

# The Canadian Journal of Medicine and Surgery

A JOURNAL PUBLISHED MONTHLY IN THE INTERESTS OF  
MEDICINE AND SURGERY

---

---

VOL. XXIV. TORONTO, OCTOBER, 1908. NO. 4.

---

---

## *Original Contributions.*

### A CASE OF ACUTE MECHANICAL ILEUS—OPERATION— RECOVERY—REMARKS ON DIAGNOSIS AND TREATMENT.\*

BY G. T. McKEOUGH, M.D., M.R.C.S., (ENG.), CHATHAM, ONT.

“The frequent necessity of resection for the relief of intestinal obstruction is a sombre commentary on the diagnostic ability of the profession. In the very large majority of cases, delay in surgical interference is responsible rather than the primary cause of the ileus.”

These are the opening sentences of an article read in the section on Surgery at the last meeting of the American Medical Association by William J. Mayo. Notwithstanding such comments of so weighty an authority, for obvious reasons it is not unlikely that resection will for some time be necessary in cases of ileus to give a patient a chance for life. The general practitioner does not meet with cases of obstruction of the bowels so frequently that the diagnosis will ever become so manifestly easy that his acumen will enable him to operate himself or to turn over such cases to the surgeon before necrosis supervenes. Indeed, to the most experienced, the diagnosis is not always clear, but often exceptionally difficult. The late Dr. Nicholas Senn wrote, “That the weak side of intestinal surgery to-day is the uncertainty of the diagnosis.” Vascular strangulation occurs so rapidly in most cases that relief can be obtained only by removal of the damaged intestine.

It is more for the purpose of inviting a discussion of the most important question of the diagnosis and early recognition of cases

---

Read at the meeting of the Canadian Medical Association, Ottawa, June, 1908.

of obstruction of the bowels, rather than to publish a successful case of surgery that I wish to report the following:

Mrs. S., aged 30, with a good family and personal history. Has had one child and one miscarriage; after the latter she was cured, and this was followed by some tubal and pelvic inflammation. She was taken suddenly ill Monday night, August 8th, 1907; she had been as well as usual all day, performing her ordinary duties, but shortly after going to bed was seized with pain in the abdomen and vomiting.

Dr. Musson was called about midnight. He found her in great distress, pain, apparently general over the abdomen, not localized, possibly slightly worse in the epigastrium and umbilical regions. There was no distension, rigidity or localized tenderness, but she expressed herself as feeling very ill. The doctor ordered applications of heat and administered remedies, which relieved the patient's agonies. The following day the symptoms remained about the same, nausea, vomiting, pain and constipation, and on the morning of Wednesday the patient's condition was reported somewhat better. Enemas relieved her of some gas. Dr. Musson saw her during the afternoon; not finding her condition so well he had her transferred to the St. Joseph's Hospital. Her condition the following morning being more grave, I was asked to see her. Her temperature then was 99.2-5, pulse 112, nausea and vomiting still persisting. Abdominal pain was severe, of an intense violent character almost continuous, with slight intervals of subsidence, diffuse but referred in its greatest intensity to the epigastrium. There was general tenderness more marked on the right side, which was dull on percussion below the umbilicus; bowels absolutely constipated. She was pregnant about three months. I suggested an immediate operation, as I thought it offered her the only hope of relief, in which opinion Dr. Musson concurred.

It was, however, late in the afternoon before the patient and her friends would agree to any surgical means of relief. By that time the tympanites was greatly increased and her pulse 136 when the anaesthetic was commenced. The patient had the appearance of great depression at that time. The vomited matter during the afternoon had a strong intestinal odor.

The abdomen was opened through the right rectus. The distension, rigidity and tenderness being greater on the right side than on the left. As soon as the abdomen was opened a large loop of ballooned intestine of a chocolate color with spots quite black was observed. The surface of this bowel was also dull and cloudy.

The bowel above the seat of strangulation was dull red, congested and much distended. The obstructed gut was so largely distended and fragile looking that Mayo's method of going down to the ilium at its caecal termination and tracing the collapsed intes-

time to the point of disease was followed, rather than handle the blackened gut. The strangulation seemed to be due to a band or drawn out adhesion resulting from old inflammatory exudate connecting the uterus, ovary and mesentery. A loop of intestine being snared and constricted.

Cutting the band at once released the gangrenous coil, notwithstanding that every care was taken in handling the diseased gut which was very rotten, it unfortunately ruptured, after, however, it was taken out of the abdomen. Through the rupture we were enabled to empty the bowel of its noxious contents. Treves says that the addition to the operation, of emptying the bowel contents has reduced its mortality 50 per cent. Wilms in his work on Ileus is of the opinion that auto-intoxication in many cases is the chief cause of death, and in all cases of resection it is therefore important to evacuate the toxic-bowel contents and prevent them from passing down into the healthy distal intestine. Nearly three feet of bowel was excised, and end to end union by a Murphy button was employed, as the patient's condition was extremely critical.

As soon as the patient was under the influence of the anæsthetic normal saline solution was transfused under the breasts. The stomach was lavaged before the patient was taken from the table. On being placed in bed she was raised to a semi-sitting posture and rectal infusion of saline by the Murphy method employed. There was no more nausea nor vomiting after the operation. The bowels moved spontaneously on the third day; she aborted on the fourth day; the button was passed on the tenth day after the operation; and with the exception of a slight post-operative Thrombo-phlebitis in her left leg her recovery was uneventful and perfect.

The early recognition and diagnosis of Ileus is of vital importance because there is only one procedure for its treatment, and that is surgical. The sooner the diagnosis is reasonably clear and operation undertaken the fewer the difficulties met with, and consequently the gravity of the case so much lessened. The most serious feature in the management of obstruction of the bowels is delay. Every hour of delay jeopardizes the only chance of relief.

Treves says, "There can be no purpose in delay; the expectant treatment has had a very extended and deadly trial in the past. It is one of the most serious as well as one of the most fatal conditions a medical man is called upon to face, and operation which is so often regarded as a last resource should invariably be considered as the first and only resource." Hence the urgency of the diagnosis.

Murphy defines Ileus as a complexus of symptoms occurring usually in a fairly regular form and order and represented by pain, nausea, and vomiting, meteorism and coprostasis. The symptoms in the early stages of mechanical intestinal obstruction are first and

most important, severe abdominal pain with nausea and vomiting; there is usually no distension or tenderness, and an absence of fever. When you have severe pain, vomiting and obstinate constipation without fever, without distension and without tenderness or rigidity, which usually comes later, you have a strong case for obstruction, and one should not wait for all the classical symptoms, such as tympanites and faecal vomiting before opening the abdomen. Several acute lesions, however, within the abdomen, such as perforation of a gastric or duodenal ulcer, rupture of a pyosalpinx, passage of a gall-stone, perforation of a vermiform appendix, acute pancreatitis, twisting of the pedicle of an ovarian cyst, etc., are ushered in with symptoms very much similar to those which follow the strangulation of a loop of intestine and often some hours must elapse before differentiating the cause of the sudden abdominal crisis.

The weight of authority, I believe, favors the view that symptoms of obstruction are rather the results of auto-intoxication than of a mechanical disturbance of the nervous structure in the intestine. Pain is always a pronounced and conspicuous symptom. It is usually violent and persistent when the obstruction is complete, generally more or less diffuse but often referred with greater intensity to the neighborhood of the umbilicus which corresponds to the site of the superior mesenteric and solar plexus. There is often slight periods of subsidence, the pain however, renewing itself again with greater intensity. At first the pain may be relieved by pressure.

Coincident with or quickly following the advent of pain, is nausea and vomiting; rarely it may precede the access of pain. The vomiting is copious and persistent, the vomited matter at first consisting of the contents of the stomach. Then it becomes bile-stained or thin brownish or pea-soup like, and finally, stercoraceous and filthy. Formerly the stercoraceous vomiting was thought to be due to auto-peristaltic movements, but recent experiments have demonstrated that it is produced by contraction of the abdominal muscles and diaphragm and of the mutual pressure that the distended coils of intestine exercise one on the other along the normal peristaltic movements of the bowel. The vomiting usually persists unless the case is relieved, until death.

Obstinate constipation due partly to reflex nerve action, but chiefly to the absolute obliteration of the lumen of the gut, usually appears as soon as the occlusion takes place. The contents of the rectum and sigmoid flexure may be lavaged with enemata, but one rarely sees a spontaneous evacuation of intestinal gases or faeces.

Meteorism is usually a later symptom of strangulation by bands or from hernia; it is most marked when the colon is the seat of the obstruction, and is especially pronounced in volvulus of the sigmoid flexure.

Meteorism is often localized at first in the snared loop of intestine and that portion of the gut above the strangulation; hence the least asymmetry of the abdomen should be carefully observed. The tympanitic abdomen in peritonitis does not depend upon a mechanical stricture, and it must be remembered that meteorism is not due to a mere collection of gas that cannot escape, "the conditions which most favor it are such as lead to gross disturbance in the circulation of the bowel and mesentery."

The degree of shock which is often a marked feature of the commencement of acute strangulation varies greatly in different cases, depending upon the suddenness of the onset, the amount and character of the bowel involved, being much more pronounced when either the jejunum or sigmoid are complicated, owing to their larger and more susceptible nerve supply. It is more marked in the young and vigorous than in the old and decrepit. Collapse is at times quite profound, so that cases of ileus have been diagnosed as cholera and again when a voluminous coil is involved the shock may be of only moderate degree. The early collapse usually passes off again to manifest itself more insidiously in the terminal stage of the disease, presenting a picture which has been so graphically described by Treves, and which we have all too frequently viewed. A condition due to auto-intoxication and identical with that which marks the closing scene of a fatal peritonitis or sepsis.

A study of the urine, faeces and blood of the patient sometimes aid in establishing a diagnosis. Indicanuria has been considered of some diagnostic importance; when indican is found in large quantities in the urine it is said by some authorities to indicate either acute peritonitis or obstruction of the small intestines. If collateral evidences point in that direction, and if acute peritonitis can be excluded the sign would indicate occlusion of the intestines.

Not much can be learned by inspection of the faeces; blood in the stools has a limited significance, except in invagination, when bloody stools are frequently characteristic. Bloodgood, of Johns Hopkins, states that one of the most important early signs of intestinal obstruction is a rise in the leucocyte count; that in his experience of either post-operative obstruction as well as primary obstruction there has been a leucocytosis varying from 15,000 to 30,000 but in the early hours unfortunately there are other intra-abdominal conditions which may account for the leucocytosis, therefore as a diagnostic symptom it cannot be depended upon.

Moynihan, in his magnificent address on the "Pathology of the Living," states, "That so far as abdominal diseases are concerned, he is the best diagnostician who spends most of his time in the operating theater. The lessons there to be learned are far greater and far out-weigh in value those that can be learned in the post-mortem room, in so far as they bear any reference to the treatment of the living."

"He would therefore urge upon all those engaged in practice the desirability of following their patients to the operating table whenever opportunity occurs. The lessons there to be learned will in practice be of a value beyond all reckoning, and interest in the daily work will thereby be quickened to an unaccustomed degree."

In conclusion I should like to again add that the early diagnosis of intestinal obstruction is of supreme importance, for, unless the patient is relieved, the case can only end tragically. Therefore, when symptoms suggesting intestinal obstruction appear they should be given careful and watchful observation, and even when an accurate diagnosis is unattainable, but a presumptive diagnosis is reached, prompt operation is demanded. Operation will save many an unfortunate patient such as has been permitted in the past to perish by inaction.

Discussion by Dr. Hicks, Port Dover, on Dr. McKeough's paper on Mechanical Ileus.

In relation to diagnosis, it is well to remember that in some of the worst cases we will have but little distention and great and immediate symptoms of shock. These cases usually mean a large strangulation badly strangulated. Von Bergmann's work makes especial of this type of case.

Dr. McKeough has already insisted on examination of the urine, faeces, etc.; I think to this we should add washing out the stomach as a diagnostic measure. In a recent case two practitioners diagnosed a mechanical obstruction from pain, vomiting, localized bulging and peristaltic movements with some collapse. I saw the case on the third day, and the use of the stomach tube brought up a further quantity of stomach contents and cleared up the diagnosis. The case was one of prolapse and dilated stomach.

Providence at times provides us with an easy way out of some cases. In a case of volvulus, which I have reported before associated with an old incarcerated femoral hernia, the gut of which was above the volvulus. I was able to practically lance the hernia, making an artificial anus and allowing the faeces to escape freely. The patient picked up at once and had a subsequent operation, when in good condition, with recovery.

Closing discussion:

A case where two practitioners had diagnosed obstruction, proved to be dilatation of the stomach, and washing out the stomach relieved all symptoms. Pain, excessive and almost faecal vomiting, and constipation were present.

Note that distention is not an essential in diagnosis, as the worse the strangulation the less the distention in some cases.

Note use of hernia in making an artificial anus. In two cases one recovered and one died.

CLINICAL REPORT.\*

By E. SEABORN, M.D.

M. S. Aged 72.

In 1895, when 63 years of age, he was troubled so much with frequency of micturition and pain that he began to catheterize himself. He continued doing so for some 9 years, sometimes as often as every 15 minutes during the day. He never boiled or even washed a catheter. When the lumen became clogged he would clean it out with a piece of wire. To obtain a menstruum with which to moisten the catheter he would expectorate into his hand and rub the catheter into that, regardless of what his occupation was at the time. He, of course, at no time took the trouble to wash his hands. He carried the catheter in his pocket. During this time, and especially for the last two years, he had suffered great pain.

