

nor laughs. It is absolutely apathetic, sits quietly without manifesting any special wants. It may, however, show signs of hunger or thirst, either by crying like an infant or by grunts or inarticulate sounds. In a higher grade, a few words may be spoken, there is recognition of parents and familiar faces and even a show of affection for them, but beyond the limited vocabulary no progress can be made, even the alphabet being beyond them. Still higher grades may speak fairly well, be free, though slow and deliberate, in their movements, etc., but fail to develop thereafter, even if they attain old age, which is not often the case.

The brothers Wenzel have divided these cases into three classes: the *cretins*, who are unable to speak, and lead a purely vegetative life; the *semi-cretins*, who are simple-minded, but whose language is limited and imperfect; and the *cretinoids*, who are endowed with some intelligence, but show the physical signs of cretinism. There is another type, the *mongolian*, called thus because of their slanting eyes, which closely resembles the cretin of a higher order, but this type shows more intelligence and seldom yields to the effects of thyroid preparations.

The thyroid, in about two-thirds of the cases, is more or less atrophied, to such a degree in some that it cannot be detected by palpation. In the remaining third, and usually in the endemic cases, there exists a more or less developed (sometimes voluminous) goiter.

ETIOLOGY.—It becomes necessary in this connection to distinguish between the two general classes, endemic and sporadic cretinism.

Endemic cretinism, often a family disease, and observed in a number of cases in special localities, is believed to be due to some chemical substance or micro-organism peculiar to the waters available in those regions.

This type has been connected with special localities by proofs from various directions. Not only is cretinism common in these regions, but normal individuals may, on moving to them, have cretinic children therein, and normal children in healthy regions. Again, animals from the latter were found to develop goiters (the preliminary cause of endemic cretinism) in the contaminating districts by drinking their water, while this

water carried afar to healthy localities and given to dogs as sole beverage also caused goiter in these animals. Whether it is a mineral salt, a vegetable mold or some other pathogenic micro-organism is not established, but for the time being the germ theory seems to prevail.

The question of heredity in these cases is a debated one. We have seen under "hypothyroidia" that syphilis and alcoholism tend to leave their imprint upon the thyroids of descendants. Some oppose this view in respect to cretinism on the ground that the positive signs of cretinism only appear when the child is weaned, and contaminating water is given to it. But this is obviously wrong: Cretinism can readily be detected in a child one month old and earlier by observers who are thoroughly familiar with the morbid effects of hypothyroidia. The latter condition in the mother is also well known to result in hypothyroidia in her offspring—a fact which brings us back to any maternal defect inherited, such as hypothyroidia, syphilis, alcoholism, etc., that may be present as the origin of the hypothyroidia in the child. In other words, there is at present no sound foundation for antagonism to the prevailing view that endemic cretinism may be congenital in a certain proportion of cases.

Sporadic cretinism, which has also been termed "cretinoid," or "*myxædematous, idiocy*," and "*cretinoid pachydermia*" occurs in any country, in localities that are entirely free from cretinism, and in healthy families. It is mainly due to some lesion of the thyroid caused by an acute febrile disease or some intoxication capable of inhibiting or arresting its functions, either before or after birth.

How a general infection can produce such lesions in the thyroid is admittedly unknown. From my viewpoint, it finds its explanation in an autodigestive process similar to that which occurs in the pancreas under certain conditions. As previously stated, I have attributed to the thyroid secretion properties similar to those of Wright's opsonins, a view recently sustained by Marbé and Stepanoff, at the Pasteur Institute. The antitoxic and antigerm constituents of the blood circulating in the thyroid (and parathyroids, which may also be the seat of similar lesions), it is obvious that undue accumulation of thyroid secretion in the

organ itself will oversensitize its own parenchyma or its vascular elements or both, and render them vulnerable to proteolysis—along with any germ or toxin that may be present in the organ. The autodigested areas are replaced by fibrous tissue, and a process of cirrhotic atrophy is started which sooner or later annuls the functions of the organ.

The diseases which have shown themselves to be the most frequent causes of sporadic cretinism are typhoid fever, scarlatina, pneumonia, and pertussis—the identical series which proves most prolific in the genesis of the infantile encephalopathies, another source of idiocy, but in which the cerebral lesions are the direct pathogenic factors.

