

of enuresis in a 9-year-old boy in which he tried removal of the adenoids. The operation made the boy much worse, however, and, believing that the removal of the adenoids deprived the boy of a necessary internal secretion, he then gave him thyroid extract, $\frac{1}{2}$ grain (0.033 Gm.) twice daily. The result was instantaneous and complete, the boy no further wetting the bed. Twenty-four other cases were thus treated. Only one of these proved rebellious to the treatment. The essential point to remember is that thyroid gland is useful mainly in cases in which there exists hypothyroidia, some sign of which can always be discerned if it is at all present. Firth obtained marked improvement in 16 out of 28 cases with small doses, especially when the enuresis had persisted since birth.

SKIN DISEASES.—A prolonged trial of thyroid preparation in many diseases of the skin has led dermatologists to the conclusion that they were indicated in disorders due to deficient metabolism. As stated by Winfield, these include the erythematobulbous type, which includes *dermatitis herpetiformis*, and the psoro-eczematous type, to which belong *prurigo*, *psoriasis*, and *chronic eczema*.

This is explained by the action of thyroid products on oxidation and metabolism, as is well shown in the effects noted by Don: 1. Increased nutrition of the skin; hence its probable remedial action in ichthyotic conditions: an effect produced without any necessary abnormal perspiration. 2. Increased action of the cutaneous glands, accelerating excretion of waste-products, thus keeping the surface in a supple condition. 3. Regrowth of hair, as shown in myxœdema and some cases of general alopecia. 4. Increased activity of the epidermal layers, causing desquamation of unhealthy epidermis and reproduction of a new covering, as observed in ichthyosis, psoriasis, dry chronic eczema, and at times in myxœdema and cretinism.

Eason⁵² reported several consecutive cases of *eczema in young children* successfully treated by thyroid. In the first case, 14 months old, the baby had suffered from eczema of the face for nearly a year. This had been entirely resistant to the usual applications and internal treatment; nor was hospital

⁵² Eason: *Scottish Med. and Surg. Jour.*, May, 1908.
^{52a} Firth: *London Lancet*, Dec. 2, 1911.

treatment more efficacious. Two and a half grains (0.165 Gm.) of a thyroid tablet was given daily. In a little more than one month the child was entirely well. His cure persisted for nearly a month, when the disease showed a tendency to recur. The second course of thyroid was followed by a permanent cure. The 4 other cases gave similar results. Moussous⁵³ observed 2 cases of eczematous seborrhœa successfully treated with thyroid. In the first case the scalp was normal at the end of two weeks; in the second in one month. Complete cure occurred in both cases, and has persisted.

In *psoriasis* thyroid is harmful when the eruption is developing, but it sometimes acts with surprising efficacy in fully developed cases. The untoward effects observed by dermatologists, however, are in great part due to the fact that they use too large doses. These, as previously stated, enhance metabolism violently and increase the waste-products in the blood and therefore the cutaneous disorder.

Pedrazzini⁵⁴ observed 5 cases of *scleroderma*, in 4 of which the thyroid was small and atrophied, while in the other the thyroid was large and hard. Thyroid treatment gave good results in the two in which it was applied, commencing with small and progressive doses. None of the patients presented signs of nervous changes suggesting atrophic origin, but everything confirmed the assumption of some connection between the cutaneous affection and the thyroid gland.

Thyroid has been tried in *lupus* by a number of observers. Though the results were contradictory, the bulk of the evidence indicates that it is worthy of more extensive trial. Owing to its influence on oxidation it enhances the nutrition of the skin and thus antagonizes the destructive process while promoting that of repair. As full doses have to be used during a prolonged period, the patient should be carefully watched. Thyroid has been tried in *leprosy*, but the results were not encouraging, though the remedy was pushed as far as safety would allow.

In a case of *hypertrophic rosacea* which has resisted all forms of treatment, Isadore Dyer, of New Orleans, used thyroid with, for local use, a salve containing resorcin ᠑j ; rose water

⁵³ Moussous: *Archives de méd. des enfants*, Mar., 1908.
⁵⁴ Pedrazzini: *Gaz. degli Ospedali*, Aug. 1, 1909.

