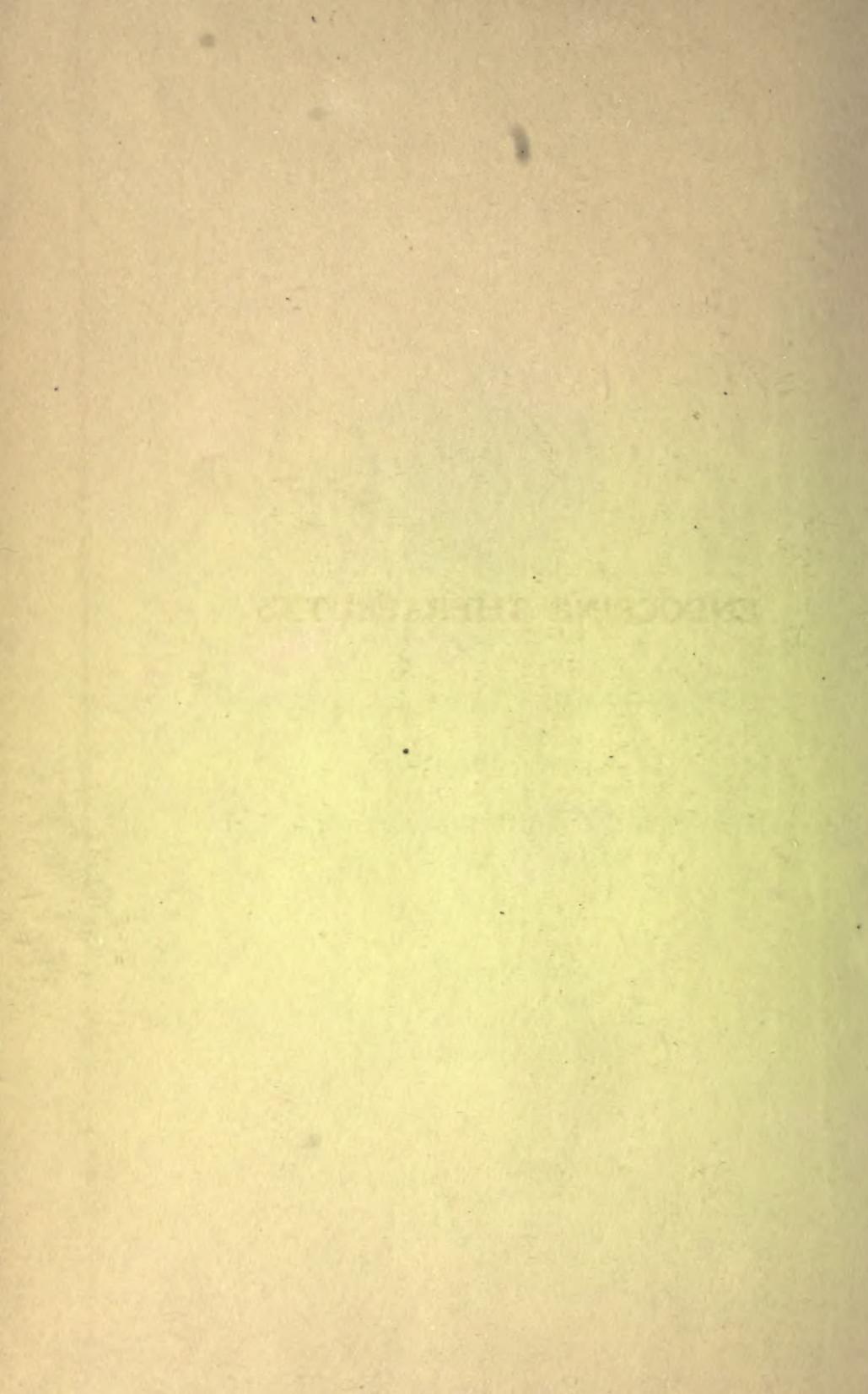


ENDOCRINE THERAPEUTICS

THOMAS BODLEY SCOTT



3 1761 06704460 2



REVIEW COPY
WITH COMPLIMENTS

ENDOCRINE THERAPEUTICS

BY THE SAME AUTHOR

**MODERN MEDICINE AND SOME
MODERN REMEDIES**

Practical Notes for the General Practitioner

Second Edition. Crown 8vo. 6s. 6d. net

MBI
S

ENDOCRINE THERAPEUTICS

PRACTICAL SUGGESTIONS

BY

THOMAS BODLEY SCOTT

AUTHOR OF "MODERN MEDICINE AND SOME MODERN REMEDIES"

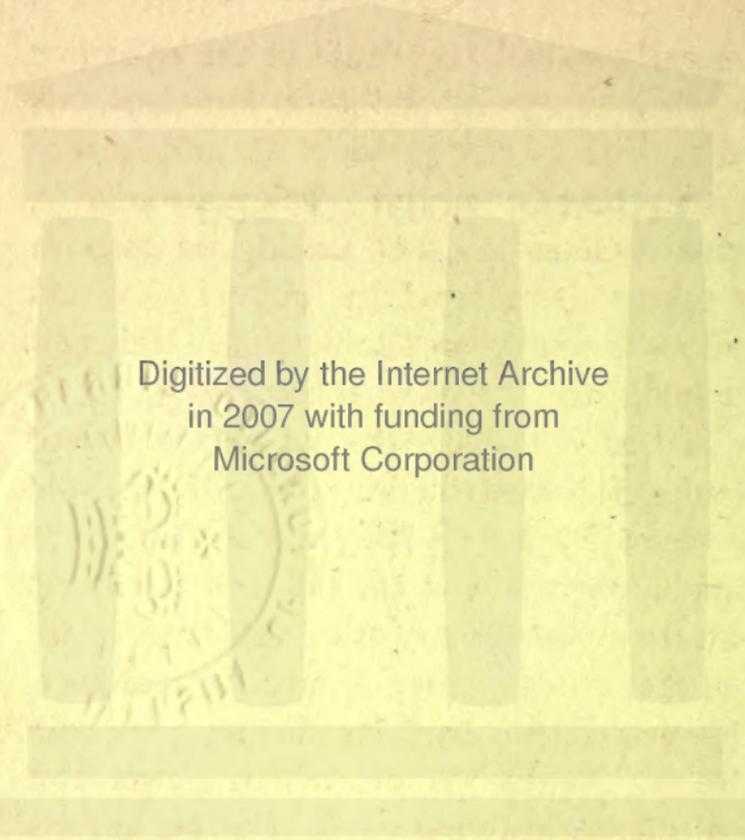


460960
21.4.47

LONDON

H. K. LEWIS & CO. LTD.

1922



Digitized by the Internet Archive
in 2007 with funding from
Microsoft Corporation

PREFACE

OUR recently gained knowledge of the endocrine glands, their secretions and their functions, has opened up entirely new vistas of life and its controlling directing mechanism. This knowledge is, of course, rudimentary, but already we perceive a new science of therapeutics, physiological and rational in its conceptions and actions : this new science fulfils also the original meaning of therapeutic in that it includes the prevention as well as the cure of disease, the way of health, the way of life versus death. Of late years we have been worshipping the power of the will, and have been concentrating perhaps too much on the development of that power ; often, it must be confessed, with happy results. In doing this we have been tempted to neglect the marvellous power and scope of the vegetative system. Our will directs our movements, and to a large extent our thoughts and actions, but the great laboratory work of life, silent and almost unseen, is carried on outside will and even outside consciousness.

A rough but instructive parallel may be drawn

between our bodies and a motor-car : the early cars had all to be started by a laborious winding-up process, equivalent to will power ; the later, by what is known as the self-starting process, electricity in place of muscle. All the unseen intricate work of our bodies, the chemical changes we call metabolism, growth, renewal, and excretion of waste, has to be done by self-starters, almost outside consciousness or control. The parallel may be extended, for each endocrine gland is an individual motor, and discharges its own particular variety of petrol into the big motor, the body : on the proper mixture of these, and on their healthy formation, life and health depend ; again, the brakes and accelerators of our bodies are largely vegetative, for they depend on endocrine co-ordination, without which the engines would soon race and wear themselves out or go so slow that life would cease. We can without doubt trace the greater part of the unconscious vegetative business of life back to the influence of these glands, but still the mystery of life, the initial force, the power behind the throne remains unsolved ; to get a glimpse of this we must try to visualize the great unseen force that governs the Universe, that controls the movements of the amœba, that directs the courses of the sun, the

moon, and the stars, and that is to most minds convincing evidence of Divine purpose and omnipotence. Dimly perceiving these facts we stand lost in wonder and admiration of the delicate, intricate, almost perfect machinery of our bodies which has been gradually evolved; then we turn our minds to contemplate the Machinist, and words fail. The materialist here may think that he has sounded the depths and touched bottom, but the spiritual mind will see only more cause for adoration, and further will realize that the Divine scheme of evolution is far from its goal as yet. We, as doctors, must be devoutly thankful for the new knowledge that will enable us to cope more effectually with the misery of disease.

Dr. Louis Berman, of Columbia University, eloquently says: "Our knowledge of the glands of internal secretions as an interlocking directorate presiding over all the functions of the organism is still exceedingly meagre. As yet we seem to be knocking at the portals of the chemistry of the imponderable. There are holes in the bronze doors, and we glimpse the unfathomable distances of unexplored regions. But we do see something, and we do glimpse a beginning. Already the outlines of a differential anatomy, a differential

physiology, and a differential psychology, which will explain to us the unique in the constitution, the temperament, and character of an individual, emerge.”

May this little book throw a little more light and a little more hopefulness on modern therapeutical enterprise.

CONTENTS

CHAPTER I

	PAGE
INTRODUCTORY	I

CHAPTER II

THE ADRENALS	20
------------------------	----

CHAPTER III

THE THYROID GLAND	45
-----------------------------	----

CHAPTER IV

THYROID INSUFFICIENCY IN LATER LIFE	56
GRAVES' DISEASE	78
THE THYMUS GLAND	89
ORCHITIC	94
THE PINEAL GLAND	95
PITUITARY	95
ANTERIOR PITUITARY GLAND	101

CHAPTER V

CONCLUSION	113
INDEX	117



ENDOCRINE THERAPEUTICS

CHAPTER I

INTRODUCTORY

FIFTY years ago, the science of Therapeutics, if it deserved such an honourable title, was little more than chaos.

Tradition, with its big sounding words, was in authority, and almost the only advances were by the way of empiricism. We were taught confidently that such and such a medicine was alterative, but what it altered or whether for better or for worse was left largely to our imagination ; there was no precision, and yet the science of healing is our very *raison d'être*. Physiology, biological chemistry, pathology, bacteriology, are all most excellent and necessary, but they are only the servants that wait on the relief and healing of suffering humanity. About that time Gull and the Guy's school initiated a short reign of scepticism and agnosticism, which did much good by clearing away rubbish and by concentrating

attention on the pathological and physiological side of disease ; but in itself it promoted no new departure.

Then at St. Bartholomew's arose a new light : Sir Lauder Brunton, young in enthusiasm but mature in knowledge, systematized our old traditional ideas and brought them into relation with physiology and organic chemistry. This was largely due to his work and experience in the laboratories of Holland and Germany, but by his own original work in Edinburgh on digitalis and on the influence of the nitrites on blood-pressure and on the circulation, he started a new conception of cardiac therapeutics. This was supplemented to an extraordinary degree by Schäfer and Oliver in their investigations of the action of suprarenal extract on the heart and the arteries.

Thus arose the new science of endocrinology, which is beginning to revolutionize medicine. This is not a renaissance, but an entirely new birth which opens up unthought of vistas, some perhaps mirages, but others of hope that will end in certainties of incalculable value to the well-being of man.

In therapeutics we must above all things keep the open mind. Our knowledge of disease and

what we call health is so small that humility is the only true mental attitude ; but it must be humility stimulated by hope and encouraged by success. The orthodox horizon, which may seem to some of us a fixed line, will always be for the enthusiast and the worker shifting forward. The word normal may become an obsession that means stagnation, and that is a hindrance and almost an insult to the conception of evolution ; the normal of to-day should be only a milestone by which those that come after may measure their progress or the other thing. In the study of therapeutics we must think of it as the preventing of disease, as the maintenance of health, and still farther as the attainment of a higher standard of life, physical and moral, than we have hitherto known. The word in Greek originally contains, not the idea of healing, so much as service in all things relating to man and his health.

The intimate knowledge of bacteriology and of organic chemistry in its new and rapid growth has opened out new fields of biological interest, which will enable our ideas of service and of the cure and prevention of disease to be largely extended.

Our human laws are often mere changing compromises, serving their purpose for a time, but the Divine law that we observe in nature is one

only, never swerving, unchangeable, just and true. We are only now getting glimpses of its higher potentialities and of its Divine simplicity. There seems to be one power alone that governs and moves the whole universe, matter and mind alike.

In practical therapeutics it must be our aim to get knowledge of this power and to utilize it, as Christ did in the service of mankind. We must, I think, look on His miracles as evidences of His knowledge and use of natural powers that are as yet unknown to us. As yet, our low spiritual development and our selfishness, national and individual, would render such powers dangerous weapons. "Such knowledge is too wonderful for me ; I cannot attain unto it," says David, but higher spiritual and altruistic ideals will fit us for the glorious possession.

Hitherto we have been looking on the science of therapeutics far too much from the material point of view. We have been very little above the veterinary surgeon, who perforce has to observe and treat almost entirely the objective symptoms of animal diseases. The more honour to him for his frequent successes. There is more of psychological interest in a horse or a dog than in a cow, but not enough for a foundation of treat-

ment. In men, and especially in women, we get often a long history of subjective ailments and symptoms that may help us to form a diagnosis, or that may make it very difficult to get at the kernel of truth. In both cases a great deal of the sifting process is necessary. But when we have done this, we still treat objectively, we attack by medicines, by vaccines, by various forms of electrical or hydropathic treatment, often with a moderate amount of success and often with none.

Where we fall short or fail completely, is in our persistent objectivity. The poor owner of the diseased body is almost left out of the problem, and yet in him lies the very fountain of successful healing, a source however that is often sealed, stagnant and sometimes, alas! that is in opposition, counter-suggesting and frustrating the good we would gladly do.

The initial fault that has produced the disease may be subjective and due to ignorance, or to lapses from physiological law; these, if not corrected by knowledge and by will power, will go on recurring. The initial fault, again, may be outside, as from infection, or from some other microbic attack, and in such the attack must be largely from outside, but the proprietor of the disease we mostly treat as a nobody. Is

that fair or politic? Surely he can help greatly or greatly hinder; the passive neutrals are rare.

We see every day the depressing influence, of a body sick or in pain, on a previously healthy mind. This is largely due to the circulation of impure blood in the brain, our thinking machine and our nervous motor; but the brain is not the ego, the Divine indissoluble part of each of us; it is only a wonderful part of our machinery. Back of body and mind lies this spirit power, in a fathomless reservoir, waiting to be used, eager for work, but in most of us so enclosed in a hard shell of materialistic blindness and doubt that it is a locked up force.

We should always have before our minds the great fundamental difference between the animal and the man. The animal has to a limited extent reason and memory. It has conservative instincts which protect from danger and which preserve its young, but beyond these it has no creative power and no appreciation or realization of its own ego. In association with man it develops and inherits astonishing powers of usefulness and reason, but separated from man it lapses in a few generations into its old, wild state. This consciousness of his own individuality and of his almost unlimited creative power should

convince man of his Divine origin and of his potential inheritance, but alas ! the world and the flesh obscure his eyes, and he wanders on, aimless and fruitless, in the murk and darkness of faithless materialism.

