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BY

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The Internal Secretions — Some Clinical Aspects Illustrated.*†

By

William Seaman Bainbridge, A. M., Sc. D., M. D., C. M.,
New York City.

The Talmudic belief in the usefulness of all created things has received therapeutic endorsement in practice from the beginning of time to the present day. The Hebrew prophets sang: "The Holy One, blessed be He, created nothing in the world without a purpose. He created the snail or leech as a remedy for contusions; the fly for the sting of the bee; the gnat for the bite of the serpent; the serpent for the cure of the scab; and the lizard for the sting of the scorpion."

The literature of all nations and all times seems to contain allusions to the use of "created things" in the treatment of disease. Not only herbs and roots, insects and birds, fishes and animals, but man himself has furnished ingredients for the broth or decoction, powder or poultice, with which the sick have been treated. "Hardly an animal," as I have said elsewhere, ‡ "has escaped making its

*Oration in Surgery, presented, by request, before the Annual Meeting of the Maine State Medical Society, Poland Springs, Me., June 9, 1915.

†One of the purposes of this paper is to emphasize the importance of the admonition; "Stop; look; listen!" as applied to many obscure and seemingly trifling conditions, some of which have only recently come to be considered as pathological states, calling for early diagnosis and treatment, surgical or non-surgical, or both. While the subject of the physiology and pathology of the internal secretions is being evolved by the many investigators who are directing attention to it, the clinician, in whatever special field engaged, should be on the alert and not dismiss with careless indifference cases which he or some of his confreres might possibly save from a life of incompetency and suffering.

‡Bainbridge. — The Cancer Problem, 1914, p. 2.

contribution, in hair or hide, tooth or toe-nail, thymus or thyroid, liver or spleen, in the tireless search of man for a means of relief. The hand on the dial has turned many times to the same point of effort during the progress of the centuries."

Many a time in her march forward, Medicine, the offspring of the Superstition of the Past, has stood on her pinnacle of achievement and looked backward, with mingled awe and confusion, over the devious trail by which she has advanced.

The immortal Shakespeare, perhaps unwittingly, gave us a glimpse of the birth of Medicine when he led us, in fancy, with Macbeth, into the witches' cavern, when he revealed to us the cauldron, and let us hear the song of Hecate and her sisters as they danced and sang while brewing the witches' broth, with its

"Eye of newt and toe of frog,
Wool of bat and tongue of dog,
Adder's fork and blind worm's sting,
Lizard's leg, and howlet's wing."

It has been said that this masterpiece of poly-pharmacy, with its twenty-four ingredients, was suggested to the Bard of Avon, who was "a master in combining poetical fancy with devotion to fact," by his familiarity with the Dispensatory of Cordus. This book, the progenitor of all pharmacopeias, was published in Nuremberg about the middle of the sixteenth century. This celebrated compilation contained the "Mithridat," a product of poly-pharmacy which Mithridates the Great (about B. C. 134-63), King of Pontus, is said to have administered to criminals as an antidote for poisons which he had previously given to them. It is related that, after experimenting in this manner upon these unfortunates, he would take both poison and antidote himself, and that in this way he rendered himself immune to all poisons, of which he had an abnormal fear. This "antidote," with which his name is associated, subsequently became popular as a "remedy" for fevers. It is said to have been "not very complicated," and to have been "improved upon" by one of the body physicians of Nero. In this improved form, it contained *only fifty-five* ingredients! It was incorporated, with additions, in the Dispensatory of Cordus, with which Shakespeare is supposed to have been familiar. Another of Nero's body physicians still further improved upon this decoction, adding flesh of snakes, and giving it the name "Teriac," or "Theriac," from the snake, "Tyros." This body physician, Andromachus by name, who was likewise a poet, dedicated a poem to Nero in which he enumerated all the ingredients of this royal remedy. The "Theriac" of Andromachus, we are told, was to be found in the Pharmacopeia Germanica of 1882. The "Theriac" of the Dispensatory of Cordus

contained sixty-four ingredients, but by the time it reached the Pharmacopeia Germanica it had been reduced to twelve. Doubtless the witches' broth was inspired by the un-expurgated prescription for this celebrated remedy.

In the dispensatories and pharmacopeias of the sixteenth century were mentioned such animal products as "distillates of capon and pullet;" wolf liver; fox lung; deer spine; inner membrane of chicken stomach; sheep's wool; toothed jaw of pike; rabbit's hair and foot; gallstones of ox; ashes of swallows, sparrows, scorpions and centipedes. The pharmacist of that time, according to accounts, had to keep in stock "poor sinner's fat," "cranium humanum," "oleum ossium humanorum," and other products which may be said to have foreshadowed the organic therapeutic preparations to be found in the pharmacy of today.

It goes without saying that all this was empirical; yet the ancient Egyptians, the Persians of the time of Susruta, the Greeks and Romans of the times of Hippocrates, Pliny, and Galen, who employed healthy animal tissues, organs or secretions, in the treatment of disease, must have had some conceptions which suggested, however vaguely, the possibility of the presence in certain organs of substances which might exert a regulatory influence upon the functions of similar organs and of the body as a whole.

Thus we see that the relatively new science which deals with the study of the internal secretions and their effects may be traced far beyond Brown-Séquard, and his organo-therapy, beyond Claude Bernard and Berthold, who laid the foundation for the scientific study of the ductless glands; still further backward to Susruta, Galen, Hippocrates, and others of our medical forefathers who, in the distant past, foreshadowed endocrinology, hormone-therapy, hemadenology, or the study of the internal secretions, by whatever name the science may be called.

It was not, therefore, a perfectly new idea which Berthold, Claude Bernard, and Brown-Séquard suggested and elaborated, when they declared their belief in the physiological influence exerted by the secretions of the ductless and other glands.

Much of the primitive and entirely empirical conception of the treatment of disease by means of animal tissues was the result of the age-long and world-wide search for the Fountain of Perpetual Youth—"perpetual youth" meaning to the Ancients very largely a matter of the maintenance or restoration of sexual vigor.

It is not to be wondered at, therefore, that perhaps the earliest and most conspicuous reference to organo-therapy related to the use of the orchitic substance in the treatment of impotence, credited to

Susruta, the Persian, who lived about a thousand years before Christ. It is also recorded that the ancients sought to convey to human beings characteristics of certain animals by the administration of fresh organs of the animal. For example, the testes of the fox, the liver of the wolf, the lungs of the deer, were given when the distinguishing characteristics of these animals were desired. Pliny is said to have recommended something like fifty preparations from the hyena for as many different ailments.

All the early ideas concerning the use of animal tissues or organs were without scientific basis, and were as entirely empirical as was the use of "black draught," "witches' broth," "green-frog poultice," "boiled puppy decoction," and like remedies in the treatment of cancer. They are none the less interesting illustrations, however, of the pointing of the hand on the dial to "the same point of effort" in the search for truth.

It was not until the experiments of Brown-Séguard with testicular extracts, which he administered to himself and some of his co-workers, that the theory of the existence and function of the internal secretions was put to the test of a practical application. His work is familiar to all, and need not be recounted here.

Since the way was thus fairly opened by these early investigators, the ductless glands have been studied one by one, in turn, and the question of the possibility of an internal secretion applied to other organs and tissues, until there has developed what may justly be termed a new science. Not only does this embrace the study of the internal secretions of the various glands and organs, but it involves also the study of the correlation of the functions of these organs with others and with the body as a whole, together with the utilization of the healthy glands or their secretions in the treatment of diseases, special and general. It likewise includes the surgical removal of the diseased gland, in full or in part, and the homoplastic or heteroplastic transplantation of healthy organs or parts thereof, in the effort to preserve their function or to offset the interference therewith by disease.

Growing out of the knowledge thus developed has come the recognition of the need of systematized study. To this end clinics have been established for the investigation of the diseases of the ductless glands *per se*, and for the study of the relations of the internal secretions to general diseases and diseases of special organs, among which the ovary will receive conspicuous attention. One such clinic has been established in Paris, under the patronage of Baron Henry de Rothschild, and under the direction of Doctor Leopold-Levy; another in Philadelphia, at the Charity Hospital, under the direction of Dr. Sajous.

With this crystallization of effort into actual clinical observation upon many and diverse conditions, it is to be hoped that the confusion and the contradictory evidence which now clouds so many of the issues concerned, will be cleared away, and that in the near future the relations and correlations of the internal secretions will be reduced to the category of established scientific fact. Perhaps, too, light will be thrown upon certain diseases and conditions, the etiology of which is still obscure. Cancer has already been suggested as one of the disease enigmas which may possibly be solved in part by a clear comprehension of the role or roles of the internal secretions. So, too, with chronic intestinal stasis and some of the conditions associated with it. Many questions of metabolism will undoubtedly be more clearly comprehended when a fuller knowledge has been obtained concerning the ductless and other glands and their secretions.

Biedle, who has devoted so much study to the subject under discussion, calls attention to the fact that the oldest, and undoubtedly the most valuable, information concerning the internal secretions is that which is derived from clinical observation. In accordance with this idea, I shall pass in brief review some of the clinical manifestations of disturbance of the functions of the glands of internal secretion, illustrating these, as fully as possible, out of my own experience or that of others, dwelling upon certain phases of the subject which have a practical clinical bearing.