3iv; lanolin ad 3vj. After two months there was decided improvement, the skin being soft and normal to the touch and the color greatly improved. The patient was discharged cured after three months of thyroid medication.

HÆMOPHILIA.—The various preparations of thyroid gland are extremely valuable in this dyscrasia, due to a deficiency of fibrin ferment in the blood. As this body, according to my researches, is mainly composed of the adrenal product, the increased functional activity of the adrenals, provoked by thyroid preparations administered, increases the blood's asset. The coagulation time in hæmophilia may be brought down from over ten minutes to three or four minutes in adults by 2-grain doses of the desiccated thyroid three times daily after meals. This is equally effective when operations become necessary.

Examples of the value of thyroid gland in a large proportion of cases of hæmophilia (we might say all, for the cases of recurrent hæmorrhage in which it fails are doubtless due to other causes) are now numerous in literature. Combemale,⁵⁵ for instance, cites the case of a woman who, for the preceding two years, had been suffering from hæmorrhages from the larynx. She was covered with purpuric spots, her gums bleeding. She was extremely weak and exhausted. Treatment with thyroid tablets was commenced; in ten days very marked and evident improvement; there was no purpura, no bleeding from the gums. In ten more days she had perfectly normal menses; all other hæmorrhages stopped. Scheffler⁵⁶ reported a case in which hæmophilic epistaxis was absolutely unaffected by ordinary therapeutic agents, and the epistaxis became so persistent and exhausting that permanent blocking of the nasal fossa was necessary. Treatment by thyroid extract exerted an immediate and beneficial effect, and was followed by cure. In three days the violent and persistent epistaxis had practically stopped. In six days, about 8 grains (0.53 Gm.) of thyroid gland having been given daily, the purpuric eruption ceased. A marked case in which the patient had become extremely anæmic was also reported as recovered by Rugh,⁵⁷ under the use of 5-grain (0.33 Gm.) doses three times daily.

⁵⁵ Combemale: *La médecine moderne*, April 30, 1898.

⁵⁶ Scheffler: *Archives de méd. et de pharm. militaire*, March, 1901.

⁵⁷ Rugh: *Annals of Surgery*, May, 1907.

The value of thyroid in the preparation of hæmophilic cases for serious operations is well illustrated by W. J. Taylor⁵⁸ in 3 cases. The coagulation time was reduced with 3-grain (0.2 Gm.) doses three times daily from twelve minutes to three minutes, and the operations, including a nephrectomy, proved drier if anything than if they had been performed in a non-hæmophilic subject. The desiccated thyroid on the market, especially the standardized product, being stronger than that available in former years, 2 grains (0.12 Gm.) three times daily need not be exceeded even in these cases.

SURGICAL DISORDERS.—We have seen that in 1907 I pointed out that the thyroparathyroid secretion corresponded with what Sir A. E. Wright has termed opsonin. During the same year I urged that thyroid preparations, owing to their influence on oxidation and their power to increase both the opsonins and the germicidal activity of the blood, were indicated in the *early stage of tuberculosis*—mainly on account of the content of the tubercle bacillus in phosphorus, viz.: 55.23 per cent. of its ashes—a fact sustained clinically. Recently, Frugoni found not only that thyroid gland markedly raised the opsonic index of tuberculous animals, but also the active germicidal power of their blood. That this should entail in the surgical field marked progress in the treatment of all conditions due to tuberculosis is self-evident. In *hip-joint disease* and other *tubercular bone processes*, for example, thyroid is clearly indicated.

Besides its powerful stimulating action on the defensive functions, thyroid gland, as shown by Parhon, Macallum, and others, hastens calcium metabolism. This accounts for its value in *osteomyelitis* and *rhachitis*. We have striking evidence of its efficiency in the treatment of deficient metabolic activity in osseous tissue in the rapid growth of the skeleton in cretinism brought about with its aid. This has suggested its use in *delayed union in fractures*—where it is valuable only when more or less hypothyroidia exists—and accounts for its greater value for this purpose in the young than in the adult, its therapeutic action in this class of cases growing less as age advances.