Christ, in answer to the Pharisees, said those memorable words of spiritual insight : " The kingdom of God cometh not with observation ; neither shall they say, Lo here ! or, lo there ! for, lo, the kingdom of God is within you." It is the kingdom of God within us, this spiritual force that is the sole motive-power of life and movement in the whole universe which is at once electrical, chemical, and biological, that we should aim to harness to our car of healing. If we could only convince men and women of this Divine possession and show them that they, all of them, are a part of the Divine scheme and partners with Christ and with one another, then the reign of faith and love would sweep away our doubts, our wars, our fears ; then the thousand petty worries and illusions of life as it is now, would vanish as a dream ; then the therapeutic art would have the spiritual collaboration of the sufferer in place of the doubting, halting opposition of a Thomas. Already we see this spirit at work in psychotherapy, in Christian Science, often foolishly

and unscientifically directed, but producing results that in our ignorance we call miraculous.

We call a disease incurable, but why? Myxœdema was incurable a short time ago. Surely this word "incurable," like "supernatural," should only be regarded as the limit of our present powers. Much of our old medical lore will no doubt have to be scrapped, but it has served its purpose, and has been a stepping-stone to truth. We now need, and, thank God, are getting, a new orientation. True science and spiritual consciousness will flood the world with a new light. The fear of death and doubt of God's goodness, implied in almost every thought and action of our lives, will be supplanted by faith here and hope in the future.

Faith in God's purposes and faith even in a doctor are drugs of great price, which combined with hope will often remove mountains.

Now one will ask, what has this rather hackneyed transcendentalism got to do with endocrine therapy? The connexion is not at first obvious, but none the less real.

Consider for a moment the mental state of the cretin, or in later life of the myxœdematous, and again that of Graves' disease, and we shall see how the health of the body is controlled by

and involved with the harmonious working of the endocriné glands.

The mind will rise above and triumph over most diseased conditions, but endocrine disease and disharmony will quench thought and faith alike, and thus turn the whole life into failure.

Tuberculosis may be conquered or for a time ignored, cancer may be removed by surgery, but endocrine disease or abnormality strikes at the very roots of life, of the vegetative system as of the autonomous, and the most powerful mind goes under.

We must acknowledge that there are a few diseases—but very few—that we can treat and cure entirely from without, such as ringworm, scabies, and rodent ulcer. The great mass of morbid conditions must of necessity be attacked from within, and yet this in a sense is wrong, for it is not the disease that has to be attacked but the owner of the disease. A very clever writer who writes without a name says, “ Know that there are two ways to be rid of a vice, a right way and a wrong way, the one being slow and uncertain, the other being speedy and sure ; for just as the foolish physician studies disease in order to bring about health, so the wise physician studies health in order to annihilate disease, saying to his

patients, ' Fulfil the conditions of health, and diseases will fall away from you of their own accord.' "

Except by surgery very few diseased structures can be removed or annihilated : it is the soil on which they grow that must command our attention and that will get us our results. A clean land will grow good crops fit for man's use ; foul land will grow only useless weeds. Again, the good crops will starve out the rubbish. Look at a good field of wheat or potatoes : in farming language they clean the land. A wise psycho-therapist does not attempt to forcibly eradicate a vice, for that would leave the soil empty, swept and garnished and ready for another inhabitant perhaps worse than the first, but he implants a virtue, a healthy idea, which squeezes out the morbid one ; he weeds out and cleans the mental soil so that wisdom thrives. Much after this method must we deal with physical infirmities.

A great number of morbid conditions, perhaps the majority, can be brought under the heading of deficiency diseases.

In childhood they are chiefly due, in overcrowded cities, to oxygen deficiency and to food or vitamine deficiency. These lead to red-cell and hæmoglobin deficiency. Then the endocrine glands,

lacking their proper nourishment, fail to develop normally and we see especially thyroid and pituitary deficiency. This, again, results in imperfect growth, mental and bodily, and to faulty metabolism. In adolescence, gonad deficiency is perhaps the chief trouble.

In early adult age, the joy and urge of life, as a rule, for a time will overcome all these difficulties and defects, and the cure may be permanent; but more often strains and settlements will show the faulty foundations. In later age we see, again too often, the old endocrine deficiency reasserting itself, the health and the mind failing for lack of their natural food and stimuli.

There is another condition, the gouty, which is often due, in the first place, to excess rather than to deficiency: food and alcohol are taken in excess of the body's needs, and the tissues become charged with effete, unconsumed material, but this almost comes under the deficiency clause, for it is the excretory organs that fail to cope with the unnatural demands.

From without daily, hourly, we lie open to attack from germs of disease, from tuberculosis, the infectious fevers, pneumococci, streptococci, and others that as yet are beyond our ken.

Seeing, then, that we are encompassed about by so great a cloud of enemies, it were surely folly to try to stay them by direct attack only. It must become more or less a trench warfare of defence: our phagocytes and our endocrine glands can in health deal with any ordinary assault; these are our *φυλακες*, our real prophylactics. When we realize their importance we grasp the fact that non-immunity is chiefly due to blood and endocrine deficiency, and that here lies our main hope of waging successful war. The production of immunity by vaccines and sera is an established fact and a great ally, but manifestly too inaccessible for the daily help of the multitude. We must look unceasingly to the garrison and see that its members are in good health and sufficiency. This we can do by curing anæmia, and by finding out if there is any gland in error, an error which is not always obvious, but which soon becomes a most interesting investigation. In substitution treatment by the corresponding animal glands we can generally effect our purpose, and by these means we can also re-educate the defective glands to take up again their proper work. This can readily be done in early and middle life, but in old age the substitution treatment will often have to be

continuous. This all tends to open up a new hope for therapeutics. In place of uncertain remedies that are foreign to our tissues and that intrinsically are often poisonous, we supply what is lacking from the animal kingdom; moreover, by supplying one gland essence that is deficient we can help to set the others working together again in their proper harmony.

It is the anæmic and those with thyroid and pituitary deficiency that succumb most readily: the cretin, the myxœdematous, those with the perverted thyroid of Graves' disease, who mostly die long before their time and almost always of some intercurrent disease.

During pregnancy careful observation will often show signs of endocrine deficiency or excess, and these will surely tell on the health and development of the foetus. The blood-pressure should be tested from time to time and the urine examined: high pressure and slight albuminuria will point to thyroid deficiency, which can easily be corrected. Low pressures, headache, and depression will point to the pituitary as cause.

It can hardly be doubted that the frequent developmental failures that we see in early childhood must be due to inherited endocrine causes or to material deficiencies before birth.

Half a century ago therapeutic scepticism was the common and fashionable state of mind, and not unnaturally ; the older therapeutæ were able to give but a poor explanation of the faith that was in them, and the materialism of that time would accept nothing that could not be proved. They were without imagination. As the knowledge of the blood and its cells grew, and as the mechanism of the circulation began to be tested by the sphygmograph and the manometer we began to see the reasonableness of some of the old drugs.

For the scientific, the physiological and biological bases of the new therapeutics, I must refer my readers to such brilliant writers as Schäfer, Sajous, and others whose accurate, honest, and painstaking work has been most inspiring. At the same time I would like to point out that the general practitioner has before him a most interesting field of study, one full of speculative and practical idealizations. All these gland extracts can be given without any risks to life, so the rank and file of the profession, with the laboratory teaching of the physiologists as their guiding power, can launch out on to this new sea without fear of storm or shipwreck. In Stevenson's hopeful words, " The conditions of conquest are

easy. We have but to toil awhile, endure awhile, believe always, and never turn back."

Schäfer's definition of an endocrine gland seems to be as accurate as possible. "Material which is passed into the blood or lymph from any tissue or organ of the body forms its internal secretion, and organs which are not known to possess any other functions than that of passing such material into the blood or lymph are internally secreting or endocrine organs."

This term is not usually extended to the lymphatic glands. Strictly speaking, then, we must consider the thyroid, para-thyroid group, the suprarenals, medullary and cortical, the pituitary gland, anterior and posterior, the pineal and the internal secretory part of the pancreas as the endocrine glands with which we have to deal.

The testes, the ovaries, and the thymus all come nearly into the same category, but not entirely; they can all, however, be harnessed for our work. With one or two exceptions the internal secretion is a matter of surmise only, but the evidence from the physiological side and from the clinical is so strong that doubt vanishes; the most sceptical must allow that we have at least a good working hypothesis and one bearing good fruit.

Professor Pawlow says : " The world of pathological phenomena is nothing but an endless series of the most different and unusual combinations of physiological occurrences, which never make their appearance in the normal course of life. It is the interlinking of events the like of which could never enter into the mind of the present-day physiologists."

These are the puzzles we have got to solve, the entanglements we have to untie.

The therapist of fifty years ago had to work largely by faith and not by sight. He had very little sure ground to stand on, and naturally his results were very uncertain. It is said of Sir William Gull, after a hard morning's work in his consulting-room, that his final soliloquy was, " To think of all these people coming to see me, when the only things certain in medicine are the actions of castor oil and ipecacuanha !"

This wave of scepticism no doubt swept away a lot of useless rubbish, but in itself it was only a negation and the old proverb " *Ex nihilo nihil fit*" was as true as ever. Then followed careful study of the natural history of disease, mostly uncomplicated by medicine. One may say, justly, I think, that in London there was no scientific teaching in medicinal treatment till

Sir Lauder Brunton came to St. Bartholomew's. He had a keen foresight of the possibilities of endocrine treatment, but it is for this generation to develop it.

Without the least hesitation one may say that in the past there have been no such curative weapons in one's hands as the endocrine extracts, and they explain the good action of some of our old friends. Strychnine is a tonic, because it stimulates the output of adrenalin; the iodides produce their effects chiefly by stimulating the thyroid to greater activity, and the future will show further extensions of these glandular reactions. These glands are all linked up together, partly by nerves and partly by their hormones acting through the blood stream, and they thus become the great regulators and coordinators of the bodily economy, of growth, nutrition, and of metabolism.

Some of the immediate results of our experiments are so striking that one is in danger of being led into unreasoning enthusiasm; the old muddle between *post hoc* and *propter hoc* is still with us, and one must not lose sight of the fact that our striking results, in the nature of things, must have side effects which demand consideration. There is some confusion of thought about

the word hormone, the literal meaning of which is something that excites. Schäfer, appreciating the fact that some hormones inhibit, invented a new word, chalone, for these ; he groups hormones and chalones together as autacoid substances, because of their drug-like action. Quoting from Bainbridge's *Essentials of Physiology*: " In such a community it is clearly of the utmost importance that the various groups should work in harmony, and, to ensure this, they must be linked up by some controlling mechanism. Two such mechanisms are found in the body, (1) a system of chemical messengers or hormones, and (2) the nervous system. The former is the more primitive of the two methods. A hormone is produced in one organ and is carried to another, exciting or restraining its activity. For example, as the acid contents of the stomach pass into the bowel, they lead to the production of a hormone in the intestinal wall. The newly formed substance is taken up by the blood and carried to the pancreas, which it stimulates to secrete the juice required for the next stage of the digestive process. Such a method of communication is comparatively slow, and where rapidity of transmission is important the messages are conveyed by the nervous system."

The action of adrenalin on the nerve ending of the sympathetic nerves, with the almost instantaneous results, is a case in point. As our knowledge increases we shall be able to see and to utilize the hormonal and chalone effects of the internal secretion of one gland on another.

CHAPTER II

THE ADRENALS

IN the endocrine republic, the presidency must, I think, be accorded to the suprarenal glands. (If they are entirely removed death occurs in two or three days. Death eventually comes after complete removal of the thyroids, the parathyroids, and the pituitaries, but not so rapidly.) The suprarenal secretion seems to be the active agent that enables us to meet successfully the great emergencies of life and to promote the rapid response to their demands that safety needs. It is the automatic activator of the whole sympathetic system. If, further, Professor Sajous' contention is proved, viz. that the physiological function of the internal secretion of the adrenals is loosely to combine with the oxygen of the air in the pulmonary alveoli, and to endow the blood with its oxygenizing properties, it takes a still higher place in the animal hierarchy.

As an introduction to suprarenal therapy, I will

go over briefly the known physiological actions of adrenalin. The gland is divided into the cortical part and the medulla. The function of the cortex is still in doubt, though it is known that in early life tumours of this may produce abnormal sexual development. Given by the mouth preparations of the whole gland are far more active than adrenalin *per se*. This points to the cortex containing something of its own, and that something of no small value.

In support of this I give the following extract from Dr. Louis Berman's great work :¹

“The two parts of which each gland is composed are known as the cortex, or outer portion (literally the bark), and the medulla, or inner portion (literally the core). No clean-cut boundary sharply delimits the two, as strands and peninsulas of tissue of one portion penetrate the other. In the history of their development in the species and in the individual, and in their chemistry and function, a sharp difference contrasts them.

“The size of the cortex varies directly with the sexuality and the pugnacity of the animal. The charging buffalo, for example, owns a strikingly wide adrenal cortex. The fleeing rabbit, on the

¹ *The Glands Regulating Personality.* The Macmillan Company, Publishers, New York and London.

other hand, is conspicuous for a narrow strip of cortex in its adrenal. Human beings possess a cortex larger than that of any other animal.

“No definite chemical substance has, as yet, been isolated from the cortex. That remains a problem for the investigator of the future. But certain observations, especially concerning the relation between the development and behaviour of the so-called secondary sex characteristics, those qualities of skin, hair, and fat distribution, physical configuration and mental attitudes, which distinguish the sexes, and the condition of the gland, indicate clearly that an internal secretion will be isolated, and that it will in its activity furnish certain predictable features.

“Three different layers of cells, arranged in strings, that interpenetrate to form a network directly bathed by blood, that breaks in upon them from *open* blood-vessels, compose the cortex. Most remarkable is this method of blood-supply, for it is exceedingly common among invertebrates and rare among the vertebrates.

“In certain disturbances of these glands, especially when there are tumours, which supply a massive dose of the secretion to the blood presumably, peculiar sex phenomena and general development anomalies and irregularities are

produced. If the disease be present in the foetus, taking hold before birth, and so brought into the world with the child, there evolves the condition of pseudo-hermaphroditism. The individual, if a female, presents to a greater or lesser extent the external habits and character of the other sex. So that she is actually taken for a man, although the primary sex organs are ovaries, often not discovered to be such except when examined after an operation or death. How closely such an occurrence touches upon the problems of sex inversion and perversion comes at once to mind.

“If the process involving the adrenal cortex attacks it after birth, the symmetrical correspondence and harmony of the primary sex organs and the secondary sex characters are not affected. But there often follows a curious hastening of the ripening of body and mind summed up in the word puberty, a precocious puberty, with the most startling effects. A little girl of 2, 3, or 4 years of age perhaps will come to exhibit the growth and appearance of a girl of 14. She begins to menstruate, her breasts swell, she shoots up in height and weight, sprouts the hair distribution of the adult, and the mentality of the adolescent, restless, acquiring, doubting, emerge. A tot bewitched into puberty! A boy of 6 or

7 may suddenly, in the course of a few weeks or months, become a little man, robust, rather short and stocky, but moustached, with the muscular strength and the sexual powers of a man and thinking of a man. It is all as if into some fermentable medium or solution a little yeast were dropped, that changed the quiet calm of its surface into a bubbling, effervescing revolution. It suggests at once that maturation, the transformation of the child into the man or woman, must be due to the pouring into the blood and the body fluids of some substance which acts like yeast in the fermentable solution. The adrenal cortex is one source of the maturity-producing internal secretions.

