheless, this patient who is now comfortable and apparently free from cancer, certainly owes the respite and relief to this decompressing operation and the *x*-ray therapy.

THE POSTOPERATIVE TREATMENT OF THE EXOPHTHALMIC GOITER PATIENT

FRANK S. GIBSON

AN intelligent postoperative handling of the exophthalmic goiter patient must be expectant in character and based upon a knowledge of the probable reaction each individual may show to each particular form of stimuli. This knowledge is obtained from the significant facts revealed in the patient's history, the physical examination, and the laboratory tests. Sum these, add certain incidents from past experience, and proceed to treat the patient well in advance of any approaching complication.

Consider a patient who presents herself for operation with the complaint, among others, that for some months, owing to an irreparable emotional and nervous disturbance, she has avoided the entertainment of her most intimate friends and even at times the companionship of her own family. Would it be wise to permit the attendance of the family and friends in the sick room of such a case when the quiet attention of the physician and nurse in charge insures a restful, tractable attitude? This incident, though it seems trivial, serves to exemplify a course of procedure which, when exercised in every detail, renders the cure of even the most acute exophthalmic goiter patient simply an interesting psychic and physical problem with the happy assurance of a good result.

Intelligent and anticipatory treatment has, therefore, become our slogan, and we use the word "intelligent" because the initiation of all precautionary measures in

whose efficacy one might have confidence would add a needless burden to the patient. On the other hand, having previously determined the points of least resistance in each individual by simple, commonplace methods, the reserve may be strengthened at these points before even the first lines of the defense have been broken.

A DISCUSSION OF SOME METHODS OF PROCEDURE WHICH ARE SIMPLE, APPLICABLE TO ALL POSTOPERATIVE CASES, AND THEREFORE ARE ROUTINELY EMPLOYED

During anesthesia and immediately following an operation all patients perspire quite freely, rendering the operative clothing wet and cold. These garments are removed and warm dry flannels substituted before the patient is taken from the operating room, and the bed to which the patient is to be returned is warmed with hot-water bottles.

This dehydration of the tissues occurring coincident with the operative procedure, coupled with a temporary abstinence from the administration of water by mouth, plays a considerable part in the incidence of the hyperpyrexia so frequently seen after operations for exophthalmic goiter. This situation is met by the subcutaneous administration, under the pectoral muscles, of normal saline in quantities ranging from 1000 to 2000 c.c. The beneficial results which have been seen to follow the flooding of the body tissues with water in this manner has brought the procedure into routine use as a postoperative measure.

It is extremely important that these patients be kept composed and comfortable, as a nervous, suffering patient soon becomes restless and irritable, a condition which predisposes to and abets the exaggerated postoperative reaction. The patients are placed in bed in the sitting

posture, with the head and knees slightly flexed. Pillows are banked around the body so as to permit complete relaxation without danger of moving, as these patients fear the slightest movement which may cause pain.

The hypodermic injection of a sedative suitable to the patient's needs and condition is administered immediately upon return from the operating room, and repeated as often as necessary to secure comfort. Morphin sulphate in $\frac{1}{6}$ -grain doses is the drug and amount commonly used, and is found to be well tolerated when given in conjunction with hypodermoclysis, even in cases that have an idiosyncrasy against the drug when given alone—that is, without watering the tissue.

Ice-bags to the number of six are placed about the body external to the sheet or blanket which covers the patient, one over the heart, the remainder over the loins and extremities. A cold wet cloth is placed over the face and forehead. These we consider to be of distinct aid in stabilizing the body temperature.

Water is urged as soon as the patient is able to take it, soups and soft foods on the day of operation and the following day, after which any form of food listed on the regular hospital menu exclusive of highly seasoned foods, meat and coffee, may be given; the latter restriction in diet being advised for a period of from three months to one year, or even longer, depending on the severity of the case.

The postoperative period of absolute confinement in bed varies from two days, in the case of a small adenoma, to eight days, in the case of severe exophthalmic goiter, after which the patients are allowed to be up for two hours each morning and afternoon. They are discharged from the hospital after from six to twelve days, with instructions to

avoid all social activity for the succeeding six months, and during that time to go to bed early at night, to rise late, and also to rest each afternoon from two to five o'clock. It is made clear to the patient that he himself has an important rôle to play in the convalescence and that the result obtained is in a large part dependent upon his hearty co-operation. The above rules of government for the convalescent period are not applicable to the patients with adenomatous type of goiter, for whom only such general measures as will tend to improve the general welfare are initiated or advised.