PATHOLOGY.—The end lesions are the same in both forms. In the endemic form there is a marked proliferation and overgrowth of interstitial tissue or connective tissue, causing both enlargement of the gland—goiter—and obliteration of the glandular tissue. Some glandular tissue usually persists; even this remnant, however, shows evidences of degenerative change.

The symptomatology of both forms indicates clearly, we have seen, that deficient oxidation, metabolism, and nutrition underlie the resulting general physical phenomena. This applies as well to the mental phenomena, symmetrical arrest of development affecting more or less all the elements of the brain. There are occasionally found localized lesions of the nature of infantile cerebropathies, porencephaly, etc., but it is probable that these are concomitant changes rather than components of the typical picture of cretinism *per se*. Briefly, we are dealing with arrested nutrition and development of the brain as a result of the absence of the secretion which sustains these fundamental processes.

TREATMENT.—Before the introduction of thyroid gland in the treatment of this distressing condition, there was practically nothing to be done. While its use must be continued, relapse (excepting the body growth) occurring invariably without it, though, as a rule, with much less intensity, the fact remains that the changes produced in the child, particularly in sporadic cases, are truly marvelous. As early development of the disease inhibits the mental development accordingly, the later in childhood it appears, the better are the results of treatment, in so far

as the intelligence is concerned. The physical restoration is not materially influenced by the age at which the disease first appeared. Children grow with surprising rapidity in some instances, over one inch per month in some cases, until the normal stature of the corresponding age is reached. The brain responds more slowly; but considerable intelligence is gained, though it does not reach, as a rule, that of normal children. They learn slowly and develop only very gradually their vocabulary. They should be gently assisted in this direction.

When the thyroid treatment is instituted the case should be carefully watched, as the tolerance varies greatly in different children. They should be kept from any violent exercise lest heart-failure occur. Another important reason for this precaution is the fact that the growth of the skeleton is so rapid that the bones tend to soften, and, therefore, to yield and bend. The tibia and fibula are especially exposed; braces should be applied to offset this tendency if it shows itself, until the normal height of a child of a corresponding age has been attained. Syrup of calcium lactophosphate of the U. S. P., one teaspoonful or less, according to the age, is a useful adjuvant to thyroid gland in this connection. This is accounted for in the opinion of Parhon and Papinian¹¹ and others, based on many published facts, that the thyroid gland plays an important rôle in the assimilation of calcium. Thymus gland 5 grains (0.3 Gm.) *t. i. d.* is also useful.

Large doses are not only dangerous, but they inhibit the beneficial process. Again, it must be remembered that the thyroid active principle is cumulative in the sense that the organism will utilize a certain quantity—which varies with each case—and that any excess may prove toxic. This stage may be reached early in one instance and late in another. I have seen it produced in three weeks with 2-grain (0.132 Gm.) doses; conversely, in a case reported by Freund in a girl of 14 years, 6 grains (0.396 Gm.) daily in divided doses caused a sudden rise of temperature to 104° F., a pulse of 160, rapid breathing, and death the next day, though she had been taking the same agent nineteen months. The *danger signals* are rapid pulse, vertigo, general weakness, pains in the back and limbs, syncope, and, if

¹¹ Parhon and Papinian: *România medicala*, 1904, cited in "Sécrétions Internes," p. 17, 1909.

the intoxication be severe, nausea and vomiting, a marked rise of temperature, and collapse. When any untoward effect occurs, cessation of the remedy a few days suffices. They are more likely to appear when the preparation used is old, a fact which suggests that it may have undergone putrefactive changes when long kept.

An infant can be given $\frac{1}{2}$ grain (0.033 Gm.) daily of desiccated thyroid, and a child of 2 years, twice daily, and older children thrice daily, or 1 grain (0.066 Gm.) can be given at dinner and another on retiring. I have never seen such doses produce untoward effects, the recumbent position after the second dose, as urged by Murray, preventing them. When it is necessary to increase the dose, the patient should be seen frequently. As much as 5 grains (0.33 Gm.) have been given three times daily with safety; but it must be remembered that the preparations now available are better and more efficacious. The preparation I now use is Burroughs, Wellcome & Co.'s standardized desiccated gland substance (in tabloids), which contains 0.2 per cent. of iodine in organic combination. Cretins usually stand larger doses than others. A good guide in them is the temperature, which tends to rise to normal; as a rule, the dose that will do this suffices to bring about the desired results. When this is attained, 1 grain (0.066 Gm.) on retiring suffices to prevent recurrence. But it must not be neglected; otherwise, the disease will certainly return.