“ If trouble in the adrenal cortex starts after puberty, phenomena of the same type, but of a different order, exhibit themselves. A woman, say in the thirties, becomes thus afflicted. Slowly or quickly her body will be covered by an abundant growth of hair, more or less of a beard and moustache appear on her face, her voice will become deep and penetrating, her muscles will harden, and she will show a capacity for hard physical labour. Sexually she appears to be made over; masculinity now predominates in her make-up. Virilism is the name by which the French, in

particular, have popularized the knowledge of the condition. Virilists have to shave, or be shaved, regularly, and are not bothered in the least by the cares, responsibilities, jealousies, and anxieties of personal beauty, for the change in their spirituality makes them immune to the preoccupations of the feminine. The cause of such a transformation in a previously entirely normal woman has been found to be a tumour of the adrenal cortex.

“But not only is sexuality, and the conduct of the secondary sex characters, connected with the adventures of the adrenal cortex. The development of the master tissues of the body, the brain, the pride and darling of evolution, is in some subtle way correlated with it. The adrenal cortex contains more of the phosphorus-containing substances of the general nature of those found in the central nervous system than any other gland or non-nervous tissues in the body. During human intra-uterine life the adrenal glands are large and conspicuous, in the first half of the second month being twice as large as the kidneys. Most of this relatively huge size, which happens in the human alone, and not in other animals, is due to enlargement of the cortex. Should this preponderance of the cortex over the medullary portion not

occur in the human, that is, if the proportions remain like those of other animals, the brain fails to develop properly, or an entirely brainless monster is generated. The human brain, therefore, probably owes its superiority over the animal brain to the adrenal cortex, in development anyhow. The growth of the brain-cells, their number and complexity, are thus controlled by the adrenal cortex."

The medulla contains and secretes adrenalin, a substance that has also been made synthetically. If the gland is hardened in a chromate solution, the medulla stains brown the chromate combining with the adrenalin; thus arises the name chromaffine. There are other small scattered groups of chromaffine cells that are found along the course of the large abdominal blood-vessels. The duration of life varies in animals after removal of the gland; this is probably due to the varying number of these accessory portions.

Adrenalin is not found in the cortex. Bainbridge says: "When a small amount of adrenalin is injected into a blood-vessel, it produces constriction of almost all the arterioles of the body, and, if the vagus nerves have been divided, an enormous rise of blood-pressure is produced.

When the vagus nerves are intact, the rise of blood-pressure is less, because, in accordance with Marey's law, slowing of the heart takes place. The action of adrenalin is not confined to the blood-vessels, but extends to every structure of the body, which is normally supplied with nerve fibres from the sympathetic system. It stimulates the nerve endings of these fibres in the structures which they supply, and the results of the injection are identical with those of stimulation of the entire sympathetic system. Thus it increases the force and (if the vagi are divided) the rate of the heart, and at the same time dilates the coronary vessels, so that in spite of the rise in arterial pressure the efficiency of the heart is maintained and its output may even become larger." This effect on the coronaries is very important, and helps to explain its great therapeutic value in some conditions of dyspnœa. Its action on the movements of organs of digestion is rather inhibitory, and it may cause dilatation of the pupils.

The arteries that are most affected are those of the splanchnic area and the cutaneous vessels all over the body; the pulmonary arteries and the cerebral are very slightly influenced.

Schäfer says, "It is always the smaller vessels which are most affected, and in consequence of

the great rise of pressure which their contraction produces the larger arteries tend to become passively dilated ; this dilatation may be very great." This must be borne in mind in aneurism and in aortic atheroma. Bainbridge says : " In all probability, the varying activity of the supra-renal glands, brought about by impulses reaching them from the splanchnic nerves, plays an important part in the adjustment of the vascular system to the changes constantly taking place in the body. A striking instance of this adjustment is seen in states of violent emotion, such as rage, pain, or fear. The additional adrenalin sent into the blood stream, in these circumstances, increases the amount of glucose passing from the liver into the blood, thereby providing a further supply of sugar to the skeletal muscles ; and in so far as it raises the blood-pressure, it also improves the nutrition and efficiency of the heart and the blood-supply to the brain. In this way the reaction of the animal to those emotional states, by movements of attack or of defence, is rendered more effective."

To the local effect of adrenalin in causing the contraction of vessels on a bleeding surface, I need not further refer. These seem to me to be the principal points in the physiology of this organ

that we should bear in mind when applying our knowledge to treatment.

The suprarenal is the organ of self-preservation, the primitive universal instinct of all animal life. It is the real fundamental egoist ; it belongs more to war than to peace, more to the flesh than to the spirit. Nevertheless, it is the necessary foundation of physical success ; controlled by, and working with, other powers, it will help man to transmute his egoism into altruism, his man power into humanity's service. This power we must determine to use in our fight against the unseen enemy we call disease ; it must be one of our chief allies.

In the experimental injection of adrenalin or of the extract of the whole gland into the veins, the most prominent and probably the most important symptom is the big rise of blood-pressure ; this is rapid, but does not last long. In the ordinary medicinal use, either by hypodermic solution of adrenalin or by whole gland extracts by the mouth, the results are more gradual and rarely go beyond the normal pressure point of 140 mm. Professor Sajous says, " The supposed blood-raising power of adrenalin in medicinal doses proved misleading. Indeed, one of my workers found that if there is one thing

that adrenalin did not do, it was to raise blood-pressure." Probably these tests were made on healthy folk, but in the very low pressures of acute fevers, such as diphtheria and pneumonia, there is nothing in my experience so certain to raise pressure as suprarenal, but it only lifts it to the normal, and doing this it is the safest and the most efficient tonic we possess. Strychnine acts chiefly by increasing the output of adrenalin. In these acute diseases, however, the gland has almost struck work, for the adrenalin contents of the gland after death have been proved to be almost *nil*. Surely it is wiser to supply freely the deficiency from without than to attempt to flog a dying gland into activity. In such cases the sphygmomanometer should be our constant guide. It is quite safe to give a 5 grain tablet of the fresh gland (such as is always on the market) every 4 hours or oftener, till the pressure amounts to 130 mm. or to 140 mm., the former in children and the latter in adults. Death in these diseases is often said to be due to heart failure, but the chief cause of that failure is adrenalin starvation.

That the heart muscle is strongly stimulated by adrenalin is shown by this experiment: a frog's heart, removed from the body, that has just ceased to beat will at once start again if placed

in a bath of adrenalin solution. Adrenalin given by the mouth has not a very dependable effect ; it may be that its blanching effect on the gastric mucous membrane prevents or delays its absorption. Lesné (*Bull. de la Soc. méd. des Hôp. de Paris*, Nov. 6, 1920) says: " Adrenalin is not destroyed by pepsin or pancreatin, but the liver seems to deprive it of some of its toxicity, so that it has to be given in large doses to obtain effects. It is much more toxic when given by the rectum, and he infers that the abundant anastomoses of the hæmorrhoidal veins enables it to be carried direct to the vena cava, and so to the heart. This should give us far more speedy results than hypodermic injection. There seems to be somewhere an inhibitory force that prevents any extreme rise of pressure, even from large doses, when given in the ordinary ways (intravenous, of course, excepted). This may possibly be due to thyroid stimulation maintaining the balance. Thyroid deficiency tends to cause atheroma of the large arteries with high pressure (this has been amply proved in thyroidectomized lambs). One would think that the continual use of adrenalin might have the same effect, but in chronic asthma, which is often relieved by adrenalin injections, this is not the case. An old patient of mine

who died at 80 years of age, had three or four injections of adrenalin daily for eight years, but her pressure never rose above the normal, and there were no signs of atheroma.

In ordinary spasmodic asthma, adrenalin injections probably give relief more quickly than anything else (with the exception of hypodermic morphia, which one naturally avoids as much as possible).

If blood-pressure be normal or above, the combination of 2 minims of liq. trinitrin with 7 or 8 minims of liq. adrenalin often gives better results; it is better to dilute them by filling the syringe with boiled water. Neat adrenalin sometimes produces pallor and a feeling of faintness, which is more alarming to the friends than to the patient.

If the blood-pressure be sub-normal the addition of pituitrin (ampoules of this combination are sold by the chief wholesale houses) instead of the trinitrin is often very useful. In the acute dyspnoea of œdema of the lungs or of cardiac dilatation, with or without high pressure, adrenalin injections act generally like magic. This is due to two causes. Firstly, the coronary arteries of the heart are dilated, giving the heart muscle a larger flush of blood, and consequently greater

power to overcome resistance, and secondly, a still more important action.

While the arteries of the great splanchnic reservoir and the superficial vessels of the skin are contracted, the large deep vessels of the limbs are dilated, and the blood flows freely from the centre to the periphery; thus the engorged areas round the heart and lungs are bled into the limbs, where hyperæmia can do no harm. This fact has been proved by plethysmographic measurements. Here again the manometer should be the guide to the use of adrenalin plain or in combination. The fact that the pulmonary arteries and the cerebral are not constricted by adrenalin renders its use practically free from danger, as far as those organs are concerned.

There is another use for adrenalin in hæmatemesis: this may almost be regarded as an external use, for the control of the hæmorrhage is due to the local action, and not to its action on the circulation. In hæmoptysis it is probably of no use. In the various states known as neurasthenic, the whole gland extract is very valuable, especially perhaps in low-pressure cases which form the majority. It is often combined with other gland extracts, such as thyroid, ovarian, orchitic, and pituitary, and is known on the market as

hormotone. A little thought and experience will show which combination to use. In high-pressure cases it is well to leave out ovarian, orchitic, and post-pituitary, but a moderate amount of suprarenal will help. It may seem foolish to give a pressure-raiser like suprarenal in combination with thyroid, but experience shows it to be most useful; the troublesome irregular heart action that thyroid often produces can be entirely controlled by suprarenal, and with it full doses of thyroid can be given: this is really of importance, for many patients will not persist with thyroid if the heart trouble be not relieved. In general practice the regular use of the manometer will show many cases in which unexpectedly there is plus or minus pressure, and in which the pressure variation is the cause of trouble; no ordinary drug can alter these variations. In old age, we often meet cases that complain of vertigo; in the majority the symptom is due to raised pressure or to actual atheroma of the cerebral arteries, and the indications are clear for thyroid or some other tension depressor, but one occasionally comes across a case where the vertigo is due to very low pressure. (I have a case now in a man of 86, whose pressure is only 110 mm. Thyroid in such a condition would aggravate, while supra-

renal is steadily raising the pressure and the vertigo is lessening.)

Without the manometer it would be impossible to gauge such a case accurately. I suppose there are still a few men who think they can estimate blood-pressure with the finger touch, but failure and error must always be their portion. In all glandular treatment we must bear in mind and follow Hippocrates' doctrine of assisting nature : the *vis medicatrix naturæ* is no mere phrase, we more or less unknowingly acknowledge and work with it every day : treatment by rest, by exercise, by dieting, by starving, all are founded on the theory of this unseen force. In this new line of therapy also, we must follow the light of nature, and remember the important fact that none of these glands in life work singly ; they help and compensate one another ; faulty action of one disturbs the body's harmony, but the healthy glands try to take up the failing work of the affected ones, and to some extent succeed. Following nature's action intelligently we can often lend a strong helping hand, and by substitution treatment set the weak gland on its legs again. As I have said before, during the greater part of life failing glands can be re-educated. At the same time we must bear in mind that when we

give one gland extract, its action is not entirely confined to the corresponding gland in the body, but must affect other glands through their intricate relationship.

In some cases this may be harmful, but generally speaking it is beneficial.

What I have just said refers only to functional failure, not to diseases like Addison's, where the real trouble is destruction by tuberculosis, nor to any form of malignant disease that primarily or secondly affects the glands.

This nature force, the *vis medicatrix*, is largely bound up with the action of the internal glands, and especially with the adrenals and the pituitary; they are the raisers of vascular tension, the stimulants to the muscles of the heart, the increasers of the oxygenation of the blood, and so of general metabolism. In the hypoadrenal stage of the acute disease, such as diphtheria, pneumonia, and typhoid, their administration increases immunity against further and other infections; that there is such a liability is of frequent observation. In such cases, to give these extracts in the early stage, when pressure is up, is probably a mistake, for in the first stage of these the suprarenal gland is generally congested and swollen, and under increased pressure

hæmorrhage into it may easily occur. This is a serious complication, and often brings about a very rapid fall of pressure with great prostration.

Under modern social conditions the well-being of infants and young children becomes a very important matter, for the future of the nation depends on the health of the individual. The mother who suckles her child gives it a start in life that, except for accident or carelessness, it should never lose. It has been proved in human and in animal life that milk is capable of conveying antitoxin substances to the offspring after these have been injected into the mother ; this is transmitted immunity, but what is far more important is inherited immunity.

Probably all infectious diseases in a civilized people eventually lead to a condition of partial and increasing immunity. This takes place partly *in utero*, but largely through the mother's milk during the first year of the child's life. In artificially fed babies this latter immunity giving power is of course absent, and such are far more vulnerable to outside attack. This vulnerability can only be met by increasing the defensive powers, and these are chiefly the adrenal and thyroid internal secretions. The unhealthy conditions of adenitis in childhood, of anæmia, liability to catarrh,

adenoids, and slow mental and bodily development are caused mostly by hypoadrealism and hypothyroidism, and need the preparations of both glands as routine treatment. In deficient growth of limbs the anterior pituitary secretion is probably deficient also, and can be added. As a rule, the child that is markedly sub-thyroidic is also an adrenal deficient, and the two gland preparations help one another in action.

By filling up these deficiencies we not only promote development but increase resistance to attack, and help the glands to take on for the rest of life a more complete function.

This artificial immunization cannot, of course, compare with that given naturally by the mother's milk. Healthy mothers, feeding healthy babies with nature's food, will go far to produce an A I nation. Every master and mistress who teaches children should go through a short course of endocrinology. They would then learn to correct their views about the moral responsibility of the dull, stupid child, that cannot learn its lessons, and the imp who is always in mischief; their convictions on the subject of original sin may also require revision. It is wonderful to see the sub-thyroid child who is to all appearance an unhappy failure wake up into new life and become

a smiling capable normality. Beyond the years of childhood criminality can almost always be traced to hereditary endocrine deficiency. On the physical side adrenal competency in childhood is one of our greatest protections against tuberculosis. In chronic tubercular disease hypoadrenia is nearly always present, and we rather neglect it. In chronic phthisis the blood-pressure is generally very low, and adrenal extract should form the basis of all treatment. It is the best of all tonics, and increases their powers of resistance to all microbic attacks. As the pressure rises the fever falls.

Daily observation will show the intelligent physician the importance of this secretion in all concerns of life.