Another indication for thyroid preparations, owing, however, mainly to their influence on general oxidation and metabo-

⁵⁸ Taylor: *Monthly Cyclopædia*, July, 1905.

lism, is in *hypothyroidia in operated subjects*. The presence of this condition, a larval and covert form of myxoedema indicated mainly by a tendency to obesity, cold hands and feet, dry skin, brittle hair perhaps, mental and physical torpor, rheumatic pains in the occiput and back usually treated unavailingly for rheumatism. Here deficient oxidation and metabolism entail a correspondingly deficient production of opsonin and other protective bodies. Such cases are readily infected, and their recovery after any operation, even sometimes after a trivial one, is unusually slow. A preparatory course of thyroid gland transforms completely such a case into one in which the chances of a successful result are as good as in a normal individual.

In *febrile infections* the thyroid gland is sometimes so active that it becomes enlarged and even quite painful. This is now recognized as a distinct effort to raise the protective process to adequate efficiency. In surgical diseases such as *septicæmia* and *erysipelas*, aid afforded to the gland by administering thyroid preparations has been found to curtail these diseases. It fulfills in a measure the rôle of antistreptococcic serum. This applies also to *suppurative processes* of all sorts due to general adynamia; the rapidity with which it produces beneficial effects in this class of disorders is sometimes striking. This applies also to suppurative processes situated in special organs, such as eye, ear, nose and throat, and the sinuses.

When the purpose is to increase the germicidal and anti-toxic power of the blood, and also phagocytic activity, in any of the foregoing disorders, excepting pulmonary tuberculosis, the dose required must be somewhat larger, but not excessive. A condition similar to Wright's negative phase in vaccine therapy is readily brought about by excessive doses. In the laboratory such doses decrease instead of increasing the resistance of animals to infection. Again, as personal investigations have suggested, there is good ground for the belief that the so-called untoward effects observed under thyroid medication are closely allied to anaphylaxis. Two grains of the desiccated gland in tablet form slowly increased to 3 grains, three times a day, is the maximum that should be administered in the adult, and the patient should be carefully watched to forestall any undue

action of the remedy. The best indication of any untoward effect, we have seen, is the pulse. Any considerable quickening or palpitation indicates that the remedy should be discontinued a few days, then resumed in smaller doses. Again, the preparations on the market vary in strength. The above dose refers to Armour's or Burroughs, Wellcome & Co.'s desiccated gland, which is standardized two-tenths of 1 per cent. of organic iodine.

In *cancer*, as will be shown in the second volume (see page 1389), thyroid gland is valuable in inoperable cases and after extirpation to prevent recurrence. As I emphasized in 1907, however, its best effects in the treatment of the disease are obtained when X-rays or radium and saline solution are employed concomitantly.

PARATHYROID ORGANOTHERAPY.

The physiology of the parathyroids was reviewed in the third chapter. We saw therein that the prevailing view was, that their secretion served to neutralize the toxic wastes which give rise to tetany, and that it influenced calcium metabolism. I defended therein Gley's opinion, that it supplemented the function of the thyroid gland, and, moreover, my own previously advanced conclusion, that thus combined the thyro-parathyroid secretion increased the germicidal and antitoxic power of the blood by endowing the albuminous portion of the hæmoglobin with sensitizing properties, and that, as such, it was the blood constituent Sir A. E. Wright had termed "opsonin." Just what rôle the parathyroids fill in the dual process cannot at present be determined, but the fact that, as shown by Gley, the proportion of iodine in them is much greater than in the thyroid proper suggests that it supplies the most active component of the compound secretion, that part of it which has to do with the sensitizing or opsonic action. This is due, we have seen, to the iodine itself, owing to the peculiar property it possesses of increasing the inflammability of phosphorus.