The younger the patient, the more marked the improvement, as a rule. In adult cretins, the results are meager if any at all are obtained. The improvement is much more marked in sporadic than in endemic cases, owing probably to the fact that up to the onset of the causative disease physical and mental growth had proceeded normally. In the Mongolian type, the thyroid treatment is useless.

Grafting of thyroid tissue to render the constant use of thyroid preparations unnecessary has been tried by various investigators. It is only in recent years, however, that a promising method has been introduced by Christiani,¹² of Geneva. The conditions are that only normal and living tissues be used; that the grafts be small (about the size of a grain of wheat), but

¹² Christiani: *Semaine médicale*, March 16, 1904.



Fig. 1

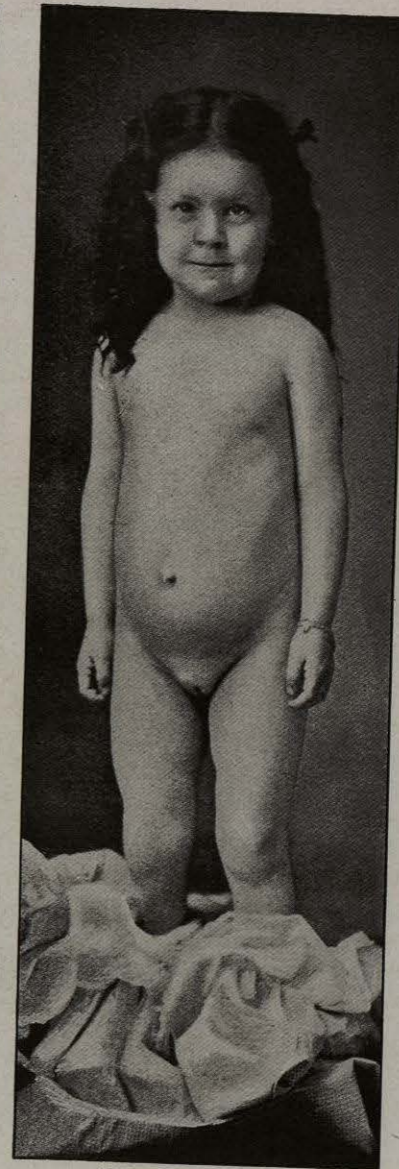


Fig. 2

THYROID EXTRACT IN CRETINISM. [J. B. McGee.]

Fig. 1. Cretinic idiot 7 years old when thyroid treatment was begun. Had ceased to develop when 3 years old.

Fig. 2. Changes after one year's treatment. Growth, $6\frac{1}{2}$ inches.

[*Cleveland Medical Gazette.*]

very numerous; that they be inserted in very vascular subcutaneous cellular tissue, and that only human thyroid be employed. This makes it possible to obtain small grafts from a removed goiter containing areas of normal tissue, and to transplant them into the cretinous subject. The tissue can be kept alive an hour in physiological saline solution. A very sharp instrument should be used to cut the grafts to avoid crushing them. They are then introduced *in situ*, where they gain a perfect foothold, becoming perfect thyroid parenchyma. More recently, Charrin and Christiani¹³ obtained good results with sheep's thyroid. Six months after the operation, the patient (a case of operative myxœdema) became pregnant, and it was found that each graft became enlarged, in keeping with the physiological process which occurs normally in the gland proper under similar circumstances. Christiani¹⁴ reported distinct improvement in 60 per cent. of his cases, which included myxœdema, cretinism, dwarfism, etc., remarkable results in 34 per cent., and no result in 6 per cent. The most striking results were in the various types of cretinism.

MYXŒDEMATOUS INFANTILISM.

This disorder, first attributed to the thyroid by Brissaud, resembles cretinism very closely, but its retention as a separate class is warranted by the fact that the arrest of development manifests itself mainly by the persistence of the characteristics of childhood, physical and mental, without the evidences of true idiocy, and often without dwarfism. The thyroid apparatus, either through inadequate development of congenital origin, organic lesions, especially sclerosis, acquired in the course of acute infections during infancy, or from some other cause, is unable to supply enough of its secretion to subserve the needs of both metabolism and growth (which involves an excess of metabolic activity), and the latter ceases, while normal metabolism, enough to sustain the vital process, continues.

