bottom and sides of water channels, tanks, wells, etc., contaminating the water used. The participation of calcium in the pathogenic process is explained by the fact that the organism requires a calcareous soil to flourish. It may be conveyed to places where the disease has not hitherto prevailed and, if the conditions are favorable in that location, it can provoke goiter. The feces constitute the probable medium through which the germ, toxin, or virus leaves the body, all evidence pointing to the intestine as intermediary in the process of infection.

My own view is that bacterial infection may also occur through the intermediary of the tonsils; local treatment of these organs when the seat of catarrhal disorders, either general or limited to the crypts, having enhanced materially the beneficial effects of general measures. The entire nasopharyngeal cavity, the lingual tonsil, the teeth and gums—the latter being frequently the seat of pyorrhea alveolaris—and all structures, in fact, through which a continuous process of infection may occur, can thus harbor the pathogenic factor of goiter.

Various organisms of the ameba type have been shown to provoke goiter, doubtless through a toxin or endotoxin produced by them. Waters incriminated an organism resembling the hematozoön of malaria. Grasset also found this parasite in recent cases. Chagas traced cases to the bite of an insect, *Conorrhinus megistus,* and Brumpt to various insects, especially the bedbug, which act as hosts for some pathogenic organism.

Marine[59] found recently that the feeding of liver and heart to trout produced goiter. Reid Hunt obtained a similar result by feeding liver to mice. This recalls that excessively nitrogenous foods were included by Munson in 1895 among the causes of goiter. Baumann also noticed that a flesh diet stimulated the thyroid in dogs to active hyperplasia. This again is due to intoxication by intermediate protein wastes and nucleins. The latter, as I have shown, are the source of the toxemia to which the form of exophthalmic goiter, caused or aggravated by a persistent and hyperplasic thymus, is due.

On the whole it is evident that *goiter may be caused by*

[59] Marine: Jour. of Exper. Med., Jan. 1, 1914.

various kinds of toxics, organic as well as inorganic, and endogenous as well as exogenous.

Goiter occurs more frequently in females than in males, and in children than in adults. Many instances have been recorded showing that the disease may be hereditary, but this is doubtless due to the fact that the defensive functions against intoxications of various kinds are themselves deficient in many families.

How do the various toxins, individually or severally, bring on the enlargement of the thyroid identified as goiter? This question can only be answered by adopting my personal view that *the thyroid gland—including always its parathyroids—is intimately connected with the autoprotective or immunizing functions of the body.* Goiter being due to intoxication from some poison, organic or inorganic, we are logically led to the conclusion that inasmuch as infections, toxic wastes, etc., cause enlargement of the thyroid, it is because this organ is the seat of a defensive reaction that it becomes enlarged.

While the disease may be the result of prolonged overactivity of the gland, characterized by typical histological lesions of hyperplasia and hypertrophy, with symptoms of hyperthyroidia, these lesions may also occur in a gland which is unable, even under violent stimulation, to react adequately to the poison. Driven, nevertheless, to inordinate activity, it undergoes violent congestion, thus causing the development of a relatively rapid form of the disease. When this identical morbid process develops slowly under the influence of a given toxic, hyperplasia develops as a result of the persistent congestion and what is usually termed a simple or parenchymatous goiter results.

VARIETIES.—Interpreted from my viewpoint, *i.e.,* in the light of the above-described pathogenesis, goiter may be divided into five distinct types: 1, *simple hypothyroid non-toxic goiter* (generally termed simple or parenchymatous goiter), the underlying cause of which is an inherent inability of the thyroid apparatus to produce enough of its secretion to carry on its antitoxic functions beyond those of normal health, any excess of functional activity to meet the needs of an intoxication of endogenous or exogenous origin provoking congestion, hyper-