It would be impossible to give, even in very brief outline, the experimental work which substantiates the clinical observations and conclusions with reference to the conditions under consideration. Nor would it be expedient, in this contribution, to endeavor to classify the clinical manifestations of perversion of function of the internal secretions according to the organs or systems of organs chiefly involved. Indeed, the correlation of the functions of the different organs is so close that complete differentiation and separation is practically impossible. The clinical manifestations of perverted function of the internal secretion of one organ are sometimes difficult to differentiate from similar results following disturbed function of another.

Examples of the oldest and most familiar clinical observations with reference to perversion or loss of function of organs supposedly having a regulatory influence over development, health, and even life, may be found in the study of the effects of castration upon man and animals. Clinical observations in this regard have been supplemented by a large number of interesting experiments upon animals. Some of these have been in the nature of indirect proofs, as it were, having for their purpose the determination of the effects of castration, thus by inference, learning the influence of the healthy organs upon the or-

ganism. Others have been indirect, seeking to ascertain the effect upon castrated animals of the transplantation of ovarian or testicular tissue from their normal habitat to another situation in the same body or from another animal. Likewise, a long series of investigations, clinical and experimental, have been conducted to determine the effects of preparations of these glands, administered under different conditions of health and disease, normality and abnormality.

The extensive observations upon animals, as well as clinical observations upon human beings, have established the existence of close connection between the generative glands and development, and it is held by many that practically no organ or tissue of the body is free from influence of this origin. It is conceded, however, that no one gland controls development or maintains health. The present state of our knowledge does not permit of a clearly defined statement concerning the extent of the control exercised by each gland or organ coming within the scope of this discussion.*

OBESITY OF ADIPCSIS.

(Hypo-endocrinism.)

(Figs. 1 to 7.)

One of the most conspicuous illustrations of perversion of function and confusion of results of such perversion may be found in certain forms of obesity. The well known effect of castration which manifests itself in a deposition of adipose tissue, has its parallel, at least to a certain extent, in the tendency toward the assumption of fat after the menopause, in both males and females. In like manner it is held that perversion of the function of the sexual glands (ovaries and testes) presumably due to hypoplasia, manifests itself in some forms of obesity of childhood. It is difficult, however to differentiate between obesity of genital origin and that provoked by changes in the hypophysis cerebri or pituitary gland, first described by Frölich, in 1901.

Dystrophia adiposa-genitalis (Frölich's syndrome) is the term applied to the syndrome characterized by accumulations of fat and disturbances of the genital functions. This condition is supposed by some investigators to be due not only to pituitary tumors, but to tumors

*Whenever, in the text or in the appended table, an interrogation point appears, it signifies lack of definite knowledge as to whether the abnormality of the given endocrinous gland is one of hypo- or hyper-function; or some other point upon which there is no conclusive opinion.

**For captions of all pictures, see pp. 49-51.

at the base of the brain. Some hold, with Fischer, that the condition is due to disturbance of function (deficiency) of the posterior lobe; others, with Cushing, that the anterior lobe is the part involved.

Obesity of a pathological character has been traced by Marburg and Hempel to disturbances of function of the pineal gland. It has not been definitely determined, however, whether this is due to hypo- or hyper-function of this gland. In a case of carcinoma of the pineal body reported by Hempel, marked obesity, noted at the beginning, was followed by extreme atrophy of the adipose tissues.

Sprinzles has noted a pathological type of obesity in thirty-three cases in which he found enlargement of the parotid gland. The accumulation of fat in these cases involved chiefly the face, breasts, and abdomen. From these and similar observances it is inferred that the parotid glands may come within the category of endocrinology. The relation between mumps and orchitic enlargement in some cases is cited in substantiation of this idea.

Adiposis dolorosa (Decum's disease), a form of painful obesity, is usually found in women. (Fig. 6). The etiology of this condition is still obscure, and may be cleared up through the further study of the internal secretions.

It is held by some that hypo-oöphorism frequently results in hyperpituitarism, this combination of internal secretory disorders favoring suboxidation of fat, and consequent obesity.

From the above it has been seen that the glands of internal secretion generally supposed to be associated with obesity are the genital glands (ovaries and testes), the pituitary, and the pineal, and that the condition is the result of hypo-function or ablation of function. The secretion of other organs may be involved, and for this reason some advocate the use of "polyglandular" preparations in the treatment of these disorders. It may be said, however, that the treatment of cases of pathological obesity, like many other conditions resulting from disorders of the endocrinous organs, is largely empirical, an example of which may be found in the administration of thyroid extract in these cases. When given without careful consideration of the individual case more harm than good may result from organotherapy.

When cases of marked obesity present themselves in practice it behooves the clinician to seriously study the case to ascertain whether there is not a definite pathological history, or whether the accumulation of fat is merely the result of an acquired or inherited tendency toward obesity, and to administer treatment accordingly.



Fig. 1



Fig. 2



Fig. 3



Fig. 4



Fig. 5



Fig. 6



Fig. 7

EMACIATION.

(Progressive Muscular Dystrophy.)

(Hyper-endocrinism.)

(Figs. 8 to 9.)

The conclusion might be reached by inference, without careful consideration, that if hypo-endocrinism involving one or more glands of internal secretion leads to general or localized accumulations of adipose tissue, the opposite condition or function, hyper-endocrinism, must lead to loss of adipose tissue. We know that the antithesis of the fat subjects may be found in the lean ones. The "fat lady" has for a side-show companion, in some instances, the "living skeleton." The various muscular dystrophies, including progressive muscular dystrophy or atrophy, have long puzzled clinicians, and their etiology has not been satisfactorily cleared up. It is probable that further study along the lines of endocrinology may throw light on the etiology, and suggest a definite line of treatment by which the unfavorable prognosis which has always applied to these cases may be rendered more hopeful. The extreme cases shown in the pictures are pitiful evidences of lack of knowledge on the part of the medical world.



Fig. 8



Fig. 9

OSSIFICATION.

(Hypo-endocrinism?)

(Fig. 10.)

Another type of "living skeleton" is represented in Fig. 10. The bony framework, in these cases, is primarily involved and the muscular system secondarily. The cases are extremely rare, and naturally the etiology is little understood. It is thought by some that the condition may be accounted for on the basis of disturbance of function of one or more of the ductless glands. The picture represents the condition as exemplified in a museum adjunct who was long familiar to circus devotees. A similar case has recently attracted the attention of the medical profession in a western community.

The organs most concerned, presumably, in the disturbances of the osseous system, are the sex glands (gonads) and the thymus.



Fig. 10

OSTEOMALACIA AND PSEUDO-OSTEOMALACIA.

(Hyper-endocrinism.)

(Fig. 11.)

Hyper-oöphorism is supposed by some investigators to account for the condition of the bony structures known as osteomalacia, or softening of the bones. So convinced have some become of the production of this condition by oversecretion on the part of the ovaries that castration is recommended as a cure. Others, considering this too radical a procedure, recommend the administration of pituitary and adrenal extract, or preparations from other glands, as the thyroid. Until the gland or glands involved are more definitely determined, and the particular manifestation of abnormal function thereof ascertained, such medication must of necessity be empirical. The subject is worthy more extended study, and may lead to a solution of the etiology and treatment not only of osteomalacia and pseudo-osteomalacia, which is a pronounced form of rachitis, (Fig. 11) but of rachitis as so often encountered in practice among children, and perhaps, likewise, of rachitic dwarfs.

A good deal of attention, in this connection, is being devoted to the thymus, largely, of course, in animal experimentation.

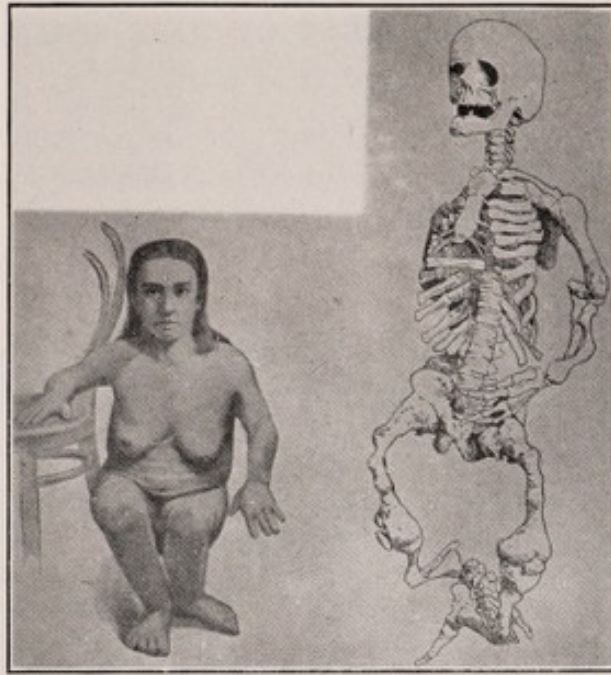


Fig. 11

PRECOCIOUS OLD AGE (PROGERIA).