In March, 1906, in using an old catheter, a piece (specimen exhibited) some 5 inches long was broken off partly in urethra and partly in the bladder. He pushed this piece of catheter into the bladder with a bit of wire and introduced another catheter. He did not consult a doctor then, nor for some several weeks after. Then he was sent to a hospital in one of the Southern States and an operation to remove the catheter and prostate at the same time was performed. His condition was extremely critical for some weeks.

On Oct. 20th, 1906, he consulted me.

*His Condition.*—Had great pain at end of micturition along the penis and in the glands. He did not use a catheter. There was a small urinary fistula above the pubes. He held his thumb over this during micturition; at other times there was only slight oozing.

The urine was loaded with albumen pus and epithelium. On examination, per rectum, it was evident that the prostate had been removed. The opinion was given that there might be some infected stitches in the bladder wound or some concretion.

He was advised to have the fistula explored at first. He entered the hospital on October 23rd, and before operation had his bladder irrigated repeatedly. An attempt to examine the bladder with a cystoscope was made, but was not successful, as the urine was cloudy even after prolonged irrigation.

On cutting down to the bladder through the fistula, a cavity was found between the skin and bladder, containing very soft granulation tissue and pus. This was scraped away and the edges of

\* Read at the Canadian Medical Association Meeting, Ottawa, June, 1908.

fistula in bladder were freshened. It was hoped that this abscess had been the source of the bladder infection. He had stipulated that the bladder was not to be opened, if it were at all possible to avoid it.

His condition was not improved, and on Nov. 28th, 1906, he went again to the operating room, and the bladder opened and the piece of catheter removed. The irrigations were continued, and the bladder wound closed with great rapidity, and on Dec. 18th he left the hospital.

I saw him some months ago, and he said his only discomfort was that he had to urinate oftener than usual, and that when he felt that he should have a discharge of semen none was ejected, but came with the next urine.

At the last operation careful examination was made and no prostate was found, but only some thickening between the rectum and bladder, presumably the sheath of the prostate. He identified the catheter as the one he had introduced before his first operation.

Dr. H. Williams was present at the last operation and verified the opinion that the prostate had been removed.



## *Selected Articles.*

### THE PHYSIOLOGY OF THE THYROID GLAND IN ITS RELATION TO EXOPHTHALMIC GOITER.\*

S. P. BEEBE, M.D., NEW YORK CITY.

THE investigations of the last twenty years have given to the thyroid gland a physiologic importance of the first order. So enthusiastic have some observers become in their belief in its primal position in physiology and also, on the part of a few, in therapeutics, that one is almost tempted to compare its supposed potency to the famed fountain of eternal youth whose magic healing and rejuvenating properties was the hope of the aged, infirm explorer. I must confess myself as among those who share the belief that the thyroid is a true gland, whose proper functioning plays such a part in the physiologic rhythm of the body that it stands very near to, if, indeed, not in, the list of viscera to which the term vital is properly applied. I share also in the belief that the thyroid proteids have a wide range of beneficial therapeutic activity, and yet I must, in the beginning of this discussion, call attention to how little scientific knowledge we have of the real significance of the gland and its mode of functioning, and to how large a degree our knowledge is the plainest empiricism.

We know that complete removal of the thyroid apparatus, *i.e.*, thyroid and parathyroid, leads in most species of mammals to a fatal issue in the majority of cases. We may now safely conclude that such a result is due wholly to the removal of the glands and not to a traumatic injury of the nerves in anatomic proximity to the gland. Death from such a complete operation is generally sudden and follows a varying period of severe tetanic convulsions. I think that as a result of the experimental work of the past ten years we may go further and state that the thyroid apparatus is complex and has two well differentiated histologic structures, thyroid and parathyroid, and we have good reasons for believing that the different histologic structure corresponds to a different

\* Read in the joint session of the Sections on Practice of Medicine, Surgery and Anatomy, and Pathology and Physiology, of the American Medical Association, at the Fifty-eighth annual session, Atlantic City, June, 1907.

function. Removal of the thyroid alone is followed in most cases by a cachexia, which may in large part be relieved by the administration of thyroid substance. Removal of parathyroids, if complete, is followed by an acute fatal tetany which supervenes in a few hours or a few days.

During the last few months I have carried out some further experiments on this line which give additional evidence of their different function. The experiments have in all cases been made on dogs. The acute tetany has been induced by operative removal of the parathyroid glands. While the animal was in severe convulsion, a hypodermic injection of beef parathyroid nucleoproteid has been given with the result that in from thirty minutes to two hours nearly all the animals have temporarily recovered a normal condition. The improved condition does not last, however, for muscular twitchings begin again in from 24 to 60 hours, and the animal rapidly passes into a tetanic condition. Another injection of the parathyroid nucleoproteid a second time will relieve the animal. The whole procedure may be repeated a third time, but we have not thus far succeeded in keeping an animal alive longer than three weeks after such an operation, but we can nearly always prevent death in the acute tetany. We have some evidence that the convulsions following the operation are due to a toxic condition of the blood, for if animals are fasted for a few days or if they are fed on meat-free diet the convulsions are less severe and appear later than they do if meat is given. Severe convulsions can be brought about in two or three hours by giving an operated animal a heavy feeding of meat. MacCallum's experiments have shown that bleeding the animal in tetany and infusing with normal saline will likewise relieve the convulsions. Further, the blood of an animal in tetany was found to be very toxic to an operated animal before enough time had elapsed for the animal to have tetany from its own operation. The globulin from the parathyroid has thus far failed to relieve the symptom, a fact which indicates a difference in chemistry from the thyroid, as in the latter gland the peculiar iodine group is in combination with the globulin and is, therefore, the proteid of particular physiologic activity.

The older experiments did not differentiate between thyroid and parathyroid, so that the acute tetany following the complete operation has been by them ascribed to the thyroid insufficiency. There are observations on record of relieving the acute symptoms by large doses, 4 to 5 grams, of iodothyron per day. Such doses are far beyond the limits of the physiologic and are not to be compared to the very small amount of parathyroid-nucleoproteid required to do the same thing.

The observations on the effect of operative removal of the glands and on the administration of various components of the glands to animals operated on, and to normal animals constitute

the most important known facts about the physiology of these structures. And the facts are briefly as follows:

1. Removal of the thyroid causes cachexia thyreopriva, the symptoms of which may in large part be alleviated by administration of thyroid preparations. Thyroid extracts owe their activity largely to the organic iodine group therein contained.

2. Removal of the parathyroids is followed by an acute tetany. It is on the above observations that all the interesting and suggestive theories useful in the physiologic and therapeutic value of the glands have been founded. Some of these theories have sufficient dignity to command serious respect, but in many of them there is a lack of regard for the fundamentals.

It is a well-authenticated fact that thyroid feeding stimulates nitrogenous metabolism, and it may be that such a stimulation is accompanied by a heightened oxydative capacity of the organism by which toxic products of metabolism are rendered harmless. Hunt has recently furnished the first experimental demonstration of the detoxicating action of thyroid by showing that mice fed with thyroid preparations are able to stand larger doses of acetonitrile without fatal effect than control animals. The beneficial effects in these experiments are not to be ascribed to a direct chemical union of thyroid with acetonitrile, but rather through the metabolic stimulation which the gland extract caused. Although the detoxication theory of thyroid function has very little direct experimental evidence to support it, there is some empiric clinical evidence in its favor, and it has been used by Moebius as the foundation of his treatment of exophthalmic goiter. The blood of thyroidectomized animals contains a somewhat different distribution of proteids than is found normally, in that there may be an increase in the ratio of globulin and a diminution in the hemoglobin, but there is little experimental ground for supposing that the blood of thyroidectomized sheep contains a toxic, and there is absolutely no reason to believe that this toxin, if it does exist, can combine in quantitative chemical fashion with human thyroid secretion. The supposed mechanism of this therapy is purely hypothetical and is without any analogy in known physiologic action. To Moebius belongs the credit for first formulating our notions of the hypersecretion theory of exophthalmic goiter, but his means of treatment has the most empirical foundation.

A unique detoxication theory of the function of the thyroid and its rôle in exophthalmic goiter has an ardent supporter in Blum, who believes that there arises in the course of metabolism a toxic globulin which is detoxicated in the thyroid by the chemical addition of iodine. The colloid is, therefore, an excretory product and the more perfectly it is iodized the less toxic effect should it have. (According to this theory exophthalmic goiter is caused by the escape into the circulation of large quantities of this par-

tially iodized proteid.) The theory is based principally on Blum's observation that iodine can be added to the thyreoglobulin *in vitro* with the result that its peculiar physiologic properties are completely lost. The latter observation is probably correct, but granting that it is, no conclusions worth entertaining can be drawn from it. Blum's theory contradicts the experimentally demonstrated facts that the iodized proteid from the glands is responsible for much of their physiologic activity, and the equally well demonstrated fact that the activity is proportional to the iodine contained. If potassium iodide be given to an animal there is an increase in the content of physiologically-combined iodine in the gland. Roos has shown that when the glands from animals fed with large quantities of potassium iodide are tested physiologically they show an activity proportional to their iodine content, whereas, according to Blum's theory, such glands should have less physiologic activity than the normal. The artificial iodizing of a proteid *in vitro* is a violent chemical action not to be compared to the behavior *in vivo*. We know, furthermore, that the beneficial effects of thyroid treatment in myxedema may be produced by the circulation of the organic iodine group, a fact which is directly contrary to Blum's hypothesis. His theory of thyroid function will not bear close inspection, but the cause of the exophthalmic symptoms, by an escape of large amounts of partially iodized globulin into the circulation, is identical with the belief generally held to-day. I am personally inclined to believe that one function of the gland may be a detoxication, but I do not believe that this is accomplished by a direct chemical union of the thyroid secretion with a metabolic toxin, but rather by the stimulating and regulating effect which is exerted on other viscera.

Chemical studies of the gland have demonstrated the presence of three forms of proteid, nucleoproteid, globulin and albumin, in addition to a number of the simpler cleavage products of proteid, the latter being bodies of no especial significance. The normal thyroid contains relatively little of the nucleoproteid, much globulin and a smaller amount of albumen; the parathyroid, on the other hand, contains a large amount of nucleoproteid, a very small proportion of globulin and still smaller amounts of albumen. These findings agree with what we should expect from the histology, and in each case the proteid present in greatest abundance is the one most active physiologically. Since the discovery and isolation of the organic iodine group by Baumann most of the chemical study of the gland has been directed toward that compound and the proteid of which it forms a part—thyreoglobulin. This is proper from a physiologic point of view, but from the pathology of the gland we must not fail to consider the nucleoproteid. I have had an opportunity during the past two years to separate the nucleoproteid and globulin from a large number of

thyroid glands, normal, simple hyperemic, glands with marked cellular hyperplasia, simple adenoma, colloid goiter, and glands from practically all stages of exophthalmic goiter. In most of the glands from the latter condition there has been found a much larger proportion of nucleoproteid, particularly in the fatal cases. The normal conditions may be entirely reversed and the nucleoproteid be found in as great preponderance as the globulin in the normal gland. Additional confirmation of this point is found in the statements of Kocher and Aeschbacher, that when the gland is rich in phosphorus it is poor in iodine. The phosphorus comes chiefly from the cell nuclei which are much more abundant in the exophthalmic gland. Histologic evidence supports this finding, as in the late stages of exophthalmic goiter there may be found considerable cellular hyperplasia with relatively little colloid. There is practically no experimental evidence on the function of the nucleoproteid as distinct from the globulin, yet in certain pathologic conditions the former must play an important rôle and one of which we are as yet entirely ignorant.

The study of thyroglobulin and its content of iodine has been the main chemical contribution of recent years, and it is especially to Oswald that we are indebted for much of the work since Baumann's time. Oswald has determined the content of thyroglobulin and iodine in many normal glands and simple colloid and parenchymatous goiters. He finds in goiter a great variation in the relative and absolute amounts of globulin and iodine, but his findings may be summarized by the statement that in goiter there is a relatively large amount of globulin poor in iodine. Although he has reported only four analyses of these glands, he bases thereon his latest theory of the disease, viz., a flooding of the system with a globulin poor in iodine. Such a theory really means a hypersecretion of a product of less physiologic activity than the normal. If we consider, however, that normally the blood supply is so great as to permit the entire volume of blood in the body to pass through the gland fourteen times in twenty-four hours, and consider also to how great an extent this blood supply is increased in exophthalmic goiter, we must conclude that this theory means simply an excess of effective thyroid secretion in the circulation. Even though there is less iodine in the proteid than normally, there is no evidence that this indicates a change in the essential character of the proteid. There may be less activity per unit of globulin, but since there is such an increase in the number of units in circulation the conclusion of the chemical study is in favor of the hypersecretion theory. Oswald entirely ignores other proteids than the globulin, a decision which I wish to emphasize again is not satisfactorily explained. The chemical findings in colloid goiter can not be used in an argument on exophthalmic goiter, since in so many cases the nucleoproteids in these latter

glands is quite as important a constituent as the globulin. Although the chemical studies indicate that in exophthalmic goiter the globulin contains proportionally less iodine, such a result does not imply a dysthyroidization as a factor in the disease, for the iodine in the proteid is a measure of a quantitative rather than a qualitative change. The clinical argument that the many types of the disease can only be explained by a dysthyroidization may have some support in the fact that nucleoproteid and globulin are found in glands of exophthalmic goiter in different ratios from those in the normal gland, but an equally probable explanation is to be found in the personal idiosyncrasy toward active proteids.