plasia and enlargement of the thyroid, *i.e.*, goiter; 2, *hyperthyroid or toxic goiter*, an aggravated form of the simple hypothyroid type due to excessive secretory activity occurring as a result of the congestion and hyperplasia, and provoking the characteristic symptoms of hyperthyroidia, larval, or even frank Graves's disease, though in most cases without exophthalmos; 3, *hypothyroid degenerative goiter*, divisible into several subtypes such as colloid, cystic, fibrous, etc., in which the degenerative changes denoted by these terms occur probably also as complications of the hypothyroid non-toxic goiter; 4, *malignant goiter*, in which the thyroid or accessory thyroid tissues become the seat of carcinomatous, sarcomatous, or other malignant processes; 5, *congenital goiter* or *goiter of the newborn*, which corresponds pathologically in most instances with the congestive or hyperplastic type of adults, and occurs in a large proportion of cases, in the newly born offspring of goitrous parents and as a result of pressure during birth.

SIMPLE HYPOTHYROID NON-TOXIC GOITER.

The etiology submitted in the foregoing pages entails the conclusion that not all thyroid glands (including their parathyroids) are functionally equal. While a normal gland can fulfill its protective function under the stress of any intoxication or infection without undergoing material enlargement or organic change, a gland weakened through hereditary influence or local lesions resulting from focal autolysis or hemorrhages which occur in the course of diphtheria, and other diseases, is unable to stand the stress. Such a gland secreting a deficiency of its normal product, may swell and thus become a "hyposecretion" goiter. The enlargement here is the result of an effort to compensate by overwork for the deficient output of the gland. Such goiters rarely show true hypertrophy; they are mainly the seat of an active hyperemia with an increase of normal cellular elements in their active parenchyma.

The enlargement may be the first symptom noticed, and through, as a rule, undue tightness of collars previously worn without discomfort. As the goiter develops, it remains soft and diffuse, showing perhaps a tendency to grow larger on one side, usually the right.

In a large proportion of cases, casual observation will elicit no general symptoms of hypothyroidia; careful examination, however, will reveal some symptom or other of this condition. The pulse may be slow, ranging from 62 down to 40 or even lower. This bradycardia is witnessed unless some cardiac complication be present. There is a marked tendency to hyperidrosis, especially of the extremities, excessive sweating occurring under slight exertion and sometimes even without it. Hypothermia is habitual, though seldom marked, and there is a tendency to cold feet and hands. The urea excretion may be reduced one-third. There are no pressure phenomena, unless the growth is far advanced—no dyspnea, no dysphagia. Nor are there nervous symptoms such as those that are common to hyperthyroidia and exophthalmic goiter—no tremor, no exophthalmos. There is, however, a tendency to rebellious rheumatic pains, often about the nucha or between the shoulders, especially marked when the patient lies abed and, therefore, relieved by rising.

Although this form of goiter sometimes recedes of its own accord, its tendency is to persist if the cause be not removed, and to undergo colloid, cystic, or other retrogressive changes. It is a pernicious form in the sense that in the child it tends toward the production of cretinism and, in the adult, to the corresponding condition, myxedema.

A careful study of the general symptoms is necessary here to determine the true nature of the goiter. Treated in time and by removal of the cause, if the latter can be located, and with appropriate remedies, these cases usually recover. It is the form of goiter which, as Kocher states, "is not usually brought to the surgeon for treatment because it can be cured by internal medication," *i.e.*, by means of iodine or its preparations. This is readily understood when we recall that iodine supplies that which the thyroid cannot provide, in organic combination, in sufficient quantity. The halogen thus relieves the functional stress which causes the organ to enlarge.

It is very important to differentiate this hypothyroid type from that which is characterized by overactivity of the gland, the hyperthyroid type, and which therefore iodine, thyroid gland, the iodides, etc., only serve to aggravate. In the latter form we

find none of the landmarks of the hypothyroid type. Indeed, as soon as any appear other than the goitrous enlargement, they are clearly those of *larval exophthalmic goiter* or hyperthyroidia, the early signs of which are a somewhat rapid pulse, so-called "nervousness," with tremor so slight, perhaps, that it is revealed only on careful examination. As we shall see under "Treatment," however, cardiac disorders other than those due to true hyperthyroidia may attend goiter and not preclude the use of iodine or its congeners.