(Hyper- or Hypo-endocrinism?)

This is a rare and peculiar condition, to which Mr. Hastings Gilford of London gave the name "progeria" when describing a case in a boy, fifteen and a half years old. (*Practitioner*, August, 1904). Fig. 12 shows the condition in a girl eight years and three months of age. This case was reported by C. W. Rand (*Boston Med. and Surg. Jour.*, July 16, 1914). Sajous (*New York Med. Jour.*, March 20, 1915), reviews these cases, and attributes the cause of the condition in part, at least, to the thymus. Growth is arrested or delayed, and senile decay rapidly ensues.



Fig. 12

UNUSUAL DEVELOPMENT OF HAIR (HIRSUTIES).

(Figs. 13 to 17.)

An unusual development of hair, or the development of hair in unusual parts of the body, presumably indicates some abnormality. It is certainly often noted in mental defectives of different types. Figs. 13 to 17 illustrate some of these.

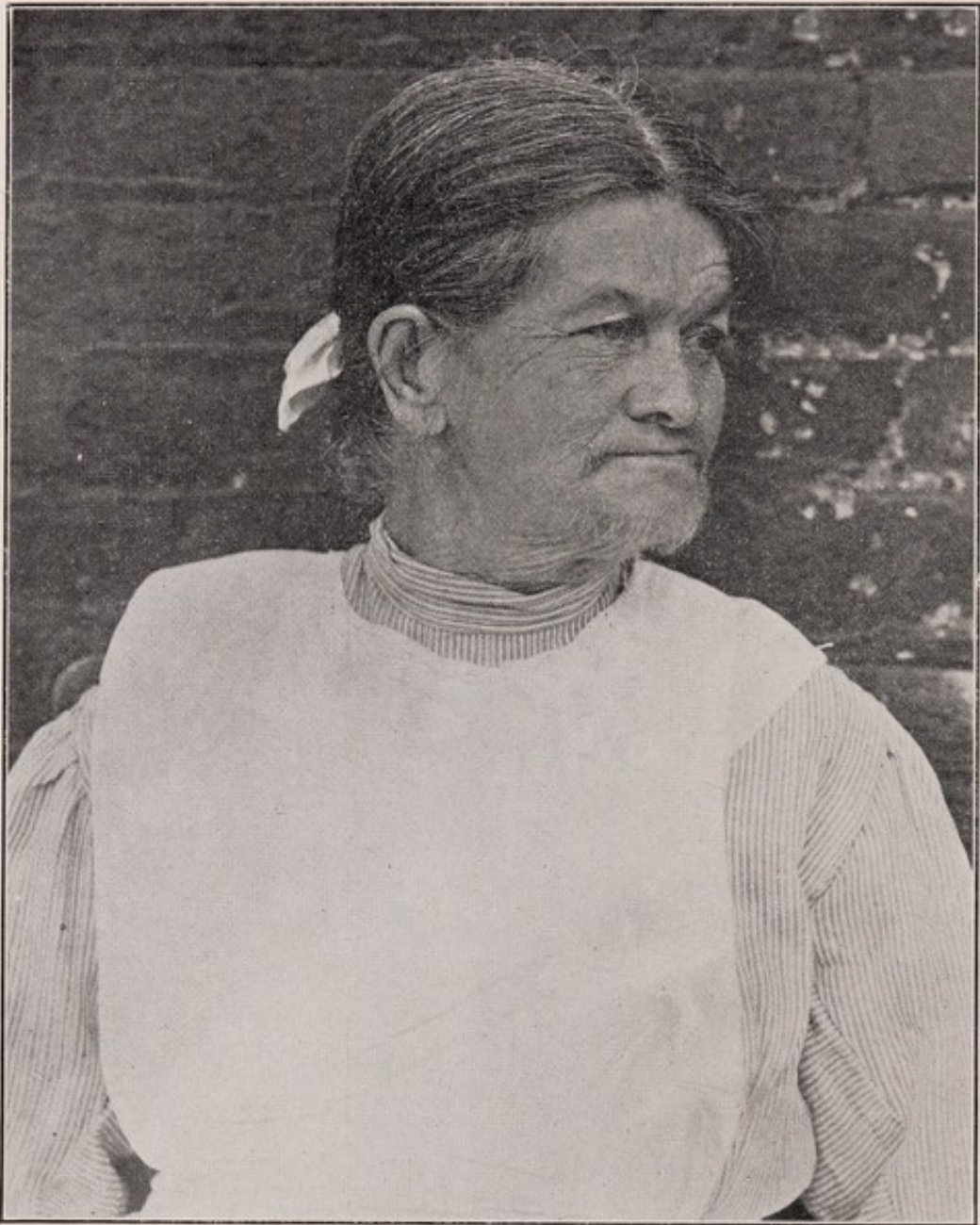


Fig. 13

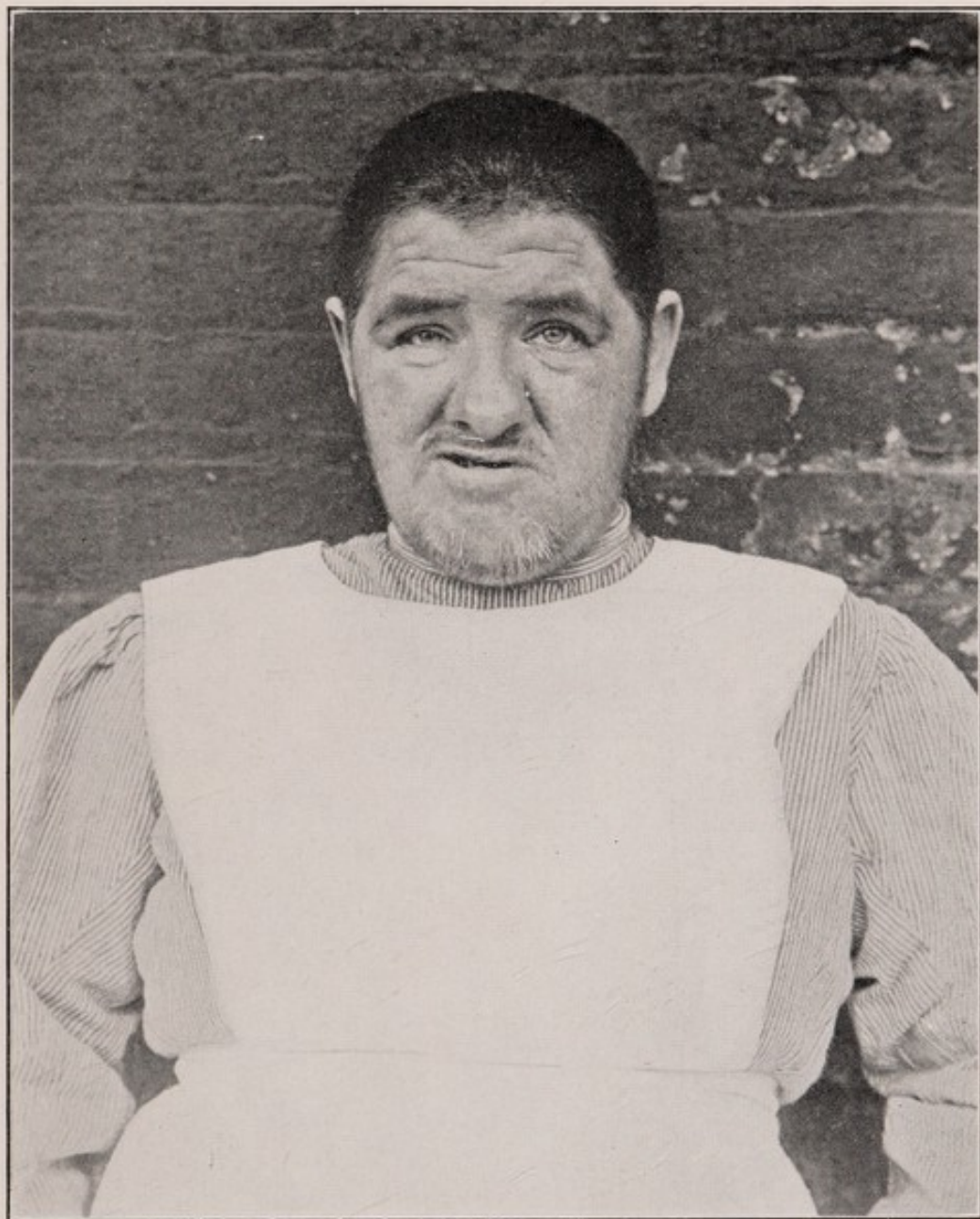


Fig. 14



Fig. 15



Fig. 16



Fig. 17

DWARFISM — MICROSOMIA.

(Hyper- or hypo-endoerininism?)

(Figs. 18 to 20.)

The fact that the surgical removal of the anterior lobe of the pituitary body in young animals has led to arrest of development has given rise to the theory that all forms of dwarfism are due to disturbances of function opposite or antithetical to those which are supposed to cause gigantism.