We know very little of what the thyroid secretion does when confined within physiologic limits, but if given in excess we see as a result many of those symptoms characteristic of exophthalmic goiter. The exophthalmos, tachycardia, tremor, gastro-intestinal disturbance, profuse sweating, increase in temperature, rapid loss in body weight, severe mental disturbance, have all been caused experimentally in animals by overdosing with thyroid preparations. It has thus far been impossible to produce the disease experimentally, and the nearest approach has been obtained by giving an excess of thyroid extracts. There is, however, a serious error in technic in most of these experiments in that the commercial thyroid has been given in intermittent doses by stomach in most cases, but if the physiologic conditions are to be simulated a saline extract of the gland from the same animal species should be given in small, frequently repeated doses hypodermatically. Even then we are not providing the most suitable conditions, as the extract of a normal gland has a distribution of proteids somewhat different from those the diseased secretion contains. One of the most interesting experiments of this kind is that reported by Dr. Matthes, who had a patient suffering from exophthalmic goiter operated on with a curative result. Later when the patient was fed portions of his own dried gland there was an increase in the nitrogen excretion with some return of symptoms.

However, granting that, as seems probable, the hyper-secretion theory offers the most satisfactory explanation of the origin of the symptoms in the disease, we as yet have no satisfactory explanation of the mechanism by which they are brought about. The tachycardia, for instance, has been variously explained, an acceptable theory to many students being that of Gley, who believes the vagus impulses are inhibited and the accelerator stimulated by the gland extracts; yet very recently some experiments on the isolated heart have indicated that the central nervous system may be in no way concerned in the matter.

The mechanism responsible for the other symptoms of the disease are in a more unsatisfactory condition than the tachycardia. The very rapid loss in weight has been repeatedly given

a partial explanation by the stimulating properties which the gland extracts have, but why and how the extracts act in this manner is a subject entirely unknown to us at the present time. The metabolism of patients suffering from exophthalmic goiter has been partially studied in a number of laboratories, and as a result we know that very large amounts of nitrogen are required to maintain an equilibrium during some stages of the disease. Recently in our laboratory more complete analyses of the urine have been made by Dr. Shaffer, and the most interesting new fact which can be drawn from these studies is that the kreatinin excretion is low compared with the normal, and the lower figures always go with the more severe toxic forms of the disease. When the patient improves there is a corresponding rise in the kreatinin output. With the low kreatinin excretion there is an increased kreatin excretion. We know little of the origin of kreatinin in the body, but Dr. Shaffer has recently advanced the theory that it is a measure of the muscular efficiency; such a theory is supported in this disease by abundant clinical evidence and by the measurements of the strength of selected groups of muscles made by Dr. Frederick Muller, who has found that in patients suffering from exophthalmic goiter the muscles are no more than one-fifth to one-third as strong as in normal individuals.

There are two commonly accepted possibilities which explain the origin of the hyperactivity of the gland. First, as a result of nervous shock; second, as a compensatory hypertrophy during a toxemia.

As to the first possibility, the investigations of the last ten years have given us a fund of information concerning the remarkable control exercised by the nervous system on glandular activity. Particularly with reference to the digestive glands we have seen qualitative and quantitative changes in their activity following an apparently insignificant stimulus. We have no direct experimental evidence to indicate in how far we can apply these results to the thyroid gland, but clinically we see many instances of marked change in the activity of the gland following some profound nervous disturbance. The condition may have been latent before and first becomes evident following some severe fright or sudden sorrow. Why the effect should last beyond the stimulus which called it out we do not know. That a new habit of abnormal activity may result from a series of repeated stimuli is an hypothesis put forward to account for many instances of physiologic overwork, and it may apply here.

As to the second hypothesis, there are some histologic studies which indicate that during the infections and also during chronic toxemias the thyroid undergoes cellular hyperplasia which may serve in the nature of a compensatory hypertrophy, *i.e.*, the additional demand for the detoxicating action of the gland results in

its growth. At present we have no method of measuring the activity which the gland has either in a normal or pathologic condition and can form only the crudest notions by the gross appearance and histologic structure. It is, therefore, rash to conclude that in those cases of exophthalmic goiter, with no goiter there is no hyperthyreosis. There are many clinical observations that support the theory of compensatory hypertrophy, and it is the mere bulk of this evidence rather than its character which is impressive.

In conclusion I must again call attention to our dearth of knowledge of the physiology of the thyroid gland and the pressing need for systematic, careful investigation, both on the part of the laboratory worker and the clinician. Theories we must have, for it is by these that we grow, but the danger lies in accepting an attractive theory as an established fact.—*Journal of American Medical Association*, October 5, 1907.

---

### THE PATHOLOGY OF EXOPHTHALMIC GOITER.

---

W. G. ACCALLUM, M.D.

Associate Professor of Pathology, Johns Hopkins University.

---

The symptom-complex, which we know under various names as exophthalmic goiter, Graves' disease, Basedow's disease, etc., has been very extensively studied, but even yet there is not perfect unanimity of opinion as to the anatomic changes which underlie these symptoms. Nearly all writers, except certain clinicians who have not made anatomic investigations, agree that there are always changes in the thyroid, although there has been much debate as to whether these changes are constant in character or not. There are others who think that the lesions must be sought in the sympathetic system or in the central nervous system, while still others regard the disease as the result of a functional disturbance of the nervous system and do not expect to find gross anatomic changes. Other attendant lesions in the eyes, in the skin, the muscles, the digestive tract and in the lymphoid tissue and thymus have been frequently described, and organs of internal secretion other than the thyroid, such as the parathyroids, adrenals, pancreas, hypophysis, etc., have been investigated with varying results. Since Moebius put forward his idea of the fundamental relation of the thyroid to the disease, attention has been centered chiefly on that organ and it has formed the point of attack in therapeutic measures, but the other lesions must still be regarded as worthy of close study, and in this paper the changes found in a rather

---

\* Read in the joint session of the Sections on Practice of Medicine, Surgery and Anatomy and Pathology and Physiology, of the American Medical Association, at the Fifty-eighth annual session, Atlantic City, June, 1907.



large series of cases will be taken up in order. It must be observed, however, that none of the changes which have been generally found and which I have found in my series have the character of primary changes. They seem in each instance to be the response or reaction to some fundamental or primary disturbance of which as yet, I think, we have no very clear notion.

Disturbances of metabolism in these cases are obvious, and these seem to be intimately connected with the fundamental activity and corresponding anatomic condition of the thyroid, but whether as cause or effect is not absolutely proved. Similarly pronounced nervous disturbances occur, the heart runs riot, the body trembles, secretions are disturbed and the mental condition and temperament are altered, but whether this is the result of chemical changes or of obscure anatomic lesions in the nervous system we are not certainly informed. Whatever vague notions we have as to the fundamental underlying cause of all these things we may discuss after describing the anatomic changes.

It has been shown by Halsted and others that if a portion of the thyroid be removed from an animal the remainder shows after some time a curious alteration, which consists essentially in the great proliferation of the epithelial cells by a process of mitosis. So great is this new production of cells that they become too numerous to be accommodated on the smooth wall of the round alveolus and the epithelial lining accordingly becomes folded in the most complicated way, each fold carrying up with it into the original lumen a supporting strand of connective tissue with blood vessels. This change in the alveolar wall is followed by a decrease in the amount of visible colloid, which loses its hyaline dense appearance and becomes pale and ragged. The whole process has been regarded by Dr. Halsted as a compensatory hypertrophy, the proliferation of the epithelium being an attempted repair of the loss of thyroid substance. A similar condition is found in a small percentage of stray dogs in Baltimore and occasionally in sheep and goats, while in certain localities, as reported by Dr. Marine, in Cleveland, in a recent paper, an enormous proportion of the stray dogs are thus affected.

What the cause of this hypertrophy can be is not perfectly clear, but Dr. Marine has observed that if these dogs be given iodids in considerable doses the alveoli again become round and filled with colloid, and Dr. Kocher tells me that the administration of iodine will prevent the development of the folded condition after the operative extirpation of part of the thyroid.

Now in exophthalmic goiter the thyroid presents an appearance practically identical with that found in these animals, and it will be my task to describe in greater detail these anatomic appearances as they occur in this disease. It is true that none of the symptoms found in exophthalmic goiter are observed in the animals

operated on nor in those in which the hypertrophied condition occurs spontaneously, but still the analogy is of great interest.

The material which I have had for study consists of sixty patients, most of whom have been operated on by Dr. Halsted for the relief of symptoms more or less typically those of exophthalmic goiter, and I am much indebted to Dr. Halsted for this material. Not all of these cases presented the complete typical picture of exophthalmic goiter; some of them, as will be recounted, showed part only of the characteristic symptoms, while some were complicated by the presence of other lesions of the thyroid and other organs. It will be of interest, however, to determine in how far the anatomic changes correspond with the development of symptoms, and this can be done briefly, more exact data being obtainable from the Table on this and following page.

From this table it is seen that in certain cases the changes in the thyroid are very well marked and are of a characteristic type, while in others they are less easily recognizable.

The more characteristic changes may be discussed first. In most instances the thyroid is enlarged, although, as a rule, not to a great size; in some cases it is not larger than the normal or it may be actually decreased in size. At operation the superficial

TABLE OF EXOPHTHALMIC GOITER CASES.

Case.	Character of symptoms.	Duration.	Character of thyroid.
W.	—Typical.....	6 mos.....	Typical.
R.	—Indefinite.....		Colloid adenoma, indefinite changes.
H.	—Typical.....		Typical.
S.	8070.—Typical.....	3 yrs.....	Typical.
C.	8076.—Typical.....	6 yrs.....	Typical combined with adenoma.
H.	2894.—Typical.....	3 yrs.....	Typical.
S.	8074.—Typical.....	1 yr.....	Typical.
M.	8066.—Indefinite, no exoph. no nervousness.....	2 mos.....	Normal.
S.	7142.—Typical.....	8 mos.....	Typical.
B.	7536.—Indefinite.....	1 yr.....	Colloid adenoma, slight hypertrophy of epithelium.
T.	5216.—Indefinite, no exophthalmos.....	3½ yrs.....	Cyst with wall of hypertrophied thyroid tissue.
D.	5045.—Typical.....	1 yr.....	Typical.
Y.	6886.—Typical.....	1½ yr.....	Typical.
E.	7425.—Typical.....		Typical.
H.	7321.—Typical.....	3 yrs.....	Typical.
R.	7278.—Typical.....	1 yr.....	Beginning folding in walls of large alveoli.
C.	7375.—Typical.....	3 mos.....	Typical.
J.	6955.—Typical.....		Typical.
S.	7351.—Moderate.....	5 yrs.....	Large alveoli, slight folding.

G.	7122.—Typical.....	2 yrs.....	Large alveoli full of colloid, complicated folding.
L.	7897.—Typical....	3 mos.....	Typical.
F.	—Indef. goiter, nervousness	1 yr.....	Beginning changes in walls of large alveoli.
S.	8071.—Indef. tachycardia.....	18 yrs.....	Exoph. changes in adenoma, not elsewhere.
S.	8046.—Indef. exoph. tremor, no goiter.....	5 yrs.....	Beginning changes in walls of large alveoli.
P.	5883.—Indef. nervousness, tremor, no exoph.....	1 yr.....	Normal.
G.	6202.—Typical.....		Typical.
B.	7153.—Indef. no exoph. tremor. wasting.....	2 yrs.....	Beginning changes in walls of large alveoli.
T.	7212.—Indefinite. tremor only, pulse 100.....	Gradual.....	Indefinite, beginning changes.
A. I.	7953.—Typical.....	6 mos.....	Typical.
N.	610.—Typical.....	2 yrs.....	Typical.
T.	2775.—Typical.....	3 yrs.....	Typical.
H.	4017.—Typical.....	6 mos.....	Typical.
H.	4055.—Typical.....	2 yrs.....	Typical.
R.	4170.—Typical.....	2 yrs.....	Typical.
C.	4538.—Typical.....		Typical.
S.	2079.—Typical.....	4 yrs.....	Typical.
W.	4808.—Typical.....	2 yrs.....	Typical.
W.	5254.—Typical.....	2 yrs.....	Typical.
D.	5334.—Typical.....	8½ yrs.....	Typical.
B.	5335.—No exoph. goiter, tremor, tachycardia.....	1 yr.....	Foci of proliferation, much colloid, lymphoid hyper.
L.	5379.—Typical.....	9 mos.....	Typical.
M.	5404.—Typical.....	3½ yrs.....	Typical.
W.	5582.—No exoph., nervousness, tachycardia, goiter.....	1 yr.....	Foci of typical change, other areas normal.
S.	5634.—Indef., goiter with tremor only.....	1 yr.....	Colloid adenoma.
G.	5199.—Goiter 28 yrs.; exoph. symptoms 5 mos.....	5 mos.....	Indef. changes in old goiter.
F.	5651.—Typical.....	2 yrs.....	Much folding in large alveoli; typical.
B.	5806.—Typical.....	8 mos.....	Typical.
S.	5873.—Indefinite.....	8 mos.....	Colloid adenoma.
E.	5914.—Slight symptoms.....	6 mos.....	Slight changes in large alveoli.
M.	—Typical.....		Typical.
L.	5991.—Typical.....	13 mos.....	Typical—focal.
E.	6019.—Typical, moderate.....	3 mos.....	Typical.
W.	—Typical.....	5 yrs.....	Typical.
H.	4744.—Typical.....	3 yrs.....	Typical.
K.	—Typical.....	2 yrs.....	Typical.
P.	—Typical, moderate.....	5 mos.....	Typical.
H.	—Typical.....	2 yrs.....	Typical.
J.	2827.—Typical.....	15 yrs.....	Typical.

veins are found to be very large and easily torn and are distended with blood so that the gland has a very congested appearance. This is not striking in the excised portion, since the vessels collapse and on section the interior of the gland tissue is rather pale. Usually the tissue is hard and rather rigid than elastic. Its normal amber red translucence gives way to a grayish opacity and the fresh cut surface, instead of being glairy or gelatinous in appearance, tends to be rather dry and granular. This varies, however, with the amount of colloid material in the alveoli, and in many advanced cases the cut surface may be still moist and give off a little glutinous material. The surface of the gland is usually somewhat nodular and rough, and this is seen to be true also of the surface, in which it is found that fine strands of fibrous tissue traverse the glandular substances, separating it into lobules.