Medication.—The postoperative administration of drugs is not routine in character, but depends entirely upon the patient's condition. Following the convalescent period no medicine whatsoever is advised in cases of exophthalmic goiter. Patients with diffuse colloid or colloid adenomatous goiters are given a prescription for the syrup of ferrous iodid, to be taken in 15-minim doses in a glass of water once daily during alternate months for a period of one year. This medication will aid in the re-establishment of the normal physiologic function of the gland and will prevent an early compensatory hypertrophy.

Care of the Wound.—Considerable drainage of serum from the wound usually occurs during the first twelve hours after operation, and it promotes the comfort of the patient to change the dressing at the end of this time and each twenty-four hours thereafter until the wound is completely healed. The small soft-rubber drain is removed after twenty-four hours. The clips which are used to approximate the skin are removed on the third postoperative day, thus avoiding any scar save the thin white line which marks the site of the incision.

METHODS FOR THE TREATMENT OF CERTAIN POSTOPERATIVE COMPLICATIONS

The acute postoperative reaction which formerly was so frequently encountered in the exophthalmic goiter patient is now seldom seen, as this unfortunate operative sequel has been almost eliminated by the preventive measures employed during and immediately after the operation; by the avoidance of suboxidation anesthesia, that is, surgical anesthesia, and the substitution of nitrous oxid *analgesia*; by the minimizing of nervous exhaustion and shock by operating on the severe cases in their rooms; by the avoidance of long operation; by the prevention of absorption of wound secretion, and by the multiple stage operation.

The signs which these cases present when handled in any other manner more disturbing to the general nervous mechanism are collectively spoken of as the "postoperative reaction," which is evidenced by hyperpyrexia, tachycardia, extreme restlessness, nausea, vomiting, and diarrhea. In some cases there may also be an acute urinary suppression. While it is true that such a condition is now seldom seen, nevertheless all cases of the more severe type are treated as though potentially capable of developing this condition. Following the operation six ice-bags are placed about the body of the patient external to the covering sheet. This number is doubled with each degree in rise of temperature up to 102° F. Should this procedure fail to control the temperature and it reaches 103° F., an ice-pack is employed in which the patient remains until the temperature has regressed to 99° F. (Fig. 100).

The technic of the ice-pack is simple. The mattress is first covered with rubber; the patient is rolled in a linen sheet and covered with a large rubber blanket. From 150 to 200 pounds of crushed ice are heaped upon the rubber

blanket and snugly packed about the patient. An ice-cap is applied to the head. An electric fan placed at the foot of the bed with the breeze directed toward the head will hasten the cooling process.

The rubber blankets will keep the patient dry without interfering with the cooling process, a fact which must be remembered, for, if the patient becomes wet, chilling will

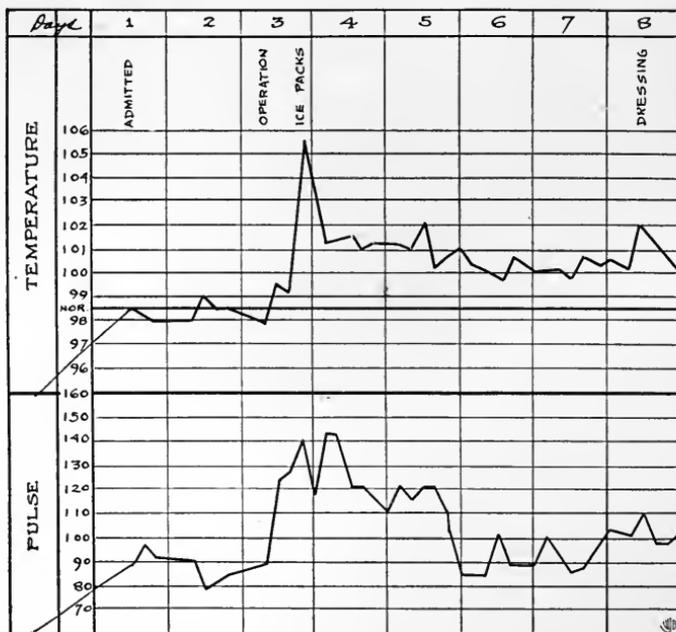


Fig. 100.—Chart illustrating control of postoperative hyperthyroidism by ice-packs.

follow and cause great discomfort, while if the patient be kept dry the temperature may be reduced to any desired point without complaint. The temperature falls at about the rate of 2° F. per hour, and should be checked carefully at least every twenty minutes. Certain emaciated cases tend to respond very much more rapidly than those possessing a more generous covering of lipoid tissue, and in such

cases the temperature reduction may continue after the patient has been removed from the pack until such a degree of subnormality is reached as to render the situation alarming. Aside from this one feature the procedure is wholly without danger.