Inasmuch as dwarfs seem less obviously pathological than do their tall fellows, the giants, less study seems to have been devoted to discovering the cause of their lack of size. So-called "true dwarfs," (Figs. 18 and 20) who seem bright, many times talented, and altogether fairly well satisfied with their lot, do not call for so much thought. The other type, however, the "rachitic dwarf" (Fig. 19), who are so irregularly developed that they may be called pathological, deserve more careful study than seems to have been devoted to them, particularly in the light of what endocrinology has taught and is teaching in greater measure as the study is pursued.

In addition to the types of dwarfs illustrated, there are many other dwarf or pygmy individuals and races, among which may be mentioned the various inhabitants of Africa. There is little reason for believing that these under-sized persons are of necessity pathological specimens in any regard.



Fig. 18

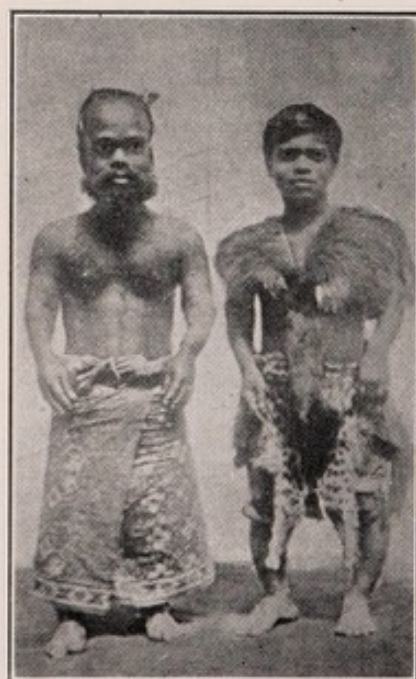


Fig. 19

GIGANTISM — ACROMEGALY.

(Hyper- or Hypo-endocrinism?)

(Figs. 20 to 21-b.)

Acromegaly is generally considered as the result of perversion or ablation of function of the pituitary gland, though investigators are not agreed as to the character of the pituitary abnormality. Marie, who first associated the clinical condition with the pituitary body, held that acromegaly is the result of destruction of the gland, and consequent complete loss of its function. The opposite view, however, that acromegaly is due to hyper-function of this gland, seems to have come into more general acceptance. Fig. 20 illustrates the relative size of giantess and dwarf. Fig. 21 is another giant, the celebrated Irish giant. Fig. 21-a represents a case of acromegaly not associated with giantism. Fig. 21-b shows the progressive enlargement of the hands in acromegaly.

In this condition, as in all others due to disturbance of function of endocrinous organs, the pathological state seems to be the result of disturbance not of one, but more than one of the glands of this system. According to Biedle, "The whole of the anatomical material which we at present possess points to the hypophysal tumour, and consequent increased hypophysal internal secretion, as the causative factors in the production of the symptom-complex of acromegaly. The weightiest argument in support of this theory is the fact that, in all cases where hypophysal tumour is associated with acromegaly, the tumour is composed of true hypophysal tissue." This author further says: "From the nature of the evidence, it appears unquestionable that the hypophysis is the site of origin of acromegaly, and that the nature of the illness is dictated by hypersecretion on the part of that organ. But the question as to whether we are to regard the pathological condition of the hypophysis as primary, or merely as the secondary result of organic affection in other parts of the body, remains unanswered. The latter assumption is permissible, for numerous experiments have shown that there is a physiological interrelationship between the hypophysis and other internal secretory organs, namely, the thyroid, thymus, suprarenals, and especially the sexual glands. Moreover, pathological conditions of these organs are associated with profound changes in the hypophysis."

Because of the presumptive poly-glandular origin of acromegaly, the condition has been treated with poly-glandular preparations. However, any organotherapeutic measures in the treatment of this condition must be considered as more or less empirical. Surgery has been invoked in the treatment of cases presumably due to hypopyseal tumors.

With reference to the so-called "true giants," who, like the "true dwarfs," are supposed to be congenitally so, and to develop symmetrically, though on an enlarged scale, Biedle says: "It is only the giants of fairy tales who, in addition to their size, are favoured with exceptional physical and mental advantages. A closer acquaintance with the giants of our day, as well as a careful analysis of the descriptions which have come down to us of the giants of old, shows that normal giants—that is to say, persons of exceptional size and free from deformity or other pathological signs, such as were assumed by Langer, and later by Sternberg—are very rarely encountered. The vast majority of giants are undoubtedly abnormal and belong to the class of pathological individuals." This fact probably led one of our popular medical writers to present "The Long Giant and His Short Story."

This abnormal condition has been described as follows by Biedle: "Gigantism is the acromegaly of the period of growth, acromegaly the gigantism of the adult stage; acromegalic gigantism is the result of a pathological process, which commences during the period of growth and continues on into the period in which growth has ceased."

Organo-therapy has proved unsatisfactory in the treatment of this condition, but further study may clear away the difficulties in the future.



Fig. 20



Fig. 21



Fig. 21-a



Fig. 21-b

GYNECOMASTIA, ETC.

(Hyper- or Hypo-endocrinism?)

(Figs. 22 and 23.)

Disturbances of the endocrinous system or systems are supposed to lead to many abnormalities of development and of function which time does not permit me to discuss in detail. One of these, gynecomastia, is illustrated in Fig. 22. Fig. 23 represents idiopathic idiocy with marked enlargement of breasts in a male. This and various other abnormalities of development have been grouped under the heading of "secondary pseudo-hermaphroditism," and are traced back to the "perversion of the stigmata of sex." Further study along the lines of endocrinology will doubtless clear up many of these obscure conditions, and may lead to ability to so treat these individuals that they may develop normally, both physically and mentally.

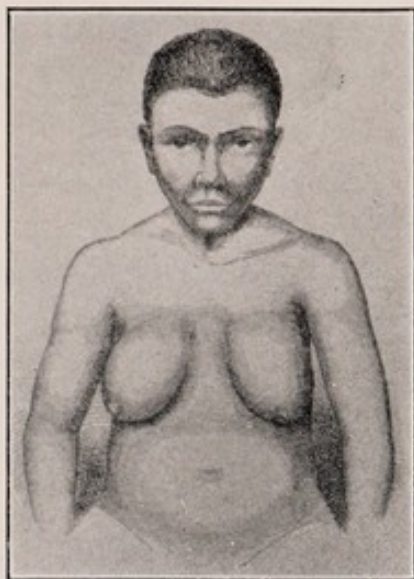


Fig. 22



Fig. 23

ADDISON'S DISEASE.

(Hypo-endocrinism.)

(Figs. 24 and 25.)

Addison's disease, characterized by brown pigmentation of the skin, results from the ablation of or interference with the function of the adrenal bodies by tuberculosis. This is illustrated in Figs. 24 and 25. The extract of the adrenal (total) is administered in the treatment of this condition, in accordance with the principles of "substitution therapy." Results have not been uniformly satisfactory, but cases are on record in which the pigmentation was diminished, the general condition improved, and the patient otherwise benefitted.



Fig. 24



Fig. 25

HYDROCEPHALUS (CHRONIC).

(Hypo- or Hyper-endocrinism?)

(Figs. 26 to 28.)

This anomaly has been studied recently in the light of endocrinology. The order is reversed, however, in this instance, the abnormal condition (Figs. 26 - 28) is supposed to be the cause of the disturbance of function of the gland involved (pituitary), rather than the result of perverted function of the gland. In a recent article (Jour. Am. Med. Asso., January 30, 1915, p. 395) Pollock says: "The disturbance of pituitary function resulting from hydrocephalus may manifest itself in two conditions, hyperpituitarism (Neurath, Cushing, Oppenheim), or in hypopituitarism. In view of the frequency of dyspituitarism in chronic hydrocephalus, the literature on the subject is astonishingly scarce."