Usually the change is diffuse throughout the whole gland, but sometimes one lobe may be much larger than the other, and in some cases the alterations described are present only in small patches here and there throughout a gland which otherwise seems nearly normal. These foci are easily distinguished by their fine grain and by their opacity from the adjacent colloid holding tissue.

Microscopically there is found the change which appears in the experimental compensatory hypertrophy. Strands of fibrous tissue run in every direction like scars through the gland and separate the tissue into lobular masses, and in these lobules the alveoli are often still separated by a fibrous tissue stroma much more abundant than in the normal gland. The alveoli are no longer rounded, full of colloid, and lined with low cubical epithelium, but are extremely irregular in size and in form. As a rule most of them are smaller than normal, while in the central part of each small lobule there are larger alveoli of very irregular outline, sending out diverticuli in every direction and encroached on by epithelial projections which extend into their lumen. With some special method of staining the connective tissue it may often be made clear that such a small lobule is probably a sort of colony in which the smaller peripheral alveoli are derived from the more centrally placed or are actually merely sections of the diverticula of the central ramifying alveolus. This alternation of large irregular alveoli with small ones ranged round them is very characteristic and evidently results, in part at least, from the separation of portions of the central cavity in the form of new alveoli.

The epithelium becomes columnar not only in the large alveoli, but in the small ones as well, and thus occupies so much space that there is but little lumen left. Indeed, the areas occupied by the small alveoli may appear almost solid, so small are their cavities and so scant the colloid. In most instances the epithelium is very regular in its form throughout and the details of its structure can be made out very clearly. The cells are plump, with a

finely granular protoplasm and a sharp outline. The free surface is very sharply marked and is sometimes slightly dome-shaped. The nucleus may lie near the base or near the free end of the cell. Mitotic figures are frequently to be found. Occasionally some of the cells appear narrow and shrunken and biconcave in form, with a very deeply stained nucleus and dark red protoplasm. These are the so-called colloid cells of Langendorff, thought by him to be especially concerned in the secretion of colloid, but which seem to us rather more like the result of some degenerative process. Only rarely could the so-called *Schmelzepithel* of Hürthle be seen and then it seemed obvious that it was the effect of mechanical dislodgement and disarrangement of the cells. Similarly the extensive desquamation of the epithelial cells which one so often sees in specimens removed at operation seems to be due to the considerable pinching and handling through which the specimen unavoidably passes during the operation. Nevertheless, we have met with one or two cases in which, in association with especially severe symptoms, there has been found widespread desquamation of the epithelium, probably not the result of pinching the gland, and this is regarded by some, especially by Dr. Bloodgood, as a feature associated particularly with very severe symptoms.

It is in these extreme cases that peculiar alterations of the epithelial cells are sometimes found. In several instances we have observed areas in which the epithelium was enormously swollen so as to practically obliterate the lumen of the alveolus. These large irregular cells no longer preserve the columnar form, but are shapeless masses of finely granular protoplasm which takes an intense pink stain with the eosin and in which the nuclei are also irregular in form and size and stain very deeply, almost black, with the hematoxylin. Usually one or two alveoli only show such a change in their epithelium, or there may be only a few cells of this form intercalated among others of the usual type in the alveolar wall, but sometimes over considerable areas all the alveoli are packed with such cells. Their significance is far from clear. Much more frequently there are found cells among the ordinary epithelial cells of the alveolar wall which are greatly enlarged but the protoplasm of which retains the characters seen in the rest of the cells and contains only a scant basophilic granulation. The nuclei of such cells are usually much enlarged and vesicular, with scattered chromatin granules.

The colloid varies greatly in different cases, but it seems that in most of the more severe cases it is markedly diminished in amount and altered in quality, the normal hyaline material being replaced by a very palely staining substance or by a ragged, shredded, granular or vacuolated mass which has no longer the refractive qualities of the normal colloid. There are some cases, however, in which there is a great deal of fairly normal looking

colloid, and this is especially true of those instances in which the hypertrophy of the epithelium is relatively slight: cases, that is, in which the process is apparently advanced, at least as far as the thyroid is concerned. On the other hand, when the colloid is greatly diminished, one rarely fails to find severe symptoms, and when the symptoms are very indefinite or in part absent it is usual to find a good deal of colloid.

The most interesting cases in this connection, then, are those in which intense symptoms exist, but in which, at the same time, the alveoli contain a large amount of colloid. There are at least twelve of these cases in our series, and although in some of them one may explain the existence of such large alveoli full of colloid, on the idea that the exophthalmic symptoms are associated with changes which have appeared in a gland already the seat of alterations such as are seen in a colloid goiter, still there remain many in which there is no evidence of such a previous goitrous change. From this it appears that the presence of quite abundant colloid is not inconsistent with the development of intense symptoms, although in most cases in which the symptoms are intense the colloid tends to disappear with the advance in the alterations in the gland. It is not improbable that the amount of colloid may bear a fairly constant relation to the stage of progress of the disease, and light may be thrown on this by the consideration of the tissues removed at successive operations. One can distinguish, however, different types of change in the thyroid in different cases, for while in one group the alveoli are not larger than normal, show elevation and folding of the epithelium and are full of colloid, another group with quite as intense symptoms will present thyroid tissue composed of very large alveoli full of colloid in which, nevertheless, the folding of the epithelial layer is most complicated. A third group comprises those cases usually milder in their course in which the alveoli are large and full of colloid, but in which the alveolar epithelium is almost flat, except in certain foci or in portions of some of the alveolar walls where it becomes cylindrical and thrown up into folds. Several of the cases in which extirpation of the thyroid was carried out with good results for the relief of indefinite symptoms, such as the combination of goiter with tremor only or with moderate tachycardia only, showed in the thyroid abundant colloid in large alveoli which are hardly at all irregular, but, nevertheless, in places show areas of epithelium which has become high and cylindrical and which is beginning to project prominently into the alveolar lumen.

Finally, in a few of the cases in which the symptoms were reduced to nervousness or slight tremor with goiter, the excised tissue shows the normal structure or that of a circumscribed adenoma. There were six of these cases which should be ruled out of the series.

The focal nature of the alterations in the thyroid is especially interesting and may be recognized in some cases in the fresh cut surface of the gland by the opacity and granular surface of the altered areas which contrast with the surrounding tissue. Apparently this, too, represents a stage in the development of the lesion, and in most of the six cases which show it the symptoms had existed only a short time before the operation. Microscopically the altered areas are quite sharply demarcated from the rest and may involve a great number of alveoli or be limited to very small foci, including only a few alveoli here and there. It is difficult to understand why the lesion should appear thus in certain areas only.

In sixteen of the cases there were found on cutting through the thyroid rounded circumscribed nodules which projected above the general level and differed in consistency and general appearance from the rest of the gland. These are the adenomatous nodules which constitute a considerable portion of ordinary goiter, and hence they are by no means peculiar nor characteristic of the changes in exophthalmic goiter. They are most commonly finely granular and opaque, occasionally flecked with yellow patches of necrosis or with hemorrhages; and on section they are seen to be composed of small round alveoli lying quite separate from one another in an abundant loose stroma and lined with cubical epithelium. In only a few of our cases did the alveoli, which make up such embedded nodules, show the folding and other hypertrophic changes which characterize the tissue round about, but in one case in which exophthalmic symptoms were well marked these changes were limited to the tissue forming such a circumscribed nodule. In another case the hypertrophied tissue was found to form the thick lining of a cyst.

The second type of circumscribed nodule is that which is composed of a tissue very rich in colloid and correspondingly translucent. The central part is often occupied by a cyst-like cavity filled with a greenish glutinous fluid. Such nodules show microscopically very large alveoli more or less radially arranged and distended with colloid. The amount of fibrous tissue traversing the gland varies in different cases, sometimes occurring in coarse bands that separate the tissue into lobules, while in other cases there are, in addition, fibres which separate the individual alveoli.

In six of our cases it was possible to study the thyroid at different stages in the progress of the disease, either in tissue removed at two different operations or at autopsy in patients who died some time after the operation. No very constant results were obtained. In four of the cases, in which the intervals between the times of obtaining the two specimens were seven months, eighteen months, forty-five days and seventy-nine days, the tissues were practically identical in the two portions examined. In the

fifth case, after a lapse of nine months, the tissue from the second operation showed that the epithelial cells had become greatly increased in height and the colloid rather more abundant. In the case in which the longest interval elapsed between the operations, two years and six months, the alveoli had changed from small compact almost solid masses of epithelium with inconspicuous lumen and no colloid to large ramifying spaces full of ragged colloid and lined with very high cylindrical epithelium.

Thus in these cases there is no tendency in the thyroid toward a return to the normal, nor should we expect it, since the second portion of tissue was obtained either after death in cases in which the symptoms had persisted or at an operation undertaken because of the persistent symptoms. It will be extremely interesting to investigate the thyroid in one of the cases in which amelioration or cure of the disease has followed partial excision, if opportunity ever presents itself.

In this connection, too, those cases seem important in which the symptoms of exophthalmic goiter have gradually given place to those of myxedema with atrophy of the thyroid.

In nearly all the typical cases there are scattered about, usually in connection with the fibrous strands, masses of lymphoid tissue which are sometimes large enough to be conspicuous, opaque white dots visible in the fresh specimen. In one instance in which there was a cyst the numerous lymphoid nodules shone through the wall of the cyst very distinctly. In some cases they are small and indefinite in outline and are composed of an irregular accumulation of lymphoid cells. Generally, however, they are well-formed lymphoid nodules with very distinct germinal centers, composed of concentrically-arranged cells with abundant protoplasm. It seems probable that this increase in the bulk of the lymphoid tissue which is practically invisible in the normal gland, is part of the general increase in size of the lymphoid structures of the neck which occurs so often.

This could be studied in a few of the cases at autopsy in which it was found that the lymph glands and hemolymph glands were enlarged, especially in the neck, but also in the thorax, abdomen and retroperitoneal region. The superficial glands are usually not so much enlarged, but the lymphoid tissue in the pharynx, the tonsils and the nodules in the tongue become very conspicuous. Microscopically it is found in all these places, as in the lymphoid nodules of the thyroid itself, that there is a great increase in the lymphoid cells, but also that the germinal centers become very large and sharply outlined and contain many actively phagocytic cells. The sinuses are usually filled with wandering cells. This change in the lymphoid tissue has the appearance of being a reaction to the absorption of some poisonous or injurious material, but whether this material stirs up the thyroid also to proliferation or is itself the product of the overactive thyroid is difficult to say.



The thymus, too, has been found by nearly all investigators to be enlarged. There are not only the usual scanty remains, but the mass of tissue is frequently seen to be as large or larger than that seen in a child before retrogression has taken place. Histologically it has the same appearance as in those earlier years, and the same processes of phagocytosis are seen to be going on. The recent statements as to its epithelial nature make this change in the thymus especially interesting and deserving of more attention than has been accorded it, particularly since there have been some favorable results from the administration of thymus extract in this disease.

The parathyroid glands are sometimes to be found attached to the portion of the thyroid extirpated at operation, even when the greatest care is exercised to preserve them. In other instances they were found at autopsy, and altogether we have had the opportunity of studying them in sixteen cases. They were practically normal in all cases. The cells of all varieties found in the normal gland were seen in these, too, in the usual proportions. In six of the cases the notes state that there was an increase in the fibrous stroma, and renewed examination of these glands shows that there is in some cases a network of scar tissue running through the tissue, just as has been seen in the thyroid in so many of these cases. Otherwise, however, the tissue in these glands seems abundant and normal. On the whole it seems improbable that the parathyroids have anything to do with the production of the symptom-complex of exophthalmic goiter when we compare these very slight anatomic lesions with the advanced changes in the thyroid.