From the standpoint of organotherapy, it is this property that we must bear in mind. We must look upon parathyroid glandules or adequate preparations of these organs as the essence, so to say, of the whole thyroid apparatus, in so far

as its antitoxic properties and its rôle in calcium metabolism are concerned. This agrees with the teachings of experimental evidence, particularly that afforded by Jeandelize,⁵⁹ which have shown that the secretory product of the thyroid gland proper is more concerned with the processes of general nutrition and development than with the auto-protective function.

The manner in which the parathyroids affect the organism and the influence of parathyroid gland as a remedy seem to me best illustrated in the symptomatology and treatment of the first condition analyzed on the opposite page (741) under the title of "hypoparathyroid tetany."

As to the preparations available, Berkeley⁶⁰ claims that the only available glands are those from the bullock, and these are hard to find anatomically—as I know from experience—and expensive. He no longer uses the preparations obtainable on the market, and employs only glands obtained fresh at the abattoirs under his own supervision. He found that the gland could be administered either as fresh gland, preserved gland or nucleoproteid solution. In the author's words:—

"The *fresh gland* is given in the simplest manner possible, minced and eaten in a bread-and-butter sandwich. The dose is from 5 to 8 glands per day. This method is, of course, available only for patients living near a large abattoir where someone has been taught how to find the material.

"In the matter of *preserving the gland*, the essential thing is to get the tissue finely divided and in intimate contact with the preservative. The glands are trimmed with sterile instruments, dried between folds of sterile gauze, and rubbed up patiently in a mortar with an excess of milk-sugar and a small percentage of boric acid to a fine, dry powder. A trace of oil of peppermint is usually added. Prepared in this way, dispensed in capsules, and kept on ice, they keep from four to six weeks. The dose is 5 to 8 per day, each capsule corresponding to $\frac{1}{2}$ a grain [0.033 Gm.] of fresh gland. They are now for sale in several New York pharmacies.

"The *nucleoproteid* (S. B. Beebe's method) is extracted as follows: The glands are thoroughly triturated—a few at a

⁵⁹ Jeandelize: "Insuffisance Thyroïdienne et Parathyroïdienne," Nancy, 1903.
⁶⁰ Berkeley: Old Dominion Journal, April, 1909.

time—in a mortar with laboratory sand. The triturate is made distinctly alkaline with lithium carbonate solution and extracted with normal salt solution in excess. The process of extraction takes twenty-four hours. The container is frequently shaken, and between whiles placed on ice. The solution is now filtered, and finally acidulated with a few drops of 10 per cent. acetic acid. The nucleoproteid settles to the bottom as a voluminous, flocculent, white precipitate. In two hours the overlying fluid, which is now clear, and contains no albumin at all, and only a little globulin, is decanted, and the precipitate is redissolved by adding a little more lithium carbonate, till a slight alkaline reaction is again obtained. This concentrated solution may be diluted to any desired strength. I usually dilute till the number of c.c. is equal to the original number of fresh glands used. The dose of the preparation is about 20 drops [1.23 c.c.] per day. It is readily preserved with a little chloroform or thyroid, and if kept on ice stays effective about half as long as glycerinated vaccine virus, or diphtheria antitoxin. To make it suitable for hypodermic use, it should be more concentrated than as described above, carefully standardized, run through a Chamberland filter, and put up in sealed tubes."

Proceeding with the consideration of the few disorders in which parathyroid has been used, it was deemed best to treat the first of these, hypoparathyroid tetany, in the same manner as other diseases of the ductless glands reviewed in the earlier chapters of this volume, owing to the important position this disorder now occupies in the clinical, and to the fact that it is scantily, if at all, treated in works on surgery.

HYPOPARATHYROID TETANY. (Tetania parathyreopriva; Parathyroid Tetany; Hypoparathyrosis; Cachexia Parathyreopriva; Status Parathyreoprivus or Hypoparathyreoprivus.)