The tachycardia which is seen in these cases is certainly of nervous origin, and is rarely associated with any

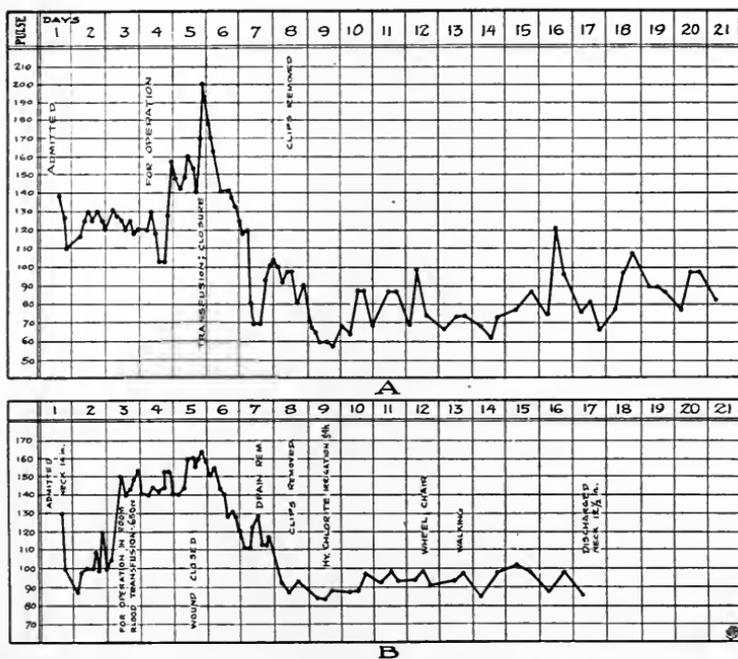


Fig. 101.—Charts showing control of postoperative tachycardia by digitalin.

sign of a failing myocardium. Even immediately preceding a fatal outcome it is rarely possible to demonstrate any sign of an acute cardiac dilatation, nevertheless a hypodermic injection of digitalin, grain $\frac{1}{25}$, is administered each hour in the hope that it may strengthen the myocardium (Fig. 101). Morphine in $\frac{1}{6}$ -grain doses, administered hypodermically, sufficiently often to overcome the nervous,

restless apprehensiveness of the patient, is certainly of very much greater benefit.

Vomiting and diarrhea are but another expression of the instability of the nervous mechanism. They are best combated by giving the gastro-intestinal tract a complete rest, withholding all fluids and nourishment by mouth until the condition is ameliorated, and relying upon hypodermoclysis to the amount of 3000 to 4000 c.c. of normal saline daily for the fluid intake.

Acute cardiac decompensation and auricular fibrillation are a not uncommon complication in advanced cases of exophthalmic goiter and in adenomatous patients with chronic myocarditis. As stated in the section on pre-operative treatment such cases receive one or more courses of digitalis before operation, that is, tincture of digitalis in doses of 20 minims or less, administered every four hours for eight to twelve doses, after which a rest period of from twenty-four to forty-eight hours is allowed, when the course is repeated. In certain cases this is supplemented by the administration of digitalin or strophanthin, the former hypodermically in $\frac{1}{25}$ -grain doses each hour, the latter intravenously, $\frac{1}{2}$ mg. in 5 c.c. of saline, given in two equal doses separated by a fifteen-minute interval.

The only other adjuvant of importance in the treatment of this condition is complete rest, in the attainment of which the value of morphin must not be forgotten.

Tracheitis, bronchitis, and pneumonia are occasional postoperative incidents. For pneumonia the usual supportive measures are employed: *spiritus frumenti*, tincture of digitalis, large quantities of water by mouth and hypodermically if necessary for the maintenance of a high urinary output. The inhalation of steam mixed with fumes from the compound tincture of benzoin is a great aid in overcoming the collection of mucus in the bronchial tree.