Hyperadrenia in childhood is so much a fault on the right side that we are tempted to ignore it, and to say, perhaps rather carelessly, that it will settle down by itself, but these mercurial children, bright and precocious, often want watching; their balance is not good, and they can overstep the mark of safety; mentally they need much judgment and care, while the unwise teachers often press their brains in order to exhibit them as prodigies. In fact, they run them for long-distance races as two-year-olds, with the

almost inevitable results. All of us, I suppose, can look back on some of our school prodigies, and have seen how rarely they lasted into after life, while the slow-developing, plodding boy turned into a successful man. Such children's brains should not be pressed, but their energies should be turned in other directions such as games or some handicraft as a diversion. Unless one can find some other endocrine fault, not much can be done by treatment for these children, but much can be done by diet; these are the children that should have almost a meatless diet. Oatmeal, milk, eggs, good farinaceous food, fresh vegetables, butter, fat bacon, and fish should be the chief foods, for all the purins are probably adrenal stimulants; in fact, these children want to be dieted in the same way as we diet patients with high pressure and arterio-sclerosis in old age. In dropsical conditions, especially in those due to kidney deficiency and cardiac failure, hypodermic injections of adrenalin have been found very useful; they must be given in large doses, 20-30 minims of liq. adrenalin, and in such doses powerfully aid the action of ordinary diuretics, such as theocin and anasarcin.

Till we get past middle life, hyperadrenia is not often noticeable, except in the acute febrile

diseases. Here all the endocrine forces are mobilized, the adrenal probably at their head, to oust and kill the invaders. We say a patient has had a narrow squeak of rheumatic fever or pneumonia, and we are right, but it is the endocrines that have silently won the day ; but where they have failed, the mobilization has exhausted and almost drained them of their virtues. Here the manometer will tell us when to step in and restock the tired glands ; I say glands, for though hypoadrenia is the most prominent symptom, the thyroid and pituitaries are played out also.

Under the stress of these acute infections it seems to be only the adrenal glands that are subject to internal hæmorrhage ; this is a cause of prostration and death that goes often unrecognized, though it might in many cases be avoided by the lowering of high arterial tension in the acute stage. This points again to the wisdom, nay, the necessity of using the manometer. The older generation of physicians thus had good reason for their bleeding, their antimonial wine, their mercury, though they often acted blindly and with unwise excess, but they had no accurate instrument to guide them. Our generation should follow their steps with sounder judgment and with far more precision in results. Sajous defines

adrenal hæmorrhage thus: "as an extravasation of blood into one or both adrenals due to rupture of some of their blood-vessels when, as a result of high blood-pressure throughout the body from any cause, toxins, toxin wastes, etc., these vessels are subjected to centrifugal pressure exceeding the resistance of their walls."

One remedy in this stage of fever and high pressure is not used or valued as it should be, that is aconite; less depressing than antimony, it helps much to reduce fever and pressure in a safe way. It is best given in drop doses of the B.P. tincture every half-hour for ten or twelve doses, or till perspiration comes on. It seems to have little or no effect on high pressure when fever is absent. Aspirin, again, is very useful often, but should not be pushed to the point of cardiac depression; in acute rheumatism the salicylate of soda is the best. Later the manometer will show us the turn of the tide, and the time for adrenal or pituitary interference. In lung cases especially, the adrenal is indicated, for it not only strengthens the contractions of the ventricles, but it hastens and increases the oxygenation of the blood. Adrenal hæmorrhage, or as it is sometimes called apoplexy, is fairly common in the first few days of infancy, and is often the unrecognized

cause of sudden collapse and death ; it is probably due to some toxæmia which rapidly raises pressure to too high a point for the fragile vessels in the gland to withstand. In the acute infectious diseases of childhood it is often the knock-out blow ; one may always suspect it, if one sees purpura. That fatal affection called black measles almost certainly has this complication. Nothing much can be done, but careful attention to the preceding fever and high pressure may ward it off. Adrenal hæmorrhage in adults is certainly rare, but probably in some cases is not diagnosed. The symptoms in a bad case are very severe ; there is great abdominal pain, diarrhœa, sickness, or both, and great collapse, with all the signs of adrenal failure in the heart and arteries.

Hyperadrenia in middle life and beyond merges into the great subject of arterio-sclerosis. This in all its forms, especially that of hyperpiesis, is preceded by a period of high tension, unsuspected generally, and therefore unmeasured in time. Careful questioning will generally show that the early symptoms have been coming on for months. These are chiefly shortness of breath on exertion, vertigo on stooping, occasional tinnitus, and a feeling of fatigue, mental and bodily, out of proportion to the work done. There is no doubt

about the presence of hyperadrenia, but the subject is so mixed up with thyroid failure that I shall go more fully into the question when I treat of the thyroid gland. But before going on to this subject I would like to quote Sajous' warning: "In old age the adrenals are deficient in maintaining the circulating activity of all organs up to their former standard. It becomes a question whether, realizing this fact, we should by artificial means excite the adrenals to greater activity. That such a step might shorten life, instead of prolonging it, is probable. In the first place, the presence of arterio-sclerosis in the aged counsels prudence, in the second place to activate the adrenals would only hasten their degeneration by imposing a greater wear and tear upon them. Drugs capable of enhancing activity had therefore better be avoided in the aged."

The wise, scientific, and safe plan is by quietly reducing arterial tension and resistance to restore the adrenals to complete or partial competency. That this can be done I hope to show in the next chapter.

CHAPTER III

THE THYROID GLAND

As a short introduction, I quote from Bainbridge's *Essentials of Physiology*: "The thyroid gland consists of two lobes, one on each side of the trachea, united by an isthmus, and it is composed of closed spherical vesicles, held together by connective tissue. Each vesicle contains a viscid colloid material. The thyroid gland contains iodine in organic combination, and it has recently been shown that the iodine is combined with tryptophane to form tri-iodo-tryptophane. This compound has been named thyroxin. The gland is richly supplied with blood-vessels and nerves. Numerous lymphatic vessels are often found, and these sometimes contain colloid material."

Probably this gland's chief function is the rule of the body's metabolism. Even in health the extract given internally increases considerably the nitrogenous excretion, and it lowers blood-pressure. If large doses are given, tachycardia with irregularity more or less is produced, and nervous excitability, flushing and heat of the skin with

perspiration, in fact, a mild imitation of the signs of Graves' disease. If full doses be continued loss of weight may be considerable. In practice we have to deal mostly with hypothyroid conditions. (The hyperthyroid disease known as Graves' disease will be dealt with separately.) There may be congenital complete absence of thyroid; this is rare, and the child living on its mother's thyroid for the first year soon after fades away. What we have to deal with generally is the state of partial hypothyroidism known as cretinism. There may be a complete, unmistakable picture of this condition, but more commonly variations and modifications.

In children, if the thyroid is removed or becomes atrophied, the following are the chief symptoms we observe: an arrest of growth, especially of the skeleton, with delayed development of the gonads; the skin is swollen, the hair thin and much inclined to fall, the face pale and puffy, particularly under the lower eyelids, the abdomen swollen, the bridge of the nose depressed, the hands and feet podgy but not properly pitting on pressure; the higher functions of the nervous system remain undeveloped, and this is thought to be due to arrested development of the cortex cerebri. Such is cretinism; we may find only some of the

external symptoms to be present, but there is always mental lethargy. This condition may be sporadic or endemic, the latter occurring chiefly in goitrous districts. The gland in such places may be large and hard, but deficient in thyroxin contents. These symptoms in breast-fed children do not come on till about the second year, when they become dependent on their own thyroxin, and not on that contained in the mother's milk. In such cases thyroid feeding is a specific, and must be carried on for some years. If the growth of the child's limbs do not improve it will help much to add pitglandin, the extract of the pars anterior of the pituitary. In most cases of hypothyroidism the blood-pressure is above the normal, but if this is not the case and the circulation be feeble—cold and blue extremities, for instance—adrenal extract should be added. Each case must be watched and treated on its merits by various combinations. There are few more brilliant or lasting triumphs in modern therapeutics. The cretin, from being a helpless burden to its parents and almost an idiot, becomes a fairly useful person, capable of education and later of mental and manual capacity. As he grows older his thyroid becomes more active, but help from outside by thyroid feeding will probably

be necessary from time to time. Without doubt this thyroid feeding acts as a hormone to the other endocrine glands, and so the whole tone of the body is raised. It may almost be laid down as an axiom that a one gland failure, existing for some time, means a general gland failure, and needs what is known as pluriglandular treatment.

In adults the same condition of hypothyroidism is known as myxœdema. The external picture is much the same, but the mental powers, having been developed, only fail gradually; there is a general impairment of sensibility. There are a few small signs which as a rule do not appear in the cretin, such as an aching back, without stiffness, and a tenderness on pressure; and a slight swelling about the ankles, not pitting and not extending to the dorsum of the feet. The puffiness of the lower eyelids is more noticeable than in children, and the general swelling of the skin of the face gives the almost immovable mask-like aspect characteristic of the disease; the hair loses its gloss and falls easily. In almost all cases the blood-pressure is raised so that the breath is short and the heart's action hurried on exertion. This high blood-pressure is probably the result of thyroxin deficiency. The body weight may increase in spite of a lessened food

intake. The oxygen consumed and the nitrogen excreted are both much below the normal ; there is also a diminished excretion of calcium salts and an increased tolerance for sugar. The general conclusions arrived at by Biedl, Eppinger, and others seem to be " that the thyroid and chromaffine system, together with the infundibular portion of the hypophysis (i.e. posterior pituitary), constitute a group of vascular glands which augment and accelerate the processes of metabolism ; that the balance is maintained by the antagonistic activity of those vascular glands, like the pancreas and the parathyroids, which exercise a restraining influence on metabolism. These two groups of glands possess physiological interrelationship with one another : the extirpation of one of these glands is followed by differing sets of phenomena. Firstly, there are the direct results, due to suppression of its specific secretion ; secondly, there are the indirect results, due to derangement of other glands, the functions of which were either stimulated or inhibited by the secretion of the suppressed gland. That the thyroid is believed to promote the activity of the chromaffine system and to inhibit that of the pancreas. The direct results of thyroid removal are the metabolism changes and failures

mentioned above; the indirect results are the absence of stimulation of the adrenals, etc., and the hyperactivity of the pancreas due to removal of the inhibitory agent. It is believed that the nervous system is the agent by which the interactivities of these glands are affected. That group which promotes metabolism has a sympathetic innervation, and stimulates the sympathetic nerves, at the same time exercising an inhibitory effect on the autonomous nerves. The group which retards metabolism possesses an autonomous innervation, and while stimulating them inhibits the sympathetic. The thyroid possesses a double function, and is furnished with both classes of nerves; it is thus able to affect both divisions of the nervous system." This special development and possession of the thyroid makes it the centre of the endocrine system, and both from the physiological and the clinical point of view must always be borne in mind. Since the above quotation was written it has become a received opinion that the intercommunication of the glands and the interactivity is carried on as much by the hormonal and chalone powers of the internal secretions as by the nerves.

It will perhaps be found that the emergency calls are transmitted by the telegraph and the

everyday calls by the ordinary post. It is with the slow postal communications that we shall be chiefly concerned in endocrine therapy; the rapid effects that we see after strychnine, adrenal, and pituitary injections are perhaps examples of the telegraph methods from outside, but probably cannot be compared for lasting efficiency with the hormonal messages that direct our everyday life.

The correctness of our observations is proved in a measure, both in children and in adults, by the comparative results of total and partial thyroidectomy. Kocher, of Berne, who has had an unrivalled opportunity of judging, says, "that if a quarter of the gland is left the symptoms of thyroid insufficiency do not appear." This probably is true of immediate results, but observation lasting over a period of years would be needed before we could lay down a working law. In children that most tiresome complaint enuresis is often connected with hypothyroidism, and will often yield to thyroid feeding when all other treatment has failed.

This weakness may continue, especially in women, into adult life. In all cases thyroid should be tried, and if by itself it fail, pituitary should be added, for this gland has a great

influence on growth, and especially on the proper development of the whole sexual and urinary apparatus. Before entering on that most important subject hypothyroidism in the latter half of life, I must draw attention to a very serious example of thyroid failure which often ends in that catastrophe eclampsia. It is only of late years that the cause of this condition has been recognized, and even now it is scarcely known. Lange writes, "In pregnant women I have observed that when the customary enlargement and over-activity of the thyroid does not occur, the likelihood that nephritis would appear is greatly increased." "Interpreted from my point of view," says Sajous, "this is because the over-active thyroid (which is the natural event) ensures the destruction of the excess of toxic wastes which the growing foetus contributes to the blood: if the organ fails to increase its activity, toxic, i.e. imperfectly catabolized, wastes are excreted in abundance by the kidneys, thus exposing them to nephritis, or if these wastes are retained puerperal eclampsia occurs. Hypothyroidism under these conditions becomes the main cause of puerperal nephritis and eclampsia."

Here prophylaxis is of the first importance: when we find slight albuminuria, we should care-

fully watch the blood-pressure and the quantity of water passed. If the pressure is up and the quantity of water below average, we must get to work at once and begin thyroid treatment, which will soon be effective and ward off danger. If, as so often happens, the trouble goes on to the end unrecognized, so that the pressure is very high and the secretion of urine almost stopped, we can still do a great deal. The patient should be put to bed, kept thoroughly warm, and the diet should be only milk and farina. Under full doses of thyroid (a 5-grain tablet of fresh gland every three or four hours) the urine will in most cases soon begin to flow more and more freely, and the pressure will go down; the urea will increase and the albumin lessen. So we may guide the patient to a safe termination. This treatment was first introduced in 1901 by Dr. Oliphant Nicholson, of Edinburgh, and deserves more notice than it has received.

The following is a typical case: A woman, aged 34, started œdema and albuminuria at the eighth month. Urine passed in 24 hours was 6 oz., which boiled solid. Œdema became general. Eight grains of fresh thyroid were given three times a day. Urine at once became plentiful and œdema lessened. She went to her full time, taking

17 grains daily ; parturition was normal, with no eclampsia ; the child died three days afterwards in convulsions.

Woman aged 28. Albuminuria and œdema came on suddenly when about a fortnight from full time. Urine passed in 24 hours only 4 oz. Œdema great, with much dyspnœa. Patient was seen at night, and 30 grains of fresh gland was given in the first 12 hours, and then reduced to 20 grains in 24 hours. Under this thyroid treatment, and without any hot packs, improvement set in, œdema and dyspnœa diminished, and the urine, though still loaded with albumin, increased to 30 oz. Parturition was normal, and the child survived. In this case thyroid was given to the child at once, and there were no convulsions.

After childhood, in girls about 15, we sometimes find considerable enlargement of the thyroid, that is tender on pressure, and that does not pulsate ; one thinks of commencing Graves' disease, but the heart's action is quiet and there is no tremor. These cases are, I think, due to the gland being left behind in the race of development. It makes a determined but futile spurt to catch up with the other glands that are going ahead normally. If this is allowed to go on unchecked the endocrine harmony is never

perfect, and an ugly parenchymatous goitre forms and lasts for life. Thyroid feeding, if begun early, will enable the gland to meet the demands made upon it ; the overstrain will cease and the hypertrophy disappear. Many an ordinary goitre in later life can be much reduced by thyroid when the external use of iodine has done all that it can do ; especially that troublesome enlargement of the gland backward which causes difficulty in deglutition will disappear.