Tetany due to hypoparathyroidia occurs as a result of any condition which temporarily or permanently arrests the functions of the parathyroid glandules. The form most generally recognized at the present time is that variously known as tetania parathyreopriva, cachexia parathyreopriva, status parathyreoprivus, which follows removal of the parathyroids along with the thyroid in goiter and other growths of this gland—a subject

already treated on page 174. The second form is due to organic lesions, such as tuberculosis, interstitial hæmorrhages, inflammatory lesions during infections, etc., of the parathyroids sufficient to greatly impair their secretory activity. These organs being the source, with the thyroid, of one of the auto-defensive constituents of the blood, as previously shown, their functional arrest allows those poisons—toxic waste-products in the present connection—to accumulate in the blood and to provoke tetany and even, in very severe cases, the clonic convulsions of epilepsy.⁶¹ In its general terms, therefore, hypoparathyroid tetany may be defined as follows:—

Hypoparathyroid tetany is a disorder due to impairment or arrest of the secretory activity of the parathyroids, characterized by more or less severe spasms or convulsions, the result in turn of accumulation in the blood of toxic waste-products, which it is one of the functions of the parathyroid secretion, as the opsonic constituent of thyroiodase, and along with other antitoxic constituents of the blood, to convert into benign, eliminable end-products.

SYMPTOMATOLOGY. *Post-operative Parathyroid Tetany.*—The symptomatology of this disorder may vary considerably in intensity and in the time and manner in which it appears. In most cases, however, the tetany begins by a sensation of stiffness around the mouth with twitching of the facial muscles and tingling or formication. This is soon followed by stiffening of the masseter muscles and fibrillary contractions or rigidity of the tongue—which causes difficulty of speech and deglutition—and finally locking of the jaws, as in true tetanus. This is often accompanied by trembling of the eyelids. The thumbs and then the hands are thrown backward, *i.e.*, in marked extension, the fingers assuming either the claw-like or “*main en griffe*” shape, or, with two fingers, the index and medius, extended, the “obstetric position.” There is at the same time flexure of the forearms, often complicated with more or less severe pains in the flexed muscles. The feet are also cramped, often in the equinovarus position, the pain being then located in the calves. In severe cases opisthotonos may occur, the body being supported only on the head, shoulders, buttocks, and

⁶¹ See pp. 1429 and 1437, vol. II, for the pathogenesis of tetany and tetanus.

heels. There is a feeling of intense tightness around the heart. The respiratory muscles, thoracic and pulmonary, being likewise contracted spasmodically, respiration becomes difficult, sufficiently so at times to provoke intense dyspnoea and cyanosis. There may also be marked strabismus, dilatation of the pupils, frothing at the mouth, and clonic movements similar to those observed in true epilepsy.

The pulse becomes rapid and weak and sometimes irregular during the attacks, and the temperature is raised. As explained in the article on tetany in the second volume, the latter symptom is partly due to the presence of an excess of adrenoxidase in the blood and the increased oxidation this entails—the adrenal center being stimulated by the toxic wastes accumulated in the blood—and partly to the rise of blood-pressure, which causes blood to be driven from the deeper vessels to the periphery, and then to congest the cutaneous capillaries. When marked this phenomenon also causes burning sensation over the entire body.

Tetany may occur almost any time after the operation, the period of onset varying greatly. As a rule, however, the first signs occur the third or fourth day after the operation, the intervening period representing doubtless that during which the supply of thyroiodase is being exhausted. The frequency of the paroxysms also varies in different cases, from one to many a day, according in a measure to the diet and amount of exercise to which the patient is subjected. In some cases the parathyroids are only injured during the operation, and their recovery ends the tetany.

Non-operative Hypoparathyroid Tetany.—The symptoms of this condition do not vary from those just described, though they are less marked. In some cases, in fact, they hardly exceed in intensity those produced by strychnine in full therapeutic doses, when the physiological limit of the drug has been reached. Here the parathyroids are able to carry on their functions only in part, the lesions produced in them by local disease, tuberculosis, interstitial hæmorrhage, etc., having left perhaps one or more of the organs or a part of their parenchyma intact. The thyroiodase formed under these circumstances being deficient in the constituent which endows it with its anti-toxic properties, it allows the spasmogenic poisons to accumulate

in the blood very gradually, and in relatively small quantity as compared to that which invades the blood when all the parathyroids are destroyed by operation or disease.