As to the physical signs, the shape of the gland is not materially changed as this enlarges, at least at first. Any increase in size can only be discerned by palpation, though inspection may elicit a local enlargement during deep respiration, deglutition, and coughing, owing to the up-and-down motion of the gland. A diffuse goiter grows in all directions, the two lobes meeting medially unless the isthmus is also involved, which is often the case. The neighboring muscles are either raised or moved aside, according to their relative position.

The growth also covers the trachea, but this canal is only compressed when one side of the growth becomes much larger than the other, causing dyspnea. This is not severe in simple hypothyroid goiters, as a rule, when the tumor is not hard, and is apt to occur only on exertion. Compression and displacements of the vessels are also rare unless the tumor be very large. We may then witness slight symptoms due to vascular obstruction: headache, vertigo, etc. Murmurs may be heard in the dilated blood-vessels of the neck, the latter usually projecting more or less from the surface while the growth itself may be seen to pulsate.

Pain does not occur in a gotier unless it be the seat of an inflammation, strumitis, which not infrequently occurs in the course of acute febrile diseases, or of a malignant growth. Unless inflamed or the seat of a cancer, the enlarged gland is freely movable.

From exophthalmic goiter, a simple non-toxic goiter is recognized by the absence of any of the systemic symptoms of the former disease, tachycardia, tremors, etc., and of exophthalmos. From the other forms of goiter, colloid, cystic, fibrous, etc., it is distinguished by its diffuse or even surface, all the latter varieties being more or less nodular under palpation, and by its more recent onset.

Examination with the X-rays is indicated to ascertain whether the case be not complicated with an intrathoracic goiter (*vide infra*) or an enlarged thymus.

Pathology.—The tissues of these non-toxic goiters, in which hypothyroidia prevails, are strikingly devoid of all signs of hyperplasia or hypertrophy, the enlargement being mainly vascular. At the Mayo clinic according to L. B. Wilson[60] less than 1 per cent. of 3563 cases coming for operation for goiter show any considerable primary hypertrophy and hyperplasia of the parenchyma of the thyroid except as associated with clinical symptoms of true exophthalmic goiter. Even mild degrees of hyperthyroidia with slight enlargement, such as occur during pregnancy, showed some signs of hypertrophy or hyperplasia.

Prognosis.—In young subjects and pregnant women, the hypothyroid non-toxic goiter occasionally recedes of its own accord, but as a rule its tendency is to persist and grow, if left untreated. Though apparently benign, it may not be so in the child, since it may initiate cretinism by depriving the body at large of a part of its supply of thyroid secretion; the adult is exposed to myxedema from the same cause. It may also represent the earlier stage of the various forms of nodular goiter, *i.e.*, those which are the seat of colloid, cystic, fibrous or other retrograde changes. Properly treated, however, before these complications have occurred, these goiters readily yield.

Treatment.—Elimination of the cause sometimes suffices to produce retrocession of the goiter. When it is endemic, the toxic is probably a water-borne one, mineral or organic. We have seen that the former include calcium as a frequent cause, and the latter pathogenic organisms, fecal pollution and other contaminating agents. A change of water used for drinking and cooking purposes is therefore an important feature of the treatment. The diet should also be controlled since a free use of meats has been found by Waters, Baumann and others to promote the growth of goiter; liver we have seen actually causes goiter in trout and mice. A meat-free diet, or at least the omission of red meats from the food, is very helpful in most

[60] L. B. Wilson: Jour. of the Am. Med. Assoc., Jan. 10, 1914.

cases by reducing the proportion of nucleins which activate abnormally as poisons the inadequate thyroid and cause it to become hyperemic and enlarged.