Much attention has been devoted to the study of the cervical sympathetic ganglia and nerves, since the idea is held by many that changes in those structures are really at the bottom of the whole disease, but the results of these studies have been very unsatisfactory; some authors have described atrophy of the cells, increase in the pigment or overgrowth of connective tissue, but quite as many or more have found the ganglia perfectly normal. We have studied them carefully in two cases and have found no pathologic alterations, unless the presence of a number of shrunken deeply-stained ganglion cells in one section can be regarded as pathologic. This ganglion was fixed in formalin and the one from the other side in alcohol. In that one no such changes were found, so that I am not disposed to attach much importance to them.

Similar results have come from the anatomic studies of the central nervous system, for while in some cases atrophy or destructive lesions have been found in the corpora restiformia, and in others hemorrhages in the medulla, the majority have shown no abnormality, and at best the lesions must be regarded as extremely inconstant.

As to the hypothesis cerebri, there seems to be few recorded observations. Häinig studied it in nine cases and found it quite normal, although in several of the cases the number of chromophile cells were striking. In the one case in which we have secured the hypophysis its tissue was normal.

Of pathologic alterations in other tissues and organs so little is known and the findings are so inconstant that they may well be passed over.

On the whole, therefore, the only lesions in this disease which are palpable and constant are those of the thyroid and of the lymphoid apparatus and thymus. All of the others are so indefinite and so often completely missed that it is difficult to convince oneself that they play a primary rôle in the disease.

From what has been said it is seen that with the appearance of definite symptoms of exophthalmic goiter there is always the same change in the thyroid. In very mild and definite cases it may be possible to find only the beginning of this change in some part of the walls of some of the alveoli. In more severe cases in the early stages the change in the thyroid may be in foci only, while the rest remains normal, but in the more advanced cases the typical change with proliferation of the epithelium and folding of the walls of the alveoli is invariably found. None of our cases came from goiter regions, although one or two had goiters before the exophthalmic symptoms developed. Even in these it is only necessary to look far enough to find the changes described above superimposed on those of the old goiter. Sometimes in nodular goiters only the intervening tissue shows the hypertrophy well, but in other cases that of the adenomatous nodules will also show it. From this series of cases we are quite convinced that this change in the thyroid in a more or less complete development is quite constantly associated with the symptoms of exophthalmic goiter.

Now this is anatomically the change produced in compensatory hypertrophy when we excise part of the normal gland, but that compensatory hypertrophy never produces a mass of tissue in excess of the normal and no symptoms result. It is the same change, too, that we find in sheep and dogs, sometimes with very marked enlargement of the thyroid, but these animals show no definite symptoms, or if they do they are rather the symptoms of myxedema (Marine). There can not be a complete analogy, then, between these lesions. In exophthalmic goiter there must be something more than the mere hypertrophy of the thyroid, either in the nature of its secretion or in some other factor quite aside from the thyroid. Nevertheless, it is certain enough that the thyroid is hypertrophied and the current opinion is that it is functionally overactive and producing an excess of secretion. This, however, remains to be directly proven, and Oswald, in opposition to the general view, believes that we really have there a condition of

thyroid insufficiency, since the gland is often nearly empty of colloid and contains relatively little iodine-holding secretion. But the removal of part of the thyroid improves the symptoms of the disease, and the administration of thyroid extract makes them worse, so that we are almost forced to the belief that the excessive activity of the thyroid is at fault.

The great question seems to remain: if the gland is hypertrophied and overactive, what has caused this hypertrophy? The symptoms of exophthalmic goiter are so like those of artificial thyroidism that it is fairly easy to believe that there is this excessive activity and that the other symptoms depend on the outpouring from the thyroid. But we have no examples elsewhere of the spontaneous hypertrophy and overactivity of an organ to the detriment of the rest of the body. Always it is a work hypertrophy or compensatory hypertrophy, but here the inconsistency appears that when you excise part of this hypertrophied gland the symptoms often disappear.

Is it possible that the fundamental underlying cause is some infection, such as influenza, which, reaching the thyroid through the pharynx, sets up such a non-suppurative thyroiditis as has been described by de Quervain, destroying many of the cells and leaving scars through the gland, after which the remainder becomes hypertrophied and its activities perverted? Gilbert and Castaigne, Reinhold, Brauer and others describe such a course of events, and, indeed, a history of pharyngitis or grippe is very common as a forerunner of this disease. It is still rather hard to comprehend the overstepping of the normal to such an extent in the process of compensatory regeneration, and the production of a harmful organ by a mechanism which usually restores to normal with such precision.

The relation of iodine to this disease is interesting, for while in a normal person the symptoms of iodism do not very closely resemble those of exophthalmic goiter, it is claimed by Breuer that in cases of exophthalmic goiter the symptoms may be made much worse or latent symptoms called out by administration of iodids.

Further, the suggestion may be offered that it is possible, since some of the symptoms are generally referred to disturbances of function of the cervical sympathetic system, that the vasoconstrictor influence of those ganglia over the thyroid may be diminished and that a consequent hyperemia of the gland may finally bring about an overactivity. Attempts to study this experimentally by the isolation of the thyroid from all nervous connections, even those which are closely bound up with the vessels, have so far led to no result.

Since the most palpable and constant change in this disease is after all in the thyroid, it seems that our efforts to explain the

disease must start with the explanation of the disturbances in structure and function of the thyroid. We must know definitely whether it is pouring out an excessive secretion into the circulation; we must be able to recognize that secretion and estimate its amount and its toxic character. Then we must learn surely whether the thyroid is doing this independently or whether it is in response to some disturbance in metabolism elsewhere. It seems possible even that it might be in response to a demand only for some other associated substance which brings with it the toxic substance, so that while the thyroid hypertrophies to meet a justifiable demand it incidentally produces a noxious substance in excess.

At all events, we must learn the underlying cause of these changes and not be content with discovering which organ is most disturbed, for only in that way can a perfectly rational therapy be devised.—*Journal of the American Medical Association*, Oct. 5, 1907.

### THE DIAGNOSIS OF EXOPHTHALMIC GOITER.\*

LEWELLYN F. BARKER, M.D., BALTIMORE.

THE part assigned to me in this symposium is the diagnosis of this remarkable disease. What I shall have to say is based (1) on an analysis of the cases which have occurred in my wards at the Johns Hopkins Hospital during the past two years,<sup>1</sup> and (2) on a study of the bibliography of the subject.<sup>2</sup>

It will be convenient to discuss (1) the character and significance of the individual signs and symptoms; (2) the diagnosis of the clinical syndrome, especially in its less obvious forms; (3) certain points in differential diagnosis, and (4) the diagnosis of the indications and contraindications for surgical interference.

On account of the necessity of brevity I am forced to limit the discussion to the features which I regard as most essential.

#### I. THE CHARACTER AND SIGNIFICANCE OF THE INDIVIDUAL SIGNS AND SYMPTOMS.

Besides the three cardinal symptoms—struma, tachycardia and exophthalmos—there are a very large number of other symptoms

\* Read in the joint session of the Sections on Practice of Medicine, Surgery and Anatomy, and Pathology and Physiology, of the American Medical Association, at the Fifty-eighth annual session, Atlantic City, June, 1907.

1. I have to thank Drs. Roger Morris and Benson A. Cohoe for help in the analysis of the material.

2. Especially helpful articles are: Moebius (P. J.): *Die Basedow'sche Krankheit*, Wien, 1896; a new edition has recently appeared with a very full bibliography. Buchan (G.): *Die Basedow'sche Krankheit*, Eine Monographie, 8°, Leipzig u. Wien, 1894. Kocher (A.): *Ueber Morbus Basedowi*, Mitt. n. d. Grenzgeb. d. Med. u. Chir., Jena, 1902: iv, 1-301. Dock (G.): *Clinical observations in exophthalmic goiter* Am. Med., Phila. 1906, vi, 271-281. Kocher (T.): *A contribution to the pathology of the thyroid gland*, Brit. Med. Jour., Lond., 1906, i, 1261-1266.

and signs to be considered, some of them more important than the exophthalmus as diagnostic aids because more frequent and characteristic.

(a) *The Struma or Goiter.*—The thyroid gland is enlarged in the majority of cases of the disease. Since we have been taught how to recognize slight enlargements, the reports of exophthalmic goiter without goiter have grown fewer, and some go so far as to deny the existence of an exophthalmic goiter without struma. It does exist, however. In twenty-one of my cases a struma was recorded in the notes dictated at the ward rounds in eighteen. The whole gland is, as a rule, uniformly involved, giving rise to the well-known horseshoe-shaped projection, but one lobe may be larger than the other. The struma is not large as a rule; the patient may even not have noticed the thickening of the neck. The isthmus of the gland is usually broadened and thickened and the pyramidal lobe is enlarged. The consistence varies according to the stage of the disease and according to the acuteness or chronicity of its course. At the beginning, and in cases running an acute course it is often softer than normal; later on, and in chronic cases, the consistence is firmer and more elastic. A characteristic feature is the granulation of the surface, usually easily recognizable on palpation and due to the lobular hyperplasia. Most important, from the diagnostic standpoint, are the vascular peculiarities of the goiter. The typical struma in exophthalmic goiter is always a struma vasculosa. The telangiectasis is recognizable (1) by the visible pulsation of the goiter, (2) in many instances by the palpable systolic expansion, (3) by the palpable thrill, and (4) by bruits audible at the point of entrance of the thyroid arteries (especially the superior) into the gland. The struma, though usually recognizable by the educated touch of the physician's finger early in the disease, is mentioned by only about one-fifth of the patients as preceding the other symptoms.

(b) *The Tachycardia or (better) Pycnocardia.*—In the semi-otic trinity the increased frequency of the heart beat is the most constant and most important sign. The pulse rate is practically always over 90 and may exceed 200 beats to the minute. A rate between 110 and 150 is very common, and the patients usually notice subjective palpitation; sometimes they complain of it bitterly. In my experience this exquisite thyreotoxic phenomenon is usually continuous and persistent. In a few cases, however, I have seen it irregularly or intermittently present. In one it was always precipitable in the early part of the disease by psychic influences and became continuous later. Very rarely pycnocardia is absent when other signs of the disease are present, and then, as Dr. Emerson has shown, the sign may sometimes be brought out by the administration of a few doses of thyroid tablets.

(c) *The Exophthalmus.*—This sign is the most striking of all

to the casual observer when it is present. It is entirely absent in about one-third of the cases, and even in many of the other two-thirds it may be so slight as not to attract attention. It is necessary to distinguish between apparent exophthalmus due merely to widening of the palpebral fissure and true protrusion objectively demonstrable as a shortening of the distance between the supra-orbital margin of the frontal bone and anterior pole of the eyeball (measurement with exophthalmometer). The former is, as a rule, a more important factor in the changed facial appearance than the latter. The prominence is usually bilateral and continuous; it may be unilateral and the intensity may vary from time to time.

(d) *Phenomena Pertaining to the Muscular System.*—The tremor noted by Trousseau and Charcot really ranks in diagnostic importance along with the pycnocardia and the struma; it is so frequently present that one inclines with Marie to designate it as a fourth cardinal sign. The tremor is rapid and vibratory, there being as many as eight to ten oscillations per second, in marked contrast with the slow tremor of paralysis agitans. It is best seen by asking the patient to hold his hand with widespread fingers between the observer and the light. The tremor may be limited to the extremities, but frequently involves also the muscles of the neck and trunk. It is not exaggerated by voluntary movement, but is increased by psychic excitation. Paresis, paralysis or atrophy are occasionally seen. In how far they are related to the fatty change in the muscles described by Askanazy is not known. Sudden "giving way of the legs" may be an early symptom.

(e) *Phenomena Pertaining to the Digestive Apparatus.*—Diarrhea and vomiting, both without apparent cause, are not infrequently troublesome symptoms in advanced stages of the disease. They are rare, however, at the beginning and are, therefore, of little help for diagnosis. Other abnormal phenomena, noticeable in the digestive apparatus, are too rare and inconstant to be of much diagnostic value.

(f) *Phenomena Pertaining to the Respiratory Apparatus.*—Here dyspnea is the most important phenomenon. It is usually a late symptom, present in relatively few cases, and generally cardiac in origin.

The respiratory curve as recorded by graphic method is flattened (Hofbauer). The lessened expansion of the thorax (Bryson's sign) is probably due to weakened muscles and is of no special diagnostic importance.

I would call attention to air-hunger and the peculiar fruity odor of the breath occasionally present in advanced cases; these are important, not for the diagnosis of the disease itself, but as indicating the existence of acidosis, which may call for an immediate therapeutic effort.

(g) *Phenomena Pertaining to the Urogenital Apparatus.*—

Here there are no constant findings. Polyuria, glycosuria, transient albuminuria are only occasionally met with. The urea-nitrogen, the total nitrogen, the uric acid and the phosphates of the urine are increased corresponding to the accelerated metabolism in this disease. A diminution of the menstrual flow is a very common accompaniment of exophthalmic goiter in women. The breasts occasionally show changes, usually of rejuvenation.

(h) *Phenomena Pertaining to the Circulatory Apparatus.*—The pycnocardia, the most helpful of the signs for diagnosis, has already been mentioned. But the heart shows other changes also. The heart sounds are strongly accentuated, and accidental systolic murmurs, due to the excited and accelerated action of the heart, are frequently audible both at apex and base. The right ventricle appears to be especially affected, and its excited action can be recognized by palpation to the left of the sternum. In advanced cases the heart is not infrequently dilated. The cardiac condition varies with the intensity of the thyreointoxication, and is a valuable criterion for judging of the latter.