In these mild cases, the identity of the disorder present may be determined by various signs: Trousseau's, tapping or pressure upon large nerve-trunks to elicit muscular contractions; Chvostek's, the production of spasm of the facial muscles by tapping over the facial nerve close to the parotid or over the muscle itself; Hoffmann's, the percussion of sensory nerves to demonstrate hyperæsthesia; Erb's, hyperæsthesia of the nerves under electric stimulation. All these phenomena are explained by the fact that, as previously urged (see also the articles on Tetany, page 1429, and Tetanus, page 1437, in the second volume), the spasmogenic toxic excites the vaso-motor center, producing thereby contraction of all vessels and driving the blood from the great deeper channels to the periphery. All peripheral muscles and nerves being rendered hyperæmic, they become correspondingly sensitive to irritation and stimulation.

Careful differential diagnosis is necessary in these cases, since tetany is also produced, irrespective of any parathyroid disorder (though the parathyroids may show active hyperplasia, as observed by MacCallum, in a fatal case of gastric dilatation), by many other disorders: gastric and intestinal, pregnancy and lactation, uræmia, violent excitement and exertion, etc.—all conditions in which the blood becomes laden with toxic substances. Infectious diseases are also prominent causes of tetany, but probably in part through the lesions of the parathyroids they sometimes produce.

TREATMENT.—Tetany should always be borne in mind when any operative measure involving the thyroid is to be resorted to, since post-operative tetany would never occur if the parathyroids were always spared. Referring the reader to works on surgery for details, it may be mentioned here that every effort should be made to protect not only the parathyroids themselves by preserving the posterior capsule of the thyroid, upon which they lie, but also to so ligate the thyroid vessels with which they are connected as to provide for uninterrupted circulation through them. I would suggest also that their lymphatic connections be as much as possible spared, since, as we have seen, the

parathyroid product reaches the venous circulation through their intermediary.

Important in this connection also is the selection of the portion of the thyroid that is to be removed. Kocher, according to Erdheim,⁶² who generally removes the central part of the gland, has "hardly ever had a loss from cachexia strumipriva or tetany." Again, complete removal of the thyroid itself is never justified, and as large a portion of the organ as possible should be left to insure the continuation of the function it fulfills in conjunction with the parathyroids. If the parathyroids are accidentally removed with the thyroid, which a careful examination of the extirpated organ should enable the surgeon to determine, they should at once be dissected out and implanted into the cervical tissues, selecting as much as possible a region rich in blood-vessels.

In some cases, operated with due care, the parathyroids left *in situ* may be injured, or suffer, perhaps, from shock. Under these conditions, mild tetanic symptoms may occur temporarily. In 500 thyroidectomies performed by von Eiselsberg⁶³ in about seven years, 15 showed Chvostek's sign, but it disappeared without treatment in a few days. In 10 cases there was well-developed tetany, with one death, total removal of the parathyroids in the latter being probable.

W. H. Brown⁶⁴ rightly criticises the indifferent attitude of some surgeons concerning the importance of the parathyroids to the organism, and sustains his position by an extremely severe case of tetany, saved only by the implantation of the thyroid with its parathyroids obtained from a small monkey, and, one month later, of three parathyroids and a piece of thyroid the size of a small walnut, obtained one-half hour after death from the body of a man who had died of Bright's disease and uræmia. These tissues placed at once in normal saline solution at 32° F. (0° C.) were implanted successfully within an hour, the simian thyroid beneath the patient's sterno-mastoid, and the human thyroid and parathyroid beneath her left rectus abdominis, under chloroform anæsthesia. Danielsen⁶⁵ also

⁶² Erdheim: Brit. Med. Jour., July 21, p. 167, 1906.

⁶³ Von Eiselsberg: Centralbl. f. Chir., Nu. 21, 1909.

⁶⁴ Brown: Annals of Surgery, March, 1911.

⁶⁵ Danielsen: Beiträge z. klin. Chir., Bd. xxxvii, p. 998, 1910.