CHAPTER IV

THYROID INSUFFICIENCY IN LATER LIFE

I HAVE dealt so far with thyroid failure, partial or complete, in the first half of life, and I hope have shown to some extent how much can be done to aid proper development and to get a fair average of health during those years. After 45 or 50 years of age we have a different but almost a more interesting problem to solve. In early life a faulty thyroid fails in development ; in later life in maintenance. Subthyroidism after 50 may be only the continuance of a life-long state, but more often it is a new condition, the earliest sign probably of premature degeneration. It must be our work to arrest this degeneration at the earliest possible moment, and not only to arrest it but to set the endocrine life going again in healthy harmony : and this we can do. We talk learnedly of arterio-sclerosis : it is a grand word, something like that blessed word Mesopotamia, but it only defines a result and shows naught of its cause ; nevertheless, it is a most serious fact and a result that destroys life and

working power in later life more than all other causes put together. We sign our death certificates as to the cause of death "senile decay," "paralysis," "angina pectoris," "Bright's disease," "heart degeneration," "apoplexy," "softening of the brain," but they all, or very nearly all, boil down to disease of the arteries. Senile decay before 80 years of age, or I would almost say 85, should be regarded as premature. We are proud of our civilization, but are we entirely justified in that pride? Though we have not, like our first ancestors, to live night and day armed against attack and death, yet the struggle for existence has only changed its character, not its intensity. They lived, fought, and died, and took their fate more like animals, free from worry and care; while we, at any rate those in the thick of the fight, have to be full of care and thought if we wish to survive or to succeed. It is this constant nervous strain that, allowing little or no rest, keeps our nerves and arteries in a state of tension. To meet this, civilization provides luxuries, food, wine, and pleasures that we take in excess, hoping to soothe our tired brains to forgetfulness and rest. To the nerve strain is thus added the physical strain of more food than we can properly

digest, of more waste products than we can properly excrete. So the vicious circle goes on till the tragic snap breaks it.

I am not contending that every case of sclerosis is due to overstrain or to over-indulgence, but the great majority come more or less under this heading. We do not only produce this condition, but we hand it on to our children, for we see it occurring in generation after generation in families who are leading lives of no particular intensity. This disease of the arteries is far more common in brain-workers than in muscle-workers. This is partly due to lack of proper exercise and partly to the lack of oxygen in the atmosphere in which they work.

Still, a man may learn to use his brain to the full and yet keep perfect health. Another cause, that is almost national, lies in our diet habits and ideas. They are altering for the better, but our forefathers consumed animal food far in excess of the body's needs, and thought that it was certainly requisite for health and work ; the same statement must be made about alcohol in almost all its forms. I am not preaching vegetarianism, but there can be no doubt that an animal diet puts a much greater strain on our excretory organs than a vegetable one, and this excretory

failure is one of the chief causes of sclerosis. Apart from the nature of our food, it has been a custom, again almost a national one, to eat a good deal more of all sorts of food than our digestive organs can cope with or than our bodies require. This leads to our intestines being loaded with imperfectly digested food, which when absorbed becomes an actual poison to the whole system, to blood, brain, nerves, and vessels. Persons who live to a great age, 90 or over, are nearly always small eaters, and at the end of life take so little that one wonders how they live at all, but they are right consciously or unconsciously.

What kills most of us is the uncleared ashbin. The thyroid gland which chiefly controls metabolism, owing to impure blood circulating through it, fails in its office, and the ashbin becomes more clogged. In all these cases we find evidence of subthyroidism, and the most prominent symptom of it is raised blood-pressure; this, if neglected, goes on to hypertrophy of the arterial coats and then to true sclerosis. The common-sense indications are to clear the ashbin, clear the flues, and for the furnace to use the right sort of fuel and rather less of it: this we surely can do.

In men the presclerotic condition comes on sometimes insidiously, and without any loud

warning. Such a case I saw recently: a man, aged 54, apparently in the best of health and condition, very muscular, playing two rounds of golf a day, with no shortness of breath, vertigo, or any sense of fatigue. His only conscious trouble was painful feet on walking. An unusually clever chiropodist, who could find no local cause for the pain, sent him to me, thinking he had high pressure: this I found to be over 200 mm. There was no albumin; the heart showed no signs of strain and no dilatation. This man felt that he was at the top of his form and lived accordingly, both as to eating and drinking; but how precarious is his state! Such men call to mind the 73rd Psalm: "They are not in trouble as other men; neither are they plagued like other men. Their eyes stand out with fatness: they have more than heart could wish"; but as the Psalm says later, "surely Thou didst set them in slippery places: Thou castedst them down into destruction." The self-denying onlooker says somewhat enviously, "Verily I have cleansed my heart in vain, and washed my hands in innocency"; but he survives while the other passes and is forgotten. It is not often that one gets such a hearty man as the above to reform his life, but if he is wise he can be saved. The

more common type is the man who, about 50, begins to get short-winded, to get fatigued in body and brain on insufficient cause, to get occasional vertigo perhaps, and insomnia. Careful observation will show an uniform rise of pressure and often slightly dilated heart; in this early stage there is usually no albuminuria. If one can get hold of these cases early one can cure them, for true sclerosis has not come on.

In women about the menopause the same trouble often occurs; indeed, every woman, I think, has a rise of pressure at this time. In quiet-living healthy folk the condition may be only temporary, but in some cases it may be the beginning of true hyperpiesis. Therefore I strongly advise that every man and woman should at 50 and afterwards get their blood-pressure tested from time to time: so much can be done in the day of small things; such tragedies wait on neglect.

The reader will perhaps ask what has this got to do with endocrine therapy? Much every way. In all these cases the thyroid has partially struck work, and with this more or less the other endocrines have followed suit. I am not arguing that the thyroid is the first offender; the causes lie beyond and in many directions, but the thyroid shows the earliest symptoms of altered function

or of disease, and also the way out. Biedl says: "If thyroxin be given continuously for two or three weeks the amount of CO_2 excretion will be increased by 15 to 25 per cent. The nitrogenous interchanges are invariably disturbed by thyroxin: the increased decomposition of albumen is expressed by a considerable increase in the amount of nitrogen excreted. The calcium excreted in the fæces, is also increased, the calcium carrying off with it much phosphorus." These properties of thyroxin fully explain its action and its uses.

In starting thyroxin treatment, patients should drink freely of soft water, or of Malvern or Vichy water: the object of this is to help the kidneys to carry off the increased output of solids that result; this will not be necessary for a continuance.

To go back to my former simile, we thus gradually empty the ashbin and clear the flues. There remains the reform of the intake, the fuel. This, of course, is imperative; without this the animal that was washed will return to his wallowing in the mire. The reformed diet is by no means an irksome one, and as the patient's sense of well-being grows, so will the old desires fade. In cases where the symptoms are urgent, particularly the head symptoms, such as vertigo, bad

occipital headaches, insomnia, and tinnitus, a purin-free diet is wise for a time: partial starvation and rest are also wise, for there is the ever-present danger of cerebral hæmorrhage. A rather drastic but most effective way of clearing the bowel and of making a fresh start is 24 hours bed, 24 hours starvation, $\frac{1}{16}$ of a grain of calomel every hour for 12 hours, and as much hot water as can comfortably be drunk: calomel is a thyroid stimulant, acting rapidly on that organ, and at the same time an intestinal bactericide.

In chronic cases the regime need not be so rigorous. Red meat should be eaten sparingly and not more than once a day: mutton is better than beef; the meat extracts such as beef-tea and rich gravy soup should be avoided. Vegetable soups made with a bone stock are quite allowable. Cheese, eggs, milk, and fish should supply the greater part of the nitrogenous intake. An approximate purin-free diet is as follows. Nuts are the most nutritious, and contain the most fat; chestnuts are the most digestible, macaroni, dates, raisins, and cheese are all purin-free. White bread, potatoes, and milk contain minute traces, but so little that it may be ignored. Cream, butter, fats, eggs, apples, grapes, figs, and honey are also purin-free; in fact, one may say

that all vegetable and farinaceous foods are allowable.

The following table of purin-containing foods is from Dr. Cautley's paper, and shows the percentage of purins in various foods.

The purin contents of food in grains per pound, pint, or teacup:

Sweetbread	70.43
Liver	19.26
Beefsteak	14.45
Sirloin	9.13
Chicken	9.06
Loin of Pork	8.48
Veal	8.13
Ham	8.08
Mutton	6.75
Salmon	8.15
Halibut	7.14
Plaice	5.56
Cod	4.07
Beans	4.16
Lentils	4.16
Oatmeal	3.45
Asparagus	1.50
Onion	0.06
Porter	1.35
Ale	1.27
Lager Beer	1.09
Coffee	1.70
Ceylon Tea	1.21
India Tea	1.05
China Tea	0.75

The question of alcohol must be decided for each individual separately, according to habits,

age, etc. Probably the less the better, but we must remember that alcohol in itself is not a pressure-raiser ; and that, especially in old age, it may be a help, while the pressure is being lowered. Alcohol wisely chosen and only used as an aid to digestion is often of value, but when used as a frequent stimulant to enable a tired mind or body to carry on or to increase endurance for pleasure and excitement, it certainly does harm. Brunton said, " All the alcohols tend to dilate vessels, to lessen blood-pressure, and ultimately to diminish activity of the nervous tissues, although at first they may seem to have a stimulant action." It contains so little nutritious material (with the exception of the sugars and extractives in wines and beers) that in itself it may be said to give little or nothing to the blood ; it only enables a man to draw on his reserves. This may be a helpful thing, but the reservoir has to be refilled. Coffee and tobacco both raise pressure slightly, and should be used in great moderation. Therapeutically in hyperpiesis we want to reduce arterial tension, and with it arterial resistance, to remove, if possible, the thickening of the arterial coats which may have commenced and to enable the heart to meet effectually the unnatural resistance it has to encounter. After

many years of endocrine experience in myself and in others, I maintain that thyroid should be our main weapon. For years iodide of potash has been used, occasionally with success, more often with complete failure. The fundamental idea is right, for by giving the iodides you increase thyroid action and excretion of thyroxin, but only if you have a fairly healthy gland to deal with. In the majority of cases that we see, the thyroid has not only struck work but is incapable of resuming it.

These are the cases when iodide fails. Thyroid feeding, on the other hand, supplies the deficiency most effectually, and causes none of the disgust and digestive upset that the salt produces. It also, I think, helps a failing gland in some measure to resume work, which the iodide certainly does not do. (If for any reason the thyroid cannot be given, I think collosol iodine is better in every way than the salts.) But what object can there be in taking such an indirect, devious path to our goal, when there is a direct, natural one? The legend of iodide in sclerosis is one of those mischievous traditions that persist, and are most difficult to kill, injurious to mankind, and an obstacle to successful therapeutics.

The increased output of calcium probably has

some good effect in lessening atheroma of the large arteries. Rendle Short says: "An increased thyroid secretion may be obtained by giving iodides. Here we find the explanation, so long sought in vain, of their effects on gummata, arterio-sclerosis, and aneurism. The beneficial agent is really the increased internal secretion of the thyroid. Two important results of observation and experiment confirm this theory. *Firstly*, in cases of myxoedema, arterio-sclerosis is early and intense. The same is true in animals after removal of the thyroid. Eiselberg gives a number of very convincing photographs of intense atheroma of the aorta in his cretin lambs, from which the thyroid has been removed. *Secondly*, thyroxin has a wonderful power over young connective tissue, as is seen by the way in which it absorbs the subcutaneous thickening of myxoedema. It is not surprising, therefore, that it should be able to also deal with gummata and atheroma."

Thyroid feeding, where sclerosis has not gone far, soon shows its merits, but a fair dose must be given. As a rule I give half a grain of the dried powder three times a day at the commencement. The pressure falls almost daily, and as it falls the discomforts, especially the head symptoms, lessen.

The brain begins to work again smoothly and easily; the exaggerated worries of life assume their natural proportion, and quiet sleep comes back again. In this early experimental stage of treatment the heart needs watching closely. Where, as often happens, there has been dilatation and, perhaps, an apex-systolic murmur, strophanthin in good doses should be given; strychnine also helps, but its action on the adrenals raises pressure somewhat. The quickest and surest plan is to give hyperdermically every day, or every other day, an ampoule of Martindale's strophanthin: this is extraordinarily effective. Digitalis as a rule should be avoided; whatever its effect on pressure may be in health I feel certain that its activity raises pressure when there is hyperpiesis. There are some cases where the liver and the kidneys are not doing their work, and where there is some œdema of the legs, in which digitalis is needed, but it should be given with mercury. The old pill of digitalis, blue pill and squills, is most effective. Mercury is probably the best and steadiest lowerer of high pressure that we have, but for obvious reasons it cannot be given for any length of time. A weekly dose of blue pill, or calomel, is a great aid to other forms of treatment. The other heart

tonics, such as sulphate of spartein, cactus, or convallaria, may be used, but are not as effective as strophanthus. The rapid action of the nitrites is of course most useful in cases of emergency, in which there is threatening heart failure or cerebral hæmorrhage, but their influence is only very transient.

Next to amyl inhalation the most rapid and effective remedy in such cases is the hypodermic use of liq. adrenalin and liq. trinitrin (7 minims of the former and 2 minims of the latter form a good proportion). In the use of the nitrites we should bear in mind that we are only treating symptoms, and those in no lasting manner, whereas with thyroid we are getting at one of the chief root causes. The wise physician will use both methods as circumstances arise.

Sir Clifford Allbutt, in his inimitable way, settles this question as follows: "In entering upon the discussion of vaso-dilation as contrasted with agents which bring about this change indirectly by modifying the causes of morbid constriction, we have to consider how far mere dilatation—brought about, that is to say, immediately and singly—serves any good purpose.

"We are told that to act thus directly upon the vessel is but to treat a symptom, and is

therefore absurd. But whatsoever be our judgment on this or any such particular effect, the common denunciation of treating symptoms, which sounds very philosophical, is surely but a parrot phrase. Why should we not treat a symptom? If in granular kidney, by mere pressure reduction the grievous headache be abated, or charmed away, we have so far, at any rate, a substantial gain.

“ In renal diseases it is generally agreed that on the whole, with due caution, to lower pressure is helpful. Moreover, if by mitigation of his suffering, the patient gets a chance of picking up in many other ways, are we not more than justified in our interference, narrow as it may seem? We never know what interference may cut a link in a vicious circle. If we cannot stop the crack in the water-pipe, we need not throw away the mop.

“ The warning should run, not against the treatment of a mere symptom, but lest, while giving our attention to the symptom and snatching at an immediate advantage, we lose our grip of the case as a whole.”

As has often been observed, failure of a single gland is sooner or later associated with failure of others, and unless this is steadily borne in mind our measures for relief may fail.

This increases the complexity of the problem, but also its interest and charm.

In writing upon the details of glandular treatment, I shall from now on write only in terms of the dried powders, and I here give a list of the proportions to fresh gland.