The radial pulse is usually small and quick. Arrhythmia is rare except in advanced cases or where the heart is otherwise diseased. The maximal arterial pressure varies. It is sometimes low, but more often higher than normal, and occasionally very high. The pulse pressure (difference between maximal and minimal pressure) may be large, indicating a large systolic output from the left ventricle. When this is borne in mind, along with the great increase in the heart rate, one begins to realize the amount of work done by the heart in this disease.

Throbbing of the carotids and of the abdominal aorta is a sign frequently present, and one of considerable diagnostic import.

Slight edema of the legs, hands or eyelids is common.

The blood shows no constant alterations, though a relative increase in the mononuclear white elements has been noted by some in the differential count.

The slight enlargement of the lymph glands of the neck so constantly seen at operations is only rarely demonstrable clinically by palpation.

(i) *Phenomena Pertaining to the Nervous System, Sense Organs and Skin.*—Both the cerebrospinal and sympathetic nervous systems are profoundly affected in the disease, the involvement of the autonomic systems, especially the bulbar, being perhaps most marked. It is surprising how many of the phenomena pertaining to the other parts of the body may conceivably be brought into relation with disturbances of the autonomic neurone-systems.

The psychic manifestations are often pronounced and may be the first to excite suspicion as to the diagnosis. Feelings of restlessness and discomfort, an indefinable anxiety or apprehension without cause and rapidly alternating moods are very character-

istic. One of my patients gradually became so irritable and violent that his wife, not knowing the cause, had him before a magistrate and bound over to keep the peace. Another became so anxious and disturbed that she lost confidence in herself and had to be sent temporarily to a closed institution pending the passing of the psychosis. Even hallucinations or persecutory ideas may develop. Insomnia is frequent and headache also. Vertigo is less common, delirium rare. Pains in the neck or jaws, and shooting pains in various parts of the body are occasionally complained of. A subjective sensation of heat in the body, independent of fever or of the external temperature, is a common symptom. At the beginning of the disease a feeling of weakness, so strong as to interfere with work, is present in many cases; easy fatigability, in young people especially, should excite suspicion.

The eye signs are among the most interesting. The pupils are usually equal and react to light, though with unilateral exophthalmus one pupil may be larger than the other. Aside from the exophthalmus and widening of the palpebral fissure, the most important signs here are (1) the failure of the upper eyelid to follow the eyeball normally in looking downward (v. Graefe); (2) the retraction of the upper lid on straight-forward vision, revealing some sclera above cornea (v. Stellwag; Dalrymple); (3) the infrequent and incomplete involuntary winking (v. Stellwag); and (4) the inability to hold the eyes in the position of convergence (Moebius). Other signs such as (5) the difficulty of everting the upper lids (Gifford); (6) the pigmentation of the upper lids (Jellinek and Rosin); (7) the failure of the forehead to wrinkle on looking up (Joffroy); (8) epiphora or overflow of tears; (9) the tremor of the eyeballs; (10) the subjective feeling of pressure behind the eyes (A. Kocher); and (11) abnormal dryness of the eyes, are occasionally met with. These signs, dubbed "fancy signs" by my colleague, Dr. Thomas, who fears a neglect of the cardinal tetrad through a search for the novel, are not without their diagnostic value; the presence or absence of all eleven may be determined in a few moments and a clue quickly gained to the unraveling of a condition which might, otherwise, easily escape detection.

The organs of hearing, smell and taste rarely present abnormal symptoms or signs. In the integumentum commune, however, important phenomena are observable. The skin is nearly always smooth, delicate, thin and moist. Sweating is constant and troublesome in a majority of the cases and accounts for the well-known increased electric conductivity of the skin (Vigouroux's sign). Vasomotor instability in the skin is a prominent feature, and the physician when making his first physical examination of the patient is often struck by the blotchy erythema of the neck and upper chest. Pigmentation is the other most important cutaneous



sign, the color of the skin may resemble that seen in pernicious anemia, or it may approach that of Addison's disease. The nature of this pigmentation may perhaps not be understood until we are better informed regarding the chromaffine systems of the body. Falling of the hair is more common than prematurely gray hair (cautities præmatura), though both are met with.

(k) *Phenomena Pertaining to the General Metabolism.*—Clinicians have long since noticed the marked tendency to emaciation despite liberal feeding in exophthalmic goiter. A loss of from 20 to 50 pounds in weight during a short period is not uncommon. The body-weight curve is important as a clue to the speed of the metabolic reactions, and thus for judging of the intensity of the disease. The metabolic disturbance consists of an acceleration of the oxidative processes (Fr. Müller; Magnus-Levy); in doubtful cases in hospitals a determination of the oxygen intake and of the CO<sub>2</sub> output by the Zuntz-Geppert method is a diagnostic aid, though it is too inconvenient for use in private practice.

The occurrence of mellituria in the disease has already been referred to. Slight fever was noticed in several of my cases. Whether or not such fever is due to a disturbance of heat-regulation, which is a part of the disease proper, is not known. It may depend on complications.

## II. THE DIAGNOSIS OF THE CLINICAL SYNDROME, ESPECIALLY IN ITS LESS OBVIOUS FORMS.

The diagnosis in typical cases of the well-developed disease could scarcely be overlooked except by an untrained or superficial observer. The coexistence of pyenocardia, struma and tremor, with or without exophthalmus, are decisive. It is in the beginning of the disease and in the atypical cases, including the so-called *formes frustes*, that some difficulty may be encountered. Once the clinician, however, has learned to recognize a beginning struma vasculosa, and to realize the significance of the so-called hyperthyreotic equivalents, especially the thyreotoxic form of the goiter-heart, the thyreotoxic neuropathic and psychopathic states, and the thyreotoxic acceleration of oxidative metabolism, he will rarely be left in doubt. It may in some instances be possible to unmask a latent hyperthyreoidism by the administration of a few doses of iodothyryn or by a Zuntz-Geppert estimation. It should be borne in mind that nearly all the phenomena of hyperthyreoidism are accentuated somewhat by the recumbent position; this may explain why the patients so often feel worse in the morning than after they have been up and about during the day. It is unusual, even in the mildest forms, not to get at least some hint from the eyes, if the various tests be run through.

## III. CERTAIN POINTS IN DIFFERENTIAL DIAGNOSIS.

A few words must be said concerning the differential diagnosis as regards (a) strumata, (b) goiter-hearts, (c) exophthalmus, (d) thyreotoxic pseudochlorosis, and (e) the conditions underlying hyperthyreosis and accounting for it.

(a) *Strumata*.—(1) Not every acutely developing pulsating struma is an exophthalmic struma; (2) the symptoms of exophthalmic goiter may become superimposed on an ordinary colloid struma, in which event the thyreotoxic symptoms appear to be mitigated (*goitre Basedowifié* of Marie, *struma Gravesiana colloidés* or *struma Basedowificata* of Kocher).

(b) *Goiter-hearts*.—It seems tolerably clear that the goiter-heart of exophthalmic goiter is a thyreotoxic phenomenon. With Friedrich Müller, I can see no reason for separating from it the milder forms of the thyreotoxic heart (*Kropfherz* of Kraus; *Kardiopathia thyreogenes levis* of His). There is every transition from the conditions in which they occur to the outspoken state. There is force, however, in the argument that the cardiopathies due to the mechanical effect of a goiter (Minnich) be separated from the thyreotoxic goiter-heart. Thus (1) disturbances of the heart due to strumata extending through the superior aperture of the thorax (Kocher), (2) the goiter-heart due to mechanical injury of the venous circulation (Rose's goiter-heart), and (3) that due to interference with respiration (dyspneic goiter-heart of Kocher), would come in this class. Though thyreointoxication may play a secondary part in such cases, it is the diagnosis of the mechanical injury that is all important and should guide the therapy.

(c) *Exophthalmus*.—It is usually easy to distinguish the exophthalmus of this disease from other forms of exophthalmus, but mistakes are sometimes made. Protrusion of the eyeballs due to the increase of intracranial pressure (especially in hydrocephalus), to aneurism, sinus thrombosis or abscess (unilateral exophthalmus), or to retrobulbar growths, especially chloromatous masses (Dock) should be remembered. An acute recurrent exophthalmus due to angioneurotic edema has also been described (Gruss).

(d) *Thyreotoxic Pseudochlorosis*.—Wunderlich observed protrusion of the eyeballs in anemic-looking girls. This is often associated with pallor, fatigability, emaciation and accelerated heart action. It was supposed to be due to chlorosis, and the goiter is mentioned in medical writings as a *struma chloroticum*. Blood examination shows, however, the presence of a normal or excessive amount of hemoglobin, and such patients are doubtless affected with true exophthalmic goiter (Fr. Müller). When they begin to lose weight, to have slight fever and to sweat freely the suspicion of pulmonary tuberculosis may be aroused. Dr. A. D. Atkinson, of Baltimore, recently showed me such a patient; a rapid tremor,

a pycnocardia, a suggestive v. Graefe's sign, a normal blood-count and slight enlargement of the thyroid gland helped to make a diagnosis of hyperthyroidism certain.

(c) *Conditions Underlying Hyperthyrosis.*—Though it is now possible for us as internists to recognize hyperthyroidism in its very early stages, we realize fully that we are far from understanding the causes of the hyperthyrosis. Hyperthyrosis, like jaundice or fever, may be excited by different causes, and we must from now on try to make out the varying etiology, be it toxic, infectious, reflex, obscure, metabolic or still other in nature. In one case recently reported a hyperthyroidism developed as a result of a metastatic endothelioma in the gland. This raises the questions concerning the justification of the terms "Basedow" and "Pseudobasedow" (Buschan) and of "essential" and "symptomatic" exophthalmic goiter (Moebius), questions which can not well be answered until we have further knowledge.

#### IV. THE DIAGNOSIS OF THE INDICATIONS AND CONTRAINDICATIONS FOR SURGICAL INTERFERENCE.

An important part of the physician's function lies in the diagnosis of the indications and contraindications for surgical interference. Formerly surgery was resorted to only after non-surgical treatment had been given a prolonged trial without success. The brilliant results of surgical treatment in the earlier and milder forms of the disease (Halsted, Horsley, Kocher, v. Eiselsberg), make it incumbent on medical men to consider operation early and seriously. Though nearly all patients improve on rest, a diet which does not stimulate the thyroid (milk), sodium phosphate and fortnightly X-ray exposures, and although occasionally a patient will get well, very many go backward again as soon as treatment is discontinued. In the very early cases surgery is capable of curing nearly 100 per cent.; even in the outspoken cases almost 75 per cent. can be cured by operations judiciously planned and skilfully performed, and the mortality, now about 5 per cent., can be further reduced. Internal medicine up to this time has been utterly unable to obtain results comparable with these. In the present state of knowledge and practice, therefore, once a positive diagnosis of exophthalmic goiter has been made, it is, in my opinion, the physician's duty and privilege to recommend operation early. I do not say that every patient presenting the v. Graefe phenomenon or an irritable heart should be operated on, but when a persistent pycnocardia associated with a vascular struma has been discovered, or whenever the grouping of symptoms is such as to leave no doubt of the existence of a persisting thyreointoxication, medical treatment, unless markedly beneficial, should not be continued long before operation is advised. The only contraindi-

cations in uncomplicated cases are a feeble heart with very high pulse frequency or pronounced psychic excitation; when these are present a brief preliminary medical treatment may be necessary; if the serious symptoms persist in spite of it and *indicatio vitalis* exist, the dangers should be pointed out and operation resorted to.

And just here a heavy responsibility rests on the physician. Fully as important as the diagnosis of the indication for operation is the choice of the surgeon. The physician should select an operator thoroughly familiar with the anatomy and pathology of the thyroid and para-thyroid glands and skilled in the special technic required. Success depends so largely on the formation of a correct judgment as to the amount of the gland to be removed and as to its removal in one or several operations, that the physician must be sure of his surgeon. Aside from the dangers of tetany, if too much gland is removed, hypothyroidism will result and the patient be doomed to thyreoid-eating or an implantation; if too little (a less serious matter) more of the gland can be taken out later. One thing seems established, that in exophthalmic goiter the symptoms retrogress in exact conformity with the amount of thyroid extirpated.

At present there is a fair prospect that the treatment of the disease may again be transferred from the surgeons to the physicians. The remarkable results already obtained in a number of cases by Rogers and Beebe through the use of their curative serum give us good reason to hope that a method will ultimately be perfected which will permit the internist to accomplish with his needle what he now asks the surgeon to do with the knife.—*Journal of the American Medical Association*, Oct. 5, 1907.

---

### MEDICAL TREATMENT OF EXOPHTHALMIC GOITER.\*

---

ROBERT B. PREBLE, M.D., CHICAGO.