SYMPTOMATOLOGY AND PATHOGENESIS.—The worst cases, in which myxœdema predominates, are virtually instances of

¹³ Charrin and Christiani: Le bulletin médical, July 11, 1906.

¹⁴ Christiani: Bull. de l'Acad. de méd., vol. lviii, 1907.

cretinism of a mild type. The patient is short, thick set, and obese, though child-like in shape, and may look old for his age. The face appears bloated, rounded, pale, and wax-like, a reddish patch being sometimes present below the cheek bones. The nose squatty and pugged, and the mouth large; the latter is usually open,—a fact accounted for by the almost invariable presence of adenoids, hypertrophy, and infiltration of the nasal mucosa and tonsils. The tongue, as in the cretin, may be thickened and the lingual tonsil likewise, rendering speech thick and difficult. The hair may be profuse, though coarse and lusterless, but about the eighteenth year it begins to fall in patches, leading, in most instances, to alopecia. In most cases hair fails to grow on other parts of the body. The skin is tense, owing to infiltration, and is also dry, because of deficient action of the cutaneous glands, and it feels rough and scaly to the touch. Pruritus is often complained of.

The teeth remain infantile, as a rule, and decay early. The abdomen is unusually prominent and hard in all cases, owing, mainly, to the stubborn constipation which causes retention of gas and fæces, the latter being only voided in some cases by engorgement and to relaxation of the abdominal muscle. The constipation is also mainly due to the loss of tone of the intestinal muscular fibers and the paucity of succus entericus. Enuresis is commonly observed. Although the respiration is apparently normal there is deficient oxidation; the extremities are cold and are readily affected with chilblains in cold weather. The face and extremities may even be cyanotic and the patient complain of constantly feeling cold. Actual hypothermia is a common feature of these cases. The part played by the thyroid in this phenomenon is well shown by the fact that Beebe¹⁵ found that "by the administration of thyroid to a cretin or patient with myxœdema it is possible to increase the absorption of oxygen from 20 to 75 per cent."

The difference between this form and true cretinism lies, as stated, in the fact that idiocy does not occur. The child may not be bright or even normally intelligent, having been slow to talk and shown deficiency at school, particularly in spelling, grammar, and arithmetic, but it is, nevertheless, quite able to

¹⁵ Beebe: *Loc. cit.*, p. 659.

hold its own for all ordinary needs; the face, in fact, unlike that of the cretin, bears an expression of intelligence. Yet the intellect retains the characteristics of childhood, both as to ideas, judgment, and emotions, a patient of twenty years, for example, preferring the company of children below ten to that of young men of his own age. These patients may show a proclivity to lie, steal, start fires, etc., especially when under the evil influence of designing normal individuals. Any unlawful act they may commit is due, in most cases, more to lack of judgment and inability to resist suggestion and a desire to please others than to an inherent proclivity to crime. Others are excitable, turbulent, and rough, and frequently break anything that is at all fragile; here, again, the element of willful harm is absent, muscular tremor and inability to prevent movements of the hands or fingers—as in athetosis—being the underlying cause of the defect.

The heart is excitable, a slight emotion sufficing to cause violent "palpitations" and tachycardia. This is mainly due to a deficiency of adrenal secretion. Dilatation of the heart from the same cause is often witnessed. The veins also show a marked tendency to dilate, the veins of the extremities and the hæmorrhoidal veins particularly. Varicocele may also exist. In a case seen through the kindness of Dr. W. Egbert Robertson, a sprig of thick veins spread upward over the mons veneris and coincided with undeveloped testicles and total absence of hair over the genitalia, in a young man of twenty years. Hæmophilia is frequently noted, an indirect result also of the hypothyroidia, since thyroid gland given orally counteracts hæmophilia by increasing the coagulation time. Epistaxis, menorrhagia, and metrorrhagia are also observed in some cases, the two latter phenomena where menstruation has developed at all, which is often not the case, coinciding with non-development of the breasts and pubic hair. The penis and testicles often remain rudimentary even when the male reaches full adult age, and his general shape and high-pitched voice recalling those of a woman.