Postoperative hemorrhage is controlled by opening the wound, tying off the bleeding point, and closing at once; or if the condition seems to be due to a general oozing, evacuating the clot, packing the wound open, and making a secondary closure after twenty-four hours. The latter condition has been seen but rarely since the initiation of the two-stage operation. The loss of blood in either case may be considerable within a very short time, and therefore immediate attention is demanded, for these patients cannot easily withstand even a moderate loss of blood. For this reason in our clinic it has become a routine procedure to transfuse whole blood to any patient in whom a secondary hemorrhage occurs. A further danger is the possibility that the trachea may collapse as a result of the increased pressure in the surrounding tissues. If this occurs, a tracheotomy must be performed, a procedure which in itself carries a high mortality rate.

Infection of the wound is treated by opening the wound widely upon the first indication and packing with plain sterile gauze. After twenty-four hours hourly irrigations with Dakin solution are instituted, with hot sterile dressings applied directly to the surface during the interim. When the infection is entirely cleared away a secondary closure is made.

A spurious form of tetany which appears after from two to twenty-four hours is not altogether uncommon. The symptoms are a slight tingling of the finger-tips; an itching of the nose. One may notice a slight pallor about the mouth and the fingers are flexed. There is also moderate spasticity of the muscles of the forearms and lower extremities. This condition is due to a transient cessation of the normal physiologic function of the parathyroid bodies produced either by trauma of their nerve supply or by the edema which results from operative procedures in their

immediate vicinity. This condition will clear up spontaneously within from six to forty-eight hours, but we usually supplement nature's endeavor at reconstruction by the administration of parathyroid extract in $\frac{1}{10}$ -grain doses, three times daily, together with 30 grains of calcium lactate every four hours, continuing this treatment for two days. We have seen this condition present at the end of an operation. The condition disappeared spontaneously after one hour and did not reappear during the convalescence.

The following instructions are given routinely to all exophthalmic patients on leaving the hospital:

"The following instructions should be very carefully followed by the patient in order to receive the maximum benefit from the operation:

"1. The diet should be a simple one, and tea, coffee, red meats, and highly seasoned or stimulating foods should not be taken. Milk, eggs, cereals, vegetables, and water may be taken in large quantities.

"2. No social functions.

"3. Reduce household cares to the minimum.

"4. Spend as much time as possible in the open air.

"5. Avoid excitement.

"6. Walking in moderation; avoid exertion.

"7. Rest should be taken as follows: First month: Arise at 10.30, breakfast in bed; rest again from 2 to 5, retire at 9. Second month: Arise at 10; in bed 2 to 4. Third and fourth months: Arise at 9.30; rest from 2 to 4.

"8. Continue this until your attending physician has found that you have received your full benefit from the treatment.

"9. Report to me your condition at the end of the first and the third month. Afterward every six months for three years."

THE PROTECTION OF THE PATIENT IN SURGERY OF THE THYROID

GEORGE W. CRILE

THE problem of the goiter patient becomes, in effect, the problem of the patient with exophthalmic goiter, since any plan of management which can safely be applied to an extreme case of exophthalmic goiter can readily be modified to meet the requirements of the individual case with a goiter of any type, or with exophthalmic goiter of any degree of severity.

As has been indicated throughout the sections of this volume, the key to the successful treatment of exophthalmic goiter is *protection*. To the extent that the protection of the patient is achieved to that extent is his recovery assured.

Against what is the exophthalmic goiter patient to be protected? He should be protected against the fatally excessive metabolism which the operation tends to induce, against failure of the already weakened myocardium, and against acidosis.

These factors may be regarded as end-effects of impairment or failure of the internal respiration of the organism. The total activity of the cell—of the liver, of the brain, of the myocardium—may be regarded as its internal respiration. What does the cell require to assure the maintenance of its normal, orderly, internal respiration? The cell requires a normal supply of oxygen; a normal supply of fresh water; a normal supply of food—mostly in the form of glucose.

What is the probable state of the cells of the myocardium,

of the brain, and of the liver in cases of advanced exophthalmic goiter? The permeability of the membranes of the cells is probably greatly increased, as is indicated by the effect of iodism on their electric conductivity. That is to say, the cells of the organs are excessively sensitive, and therefore the patient must be protected against the psychic stimuli of fear and worry before, during, and after the operation. This is accomplished by establishing confidence, by preventing knowledge of the time of the operation, by the exclusion of anesthetics that produce a stage of excitation.

The abnormal sensitization of the cells in exophthalmic goiter cases necessitates the protection of local anesthesia, even if surgical anesthesia is employed also.