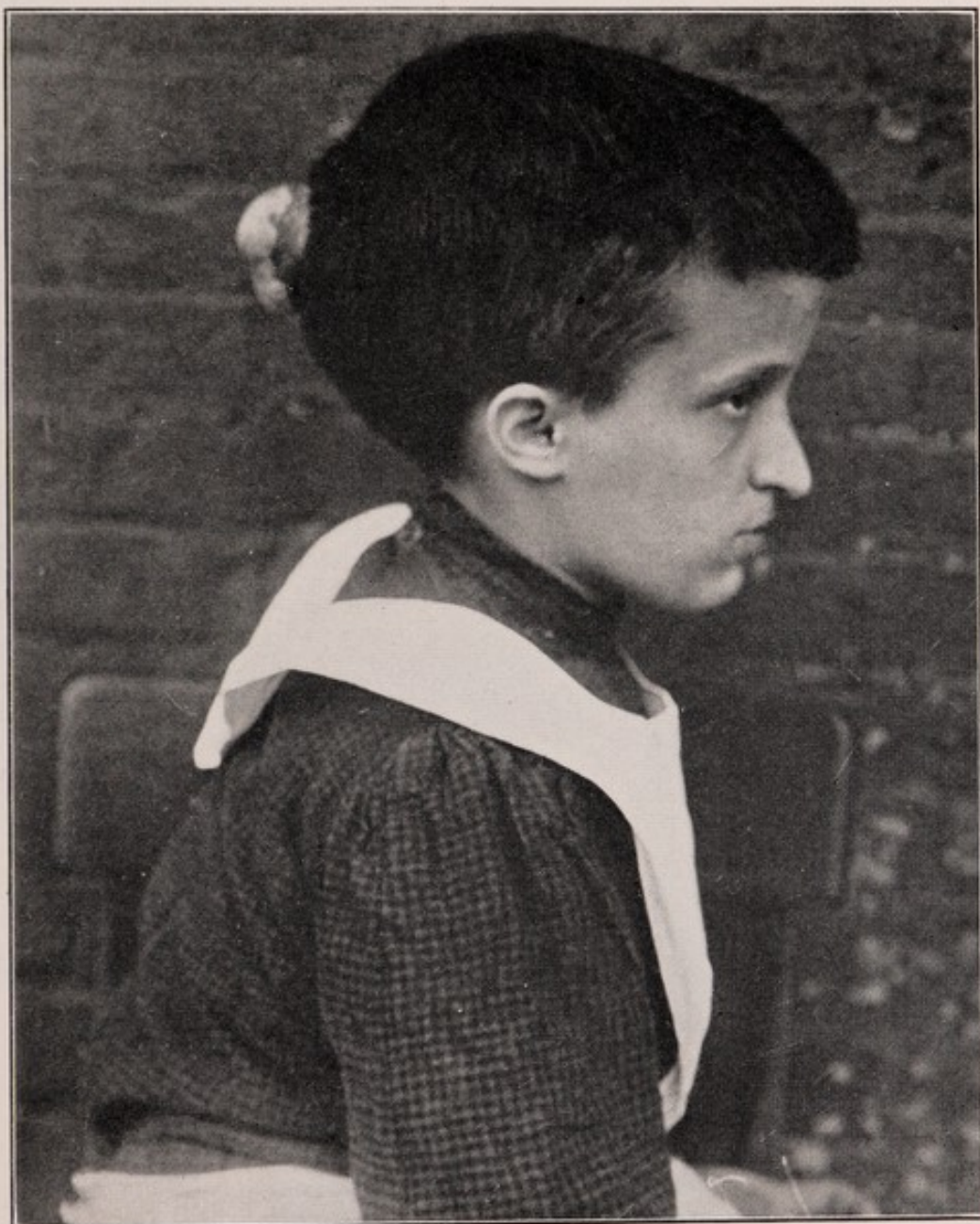


Fig. 26



Fig. 27



Fig. 28



Fig. 29

MICROCEPHALUS.

The opposite condition in point of size of the head — microcephaly — is shown in Fig. 29. These individuals, however, properly belong in the group of cretins, shown later.

HYPER- AND HYPO-THYROIDISM.

While the various other endocrinous glands—the thymus, the pituitary, the pineal, the ovary, the testis, the pancreas, and various other structures of the body—have been subjected to searching inquiry since attention was specifically directed to them, and while the interrelationship of these glands is accepted as a fact, perhaps the most far-reaching study has been devoted to the “monitor” of them all, the thyroid, “the keystone of the endocrinous system.” The literature concerning the thyroid and its functions and diseases is enormous, much of it, however, being contradictory and confusing.

Growing out of the interest which has been aroused by those who have given careful and painstaking study to this gland, there has arisen an empirical “thyroid-therapy” which is made to apply to a large proportion of human ailments. This has led to a considerable degree of skepticism along lines which might justly be given serious attention. With more or less vague ideas concerning the functions of this organ, naturally an indiscriminate application of organo-therapy in the treatment of disorders of the gland itself, and particularly of disorders of other structures by means of thyroid products, is conducive to perhaps more harm than good.



Fig. 30

HYPERTHYROIDISM.

(Figs. 30 and 31.)

The most familiar, and the most important, result of excessive thyroid secretion (according to the generally accepted views, which, however, are disputed by some), is exophthalmic goitre, "Graves' Disease," "Basedow's Disease," or, as I prefer to designate it, systemic goitre. Various other conditions, notably dementia praecox, have been attributed to hyperthyroid function.

In view of the fact that the exhibition of symptoms due to the introduction of thyroid toxins into the system characterizes the clinical picture in cases of exophthalmic goitre (Figs. 30 - 31), the term "systemic goitre" appears to me to be a fitting designation for this disorder, which is apparently of true autotoxic origin. This term is therefore employed as a synonym for hyperthyroidism and dysthyroidism—increased or perverted thyroid secretion affecting the entire body, with local enlargement of the thyroid gland as a matter of secondary importance.

According to the majority of modern investigators, more particularly operating surgeons, headed by Kocher, this disease is due to an increased activity of the thyroid or an abnormal function, or a combination of increased and perverted glandular function. Lane holds that the disease is the result of the absorption of effete products from the intestinal tract, in cases of chronic intestinal stasis. Others have interpreted the condition as a dysthyreosis, through iodine poisoning, the organ having lost the capacity of storing the iodine as iodothyronin, in the normal manner.

The manifestations of the malady are usually charged to the excessive functional activity of the gland. The onset in most patients is insidious, but it may be acute, especially after violent emotions, and it can usually be shown that a neurasthenic or hysterical stage has preceded the development of the symptoms.

Although there exist theories in plenty concerning the mutual relations between the thyroid and other glands with an internal secretion, such as the parathyroids and the suprarenals, the available data are still too unreliable and contradictory to justify a prolonged discussion of these teachings. A number of facts have also been ascertained, without definitely establishing the part played in goitre cases by the thymus, which during the time of its physiological development represents a vital organ of special significance for the nervous system. Hypertrophy of the thymus in these cases is probably a compensatory process, an excess of which may in turn involve dangers for the organism. The mutual relations between the thyroid, the pancreas and the suprarenals, have been explained as being of an inhibitory char-

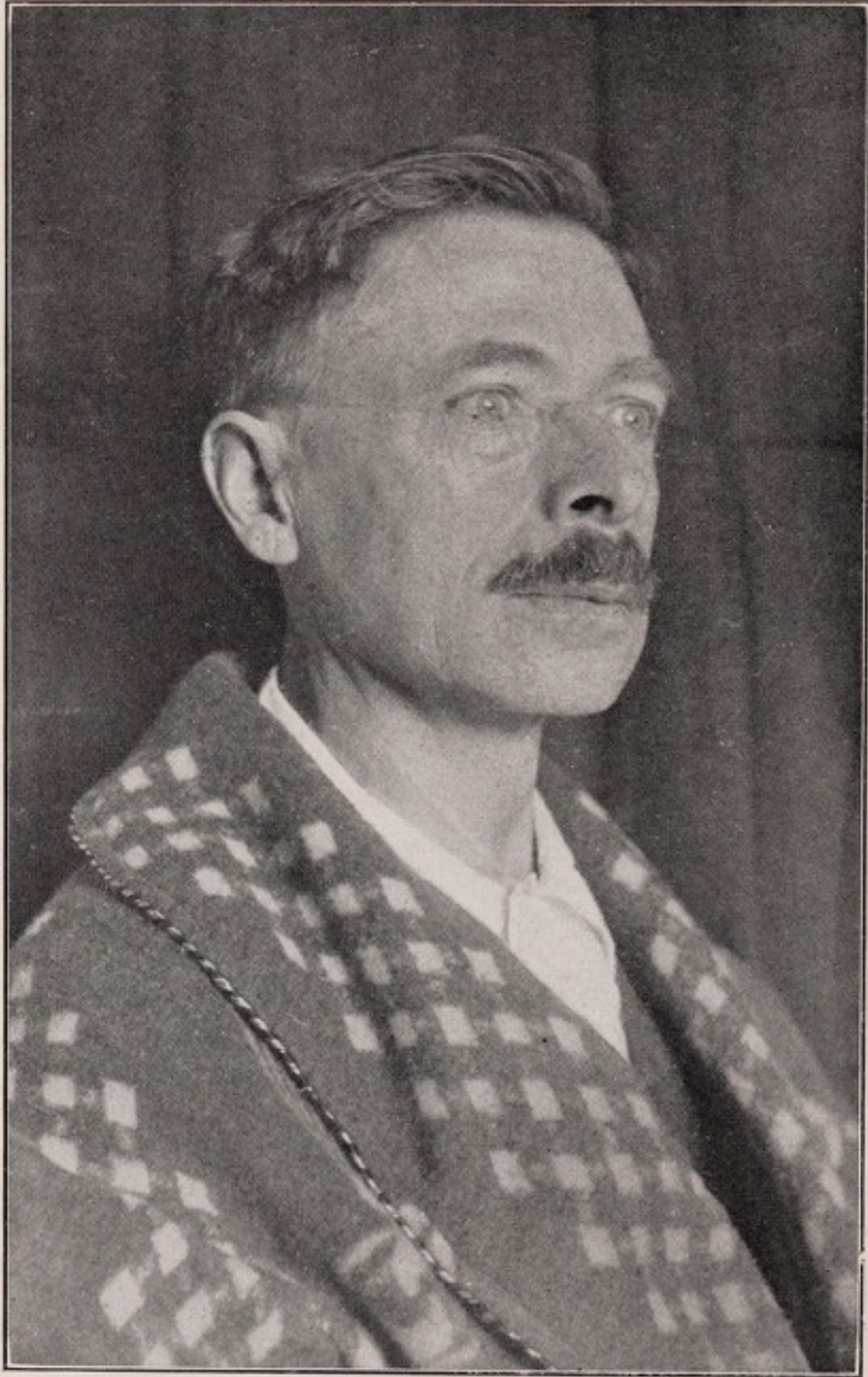


Fig. 31

acter between pancreas and thyroid, while the relation between the suprarenals and the thyroid has been interpreted as antagonistic by some, and as synergistic by others.