---

A correct estimation of the value of any plan of treatment of a given disease is easy or difficult, possible or impossible, in direct proportion to the closeness with which the disease follows a type. If the disease is acute and typical, the therapeutic value of any measure is readily determined; but if, on the contrary, the course of the disease is chronic and subject to the many spontaneous remissions and exacerbations, it is nearly impossible to reach a just estimate of the value of any plan of treatment. When, in addition to these characteristics, the pathologic phenomena are not sharply separated from physiologic processes, the difficulties

---

\*Read in the joint session of the Sections on Practice of Medicine, Surgery and Anatomy, and Pathology and Physiology, of the American Medical Association, at the Fifty-eighth annual session, Atlantic City, June, 1907.

opposed to correct judgment are further increased. There is perhaps no disease, the history of which better demonstrates the truth of these principles, than does exophthalmic goiter. An almost unending list of plans of treatment might be prepared and in regard to each the opinions of their value have varied from useful, through useless, to harmful. And to-day, although there are many reasons for the belief that we are at last approaching an adequate conception of this disease, there still reigns the greatest chaos in its treatment, and so far as I can see there will continue to be great diversity of opinion on the subject until our knowledge of its pathology, and particularly of its etiology, becomes more complete than it is at present.

It is difficult, indeed impossible, to even sketch the various things which may be done for the patient in the time allotted, and it is not likely that it would prove to be profitable. It, therefore, has seemed best to make an effort to group the various plans as follows:

1. Those directed toward the correction of the neurosis, which is believed by many to lie back of and to cause the alteration in the functions of the thyroid gland.

2. Those which are directed toward counteracting the perversion of the thyroid secretion.

There is much collateral evidence in support of the idea that fundamentally this disease is a neurosis, and independently of whether this is true or not, a very considerable proportion of the patients must be or are, at least for a time, best treated along these lines.

One of the most important and constant of the symptoms is the increase in tissue waste, a fact which immediately suggests the advisability of rest and of abundant proper nutrition. The degree of rest required varies in different patients and in the same patient from time to time, and ranges from absolute and prolonged rest in bed to a mere restriction of activities. The rest should be both physical and mental. In many instances this rest, particularly the mental rest, can be best obtained if the patient is in hospital or sanitarium. In other instances, however, the opposite is true, just as in some cases a certain amount of work may be permitted. It is not possible to give more than the most general suggestions on these points, and much must be left to the judgment and good sense of the physician in charge. The better his suggestions are adapted to the individual case and her surroundings, the more satisfactory the results will be.

So, too, in regard to the diet, thought and care are necessary. The circumstances, tastes and digestive powers of each case must be consulted. In some cases forced feeding is required, while in others the usual amounts of food are sufficient.

The influence of climate is often important and many cases

are greatly benefited by a change. Just what change should be advised can not be stated, for, while some cases are improved by a trip to the mountains, others receive greater benefit from a trip to sea-coast or an ocean voyage. If the cardiac symptoms are marked, high elevations should be avoided; and, if the patient goes to the seashore, surf bathing should be forbidden. And, wherever the patient goes, quiet, rest and good food are absolutely essential.

These general hygienic and dietetic suggestions, suitable under all circumstances and to all cases, may be combined with various other measures, such as baths, massage and electricity.

Baths of various sorts and kinds have been very enthusiastically advocated by those whose interests are centered in hydrotherapeutic methods and institutions, but, when sufficient allowance is made for this enthusiasm, there is not much left to say in their favor.

Various forms of the electric current have been extensively employed; some advocate galvanism, some faradism, some the static current. There is much diversity of opinion as to their value. But it is probable that no one of them has other than a suggestive influence, and it should always be kept in mind that the exophthalmic patients are extremely susceptible to suggestion. This is well illustrated by the statement of Moebius to the effect that anything is of value, providing only that the patient is led to think that it is.

More recently some use has been made of the X-ray. Some have reported most favorable results from this method, while others have seen no other effects than a lessening of the activity of the metabolic processes.

Turning now to the question of drugs, one finds an almost unending list which have been employed, and in regard to the value of each one finds wide diversity of opinion. The use of various iron preparations has been advocated and condemned, but the summation of experience is that if there is an anemia, particularly one of the chlorotic type, as there often is, iron is useful, but that it has no direct effect on the fundamental process.

Arsenic is another drug about which much the same may be said as has just been said in regard to iron.

Iodids, the use of which is suggested by the presence of the goiter, have been used by many, and, while their use may be accompanied by a reduction in the size of the goiter, the other and more important symptoms are intensified. This is particularly true in the cases of primary exophthalmic goiter. There are some who have seen patients improve under their use, but in general it may be said that the improvement is in spite of rather than because of. For some reason yet unknown the iodid of potassium

has proved to be more harmful than iodine itself. The use of iodothyron is to be unreservedly condemned.

Because of the prominence of the cardiovascular symptoms, drugs which influence these have been extensively employed, in particular the digitalis. In regard to the value of this, as of its substitutes, strophanthus and convallaria, there is the same diversity of opinion noted in regard to all the agents so far mentioned. Small doses accomplish nothing, while larger doses are prone to excite the signs of digitalis poisoning. Many experiences and careful clinicians, however, employ these drugs in cases where there is extreme tachycardia or any of the usual evidences of cardiac insufficiency, such as cardiac dilatation, passive congestion of the liver or edema of the feet.

It has also been natural to endeavor to lessen the extreme nervous irritability of these patients by the use of various sedatives, the bromids in particular having been extensively employed. The bromids of sodium and potassium are the ones usually given, but the hydrobromate of quinine has also been advocated, even with enthusiasm, by some. Opium or its derivatives has been used for years and, except for the dangerous possibility of establishing a drug habit, seems to me personally to be more valuable than other sedatives.

To these, the drugs most often employed, may be added others, such as quinine, antipyrin, phenacetin, salicylates, veratrum viride, aconite, cannabis indica, strychnia, nitrites, sodium phosphate.

One is forced by such a review as this, and by the diametrically opposed opinions which have been expressed by equally careful observers as to the value of each of the drugs or methods mentioned, that no one of them has any direct effect on the process and that their beneficial influence is determined solely by the skill and intelligence with which their use is adapted to each particular case.

Another group of preparations which have been used and still are to a limited extent, deserve mention more because it shows the evolution of our ideas as to the essential nature of the disease. This group contains the bodies prepared from various glands having an internal secretion and includes the thyroid, thymus, suprarenals, ovaries and testicles. In regard to all of them one finds favorable reports, but, after reviewing the entire experience, one must conclude that they are all useless, with the exception of the thyroid preparations, which are positively harmful.

Lastly come the preparations which appear to best fit with the current idea that an excessive or perverted activity on the part of the thyroid gland is the essential factor of this disease. This belief, one which I personally share, has led to the manufacture of a number of antitoxic or cytotoxic preparations. While the fundamental idea underlying these is the same, the preparations are of two

different sorts: first, those derived from animals which have suffered thyroidectomy, and, second, those derived from animals to which normal or pathologic glands have been administered. In a few instances the serum of patients with myxedema has been employed, but it is obvious that no extensive use of this is possible. The preparations which have been most extensively used are the milk, either natural or disiccated, from thyroidectomized animals, the antithyroidin of Moebius, the thyroidectin, *i.e.*, the desiccated blood of thyroidectomized sheep, and very recently a serum prepared by Rogers and Beebe by the use of the nucleoproteid and thyroglobulin from normal and pathologic glands.

It is yet too soon to express a definite and final opinion as to the value of these various so-called specific preparations. The reports so far published are to the effect that most of the cases are improved, a small number are cured and an equally small number are unaffected. Were it not for the apparently well-grounded theories which underlie this work, we would, I believe, be justified in saying that these preparations are as futile as the other methods of treatment which have been outlined, and that the cures and improvements are to be referred to the rest, hygiene and passage of time rather than to the material administered. However, no definite judgment on the question can be reached until more cases have been observed, more time has elapsed, and probably until more perfect sera are prepared.

After this discouraging review of the methods of medical treatment, it would seem as if all cases should be treated surgically, and yet I think that many, possibly a majority of the cases, should continue to be handled by medical methods, for one must always remember that the natural evolution of the disease is toward recovery. I have endeavored to formulate some rules which might serve as a guide to the selection of the cases for surgical treatment, but can not, even to my own satisfaction, go further than to say that medical treatment should be employed in every case until it is seen that, in spite of rest, proper nourishment and hygiene and intelligent effort at the correction of individual symptoms, the patient is steadily getting worse. How long the employment of surgical measures should be delayed must be determined in each individual case, but it is far better to operate earlier than is necessary than to delay too long.

If in a given case the condition is not serious, but in spite of the best of help still remains bad enough to interfere with the usefulness of the individual, partial thyroidectomy should be employed.

The same thing must be said of the resection of the thyroid as has been said of the other methods of treatment—that the results are good or bad in direct proportion to the skill and intelligence with which it is advised and carried out.—*Journal of the American Medical Association*. Oct. 5. 1907.



## THE SURGICAL TREATMENT OF EXOPHTHALMIC GOITER.\*

ALBERT KOCHER, M.D., BERNE, SWITZERLAND.

Out of 3,460 operations for goiter performed in Professor Kocher's clinics in Berne up to date, 315 have been done on 254 patients afflicted with exophthalmic goiter, of which I will speak here.

My father, Theodor Kocher, was one of the first to operate on the thyroid gland in this disease, which he always claimed to be caused by hyperactivity of the thyroid. The results of his operations on the gland have been up to date so satisfactory that he has proceeded in very much the same way for the past twenty-five years.

I will say only a few words of other operations. In three excisions of the sympathetic nerve, to which I referred in my paper in 1902, the operations had absolutely no permanent or progressive effect on any symptom of the disease. Another, done two years ago, following an operation on the thyroid gland, merely to influence the persisting exophthalmos, had a directly bad effect, so that plastic operations subsequently had to be done to the more protruding eyeballs. I need, therefore, make no further reference to this method.

Let me now, first of all, speak of the danger of the operation in exophthalmic goiter, which still keeps many a patient and often his physician away from the surgeon. We have had in the last 91 operations on 63 patients not a single death, and, in the whole, we have lost only 9 patients out of 254; that is to say, 3.5 per cent. There is no doubt that this percentage will still be lowered. If we ask why we have had a lower mortality than formerly, the answer is a very definite and short one. It is not only because of our improved technic, but because experience has shown that more prudence and care is necessary for operations in this disease than for the majority of other operations. It is not that in a greater number of cases surgical treatment has been refused, for, on the contrary, we have been able to operate in nearly all, but because we have learned to judge of the gravity of a case and to decide accordingly the extent to which the patient will stand operative measures.

Whereas, previous to my paper in 1902, extensive operations had been done (such as excision of one side and resection of a part of the other side of the gland, excision of one side together with

\*Read in the joint session of the Sections on Practice of Medicine, Surgery and Anatomy, and Pathology and Physiology, of the American Medical Association, at the Fiftieth annual session, Atlantic City, June, 1907.

ligation of arteries of the other, and ligation of more than two arteries in one session), in the last 100 cases such operations have merely been done exceptionally, and only when we were sure the patients could stand them. Very often we had to begin with the ligation of a single artery, and even this only after a long preparative treatment of the patient.

Let me tell you in a few words what we consider important for every surgeon to know before he attempts operations of this character. Above all, we have to investigate the strength of the heart. In the majority of cases, and especially if the disease has been of long duration or has presented sudden exacerbations, we find the heart dilated. We are then to decide whether or not we have to deal with a compensatory hypertrophy, the result of increased cardiac activity brought about by the tachycardia. If this is the case, the dilatation will be slight and constant, and, what is more important, blood pressure will be increased. This we find in the majority of cases. A systolic blood pressure, even of 1.95 mm. mercury (Riva Rocci), does not forbid operation, but we must be sure that the high pressure is proportional to the degree and constancy of tachycardia. If this is not the case, extreme care is necessary. If we find the blood pressure below normal and the disease highly developed, we must study the condition and especially note the action of the heart after exertion or excitement. Under these circumstances we might find a sudden, very marked dilatation of the heart, irregularity of pulse and a blood pressure which can not be measured with our ordinary methods. These patients must be carefully watched and prepared for operation and, what is more important, they should never be submitted to an immediate extensive operation.

The second point which we have to consider is the degree of the disease at the moment we are asked to operate, and this particularly concerns the degree of intoxication presented by the patient at that moment. Intoxication is evidenced by special symptoms, such as sleeplessness, extreme nervousness, great fatigue, weakness, diarrhea, vomiting and a high degree of tachycardia, with irregular pulse and a very vascular thyroid. A highly vascular gland, with expansile pulsation—that is to say, with dilatation of the capillaries (what we call struma telangiectodes) is a sign of very severe intoxication. We find these symptoms more pronounced in the early stages, especially when there has been a rapid development of the disease. Such symptoms do not warrant an extensive operation, and the patient consequently should be prepared merely for a slight operation.

Of further importance is the examination of the blood in exophthalmic goiter, for through this we are apt to find an answer as to the gravity of the disease. Up to the present time 58 cases have been carefully examined by Dr. v. Steiger, who has done

special work in hematology. In nearly all typical cases of the disease we find an increase in the number of lymphocytes and a decreased number of the polynuclear forms, the total number of leucocytes being normal or rather low. The number of lymphocytes is sometimes absolutely increased, but more often the increase is a relative one. This increase is proportional to the degree of the disease, and if there is no increase of lymphocytes the case is an especially serious one. Only in very early, undeveloped cases and in those of long standing which have improved do we find that lymphocytosis is absent. Some time after operation the numerical proportion of the different forms of leucocytes becomes either normal or nearly so, in accordance with the improvement of the patient. We know very little as yet of the significance of lymphocytosis. That form of lymphocytosis which follows infections must be regarded as a secondary hyperproduction in the lymphoid tissues, damaged by the acute infection. Lymphocytosis, on the contrary, is a primary and specific process and indicates a hyperfunction of lymphoid tissue, probably according to its want, and this can not be merely a local effect, as there is a substitution of the myeloid leucocytes at the same time.