Corpus luteum

1 gr. = 5 grs. fresh substance

Duodenal substance

1 gr. = 7 grs. fresh substance

Orchitic substance

1 gr. = 7 grs. fresh substance

Ovarian substance

1 gr. = 7 grs. fresh substance

Pituitary whole gland

1 gr. = 4 grs. fresh substance

Pituitary anterior lobe

1 gr. = 4 grs. fresh substance

Pituitary posterior lobe

1 gr. = 4 grs. fresh substance

Suprarenal

1 gr. = 6 grs. fresh substance

Thymus gland

1 gr. = 5 grs. fresh substance

Thyroid

1 gr. = 0.2 per cent iodine

5 grs. fresh substance

Parathyroid

1 gr. = 6 grs. fresh substance

The gland that seems to be the most help to thyroid in the treatment of high pressure is the anterior pituitary. This seems to help in the lowering process, and at the same time to act as a general tonic. I shall dwell more on this when I deal with my experience of the pituitary gland as a whole. Many makers put a tablet on the market that contains ovarian and orchitic and sometimes also parathyroid; the first two have a slight general tonic effect, I think, but to give parathyroid with thyroid seems rather futile. On the whole, I think, we should make our experiments as simple as possible, otherwise our results and our judgments will become confused. For general use I advise thyroid and pitglandin (ant. pit.), $\frac{1}{2}$ grain of the former and $\frac{1}{2}$ grain of the latter. In cases which show weakness and depression the pitglandin can be increased to 1 or 2 grains without any harm and with much good. The dose of thyroid, too, may have to be altered: I have a case now of myxœdema in a woman, aged 55, which needs 3 grains or more daily to produce any effect on the tension; others, again, with irritable hearts, will hardly stand the $\frac{1}{2}$ grain doses. The pitglandin, or in some rare cases, suprarenal, will help them to stand this dose, but it is not wise, except in cases

threatening hæmorrhage, to work with big doses or to try for a speedy result. In heart cases, where there is cardiac pain and distinct dilatation, the treatment should be commenced with a few days of absolute rest in bed ; with this the response will be much quicker, and one is able to form a more accurate judgment as to what is permanent and what is passing in the heart's attitude. In all cases wise advice, as to rest and exercise, is needed, and both, if well ordered, will help to lower pressure, but we must always remember that these hearts in people over 50 have not much reserve, and come to their dynamic limit rather suddenly. One is often surprised to find a dilated heart and feeble pulse with high arterial tension even of 200 mm. The work of Starling throws light on this apparent paradox. He says : " The contractile force of a muscle depends upon and is proportionate to its previous stretching, so that in its inception even cardiac dilatation is compensatory, and a rise of blood-pressure will increase the stretching of the cardiac muscle. But it is a desperate expedient, for with the overstretching complete failure may ensue." The work of many of these high-pressure hearts is like the work of Sisyphus, without help almost hopeless ; we can help them slightly by increasing

the *vis a tergo*, but far more by vaso-dilation, that is, by the lowering of the gradients in front.

Another great help to thyroid in bringing down pressure is hippuric acid in the form of hippurate of lithia or soda; introduced by the late Dr. George Oliver, of Harrogate, it has in a fair number of cases a very rapid action, and one far more lasting than that of the nitrites. Where there is no arterial thickening and the tension may be said to be only functional, it will work quite well without any thyroid at all, but I use it chiefly as an aid to the gland. It was originally made from the urine of any graminivorous animal, such as the horse or cow, but it is now made synthetically. No accurate solution of its physiological action has, I believe, been made so far, but I think it will be found that it hastens and helps the elimination of waste nitrogenous material by the kidneys. I hope I may be excused for giving a personal example. I belong to a sclerotic family, and always take my compound thyroid tablets: a few days ago I was feeling my head stupid, rather giddy, and the heart was painful. I found that my pressure was 180 mm.; this is much above my average. In addition to my thyroid I took 9 grains of lithium hippurate (in 3rd grain doses) daily for three days;

on the third day my pressure was 130 mm. This effect was produced without any feeling of discomfort, such as the nitrites often give, and all my other symptoms disappeared. The dose of hippurate is from 5 to 10 grains daily. It is easily soluble, and in cases of nerve strain or insomnia works admirably with some bromide. I have touched on most of the main signs and conditions of hypothyroidism, but in practice the careful observer, who has had his eyes opened, will be able to diagnose often some small divergencies from the normal, mostly in the direction of deficiency, and will be able to correct them quickly and happily. Such, for instance, is the unnatural falling of hair in middle-aged women, the hair at the same time becoming brittle and losing its gloss; unexplained rheumatic pains, such as fibrositis, or wandering pains in the back with a strong sense of chilliness, are often due to thyroid deficiency.

Commencing enlargement of the prostate in men is often arrested by thyroid if continued for some time: its power of absorbing young connective tissue is the probable explanation. Finally, one must always think of its powers of defence against the invading microbes of disease; a poor gland, deficient in thyroxin, cannot speak effec-

tively with the enemies at the gate. In mental diseases, apart from those that can be accurately traced to syphilis, there is probably always a functional disorder existing for a considerable time before the more definite symptoms and the organic changes appear. These are often traceable more or less to toxæmias, as in puerperal insanity, in Graves' disease, and in the mental disturbances that follow the acute fevers. These toxæmias can be studied from two points of view: first, the actual effect of the poison on the brain tissues: here not much can be done effectually with our present knowledge, but when we study it from the endocrine point of view a more hopeful plan opens. The toxæmia probably has gained its morbid power and foothold from deficiency of our glandular prophylaxis. All of us who get these acute diseases are exposed to toxæmia, but fortunately few of us succumb; this may be partly due to the severity of the dose, but much more to our means of protection. All this demonstrates the extreme importance of watching carefully through the acute stages of disease for the signs of endocrine failure or exaggeration. The pressure period needs anti-phlogistic measures, while the subsequent low-pressure period, whatever the temperature may

be, requires the actual support that we get so well from adrenal extract. Again, we must remember that in all acute diseases metabolism is excessive, and that the results may be in themselves poisonous; elimination of these is imperative, and is largely under the control of the endocrine glands. When mental disease is established the endocrine failure or error still persists, and much can be done by intelligent use of our gland extracts. For instance, in melancholia, hypothyroidism is the rule with raised blood-pressure; these two alone bring about a sense of discomfort with mental fatigue and incapacity quite apart from the mental disorder. Here the thyroid, by its action on blood-pressure and on metabolism, helps much towards the cure of the main affection. In maniacal conditions the blood-pressure is generally far below normal and metabolism excessive: here adrenal or pituitrin therapy comes to our aid. In dementia præcox careful investigation will often show endocrine failure or excess, and so give indications for suitable treatment.

When giving thyroid in brain disease, we must remember that large doses carry off a good deal of phosphorus: the brain-cells cannot spare this loss for long, and we should restore the loss by

giving phosphorus in pill or by lecithin: this will generally act as a sedative rather than as an exciter.

When once our eyes are opened we shall see more clearly day by day how much mental disturbance depends on, and is connected with, endocrine disorder; experience and thought will then show many roads to successful treatment, such as hitherto have been unattainable.

GRAVES' DISEASE

During the vicissitudes of life urgent calls are made from time to time on the thyroid gland, in pregnancy for instance; but these are nature's conservative demands that fulfil a useful purpose, and that cease when the emergency is over. The only real morbid hyperthyroidism is that which we see in Graves' disease, but the cause is rarely, if ever, in the gland itself; this is a disease in which we must treat the symptom first and worry out and remove, if possible, the cause as soon as we have traced it. As in most diseases, we must in the first place be opportunists. In this case the condition of the thyroid strikes the eye, the gland is enlarged nearly always, it pulsates visibly, and there may be exophthalmos. The heart's action and the sympathetic nervous

system appear disordered, exaggerated, and fussily futile, and to the patient, if a woman especially, the same adjectives may be applied. To give a disease a name, and so to label it, is no doubt for teaching purposes convenient, and perhaps advantageous, but on the other hand it is apt to confine our ideas and to put us off the track of deeper investigation. When we talk of Graves' disease we think of the great physician who first described this enlargement of the thyroid. When we talk of exophthalmic goitre we lay stress on a prominent symptom. And yet the disease may exist without either of these symptoms. The cardinal signs are thyroid enlargement, exophthalmos, tachycardia, and nervous tremor: the first two may be absent, the last two are always present. We must regard the disease as one with a toxic origin, and apparently the first affected organs are the endocrine glands, and chiefly the thyroid and the suprarenal: through these probably the great sympathetic ganglia are disordered. We conclude that there is hyperthyroidism, i.e. an increased output of thyroxin, because firstly we see the gland in a state of excitement and overgrowth, and secondly, because much the same symptoms can be produced by excessive thyroid feeding; but this argument

scarcely covers the whole ground. There must be, I think, functional disorder as well as functional increase.

Then, again, the same toxæmia that produces these manifest signs must inevitably affect other endocrines, and this may be in the direction of stimulation or of inhibition. We find in some cases plus arterial pressure and in some minus pressure; this points to the adrenal system suffering in one way or the other; but, I think, we must look to the parathyroids mostly. Here all points to their deficiency, or almost to suppression. These glands are the chief thyroid controllers, and when they are not in action the thyroid engine races. In other directions we see evidences of parathyroid suppression; the nervous tremor of the limbs suggests that of tetany, which follows extirpation of these glands. The wasting and increased metabolism both point to the thyroid check being out of work. In fact, to be accurate, we must look on Graves' disease from one point of view as hyperthyroidism and hypoparathyroidism combined. This idea will help us in the practical treatment of the urgent symptoms, it may help us to make a break in the vicious chain, but it does not help us to the cause, the original toxæmia. In many cases there is a report or

history of some great nerve shock, but it is doubtful if this is the *causa causans*; careful inquiry will nearly always elicit some pre-existing defect, gastro-intestinal chiefly, but often dental, tonsillar, or nasal; in women there is often evidence of ovarian or uterine disorder. If we hope to cure we must go deeply into all these errors and call in surgical help if necessary. A chronic appendix, pyorrhœa, a focus of disease in the tonsils, chronic disease of the antrum or of the posterior nares may need help or removal. In women ovarian disease or uterine may need medical or surgical treatment. Above all the intestinal tract needs watching: often there is colitis or intestinal stasis, or both. During the war Graves' disease occurred rather frequently among men in the trenches. Here we had the double causes of nerve strain or shock and the intestinal irritation set up by exposure and by food that was often irregularly supplied and of doubtful quality. To dwell minutely on these causes is outside the scope of an article that deals with endocrine treatment only, but as a preliminary to success they cannot be ignored, but must be regarded as the very foundation of therapeutics. We all know that in the early stages of Graves' disease thyroid feeding is distinctly bad;

as one would expect, the symptoms are aggravated. This brings us to the possible use of the other gland extracts, and the three principal ones are adrenal, parathyroid, and pituitary. Adrenal treatment has often been found beneficial, but not infrequently a failure. This is explained, I think, by a bad choice of cases. If the blood-pressure is uniformly below the normal point, it shows that there is adrenal deficiency, and it is these cases that will respond to adrenal treatment. Where the pressure is normal or above it will not do good, but possibly harm.

To my mind parathyroid is the chief gland indicated. I give a short summary of parathyroid physiology from Bainbridge: "Our knowledge of the function of the parathyroids is derived almost entirely from observations on the effects of the removal in animals or in men. Extirpation of all four glands is followed in a day or two by acute symptoms, which are for the most part of nervous origin. The excitability of the central nervous system is increased, and reflexes are not only evoked more readily but are usually more vigorous: tremors of the skeletal muscles, and from time to time prolonged muscular spasms, and even convulsions often occur. Since the muscular twitchings and convulsions cease after

the section of the motor nerves, they must be central in origin; and it is probable that they result from abnormal excitability of the spinal motor neurons. The condition is known as tetany, and although recovery frequently occurs, it is sometimes fatal in a few days, more especially in carnivora and in young animals. There is some evidence that vaso-motor reflexes are evoked more readily after parathyroidectomy, and that the irritability of the sympathetic system is also exaggerated. Noel Paton has shown that the injection of guanidin is followed by symptoms which closely resemble those of parathyroid tetany, and he has brought forward some evidence which suggests that the function of these glands is to control the metabolism of guanidin and that this substance accumulates in the blood when the glands are removed." Of this substance, one of the derivatives of purin, Bainbridge again says: "After its absorption the nucleic acid taken as nucleo-protein in the food is broken down by a series of enzymes, called nucleases, which are found in many tissues, notably the liver and spleen, first into complex groupings called nucleotides, and then into adenine, guanine, and other bodies. Other ferments subsequently convert adenine and guanine by a process of deamination

into hypoxanthine and xanthine. Finally, a third set of enzymes oxidise hypoxanthine to xanthine, and the latter to uric acid. Uric acid is then the end product of the action of these enzymes on nucleic acid."

It seems that any interruption in the normal sequence of chemical change from nucleic acid to uric acid may cause symptoms of poisoning: ptomaine poisoning belongs to the same group probably. The symptoms of tetany in some respects resemble those of Graves' disease. As far as I know, there is no swelling of the thyroid nor exophthalmos in tetany, but the muscular tremors are very similar; both diseases are partly concerned with parathyroid failure, and Noel Paton's work on guanidin to some extent explains the matter.

Rudinger, writing on thyroid and parathyroid relationship, says: "We have to suppose that under normal conditions the function of one gland is controlled by the other." He brings this evidence: "Moussa and Chanani found that the exhibition of the parathyroid of horses was followed by unfavourable symptoms in myxoedema, but that in Graves' disease it had a very favourable effect." Rudinger believes that the hyper-function of the thyroid in Graves'

disease is restrained by parathyroid treatment. From the further results of their experimental work he and his co-workers, Eppinger and Falta, infer that the thyroid secretion stimulates the sympathetic, while that of the parathyroid has an inhibitory effect. Stimulation and inhibition are so balanced by the activity of the two glands that, under normal conditions, oscillation is possible within a very small margin only.

It seems to me that these findings, which have been to a great extent confirmed, square pretty accurately with our clinical experience of disease or altered function of these two glands, and further that they give us distinct pointers to treatment, which as humanitarians is our chief want. I have given parathyroid for some years in every case of Graves' disease that has come into my hands, and I firmly believe that it is the agent we need in the scientific treatment of it. I presuppose, of course, that everything possible has been done to remove local toxic causes. Suprarenal helps the good effect if the blood-pressure be low. Exophthalmos is thought by some to be a sign of hyperadrenalism, and this is probably true; the unnatural disturbance of the sympathetic is probably due also to the same cause. To be effective parathyroid must be

given in full doses; the least I give is $\frac{1}{4}$ grain of the dried extract, thrice daily, and we need not hesitate to double the dose.

Whole pituitary and thymus have been tried in Graves' disease, sometimes apparently with success, but I have no personal experience of either of them. The best plan of treatment of Graves' disease has in my hands been as follows:

(1) Find out by every means at one's command the initial fault, and remove it as far as possible. (Here X-ray examination will help much, so far as abdominal faults are concerned.)

(2) Rest. This can never be more than a compromise; the nervous affection is all against it, and with a pulse rate of 120-140 it is more of an aspiration than a reality; but if by comparative rest the pulse rate can be lowered five beats a minute, much is gained.

(3) Suprarenal extract of the blood-pressure is low, one grain of dried extract three or four times a day. (This is about equivalent to the five grain tablets of the fresh.)

(4) Parathyroid always, in addition to anything else one may be giving. Full doses are needed: $\frac{1}{4}$ grain of dried extract three times a day is generally sufficient, but this dose may be increased.

Improvement should be noticeable in a week:

firstly, the lessening of the tremor and then of the rapidity of the heart, but in long-standing cases the treatment will need time and patience.

If, as sometimes happens, the heart has become much dilated, a hypodermic injection of strophanthin every other day will help much. Digitalis as a rule disagrees. The diarrhoea and colitis are generally controlled, and they may be cured by the following mixture, which is mildly bactericidal, but very comforting :

Bismuth salicylat, gr. 12
Liq. hydrarg. perchlor, m. 3
Pulv. tragacanth co., 9 s.
Tinct. chloroform et morph. co., gr. 15
(B.P. 1885)
Aq. ad ℥i ; ter die semund.