Through the better understanding of systemic goitre and the improved technic, the surgical treatment of the disease has been so greatly advanced in the last twenty years that after a long period of hesitancy operative intervention is now very widely recommended in these cases. There are many, however, who still prefer to employ the bio-chemical measures first, and, failing with these, to resort to operation. With the improved methods of inducing anesthesia, many cases can now be subjected to surgical treatment under general anesthesia which were formerly considered contra-indications to treatment by this method. Others prefer local anesthesia, a method which I have found eminently satisfactory in many instances.



Fig. 32



Fig. 33



Fig. 34

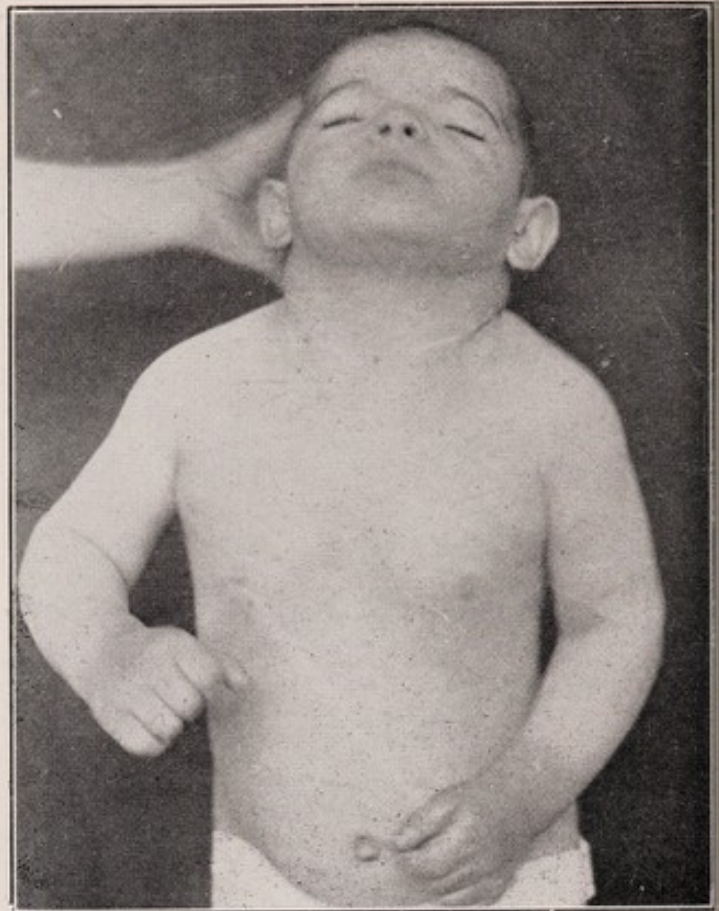


Fig. 35

HYPOTHYROIDISM.

(Figs. 32 to 62.)

According to Hertoghe there is hardly a symptom or symptom-complex which cannot be traced to the incomplete function of the thyroid gland. "If we knew exactly," he says, "the function of the thyroid gland we would no doubt be able to deduct immediately the symptom of a diminished or impoverished secretion, but we do not. However, we know something. We know that without the thyroid stimulus no cell, whatever it may be, can attain its morphological work, muscular, nervous, connective, glandular, or bone. The proof thereof is that a child born with congenital want or a child deprived completely by an operation of its thyroid gland does not grow, or grows very little. Give it a few doses of thyroid extract and it will begin to develop; stop the supply and immediately progress is stopped." "We know something more," he continues. "When a cell has done its duty for some time it decays, it is no longer desirable. It must be taken to pieces and eliminated through various channels—bowels, kidneys, lungs—especially under the form of urea. When thyroid supply is scarce the

carrying away of the cellular waste matter is slow and incomplete—mucin, fat, and other principles accumulate on the spot, and there form an infiltration and edema of a special kind—hard, non-depressible—and therefrom comes the name myxedema.” According to Hertoghe, infiltration is the constant lesion of thyroid deficiency. It may be slight, as in “benign hypothyroidism,” or “myxedema fruste,” or it may be marked, as in severe myxedema—but it is always there.

Summing up the matter, Hertoghe says: “When you encounter the association of one or more of the following symptoms: Trophic changes in hair, eyebrows, eyelashes, teeth, or gums; an habitual chilliness, biliary disturbances with lithiasis, dyspnea with asthmatic attacks; menorrhagia, recurring abortion, hemophilia; melancholia, depression, weariness of life, migraine, vertigo, sudden loss of consciousness, noises in the ears; somnolence, rheumatoid changes in the muscles, ligaments, or aponeuroses; nocturnal incontinence of urine, pollakiuria, loss of appetite and obstinate constipation—think of a possible deficiency of the thyroid secretion.”

In the treatment of hypothyroidism two methods, in line with endocrinology, have been employed; the administration of thyroid extract, and the transplantation, into the body of the subject, of healthy thyroid tissue from another person or animal. I began working along the line of transplantation in 1900, employing the gland from the human, when available, and from the sheep. Some of the cases are illustrated herewith.

Thyroid insufficiency in early life manifests itself in cretinism, illustrations of which are given in Figs. 32 - 44. Other forms of hypothyroidism are shown in Figs. 45-48.

While, as we have seen, many conditions are concerned with thyroid insufficiency, the commonest and most clearly understood of those seen in the adult is myxedema, of which the following pictures are illustrations. (Figs. 49 - 62.)

With the ages of empiricism back of us, and with the prompt sensationalizing of the theories and achievements of Brown-Séguard and his co-workers, it is not to be wondered that the scientific study of the internal secretions and their effects has been buffeted from the pillar of organotherapeutic charlatanry to the post of scientific skepticism. During the years immediately following Brown-Séguard's first efforts a few serious workers, refusing to be discouraged by the unsatisfactory publicity with which his pronouncements had been received, continued along the lines indicated, and the ranks of these increased year by year, until at the present time, such an army of investigators is in the field that there is reason to hope for a speedy clearing away of all that yet obscures the question of hormones and hormone therapy.