In a still higher type of infantilism the signs of myxœdema are hardly discernible. The growth may even exceed that of the average individual. Such cases are usually plump and even

portly; as in the preceding form, the abdomen tends to be large, but the limbs are well rounded, recalling those of a woman, with fair skin, a high-pitched, or infantile, voice to complete the resemblance. The face, axillæ, and pubis are free of hair; the penis and testicles small and rudimentary. Mentally "he is simply an overgrown child," wrote Meige,¹⁶ who gave us a close analysis of these cases. "These children, who should long before have reached the reasoning period of their lives, play with toys, laugh at a childish prank, cry for practically nothing, become angry as readily, are subject to ridiculous frights, and call their mamma under the influence of the least emotion." In the average case, however, this truly infantile type—recalling the behavior of a child of but two or three years—is better exemplified by one of seven or eight years, though he be perhaps actually beyond his twentieth year.

The feminine attributes are sometimes very marked in the male, the breasts, thighs, and general conformation resembling closely those of the female, constituting the "feminine" type. In the female, in whom infantilism occurs less frequently, the body preserves the attributes of childhood, *i.e.*, it fails to undergo the normal changes of puberty. Though tall, perhaps, the body shows no development on sexual lines: the breasts remain small and flat, no hair grows in the axillæ or over the pubis, the trunk remains cylindrical, and the hips and nates flat. The uterus and its adnexa also fail to develop, and menstruation fails to appear. Some cases tend even toward the male sex, constituting "masculinism," the voice, the physical outline, assuming a masculine type.

DIAGNOSIS.—From this type, which belongs essentially to the domain of the thyro-parathyroid apparatus, must be distinguished several types which do not.

Lorain Type of Infantilism.—In a type described by Lorain, in 1870, the dwarfism is symmetrical in the sense that the ultimate products, are symmetrical, miniature men—this form being practically always observed in the male. No myxœdematous symptoms are present; the genitalia are usually normal, though the pubic and axillary hair is wanting, and notwithstanding their diminutive stature and their slender physique,

¹⁶ Meige: *Revue Intern. de Méd. et de Chir.*, Mar. 25, 1896.

their facial appearance and expression, and their intelligence are usually quite up to the average. They depart in no way from their fully developed fellow-men, in fact, except in the stature. As shown mainly by Meige,¹⁷ this type is not due to thyroid insufficiency, but to anangioplasia, *i.e.*, defective development of the arteries and premature ossification. It is usually ascribed to parental hereditary syphilis, tuberculosis, alcoholism, and other debilitating disorders. Thyroid preparations in this form are of no value.

Mongolian Infantilism.—This type is characterized by Mongolian features, and particularly the slanting eyes. These features occur at birth, and are not traceable to syphilis, tuberculosis, alcoholism, etc., as in the Lorain type, but rather to prolonged deliveries—which account in some cases, at least, for the flat skull or bulging forehead—or to strong mental emotions during pregnancy. They are not morose or torpid like the myxœdematous cases and are usually amiable and well behaved. Curiously enough, all show a marked predilection for music and signs of unusual development of the musical sense. The tongue is usually quite thick and heavy, and the hands square and flat, the latter accounting for the clumsiness which characterizes all these cases. They usually suffer from some chronic respiratory trouble, and are apt to die early of some intercurrent infection. Their undeveloped size, their Mongolian facies, the bulging forehead, and their feeble-mindedness render the recognition of these cases quite easy. Thyroid preparations are of no avail.

Achondroplasia, or Fatal Rickets.—This type of dwarf, unlike the myxœdematous type, does not show mental deficiency, but many of the characteristics of cretinism: the relatively large head, the saddle nose, the short and bowed limbs, the prominent abdomen, and the marked lordosis. But the arms and legs are, unlike the other types, which all show some degree of symmetry, entirely too short for the body, the finger-tips never reaching the level of the hips. Again, the long bones are usually bent and deformed. The skull is unduly developed and is out of proportion with the face, which is then made to appear small. The eyes, lids, and tongue may resemble greatly those of the cretin, but the hair is normal and usually abundant, and the

¹⁷ Meige and Allard: *Nouvelle Iconog. de la Salpêtrière*, No. 2, 1898.