I maintain that the details of this treatment are in accordance with our present knowledge of the causation of the disease and with our present knowledge of endocrinology. The use of X-rays, if carefully and judiciously used, helps much to subdue the thyroid hyperactivity, but they do not go to the root of things, and only treat a symptom ; but in this disease, as in most, we cannot afford to despise any outside help.

With regard to partial thyroidectomy, I feel very jealous. I feel that the calling in of surgical help is a grave reflection on the physician. There may

be such severe cases that it becomes necessary, but those must be cases of neglect, where no intelligent treatment has been given in the early stages.

I had a very interesting case where all the acute symptoms persisted after two partial removals. This has been entirely cured by parathyroid and the antiseptic treatment of the bowels.

It is easy enough to take away thyroid tissue, but how can we put it back? In many cases of this disease a time comes when the exhausted thyroid gradually passes into a condition of deficient function, and we have to deal with signs of myxœdema; in such cases thyroid feeding may have to be continued for the rest of life. It does not do to take short views. At the back end of life we want all the thyroid that belongs to us, and most of us need a bit more. These short cuts to what appears to be a brilliant success often end in a morass of difficulties from which there is no way out. I earnestly beg my readers to be wise physicians and patient in endeavour. Spendthrift surgery should be the last resource.

In paralysis agitans parathyroid in full doses has a distinct effect in lessening the muscular tremors and movements, and, I think, retards the progress of the disease in other ways.

The walking steadies and there is not the same tendency to the quick run forward ; whether it has any retarding effect on the end cerebral failure that comes in most cases I cannot say. To sum up : The signs of complete absence of parathyroid, after removal, we know pretty well, as in tetany. In these two other diseases, Graves' disease and paralysis agitans, we have the signs of partial absence, but probably also of altered function ; in both conditions parathyroid feeding is the obvious thing and to a great extent the successful thing. These glands appear to exercise an important control over lime-metabolism, and to this may be due its extraordinary power of healing sluggish varicose ulcers.

THE THYMUS GLAND

The thymus gland must, I suppose, be thought of as one of the endocrine group. It has for years been the subject of acute controversy. Theories and observations proved and again disproved seem to cloud it in darkness. Bainbridge briefly says : " The gland is abundantly supplied with blood-vessels. In man it reaches its maximum size during the first two or three years of life ; and then becomes smaller, usually disappearing with the occurrence of puberty, and

being almost completely absent in the adult. After its removal in animals, the testes develop more rapidly, and conversely castration delays the atrophy of the thymus. The thymus thus appears to exercise a restraining influence on the development of the reproductive organs, and to undergo atrophy when their function has been accomplished."

Rational organotherapy with this gland is up to now impossible, yet so many observers have thought that distinct results have been obtained that we must keep an open mind and hope for more light. Personally I have nothing to offer.

The testes and the ovaries are not pure endocrine glands, as they have a definite excretion, but all must agree that they possess an individual hormone, which largely influences the whole body, both in its development and its behaviour. Castration in the male before puberty produces the appearance of eunuchism, and in the adult, besides impotence, various abnormal mental states. Some of us remember the disastrous consequences of the attempts made some years ago to cure prostatic disease by castration: even in old men who seemed to have long passed sexual life a fatal insanity appeared. In ovarian

removal we see somewhat similar symptoms, but not to such an extreme degree; many a woman whose ovaries have been removed, though she cease to menstruate, is a very useful member of society and leads a fairly happy life, but in both sexes there is evidence of disturbance of metabolism, for both are apt to get fat.

I think we must conclude that sexual life in women is not such a predominant fact as in men. There is good reason for thinking that the active hormone which influences the sexual characteristics comes from the interstitial cells of the testis and from the ovaries.

We are most of us, I suppose, bisexual in a measure. The masculine woman, masculine often in build and appearance and often in mental characteristics, is a familiar figure. The womanly man is also a well-recognized type. Homosexuality is to most normal men and women an impossible horror, and human law, in the interests of society, cannot make fine distinctions, but must look on it as criminality; yet from the scientific and anatomical point of view there is a small amount of excuse. In the early differentiation of sex there is sometimes a mix up of the essential sex characteristics. When this occurs there may well be temptations of which the normal man or

woman has no experience nor conception. I have touched on this delicate subject because in practical treatment by orchitic and ovarian extracts it must be borne in mind. Both extracts seem often to be most effectual on the opposite sex. In that frequently occurring period of mental depression that follows the climacteric, orchitic extract works something like a revolution, while ovarian extract completely fails. In many of these women there is absolute sexual antipathy, which the orchitic also removes. I think the same rule applies also to men, viz. that ovarian extract is a distinct nerve tonic, but here I do not feel so sure of my ground. In the ovary we have to deal practically with ovarian extracts and those of corpus luteum. Below demonstrated experimentally that ovarian extract, injected into the blood stream, caused increase of blood-pressure, increase of pulse frequency, increase of oxygen intake, and increase of carbonic acid output.

Extract of corpus luteum, on the other hand, causes diminution of nitrogen excretion, diminution of oxygen absorption, increased activity of the sweat glands, and a marked fall of blood-pressure; these differences form the basis of our clinical applications. Preparations of whole ovarian behave to some extent like those of the

adrenals: they raise pressure and are metabolic stimulants; for this reason they are often used in neurasthenic cases, where pressure is low.

Corpus luteum is clinically far more important, and if used judiciously is a great addition to our remedies in uterine disorders. In early life in girls who have painful, scanty, irregular menses, it will, if given for four or five days before the period is due, bring about a healthy state of things: the pain will cease and the character of the loss will be more natural. It should be given in 2-grain doses three times a day. It is unsuitable in most cases if the loss is very profuse. Of course, in painful menstruation, due to uterine displacement or cervical obstruction, it will do little good. During the climacteric, especially when pressure is high, it will also help to remove or lessen many of the distressing nerve symptoms.

After ovarian life has entirely ceased, it is of no avail, for it apparently only acts as a stimulant to existing corpus luteum, and not as a substitute; thyroid now takes its place. In the psychoses that one occasionally sees occurring at each menstrual period, whether accompanied by pain or not, corpus luteum is very effectual; in these cases it should be given twice daily for months, and three times when the symptoms appear.

A cure will generally result. In many cases it relieves much the vomiting of pregnancy, and by anchoring more securely the placenta to the uterine wall it helps to prevent miscarriage, and should always be tried when there is a tendency that way. It is said, and probably rightly, to stimulate and help the breast glands in lactation. It is altogether a useful extract, and deserves further study and trial.

ORCHITIC

Sajous says: "From the standpoint of therapeutics, testicular preparations can hardly be regarded as of more than historical interest." I think this is scarcely in accordance with recent experience. The interstitial cells certainly seem to behave like other internal secretions, and to have an effect greater than can be accounted for by its nucleo-albumins. It is probably a raiser of blood-pressure like ovarian extract, but as in our experience of ovarian therapy, there is probably a great difference between the extract of the whole organ and the interstitial cells, these corresponding in action more to the corpus luteum. Further investigation, I feel sure, will define its uses.

THE PINEAL GLAND

Biedl says : " The data in our possession point to the conclusion that the pineal gland is an internal secretory organ which influences metabolism, though the details of its function are at present not ascertained. Still more important is the fact that during the period of its complete development, that is to say, until the seventh year, this organ exercises a definite and apparently inhibitory influence upon the development of the sexual glands, and it is possible that it has a secondary effect upon mental development. The destruction of the pineal gland at this stage of existence leads to mental and physical precocity." If we can establish a diagnosis in such cases, pineal therapy should prove useful and carry the patient over the years of normal pineal influence.

PITUITARY

*(The following description is mostly from
Bainbridge.)*

The pituitary body lies in the sella turcica, and is connected with the floor of the third ventricle by a hollow stalk. It consists of two lobes differing from each other in origin and in structure. The anterior lobe is glandular in structure.

The posterior lobe consists of two parts, the pars nervosa, composed of neuroglia, and the pars intermedia, a thin layer, ectodermic in origin, applied to and partially surrounding the pars nervosa. Functionally the pars intermedia is associated with the pars nervosa, and the posterior lobe has apparently an entirely different rôle from that of the anterior lobe. This is shown by the observation that removal of the entire gland, or of the anterior lobe, is followed by death in a few days, although the animal survives after the removal of the posterior lobe alone. The anterior lobe is therefore essential to life, whereas the posterior is not. Partial removal or injury by disease in young animals produces more or less deficiency of growth, failure of sexual development, and often obesity; mental development is not nearly so affected as in thyroid deficiency. When this arrest of pituitary development occurs in the human subject it is known as infantilism. The failure in growth and sexual development is due to incomplete action of the pars anterior, the obesity is believed to be due to partial failure of the pars posterior. Overgrowth of the pars anterior in man causes acromegaly, the chief features of which disease are enlargement of the bones, especially of the hands, feet, and face,

thickening of the skin, diminution of sexual power, and often glycosuria. If the alteration of the pars anterior occurs in childhood, before the epiphyses have united with the long bones, these bones increase greatly in length and we get gigantism. I have thought it wise to dwell on the above facts in somewhat lengthy detail, for on them depend much the therapeutic application of these glands. Our earlier knowledge was chiefly of the posterior. The remarkable results caused by hypodermic use of pituitrin were one of the earlier lessons of endocrine action. Briefly, this lobe has no influence on growth, but has much on carbohydrate metabolism; injections of pituitrin as a rule lead to polyuria: overgrowth and hyper-activity of this lobe invariably have this effect. In disease, where urine secretion is deficient, as in various forms of dropsy, it sometimes acts as a diuretic, but not always. A more universal effect of pituitrin injection is the contraction of unstriped muscle throughout the body. Its use is well known and most valuable in uterine inertia during and after childbirth, in atony of the intestines, especially after abdominal operations, and in constriction of the bronchioles. Its diuretic action is probably due to an increased flow of blood through the renal vessels, for these

are an exception to the above rule and are dilated rather than constricted. Its property of raising general blood-pressure is due chiefly to the arteriole constriction it causes, and partly to its direct influence in increasing the force of the heart's ventricular action. Compared with the action of adrenalin, it acts directly on the muscle, whereas adrenalin acts on the sympathetic nerve always—with the exception of the kidney arteries it acts on all unstriped muscle, whereas adrenalin has an inhibitory action on the abdominal group; its action is more prolonged than that of adrenalin. Another difference that in practice must be remembered is that while adrenalin dilates the coronary arteries, pituitrin contracts them and the pulmonary also. Why the combined injection of adrenalin and pituitrin should give such relief in asthma, as it undoubtedly does, requires some thought—probably the pituitrin acts chiefly in bracing the heart, while adrenalin acts as a vaso-dilator on the coronaries, and especially on the pulmonary arteries, and at the same time increases oxygenation.

Professor Sajous, whose work commands and deserves the greatest respect, looks upon the posterior pituitary not as a true endocrine gland, but as a most important governing centre of the

whole sympathetic nervous system. His views should be read and examined in his great work *Internal Secretions and Principles of Medicine*.

The extracts of the pars posterior physiologically and clinically behave so much like other endocrine extracts that one can hardly doubt the presence of an internal secretion. Sajous looks on this as an extension of chromaffine action, but distinct differences exist between this and adrenalin which are difficult to explain; the pars nervosa may have an entirely nervous rôle. Sajous says: "The marked advantage of pituitary (meaning the pars posterior) is that it sustains the rise of blood-pressure and is reliable in shock and other emergency cases. It seems also to sustain the temperature and the muscular tone, cardiac, vascular, intestinal, and uterine, longer than the adrenal active principle. It possesses also a great practical advantage over adrenalin in that it can be administered by the mouth without compromising its effects. Moreover, pituitary preparations have seemed to me to produce the pharmacodynamic effects of both the cortex and medulla of the adrenals." Some observers have doubted the effect of pituitrin given by the mouth, but I feel sure that Sajous is right on this point: the hormotones

which Carnrick introduced some years ago depend much on this for their tonic effect, especially in the low blood-pressure cases of neurasthenia, which are the more common: in high-pressure cases, on the contrary, they often seem to raise pressure above the safety point and above the point of brain comfort. Sajous further says, "The pituitary is now granted four internal secretions: one each for the anterior and posterior lobe, one for the infundibulum, and one for the organ as a whole." As shown by Renon, "pituitary extract raises the depressed arterial tension and corrects purely functional disorders of rhythm. It is recommended in doses of 3 to 6 grains of the whole gland in myocardial weakness, particularly in that which is due to infections when the blood-pressure is receding, the pulse is becoming more rapid, and the urine scanty. While less active than digitalis as a diuretic, it nevertheless serves a valuable purpose in this connexion.

"It is contra-indicated in aortic affections, in any disorder in which high vascular tension prevails, and where there is any tendency to anginal pains, which it tends greatly to aggravate."

In England we have not as yet made the use of these powerful aids to failing circulation and

to failing powers of resistance that we should have done : we still cling to our old exoteric drugs like digitalis, strophanthus, and strychnine, and to a considerable extent find them valuable, but they can often be replaced or aided by these natural esoteric drugs and without the unpleasant side-effects that the others, especially digitalis, often cause.

The use of pituitrin in obstetrics is so well known that I need not enter into particulars.

In acromegaly one would look for much help from pituitary extracts, but so far it has only been found efficacious in the relief of the severe headache and lethargy that belong to this disease. The more we learn of these intricate actions and reactions, the greater will be our control, both of functional abnormalities and of commencing organic disease.

ANTERIOR PITUITARY GLAND ¹

Hitherto in England little clinical work has been done with pitglandin, the active principle of the anterior lobe, though, in its enormous influence on growth and development, it is more important than pituitrin. It is presumption, perhaps, to say that any link in the wondrous chain of animal vitality is more important than

¹ Much of this article appeared lately in the *Practitioner*, from which I quote by the kind permission of the editor.

another; still, in our working plans, we must differentiate somewhat between the vital and the non-vital.

To recall to mind the physiology of the subject we give this quotation from Haliburton's *Handbook of Physiology*, 1917:

“The anterior lobe consists of large granular cells and numerous blood-vessels. Its precise function is undetermined, although, probably, it is a vascular gland pouring an internal secretion into the blood, which influences growth. Abnormal hypertrophy of the pituitary produces the condition known as acromegaly, and if the view advanced above of the anterior lobe is correct the condition is caused by an increase of its internal secretion. Feeding young animals on the anterior lobe hastens the growth of their skeletal tissues.”

Later he says: “The pituitary body is essential for life.” Cushing and Horsley found that total removal of the organ is fatal in a few days. The same result followed entire removal of the anterior lobe. On the other hand, removal of the posterior lobe produces no such effect. Partial removal of the anterior lobe produces a condition known as hypopituitarism, in which adiposity, accompanied by atrophy of the organs of generation,

are the most definite signs. If the operation is done before adolescence, there is a persistence of sexual infantilism. The transplantation of the organ from another animal, or injection of anterior lobe extracts, prolongs life after extirpation, or relieves the symptoms after partial extirpation.

The work of Goetsch and Robertson has shown conclusively that the development and proper conservation of the genital functions cannot be secured without the active assistance of the anterior lobe secretion.

Goetsch, of Chicago, again, says: "Perhaps between no two of the ductless glands is a closer inter-relationship in function more demonstrable than between the pituitary and the sex glands. We know from experiments in which the pituitary gland has been partially removed in dogs, that a deficiency in pituitary secretion thus produced is followed by under-development, genital inactivity, and hypoplasia in young animals, and by impotence, sterility, and retrogressive changes in the sex glands, together with adiposity, if the animals were adult at the time of the operation.