Fig. 36



Fig. 37



Fig. 38



Fig. 39



Fig. 40



Fig. 41

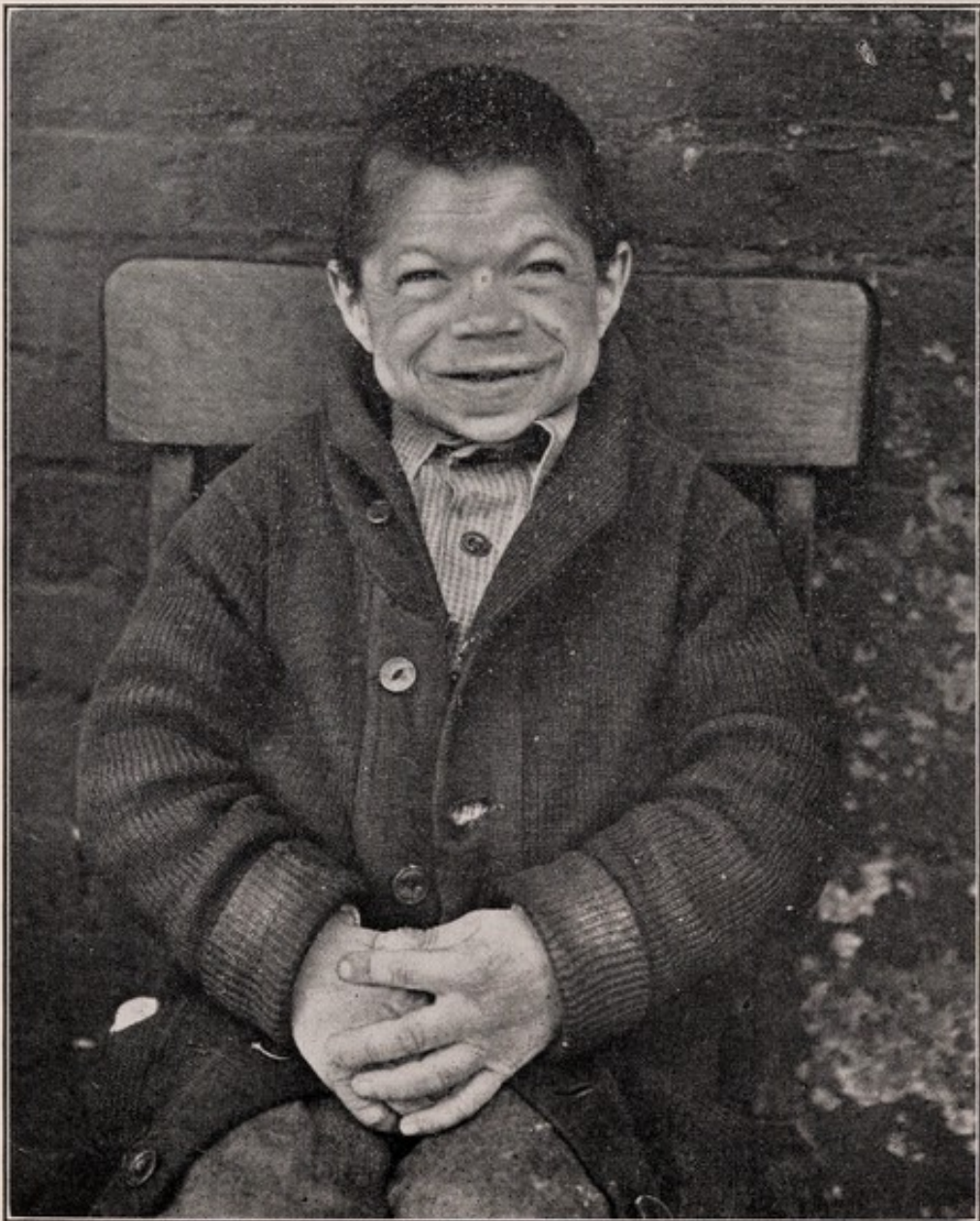


Fig. 42

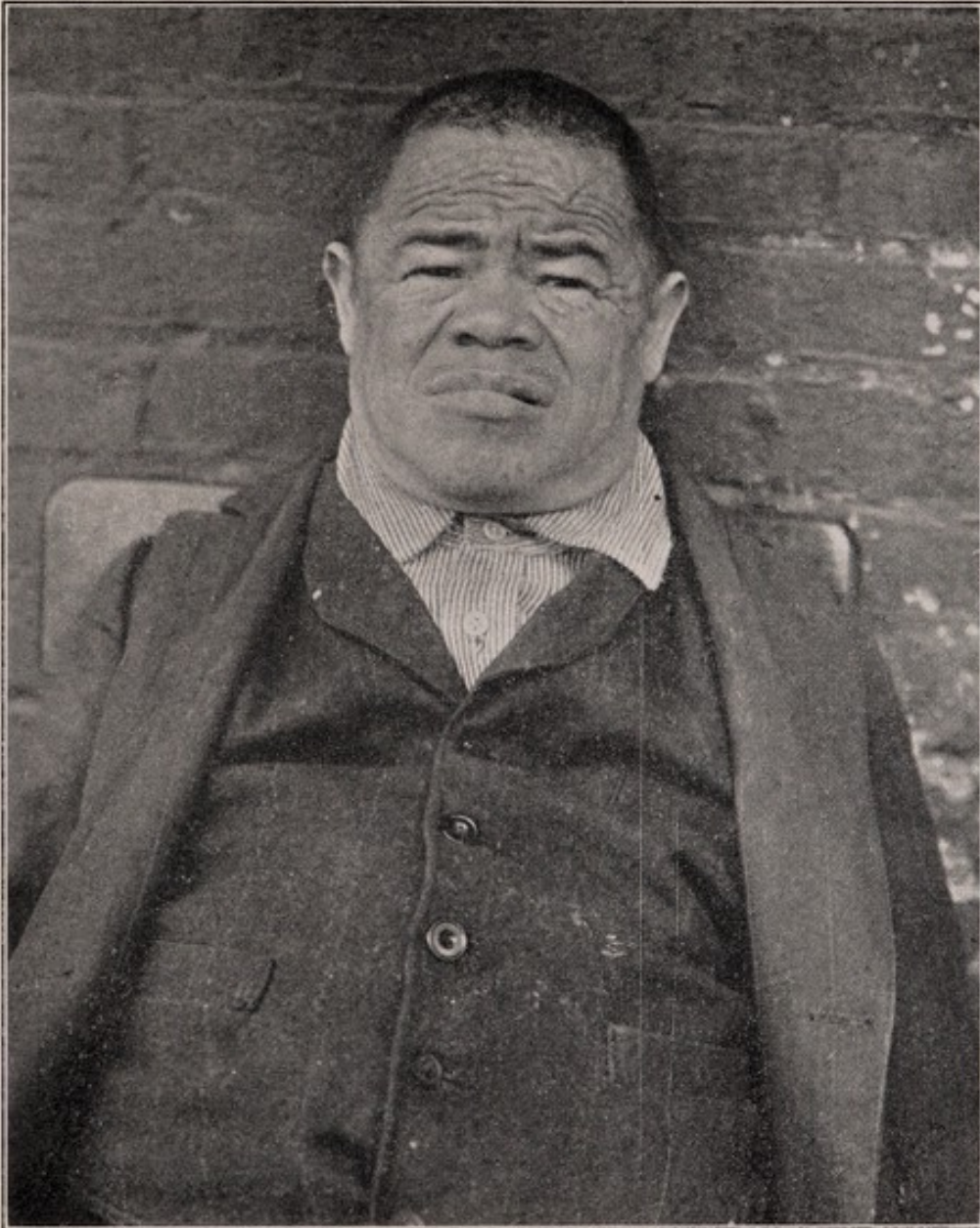


Fig. 43



Fig. 44



Fig. 45



Fig. 46

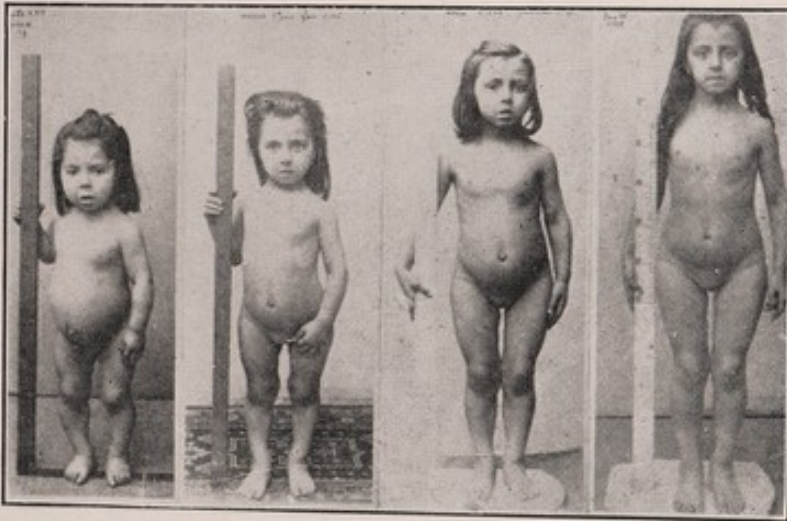


Fig. 47



Fig. 48



Fig. 49



Fig. 50



Fig. 51



Fig. 52



Fig. 53



Fig. 54



Fig. 55



Fig. 56



Fig. 57





Fig. 59



Fig. 60



Fig. 61



Fig. 62

TABLE OF ENDOCRINOUS GLANDS AND THE CONDITIONS
RESULTING FROM PERVERSION OF
FUNCTION*.

Gland	Function (Perversion of)	Condition result- ing from pervers- ion of function.	Remarks
Thyroid	Hypersecretion	Exophthalmic Goitre Dementia Pre- cox (?)	According to some observ- ers there are many other conditions, particularly of the nervous system, which result from hypo- thyroidism
	Hyposecretion	Myxedema Cretinism	
Parathyroid	Hyposecretion	Paralysis Agitans	
Adrenals	Hyposecretion	Addison's Disease	It is held by some that the adrenals are concerned in other conditions
Pituitary	Hypersecretion	Obesity	Various forms of "patho- logical obesity" come under this head, all pre- sumably associated with perverted function of the sex glands (gonads). It is not uniformly con- ceded that the disturb- ance of function is "hy- per," some holding the opposite.
		Acromegaly (Gigantism) (Macrosomia)	
	Hyposecretion	Dwarfism (?) (Microsomia)	
		Progressive Muscular Atrophy	
Hyper- or Hypo- Secretion (?)	Chronic Hy- drocephalus		
Pineal	Hyper- or Hypo- Secretion (?)	Obesity	Great divergence of opin- ion exists with refer- ence to the pineal gland. Some observers deny that it exerts any influ- ence on metabolism, and that it is of more impor- tance than a "vestigial remnant."
		Tallness in children	
		Cachexia	

Thymus	Hypersecretion	Osteomalacia Rickets "Idiotia thymica"	This gland is supposed to control calcium metabolism, and hence to be associated with conditions of the osseous system. In this regard, as in many others connected with endocrinology, marked differences of opinion exist
	Hyposecretion	Ossification (?) Arthritis deformans Exophthalmic Goitre	
Sex Glands (Gonads)	Hypersecretion	Osteomalacia Pseudo-osteomalacia Rickets Dementia precox (?)	It may be stated in a general way that the sex glands are so involved in perversion of function that it is at present impossible to clearly differentiate the influence exerted by them from that of others. In all forms of "pathological obesity", especially Adiposis dolorosa, of Dercum's disease, the gonads are supposed to be concerned, no matter what other endocrinous gland may be involved.
	Hyposecretion	Obesity Gynecomastia (?) Ossification (?) Arthritis deformans (?)	
Spleen	Hypersecretion	Pernicious Anemia Banti's disease Chronic jaundice Gaucher's disease	The functions of the spleen are still matters of dispute. Some of the recent investigations, it is claimed, tend to show that, despite older views to the contrary, the spleen may be brought within the category of endocrinous glands. Its role in this line is yet to be determined, but its influence in the causation of the diseases named is being made the subject of study.
Miscellaneous Tissues and Organs.			In the light of the findings of endocrinology, many other structures are being studied. The kidney substance, the intestine, the pancreas, etc., are among these.