Autointoxication of intestinal origin is an important factor. A rich diet may also act as an indirect cause of goiter, as urged by Waters, Baumann and others. A meat-free diet sometimes suffices to reduce the size of a goiter. The purpose here is to prevent autointoxication mainly by nucleins, and thus reduce the work of the thyroid as a factor in the defensive functions of the body.

To attain the same object purgatives are indicated wherever the intestinal action is not free. It should be maintained by means of saline aperients, preferably the sodium phosphate 2 drams (8 Gm.) daily, and if any autointoxication of intestinal origin is discernible, or if pathogenic organisms, entozoa in the alimentary tract, be a possible cause, intestinal antiseptics, thymol, the sulphocarbolate of zinc, betanaphthol, sodium salicylate or creosote carbonate should be administered. Messerli[61] advocates, on the basis of excellent results, continuous mild purgation to keep the intestinal bacterial flora down as much as possible.

A purulent focus in any organ may also provoke the thyroid overactivity which maintains, or leads to, goiter. Catarrhal disorders of the nasal cavities, including the sinuses and vault, the ears, lingual tonsil and the gums, especially pyorrhea alveolaris, should, therefore, be recognized as causes and treated with due thoroughness. The most prolific etiological factors of this nature, however, are conditions of the tonsils which in any way tend to favor the accumulation of bacteria in the crypts of these structures or behind them. Extirpation of these organs, besides being sometimes dangerous in these cases owing to the dilatation and engorgement of the neighboring vascular channels, does not afford the best results. Each purulent focus should be carefully cleansed, then cauterized with either galvanocautery or ignipuncture. Less active measures do not procure lasting results. Adenoid vegetations may also cause goiter in the young by perpetuating an autotoxic process. Coble,[62] for instance, obtained complete disappearance of a goiter

[61] Messerli: Revue Médicale de la Suisse Romande, March 19, 1915.
[62] Coble: Indianapolis Med. Jour., Feb., 1909.

in a boy of 15 years, by removing an unexpectedly large adenoid. Pelvic disorders in which ulceration is present should also be remedied.

As regards internal medication it is only, as previously stated, in these hypothyroid cases that we may with certainty expect results from iodine and its preparations or from its organic congener—that contained in thyroid gland. As advised by Kocher, however, and as my own experience has shown, iodine and thyroid gland should be reserved for the cases that are free from pressure symptoms—remembering always, however, that hysterical cases often experience a sensation of choking irrespective of the goiter—and where the growth has been growing slowly. Its mode of action suggests itself in the light of my views: it enhances directly or indirectly the antitoxic function of the thyroid apparatus, by enhancing its activity or of its secretion in the blood-stream, and thus aids in breaking down the toxic which causes the goiter. The sodium salt of iodine, sodium iodide, is to be preferred to the potassium salt, the ion of which may affect the heart unpleasantly. A dose of 5 grains (0.3 Gm.) three times a day, given immediately after a meal in a small tumblerful of water, will awaken no gastric disorder, even when gradually increased to 10 grains (0.6 Gm.) taken in the same manner. Some cases respond better to the action of Lugol's solution; 3 to 5 drops may be given in the same way as the iodide salt.

The patient should be watched carefully and, if any sign of iodism appears, the use of the iodine salt should be discontinued a few days, after which it may be resumed by starting with a smaller dose—just enough to approximate iodism without provoking it. To arrest iodism, if it should persist, Fowler's solution in 2- to 3- minim (0.12 to 0.18 Gm.) doses in half-glassful of water after meals, sometimes proves effective. But its administration should be discontinued as soon as the untoward symptoms disappear.

Steadily as the enlarged gland is aided by the halogen in carrying its antitoxic functions, it recedes if the goiter be an hypothyroid (parenchymatous) growth, and if the sources of the causative intoxication have been thoroughly eradicated.