These sensitized patients require protection against any infection stimuli; and, in extreme cases, they must be guarded against even the absorption of aseptic wound secretion or of hemoglobin.

In brief, these patients must be guarded against psychic, traumatic, biochemic, and anesthetic stimuli; against suboxidation, and, in addition, against the effects of the secretion of the thyroid itself. Whether the operation is to be performed with the patient in bed or in the operating room, on the day of operation he should see no surgeon, should see no preparation, should see no operating room, but should see only the already familiar anesthetist, the already familiar anesthetic apparatus; should experience only the already familiar odor of the gas and oxygen, and the already familiar sensation of this type of anesthesia. The end to be achieved is the maintenance of an unbroken state of negativity while the exquisitely sensitized organism is carried through the processes of the ligation of an artery, and of the removal of a part of one or both lobes of the thyroid.

In the absence of other damaging influences, to be discussed presently, the internal respiration, and hence the function of the myocardium, of the cells of the nervous system, and of the cells of the liver is not disturbed by the operation; the appearance of the clinical chart is not disturbed; the patient is safe.

Protection against excitation and against excessive activity is not the only protection required by the exophthalmic goiter patient. Protection against suboxidation is required also. The internal respiration, hence the life of the patient, is immediately dependent upon a continuous supply of oxygen; hence asphyxia, or deep inhalation anesthesia, quickly suppresses the internal respiration, and causes death, either immediately or within a few hours or a day or more. The clinical course in such a case is similar to that produced by fear, worry, physical injury, exertion, or infection. Since all inhalation anesthetics cause suboxidation in extreme cases, deep surgical anesthesia, especially ether anesthesia, is ruled out. Gas and oxygen analgesia, combined with local anesthesia, is entirely free from this serious objection. Ether anesthesia almost wholly suspends the internal respiration and is especially damaging.

As regards the adaptation of the degree of anesthesia to the individual patient, the judgment of a highly experienced anesthetist is priceless. In this respect the judgment of Miss Hodgins, chief anesthetist of Lakeside Hospital, is almost unailing.

A weak myocardium or a decompensated heart leads to serious suboxidation because of the diminished minute volume of blood supplied to the vital organs. Against this condition the patient is best protected by one or two courses of digitalis as described in the preceding section.

A much neglected requirement for the maintenance of the normal internal respiration is water. Advanced cases of exophthalmic goiter commonly have cycles of



Fig. 102.—Patient before and after removal of large bilateral goiter.



Fig. 103.—Patient before and after removal of large pendulous goiter. (Case of Dr. F. E. Bunts.)

vomiting. These may be controlled by sufficient water, for water seems to bear some relation to the cause of vomiting, which rarely occurs if a good water equilibrium is main-

tained. It is probable that the clinician fails to appreciate the great loss of water through the skin, and that because of the raging metabolism the exophthalmic goiter case requires much more water than a normal individual; just as an engine running under full pressure at 60 miles an hour requires more water than an engine running only 25 miles



Fig. 104.—Patient before and after removal of large vascular goiter.

an hour. The goiter case, like the express engine, must be protected against burning out his "boiler" by urging water by the mouth; or, if enough cannot be introduced by this normal route, then, under the protection of local anesthesia, from 3000 to 4000 c.c. may be given subcutaneously every twenty-four hours until the crisis is past.

There is evidence, although it is not conclusive, that the patient should be protected against the too sudden withdrawal of thyroid activity. This danger may be eliminated by the administration of thyroid extract before



Fig. 105.—Patient before and thirty days after removal of adenoma.



Fig. 106.—Patient before and after thyroidectomy for exophthalmic goiter: *A*, Before operation. *B*, Two weeks after operation. *C*, A year after operation.

the operation. By giving two grains the evening before and two grains on the morning of the operation the dose will become effective at the time the thyroidectomy is performed. If, later, the patient seems apathetic, it is well to continue the administration of the thyroid extract for

some days. The necessity for providing a more or less gradual decline rather than a sudden decrease in the amount of the thyroid hormone is supported also by the fact that the safest operation is a graded operation: first, a ligation of one superior thyroid artery; then, of a second; and finally, after an interval, the length of which is determined by the needs of the individual patient, a unilateral or a bilateral partial thyroidectomy. In a serious situation, even if we could "wish out" the thyroid, the sudden break might be fatal.