*In the present state of knowledge concerning the endocrinous glands and the results of perversion of their functions, it is impossible to formulate a table of exact findings in all cases.

ILLUSTRATIONS.

OBESITY. — pp. 6 - 10.

- Fig. 1. Obesity of Childhood. Age and weight not given. (Gould and Pyle, "Anomalies and Curiosities of Medicine.")
- Fig. 2. Obesity of Childhood. Age, 13 months. Shown to give idea of relative age of Fig. 1. (Gould and Pyle.)
- Fig. 3. Obesity of Childhood. Age, 9 years; weight, 201 pounds. (Gould and Pyle.)
- Fig. 4. Obesity in a Dwarf. Height, 34 inches; weight, 309 pounds. (Gould and Pyle.)
- Fig. 5. Idiocy with Obesity. Randall's Island. Age, 40 years. "Idiopathic idiocy." Members of her family who visit her show tendency to adiposity, and are probably mentally deficient. (Bainbridge.)
- Fig. 6. "Adiposis dolorosa" (Dercum.)
- Fig. 7. Idiopathic Idiocy with Adiposity, localized in right upper arm. Age, 38 years. Randall's Island. (Bainbridge.)

EMACIATION. — p. 11.

- Fig. 8. "Living Skeleton" (Progressive muscular atrophy). "Museum Freak." (Gould and Pyle.)
- Fig. 9. "Living Skeleton" (Progressive Muscular Atrophy). Female, aged 18 years; weight, 27 pounds. (Gould and Pyle.)

OSSIFICATION. — p. 12.

- Fig. 10. "Ossified Man." (Gould and Pyle.)

OSTEOMALACIA. — pp. 12 and 13.

- Fig. 11. Osteomalacia, a pronounced form of rachitis. (Gould and Pyle.)

PROGERIA. — p. 13.

- Fig. 12. Progeria, or precocious old age. Girl, aged 8 years and 3 months. (Rand.)

HIRSUTIES. — pp. 14 - 18.

- Fig. 13. Masculine type of mental defective, with beard. Age, 59. Shaved monthly. Randall's Island. (Bainbridge.)
- Fig. 14. Masculine type of mental defective. Aged 39. Heavy growth of beard; shaved monthly. Randall's Island. (Bainbridge.)
- Fig. 15. Low-grade imbecile epileptic. Aged 50. Very long beard, shaved monthly. Features masculine; voice feminine. Randall's Island. (Bainbridge.)
- Fig. 16. Low-grade imbecile. Aged 30. Heavy growth beard, shaved monthly. Randall's Island. (Bainbridge.)
- Fig. 17. Group of Figs. 13 - 16.

DWARFS. — pp. 19 and 21.

- Fig. 18. "True dwarf." Age, 20; weight, 36 pounds; height, 22 inches. (Gould and Pyle.)
- Fig. 19. "Rachitic dwarfs." Height, 3 ft., 6 in. (Gould and Pyle.)
- Fig. 20. "True dwarf" and Giantess of same age. (Gould and Pyle.)

GIANTISM: ACROMEGALY. — pp. 20 - 22.

- Fig. 21. Irish Giant. (Gould and Pyle.)
- Fig. 21 - a. Acromegaly without giantism. (Gould and Pyle.)
- Fig. 21 - b. Progressive enlargement of hands in Acromegaly. (Gould and Pyle.)

GYNECOMASTIA. — pp. 22 and 23.

- Fig. 22. Gynecomastia. Man with fully developed breasts, which hung down like those of a nursing woman. (Gould and Pyle.)
- Fig. 23. Idiopathic Idiocy, with marked enlargement of breasts and general adiposity. Abdominal fat was so annoying to him that it was removed. Note absence of umbilicus, which was removed in the lipectomy operation. Aged 48. Sexual pervert. Randall's Island. (Bainbridge.)

ADDISON'S DISEASE. — p. 24.

- Fig. 24. Uniform pigmentation of face. (Addison.)
- Fig. 25. General pigmentation, with areas of white. (Addison.)

HYDROCEPHALUS—Macroc-type. — p. 24 - 26.

- Fig. 26. Hydrocephalus, with meningocele from occipital fossa, about size of base-ball. Fronto-occipital circumference, 152 cm. Female, aged 16. Randall's Island. (Bainbridge.)
- Fig. 27. Group of hydrocephalic defectives. Randall's Island. (Bainbridge.)
- Fig. 28. Chronic Hydrocephalus (rare) in adult. (Gould and Pyle.)

MICROCEPHALUS. — p. 27.

- Fig. 29. Microcephalics, brother and sister. Girl (to left) aged 18. Boy (to right), aged 9. Marked improvement in mentality under treatment with pituitary extract. (Bainbridge.)

HYPERTHYROIDISM. — pp. 28 and 29 - 31.

- Fig. 30. Systemic hyperthyroidism, with goitre; of exophthalmic and cardiac type. (Bainbridge.)
- Fig. 31. Systemic hyperthyroidism with no apparent goitre, but with exophthalmos. (Bainbridge.)

HYPOTHYROIDISM. — pp. 28, 31 - 46.

- Fig. 32. "Congenital myxedema." Child sent to Presbyterian Hosp. for operation upon tongue. (1894.)
- Fig. 33. Negro cretin. Randall's Island. (Bainbridge.)
- Fig. 34. Cretinism with goitre. Before operation. Female. Randall's Island. (Bainbridge.)
- Fig. 35. Fig 34, after operation.
- Fig. 36. Cretinism with goitre. Randall's Island. (Bainbridge.)
- Fig. 37. Group of cretins of different ages. Randall's Island. (Bainbridge.)

- Fig. 38. Group of "Mongolian Idiocy." Ages, from left to right, 17, 19 and 11 years. Thought by some to be found in children born at end of long line of normal children, generally at end of child-bearing period, of normal parents; also, failure of some internal secretion in mother. (Bainbridge.)
- Fig. 39. Also shown in Fig. 38. Shows hyperextensibility of joints. "Great contortionist." Randall's Island.
- Fig. 40. Same as Fig. 39. Shows marked furrowing of tongue usually found in idiots of so-called Mongolian type.
- Fig. 41. Cretin, aged 37. Condition in 1907, before treatment by implantation of calf's thyroid into abdomen, and human thyroid into suprarenal region. (Incidentally, at this operation, a large stone was found in the kidney, and removed). Note absence of hair. Randall's Island. (Bainbridge.)
- Fig. 42. Same as Fig. 41, April, 1915. Note suit of hair. Improved considerably under treatment.
- Fig. 43. Probably oldest living cretin. Aged 41. Had one brother of same type, who died at 32. Randall's Island. (Bainbridge.)
- Fig. 44. Same as Fig. 43, in good humor.
- Fig. 45. Hypothyroidic alopecia. Influence of thyroid feeding. (Hertoghe.)
- Fig. 46. Mild myxedema, with loss of eyebrows. (Hertoghe.)
- Fig. 47. Hereditary paludism. First figure to left shows arrest of growth, age 8 years, height 2 ft., 10 in. Other figures show influence of thyroid feeding after 1, 2 and 5 years. (Hertoghe.)
- Fig. 48. Same as Fig. 47, 14 years after treatment. (Hertoghe.)
- Fig. 49. Mother of girl shown in Figs. 47 and 48. Mild myxedema. (Hertoghe.)
- Fig. 50. Mild myxedema. Aged 25. (1882.) (Bainbridge.)
- Fig. 51. Same as Fig. 50, showing condition in 1908.
- Fig. 52. Same as Figs. 50 and 51, showing condition in May, 1914.
- Fig. 53. Severe myxedema, before and after treatment. (Hertoghe.)
- Fig. 54. Severe myxedema, before and after treatment. (Hertoghe.)
- Fig. 55. Severe myxedema, before and after treatment. (Hertoghe.)
- Fig. 56. Severe myxedema, with predominance of rheumatoid pains. Before and after treatment. (Hertoghe.)
- Fig. 57. Severe myxedema, before and after treatment. (Hertoghe.)
- Fig. 58. Severe myxedema before treatment. (Hertoghe.)
- Fig. 60. Same as Fig. 59, after two months' treatment. (Hertoghe.)
- Fig. 61. Severe myxedema. From left to right, before treatment, after two months' treatment, after fourteen months' treatment. (Hertoghe.)
- Fig. 62. Severe myxedema, cachectic stage, three days before death. (Hertoghe.)