To activate the action of the iodine salt, a 5 to 10 per cent.

ointment of iodopetrogen (U. S. Formulary) should be rubbed into the gland daily, ceasing as soon as iodism or irritation of the skin appears. A piece the size of a small hazelnut suffices if properly rubbed in. Its application should be preceded by a period of massage of ten minutes' duration, the movements being directed downward and outward and synchronous with deep inspirations. This and the compression exerted cause a reflex contraction of the vascular channels, and hasten materially the curative process. Where iodism tends to appear, the ointment of biniodide of mercury weakened by the addition of an equal quantity of simple ointment should be used instead. If irritation of the skin is produced the intervals between the applications should be prolonged.

Formerly, iodine, iodoform and other drugs were injected into the growth. But this method has been generally abandoned owing to its dangers, death having resulted in a number of instances. Moreover, its indications being the follicular or parenchymatous type—our hypothyroid form—it affords no advantage over the internal use of iodine or its congeners.

As previously stated, any sign of hyperthyroidia or larval exophthalmic goiter precludes the use of iodine or thyroid, or any preparation of the agents; yet care is necessary to avoid attributing to hyperthyroidia symptoms which may suggest the presence of this condition and yet be due to hypothyroidia. The organ which most frequently misleads the clinician in this connection is the heart, owing to the frequency with which this organ is the seat of organic lesions. Thus, in a study of 381 cases of goiter and of the autopsy records of 720 cases, Shranz found organic lesions of the heart, irrespective of valvular lesions, in 23 per cent. of goitrous children and 49 per cent. of goitrous adults. The morbid process found to predominate in the autopsy records, 25 per cent. of all subjects examined, proved to be degeneration of the myocardium—a condition clearly explained by the participation of the thyroid secretion in tissue metabolism which I advocate. Deficient thyroid activity thus means defective cardiac nutrition, in keeping with the corresponding condition of the rest of the body when the hypothyroidia has existed sufficiently long. Dilatation of the right ventricle (Rose's goiter heart) is a form of disorder not

infrequently met with, and which gives rise to pulmonary congestion—Kocher's pneumonic goiter heart. Conversely we may encounter a condition in which the heart, as a result of a functional or organic disorder, may so influence the circulation as to provoke congestion, passive or active, of the thyroid and produce what Révilliod has termed a "cardiac goiter."

This indicates that a careful study of the heart is necessary where, as is so often the case, a functional disorder, including the more prominent sign of hyperthyroidia, tachycardia, is present. Thus, a low vascular tension due to general vasodilation, may, in virtue of Marey's law, produce a rapid pulse and lead the clinician to believe that he is dealing with a goiter which has assumed the hyperthyroid or thyrotoxic type. On the whole, a rapid pulse does not always preclude treatment for simple goiter—with cardiac complications perhaps—unless the tachycardia be accompanied by other symptoms of larval Graves's disease.

When a cardiac disorder of an adynamic type, especially dilatation of the right ventricle, is detected, the iodides are safer than thyroid gland. Unless the rare type of "cardiac goiter" be present, digitalis is of material help in the curative process; digitalin, $\frac{1}{10}$ grain (0.06 Gm.) twice daily, not only enhances the cardiac dynamism, but tends also to regulate the *vis à tergo* motion of the blood in the body at large and thus relieve the congestion of the thyroid—a prominent feature of the enlargement of this organ which constitutes goiter.