In great hazards in which, after the preliminary ligations, a period of physiologic rest has brought insufficient improvement, the thyroidectomy is performed with the patient in bed under analgesia and local anesthesia in order that the already impaired internal respiration may be protected to the utmost from too prolonged general anesthesia or from the slight disturbance which attends transit to the operating room, even when the transit is made with the patient under anesthesia. Quinin and urea hydrochlorid is used to protect the patient against postoperative pain.

If the hazard is great and the pulse runs up during the operation the wound is left open to protect the patient from the absorption of wound secretions and from postoperative pain, and also to shorten a hazardous operation by a few but possibly decisive minutes. The open wound is protected by flavine gauze dressings, or by sterile dressings which protect the wound almost as well, until its closure under analgesia on the afternoon of the same day or on the following morning. This affords a graded surgical contact.

Finally, and of the greatest importance, the patient must be protected against the so-called postoperative

hyperthyroidism. Therefore, if after operation there is inaugurated a progressively increasing temperature, with a greatly increased respiratory and pulse-rate, then, in accordance with the principle that heat increases chemical activity and electric conductivity, and that increased chemical activity and increased conductivity in turn are expressed in increased temperature, such patients are literally packed in ice. This procedure has been found to exercise a remarkable control over the destroying metabolism.

This postoperative phase of exophthalmic goiter is closely analogous to heat-stroke in symptoms and in control. It is suggestive to note that both heat-stroke and the so-called postoperative hyperthyroidism are the antithesis of shock, in which by contrast the heat center is paralyzed. In the treatment of shock, heat is as useful as cold in the treatment of hyperthyroidism or of heat-stroke. In each case the most efficient treatment is based upon simple physical laws.

In brief, the goiter patient should be protected against suboxidation; against inhalation anesthesia; against absorption of wound secretions; against infection; against fear and worry; against postoperative hyperthyroidism; against postoperative hypothyroidism.

When protection against these dangers is assured the operability of the goiter patient, even of the "bad risk" patient with hyperthyroidism, becomes 100 per cent.; and the mortality is reduced to that attending the removal of benign pelvic tumors.

The formulation of the plan of treatment described in this volume has been based upon experimental researches and upon the clinical study of 3535 thyroidectomies, among which 1958 were clinically diagnosed as cases of exophthalmic goiter.

In a study of the clinical histories of 1200 consecutive cases the following statistics were made:

185 were males, 1015 females. The ages of the patients in this group were distributed as follows:

- 75 under twenty years of age.
- 205 between the ages of twenty and thirty.
- 345 between the ages of thirty and forty.
- 279 between the ages of forty and fifty.
- 256 between the ages of fifty and sixty.
- 40 above sixty years of age.

Among the possible etiologic factors mentioned in the records a preceding infection—in most cases either tonsillitis or influenza—is noted in 278 cases; “extreme worry” in 319; fright and resultant nervousness in 154. Among the “psychic” factors are mentioned “sudden shock and extreme fright from automobile accident”; “sad news”; “severe grief”; “extreme financial worry.”

In this series the types of gland, following Dr. Graham’s classification, were as follows:

| | |
|---|-----|
| Normal | 14 |
| Hypertrophy and hyperplasia..... | 384 |
| Colloid goiter..... | 87 |
| Exhaustion, atrophy, fibrosis..... | 2 |
| Adenoma, benign (unclassified)..... | 182 |
| (1) Diffuse colloid adenomatous goiter..... | 175 |
| (2) Fetal { Pure fetal..... | 150 |
| Intermediate..... | 72 |
| Colloid | 87 |
| Adenoma, malignant | 11 |
| Carcinoma | 10 |
| Inflammation..... | 25 |
| Miliary tuberculosis of thyroid..... | 1 |

The involvement of the thyroid was bilateral in 973 cases; the right lobe alone was involved in 134; the left lobe alone in 83; the middle lobe alone in 10.

Among these 1200 histories some vocal complication is

mentioned in 51 cases; hoarseness is noted in 94 of the histories, and cough in 87.

Since the adoption of the methods described in this volume we have performed 1783 thyroidectomies, including 1022 thyroidectomies for exophthalmic goiter, with 25 deaths, a mortality rate of 1.4 per cent.; and 783 ligations with 6 deaths, a mortality rate of 0.76 per cent.

Included in this series are the following groups: One series of 194 and another of 331 consecutive thyroidectomies without a death; one series of 153 and another of 396 consecutive ligations without a death.

Since the adoption of this plan of treatment no case has been rejected as inoperable, although some have been practically *in extremis*, with edema of the extremities and with ascites.

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