"It is the secretion of the anterior lobe which is responsible for these sex changes. Clinical hyperpituitarism is well exemplified in the diseases, gigantism, and acromegaly. In the early stages

of these diseases we find an exaggerated sexual activity, and in the late stages, corresponding with pituitary involution and inactivity, a disappearance of the sexual function."

It is perhaps rather humiliating to find that our well-being, and our proper developments, bodily and mental, are so dependent on the healthy conditions of our lower animal reproductive functions, but the history of our evolutionary past is an integral part of our present make-up, from which there is no getting away.

Striving, revolting, aspiring bundles of sex, bundles of primitive fighting animalism and of spiritual potentialities, we must therefore learn so to direct and curb these elementals that spiritual and bodily evolution may advance hand in hand.

Conditions due to abnormal anterior pituitary secretion naturally divide themselves into those of pre-adolescence and post-adolescence. The former are chiefly defects of growth and development, and the latter chiefly of function. The functional failures of adult life are often the result of unrecognized developmental faults in youth. In early adults the urge of life and the call for action are so intense that for a time endocrine deficiency is almost obscured, but the poor material in the machine shows itself before long

and power partially fails. This points to the importance of careful observation in childhood. We see children developing in a hesitating way, both in mind and body, not going straight. We are too apt to think of it as a character-deficiency, or we call it laziness or wilful stupidity, but it is nearly always endocrine deficiency.

We see the extreme proof in the treatment of the cretin by thyroid, but these endocrine disharmonies are at work, unseen generally, and often very slight, through most of childhood's years. Much has been done by thyroid treatment, but still more would be accomplished if we realized that thyroid, adrenal, and anterior pituitary deficiency generally exist together.

The thyroid tells perhaps more on the brain and the nervous development, and the pituitary on the osseous and the sexual, but no fast line can be drawn between the two influences.

We see often the slow-developing, dull adenoid type improve rapidly under thyroid as far as intellect is concerned, but the body and limb growth falters. Here the combination of the three glands does exceedingly well. In girls, especially, the intellectual life may be active and even brilliant, but the uterine and ovarian development are almost standing still, unobserved

and untreated ; these girls grow up sex failures. Never advancing beyond rudimentary growth of uterus and ovaries, they swell the ranks of the disappointed, the sterile, and the nervous invalids. They often begin to menstruate at 13 or 14, and go on for a year perhaps, then comes irregularity or complete cessation. This state of things, when not due to manifest anæmia, points almost conclusively to hypopituitarism, and can be helped wonderfully by anterior pituitary medication. It should be given in good doses, 2 to 4 grains daily for two or three years, or till healthy menstruation is well established. Under its influence the pelvic organs develop as nature demands.

It is well known that children of both sexes who have enuresis often get right under thyroid, but there are failures also, and in these the combination of pitglandin with thyroid will often succeed. Failures of normal skeletal growth and osseous development especially demand pitglandin.

It should be an axiom, always in our minds, that endocrine deficiency is very rarely single, and, further, that the whole field must be considered before we can expect success in treatment.

Robertson, of Chicago, the discoverer of tethelin,

his name for the active principle of the anterior lobe, has published some suggestive observations on the periods of life in which pitglandin has most effect. There seems a short time, after lactation has ceased, when the effect is one of retardation of growth, but as the period of sexual maturity draws near, there is rapid increase in growth and probably hastening of maturity. This emphasizes its value in the late years of girlhood. The life of an imperfectly developed woman is often a silent unsuspected tragedy.

The further symptoms and effects of pitglandin abnormality are thus graphically described by Englebach, of St. Louis (*Endocrinology*, July-September, 1920):

“The effect of the secretion from the anterior lobe upon the muscular tonus is a subject which has received comparatively little attention, but which has appeared to the writer as being almost as important as the difference present in the osseous growth and development. This is particularly striking when one compares the muscular development and tone of pre-adolescent hypopituitarism (Lorain-Levi type) with those of post-adolescent hyperpituitarism (acromegaly). The extreme difference in the genital function and development is also emphasized in comparing

the foregoing two types. In the first (Lorain-Levi type) the genitals are infantile and functionless, with the presence of sterility and impotence ; whereas in the acromegalic the genitals are unusually well developed and associated with hypersexuality. In pre-adolescent varieties of both over- and under-activity of this lobe, there is a tendency to decreased genital function. This is present as a cardinal sign in the hypopituitary post-adolescent subject, and is soon acquired in the pre-adolescent hyperpituitarism, on account of the early transition to inactivity in this variety.

Decreased genital function and muscle tonus occurred so constantly with hypoactivity of the anterior lobe, that they established themselves as the best indicators of the state of activity of this lobe. Hence, the genital functions (menses, libido, and potency) and the muscular tonus (muscle fatigue, or physical capacity), taken with the temperature, pulse, and blood-pressure, were considered, at the time of their determination, the significant signs of activity. The osseous changes, genital development, and secondary sex characters were interpreted as evidence of former activity, which might have changed to the opposite state."

After 55 or 60, when we often see endocrine deficiencies producing premature senility, pitglandin failure forms a very important part of the complex; it is generally associated with thyroid failure. The symptoms are the well-known ones generally classed under subthyroidism. These are, raised blood-pressure with its usual signs of cardiac strain and fatigue, shortness of breath, and easily produced muscular fatigue. If the cerebral arteries are affected, there may be vertigo and tinnitus. In short, there are the symptoms of early arterio-sclerosis: premature sexual and vesical weakness, which so often occur, point to pitglandin deficiency. In practice it is found that hormotone treatment by combinations of the thyroid and pitglandin are most effective.

Pituitrin should be avoided, for it tends to raise pressure. The pitglandin balances effectually the depressing effects of the thyroid, but it should be given in full doses, 2-6 grains of dried extract daily. My experience shows that it restores sexual and vesical power and generally raises the tone and capacity of the whole system. It does not raise blood-pressure, but, I believe, helps to lower it. As in early life it promotes gonad activity, so in later life it reawakens those

glands and especially the interstitial gland in men.

While the anterior pituitary secretion in early life promotes growth and develops function, in old age it maintains function, and for a long time counteracts the tendency to degeneration of tissue. This and thyroid, together, are the conservators, natural, not artificial, of life and energy.

Some forms of epilepsy have been successfully treated by pitglandin in America, and, as far as my limited experience goes, it holds out much promise in senile epilepsy.

The three following cases are interesting examples: A man of 70 developed frequent attacks of epilepsy, always at night. His blood-pressure was 180 mm. or over. Three years ago he was given thyroid dried gr. $\frac{1}{2}$ ant. pit. twice a day. This he has taken ever since, and has had no attack for more than two years.

A man of 85 had three very violent epileptic attacks in four months. His blood-pressure was normal. He was given ant. pit. dried gr. $1\frac{1}{2}$ twice a day, and has continued them. He has had no further attack for ten months.

A man of 72 developed frequent attacks of petit-mal, generally when walking. His pressure

was normal. Under $1\frac{1}{2}$ grains of ant. pit. twice daily, the attacks became fewer and have now ceased for more than a month.

Another man, aged 63, with very imperfect genital development (as a child he was brought up as a girl), has had frequent epileptic attacks since childhood. Under 60 grains of bromide daily he held on fairly well, but was gradually getting depressed and peevish, and the fits were becoming more frequent. Two months ago I put him on to pitglandin, 3 grains daily, and we halved his bromide. He now often goes a week without a fit. They are steadily lessening in frequency and severity, and his altered mental state is obvious to all. He is happy, contented, and cheerful. I hope soon to wean him from the bromide that he has taken for fifty years.

The first three men had had no sign of epilepsy previously. The mental condition of the three has much improved, and their tempers also, according to the family reports.

It is quite safe to give larger doses than the above, if necessary, for there seems to be no toxic effect.

Pituitrin has been found to intensify epilepsy; this is not surprising when one thinks of its pressure-raising property.

It is rather humiliating to find that the practical science of endocrinology, from the therapeutic side, is not nearly so advanced in this country as in America. The nation that produced Sir Edward Schäfer, George Oliver, and others, ought not to have lagged behind. This may be largely due to our absorption for many years in medical subjects pertaining to the Great War. This lack of the newer knowledge was very evident in the recent discussion on Graves' disease at the Royal Society of Medicine. Hardly an allusion was made to the endocrine treatment of that condition (a typical endocrine disease), which in many hands has been so successful, both at home and abroad.

Surgery, which has been happily, and in this case justly, called the opprobrium of medicine, was in the lordly ascendant.

The ideal of endocrine treatment is essentially conservative. It is not the destruction or removal of disease, but the restoration of the normal balance of power and of function to the organs that rule our life.

CHAPTER V

CONCLUSION

IN the foregoing chapters I have relied chiefly on my own observations and results, but owing to the absence of material I have in some cases been obliged to rely on and to quote other men's work and opinions. I have tried to use only what seems to be established or to be reasonably probable. This last chapter I look on as my own in a large measure. The observations are my own and the speculations also; the results seem to me absolutely trustworthy and to be full of hope.

There is enormous and quite unnecessary wastage of work and energy at the back end of life. Men and women, who have worked faithfully and well, and who have laid up a store of knowledge and wisdom, suddenly break down with paralysis, heart trouble, or premature senile decay. Even if they survive for a time, most of their life's fruit is no longer available.

Let us get this axiom (for it almost deserves the name) into our minds, that senile decay is endocrine failure; it may pass rapidly into endocrine decay, but there is a time, a day of

salvation, in which the endocrine failure may be restored or at the worst arrested. Think of the long, silent tragedy of a paralysed life or of brain softening; think of the loss to the world of all that stored wisdom. Healthy old age may be lacking in initiative and possibly in pluck, but it is a very good adviser; it is not generally in a hurry, and if it accomplish little, it may serve a very useful purpose as a brake on the *facilis descensus*.

What is old age? Surely not a question of years alone. Why is one man played out, spiritless and inefficient, at 60, while another at 80 or 90 is full of interest in life and of good judgment? One may say it is due to the sort of life he has led, but in many cases there is no such reason that will bear investigation. Perhaps more justly it may be said to be due to the life and qualities that he inherits. One will say that old age is degeneration of tissues, of muscles and brain substance, but this is only stating an accomplished fact; it evades causes and origins. Degeneration is probably in great measure the end result of metabolic imperfection; combustion, the ever-active maintainer of life, and the clearing out of used-up material go no longer hand in hand: the machine, getting clogged with grit, runs no more smoothly, and begins to show signs of wear.

Metabolism without a doubt is chiefly governed and directed by our endocrine glands, and it is to them we must look both for the cause of degeneration and for the way of relief. Biedl, in a very able article in *Endocrinology*, September 1921, says: "Brown Sequard, the father of the internal secretions, placed the gonads as the axis of the problem of old age, and in his own person and to his own satisfaction thought it proved. This limited application of our present-day knowledge no longer satisfies." Biedl later on says: "Just as all bodily conditions and their fundamental chemical reactions are under the influence of the entire hormone apparatus, so is old age. This condition is regulated and directed in the degree and course of its development, not only by the testicles or ovaries, particularly by the interstitial cells, but just as well by the thyroid and thymus glands, by the pituitary and pineal, by the inter-renal and adrenal system, in short, by the whole endocrine apparatus, by its single parts, but before all by the harmonious co-operation of all."

In the treatment and arrest of senile degeneration we must continually keep this ideal doctrine ever before us. Individual cases will show more or less failure of individual glands, and in our treatment this guidance must be followed.

Polyglandular therapy is at present the fashion, but used without accurate diagnosis and intelligence is rather like firing into the brown, and the results often are the same.

I am not advocating the entire abolition of old age, for in the Divine order of things the night cometh to us all. Surely it is the Divine order also that we should value the great gift of life, and strive to maintain its efficiency to the last and to the utmost.

As the end draws near, the enthusiastic radicalism of youth passes almost imperceptibly into the conservatism of old age. *Laudatores temporis acti*, we some of us sigh for the land where there is rest and, as we fondly think, no more change; but some of us, optimists to the end, look forward with eyes wide open to the great adventure of the life to come. Whichever class claims us, may we be able to say in Stevenson's cheerful and characteristic words :

Under the wide and starry sky,
Dig the grave and let me lie.
Glad did I live and gladly die,
And I laid me down with a will.

This be the verse you grave for me :
Here he lies where he longed to be ;
Home is the sailor, home from the sea,
And the hunter home from the hill.

LIST OF AUTHORITIES

- Internal Secretions and Principles of Medicine.* Sajous. 2 vols. (F. A. Davis & Co. 1921.)
- The Glands Regulating Personality.* Berman. (Macmillan & Co. New York and London. 1921.)
- The Endocrine Organs.* Schäfer. (Longmans, Green & Co. 1916.)
- Essentials of Physiology.* Bainbridge. (Longmans, Green & Co. 1920.)
- The Newer Physiology.* Short. (Wright & Sons. Bristol. 1920.)
- Diseases of the Arteries.* Allbutt. 2 vols. (Macmillan & Co. London. 1915.)
- The Internal Secretary Organs.* Biedl. (Bale, Sons & Danielsson. 1912.)

INDEX

- | | |
|---|--|
| <p>Adrenal action and therapy, 20 et seq.</p> <p>Adrenal deficiency an adverse factor in tuberculosis, 38, 39</p> <p>Adrenal hæmorrhage in acute fevers, 41, 42</p> <p>Adrenalin in cardiac dropsy, 40</p> <p>Adrenalin in spasmodic asthma, 31, 32</p> <p>Adrenalin more active per rectum, 31</p> <p>Allbutt on vaso-dilation, 69, 70</p> <p>Anterior pituitary failure in early senile decay, 109</p> <p>Arterio-sclerosis, causes of, 56-8</p> <p>Bainbridge's description of</p> | <p>endocrine interlocking hormone, 19</p> <p>Comparison of effects on pressure of pituitrin and adrenalin, 99</p> <p>Death after acute fevers due more to adrenal failure than to heart failure, 30</p> <p>Definition, Schäfer's, of an endocrine gland, 15</p> <p>Differences between ovarian extract and corpus luteum, 92, 93</p> <p>Effect of adrenalin on the splanchnic arteries and on the pulmonary and cerebral arteries, 27</p> <p>Endocrine deficiency in pregnancy, 14</p> |
|---|--|

-
- Enuresis, 51
- Explanation of adrenalin action in cardiac dyspnoea, 32
- Hyperadrenia in childhood, 39
- Interaction of adrenalin, thyroid, parathyroid, and pancreas, 49, 50
- Irregular heart action caused by thyroid treatment relieved by suprarenal extract, 34
- Menopause, raised pressure, and, 61, 62
- Myxœdema symptoms, 48
- Parathyroid in Graves' disease, 82-6
- Purin contents of various foods, 64
- Schäfer's interpretation of hormones and chalone, 18
- Suprarenal and thyroid as immunity given in infants, 37
- The action of hippurates, 74
- Thyroid feeding much more effective than iodides, 61
- Treatment of eclampsia by thyroid, 52, 53
- Variations of blood-pressure in mental diseases, 77

Faint, illegible text, possibly bleed-through from the reverse side of the page.



460960

Scott, Thomas Bodley
Endocrine therapeutics.

MBL
S

**University of Toronto
Library**

**DO NOT
REMOVE
THE
CARD
FROM
THIS
POCKET**

Acme Library Card Pocket
LOWE-MARTIN CO. LIMITED