In rebellious cases the injection of boiling water into the goiter may be tried. Porter's method previously described (see page 237) may be employed. John R. Wyeth[63] recommends the following method: The skin and the area to be injected are anesthetized by means of novocaine solution, one-half of 1 per cent. A steel syringe is filled with boiling water from a caldron, and the water immediately injected by inserting the needle well into the substance of the mass. To prevent scalding of the skin, the contiguous surfaces are shielded by a covering of towels, only the point of injection being left exposed. As the steam or water is apt to escape from the needle, a gauze swab is held as a shield in front of the needle, which is thrust through

[63] Wyeth: New York Medical Record, May 29, 1915.

and into skin when the contact is made. From ten to twenty minims are forced out in one spot; after which the needle is partially withdrawn, the point carried to a new field, and the injection repeated. Three or four such areas may be injected at one sitting; injections are repeated as required, at intervals of one or two weeks, until the tumor disappears. In a case cited five injections were made in ten weeks, and in three months the goiter had entirely disappeared. Important vessels and nerves, as well as the trachea, should, of course, be avoided, and it is advisable not to point the needle immediately under the skin, as the excessive heat so directly applied may produce necrosis. A Bunsen burner or alcohol lamp held under the barrel of the syringe just as the needle is being inserted will insure the high temperature required. Care should be taken to avoid the veins.

Electricity sometimes proves of value, but only as an adjuvant to internal treatment. Galvanism may be administered by applying one of the electrodes, well moistened in saline solution, to each side of the goiter; 10 or more milliampères of the constant current should be used fifteen minutes every other day, the positive pole being placed over the goiter. For large growths, the electrodes should be broad and malleable, the one covering the entire surface of the goiter, while the other, well moistened, is applied to the back over the seventh cervical vertebra. A current of 20 milliampères or more is required to insure penetration. Cataphoresis may be carried out merely by wetting the negative electrode with Lugol's solution instead of saline solution. In most cases, however, especially where the general symptoms of hypothyroidia are not very marked, the internal administration of the iodide with galvanism will suffice. The latter contributes to the curative process by increasing the contractile activity of the blood-vessels, thus relieving the engorgement of the gland. Static electricity has also been used advantageously by some observers.

The X-rays have been tried, but the prevailing opinion is that they should not be used in hypothyroidia, their tendency being to inhibit further the functional activity of the gland—to the point of myxedema in some instances. Especially is this danger to be borne in mind in the case of goitrous children.

Vaccine therapy offers a promising therapeutic field in goiter. McCarrison,[64] in studying the amebic flora of the intestine in cases of endemic goiter in India, was led, by the uniformity of the bacterial growth, to try the effects of a vaccine made from this composite growth upon some of the cases. There followed a prompt decrease in the size of the enlarged gland and complete recovery in many cases. Upon examination of this bacterial growth it was found to consist mainly of a somewhat altered type of colon bacillus. He therefore used a vaccine made from this alone, and obtained similar good results. He also tried the effects of a vaccine made from a staphylococcus and one from a spore-bearing bacillus, with favorable results from both. He treated 33 cases in all, with most excellent results, but calls attention to the fact that the treatment is suitable for recent cases of parenchymatous goiter only, *i.e.*, the hypothyroid type. The results were best when the composite vaccine was used. By way of explanation of the action of these varied vaccines, he suggests that the cases studied by him in India, were due, as he had previously found, to an ameba in the intestine; that the thyroid is the means of combating certain toxins normally present in the intestine; that when to these there is added the specific virus of goiter (from the ameba) there is an extra strain put upon the gland, and in consequence of this it undergoes hypertrophy. By the use of one of the vaccines, which in itself is in no way specific for goiter, there is removed from the thyroid gland the added strain of neutralizing the toxins arising in the intestine from the bacteria there present, and the gland is able to return to its normal size and take care of the specific toxin of the disease. This interpretation is in accord with my own, the amebic toxin acting as pathogenic agent, which the vaccine combats by promoting the formation of antibodies, thus relieving the need of excessive thyroid activity.

Langmead[65] tried vaccines prepared from coliform bacilli from the patient's own bowel in eight cases of parenchymatous goiter. The growth disappeared in one instance and diminished in size in the rest. The initial dose was usually

[64] McCarrison: London Lancet, Feb. 10, 1912.
[65] Langmead: Monthly Cyclopedia, May, 1914.