We furthermore know very little of the function of the lymphocytes themselves. Their number is increased in slight or chronic infection, and more especially in intoxication, and we must admit that in exophthalmic goiter an analogous irritation of lymphoid tissue takes place. We know that wherever this irritation takes place lymphoid tissue can form, and it is an interesting fact that in exophthalmic goiter the lymphatic glands in the neighborhood of the thyroid are hypertrophic, and more especially lymphoid tissue and germinal centers are also present in the gland itself, which indicates that the thyroid body is the place of origin of this irritation. We find that this local formation of lymphoid tissue in the thyroid body is present also in early cases, even before there is evidence of lymphocytosis and diminution in number of polynuclear leucocytes in the peripheral capillaries, which latter is the result of the toxic influence on the bone-marrow. After excision of a part of the gland, we also find the lymphocytes diminished, whereas their number increases after ligation of arteries.

It may be seen by this brief statement what important results the examination of the blood may give as to the gravity of a case. The very fact of substitution of myeloid leucocytes by lymphocytes seems to me of further importance. It might explain why an ordinary, even slight infection or intoxication acts so badly on a patient with exophthalmic goiter, because ordinary leucocytosis can not get so far or substitute lymphocytosis. Therefore, the patient's condition may be very bad with a slight infection, or the symptoms of exophthalmic goiter may increase often to a dangerous extent. We found, for instance, in a patient with this disease who developed

tensillitis, only 7,000 polynuclear leucocytes and 3,400 lymphocytes, though the symptoms of infection were very marked and a very high temperature was present. The same fact of substitution might explain some of the sudden deaths after operation in severe cases, in analogy to the sudden deaths in lymphatic conditions. When the gravity of a case has been thus established, we can determine the time and decide on the method of operating, for sooner or later we will be able to operate without fear.

Now the second and more important question arises: Can we cure the disease by operation? Most surgeons have noted an immediate increase of the symptoms after operation, which symptoms can even become fatal. I have, in my paper in 1902, claimed that this post-operative aggravation is due mostly to hemorrhage and absorption of toxic blood, especially when gland tissue is resected and injured in any way during the operation. This opinion has since been widely confirmed. By most careful avoidance of any bleeding, by ligation of every small vessel, and by taking the greatest care not to injure the parts of the gland to be left, we can avoid alarming symptoms almost completely. As a matter of fact we see such symptoms at the present day only if, for any reason, the operation had to be done quickly and the gland tissue was injured.

When the immediate effect of the operation is over (and when it has been done under local anesthesia the disturbance lasts but a few hours), the surgeon is surprised at the striking improvement in the patient's condition. The very fact that the symptoms of the disease may disappear so soon after the operation, so that many times the patient is almost normal in a few days, seems to us to be the proof that we have touched the disease in its important place.

I think that it is generally admitted nowadays that the thyroid gland is diseased in every case of exophthalmic goiter, and it is also admitted that it shows functional alteration. It is much to the credit of American physicians that they have demonstrated what are the exact histologic changes in the thyroid gland in this disease. The proliferation of the epithelium, which assumes the cylindrical type, and the liquefaction of colloid are the most striking features and, especially when compared with the hypertrophic glands, described in Halsted's classical experiments, these changes seem to furnish proof of a functional disorder. Still it has been difficult for those who have examined large series of cases and also for those who see a great deal of other diseases of the thyroid gland, to accept the above-mentioned changes as being specific for exophthalmic goiter. We find the same enlargement of follicles with formation of papillæ and high cylindrical cells, together with the decrease in thick colloid, in glands of normal size in hypertrophic as well as in nodular goiters, without the slightest symptom of exophthalmic goiter. But we find them in a part of the gland

or in a nodule where vascularization is rather diminished, while the diseased parts in exophthalmic goiter, even if present in areas only, will be found in very vascular parts, as, for instance, in the periphery of the gland or a nodule. We must conclude, therefore, that the histologic changes themselves do not account for the symptom of the disease, but it is the change of metabolism which shows itself by the increased vascularization of these parts. Chemical experiments, which I can not discuss here, show that material, such as iodine, is taken up eagerly by the thyroid gland in patients with exophthalmic goiter and is not eliminated by the kidneys as it is in normal individuals.

Besides these histologic changes, we must consider, as characteristic for the disease, the formation of lymphoid tissue in the thyroid glands, and in special cases the presence of large cells with specially differentiated protoplasm. The diffuse infiltration with leucocytes and the desquamation of the epithelial cells, which we find very often in the inflamed gland in exophthalmic goiter and which have been described by several authors as being characteristic of the disease are secondary. This may be the result of handling and injuring the gland during operation or the result of treatment with Roentgen rays, electricity, injections, etc. We also find it regularly after ligation of arteries in previous operations.

What are we accomplishing by our operations on the thyroid gland in exophthalmic goiter? Only exceptionally a limited and well circumscribed part of the gland is diseased and can be entirely removed. It happens when the disease develops in a subject with nodular goiter and may also account for the prompt cure of these cases by operation.

Nearly always the changes are diffuse, though in areas, and it is not possible to take away all diseased tissue without depriving the patient of the thyroid function altogether. This is, in my opinion, not permissible. What we can do is to reduce the diseased tissue or its increased vascularization and thereby reduce the assimilation. It has proved that the nearer to the normal we reduce the gland, or its blood supply, the prompter the cure will be. I think it is the best proof against a perverted secretion of the thyroid gland in exophthalmic goiter, that even when we leave behind so-called diseased gland tissue, but under normal blood-supply, the improvement after the operation is immediate and goes on to entire cure. We must admit, therefore, that the so-called diseased part of the gland can assimilate normally and, more than that, it can become normal itself or rather adapted to further claims.

The fact that increased vascularization is indispensable for the development of the disease also proves that what reduces vascularization prevents its development. We easily understand, therefore, that in nodular, and especially colloid goiter, with me-

chanically reduced vascularization owing to the great accumulation of colloid, the disease does not easily develop, whereas it does readily in normal and slightly hypertrophic glands. Based on these facts, the operation has been carried out in 254 cases and the results are as follows:

There is not a single case of ours in which the patient has not been much benefited by the thyroid operation. We have cured by our operation the patients in 83 per cent. of all our cases. There are 73 per cent. of the patients with the so-called primary disease healed; 92 per cent. of the patients having the disease combined with ordinary goiter, and 100 per cent. of the patients with vascular goiters. Some of the observations date back 15 and 17 years since the time of observation, without recurrence of the disease, provided that the operation was carried so far that vascular symptoms of the thyroid disappeared completely. In cases of this type the patients are all completely cured, so that no symptom of exophthalmic goiter remains. But the time required for recovery has varied greatly, it being especially long before the heart and eyes became normal again. I wish especially to say that our chances of cure do not so much depend on the degree and the extent of histologic changes as on the duration and the secondary changes in the case.

We have had cases in which the excised gland showed excessive epithelial proliferation in all parts and in which the patient presented all the symptoms in the highest degree, and yet the cure has been just as complete and rapid as in patients showing much colloid matter and less severe symptoms. The difference between the two lies in the fact that the former, as a rule, not only develop very rapidly, but also progress rapidly. Hence an operation must be undertaken early before organic changes take place, and also before the thyroid tissue has undergone induration—that is to say, before the excessive proliferation of cells has mechanically reduced the capillary supply and a part of the functional tissue, and also before infiltration and desquamation have destroyed a part of the functional tissue. These latter changes are the cause of symptoms of hypothyroidism.

Secondary organic changes of this nature were present in 4.8 per cent. of our cases. The patients were all very much benefited by the operation, but some heart trouble, the impossibility of much exertion and more or less exophthalmos remained. These patients might present slight symptoms of hypothyroidism, but I must say that, owing to the great care my father takes in this matter, it has been the exception to see these symptoms appear after operation.

Ten patients (4.4 per cent.) were benefited by thyroid operation, but not as much as could have been expected; some of these had symptoms of other diseases and they seemed to present a

special form of the disease. But space is too limited to discuss this question. Eight patients (3 per cent.) are still under observation, the time since the operation being too short to give any definite opinion concerning them. In another group of eight cases (3 per cent.) the patients could be cured by the thyroid operation, but, being so much improved, do not wish it.

This brings us to the question, how operate? The most important condition is *nihil nocere*, and that is why I have spoken, in the first place, of the danger of operation. We have seen that careful preliminary observation of the case makes a carefully conducted operation a possibility for almost every patient. The method has to be chosen for every case. We give the preference to repeated operations with the patient under close observation and with the help of medical treatment. More than two arteries should never be ligated in one session, because of the above-mentioned changes in the gland. To remove more than half of the gland at one sitting is dangerous, and it is difficult to say whether this is ever wanted. We find it rarely necessary to resect a part of the remaining gland after excision of one side.

The question, When are we to operate? depends not alone on the physician, but also quite as much on the patient. Often the surgeon thinks it the doctor's fault that he is consulted too late, and does not imagine what an unsettled and sick mind the patient has. It is necessary to advise people to see the doctor in the early stages of the disease. Nervousness, irritability, weakness, emaciation, sleeplessness are the early symptoms and are not sufficiently dwelt on. These patients are often regarded as cases of neurasthenia. If such patients were carefully examined by medical men, especially after exertion and before or during menstruation, characteristic, although slight, symptoms could often be made out; such as tachycardia, ocular symptoms, tremor, blood changes, and especially vascular symptoms of the gland.

On these latter symptoms treatment should be decided. Distinct vascular symptoms should at once induce surgical treatment. If they are wanting, the medical treatment, with the patient under close observation, may cure, but if it does not, or if relapses come on, vascular symptoms will develop before long and be at once noticed by the doctor and induce surgical treatment. In such cases ligation of two arteries or excision of half of the gland will cure definitely in a very short time. If the doctor sees the patient only when the disease is at its worst, then we do not advise an immediate operation. Even ligation of one artery may be dangerous then, because of the increase of the discharge of toxic material from the gland and because in these cases the organism has not yet developed its own antitoxic reaction, the lymphocytosis. In these cases medical treatment is needed and cytotoxic

serum here seems to act well. If the reaction of the organism is present, operative treatment must take place.

In cases of longer duration, great benefit can be derived by operation, but here one has to be even more careful, as we have to deal with organic changes in the heart and there is the fear of hypothyroidism. I wish to mention one fact, that in all cases of long duration, whether in the so-called primary cases or in the cases combined with ordinary goiter, always the same symptoms are evident—dilatation of the heart, excitable pulse, and exophthalmos. As to the latter symptom, which is mostly caused by the dilatation of blood vessels in the orbit, the fact that the eyeball does not go back, even when it can be pushed back easily, does not in all cases come from development of fat or connective tissue, as is generally admitted, but also from the fact that the muscles of the eyeball have been distended so much and so long that they can not contract well, if at all. It is possible that electric treatment might be of benefit.

We come now to the conclusion that operation on the thyroid gland gives the possibility of an entire cure of the disease. Whether we admit a primary irritation of the sympathetic nerve, and, therefore, an increased metabolism of the gland, or a primary increase of thyroid material and from it an irritation of the sympathetic system, or both, it amounts to the same thing so far as the thyroid operation is concerned. By reducing the hypertrophic thyroid tissue or reducing its blood supply, we reduce the possibility of too extensive reaction to the primary cause and also enable the gland to adapt itself to counteract new outbreaks of primary causes which a nervous subject can easily show.—*Journal of the American Medical Association*, Oct. 5. 1907.



## ABSTRACTS.

**Pankreon.**—Pankreon, according to a report from the "Lancet Laboratory," is prepared from fresh pancreatic glands, the active principle being subsequently combined with tannic acid, the combination being proof against the action of the gastric juice. It has been administered in cases of carcinoma of the pancreas. After giving pankreon daily for six days the absorption of nutrient material is said to have been increased by 50 per cent. and the output of sugar diminished by nearly a third. Opium, too, diminished the amount of sugar, but the absorption of food material was only increased by 10 per cent.—*The Lancet*, Oct. 20, 1906.

**Suggestions of a Plan of Organizing a Hospital System for the City of New York.**—Stephen Smith gives a number of suggestions concerning the organization of a hospital system. He says that the "Department of Hospitals" should be provided for by an amendment of a charter of the city. The Department should create "Hospital Districts," the division of territory being based on the population or the laboring or tenement house classes and the sickness-rate. Certain public hospitals should become "Emergency Hospitals." Emergency Hospitals should be provided for districts where none now exist. One or more "Convalescent Hospitals" should be created on ample farm lands located on the water front within easy access of the city. The "Special" and "Contagious Diseases" Hospitals would take their proper places in this organization of hospitals.—*Medical Record*, January 5, 1907.

**Report of Two Cases of Dementia Paralytica, One Associated with a Large Hemorrhagic Lesion, the Other with Atrophy of the Optic Tract.**—Jessie Weston Fisher presents the results of a careful study of these two cases. There are not many records of dementia paralytica associated with gross focal lesions of the brain. Autopsy showed, in the brain of the first patient here described, an area of hemorrhagic degeneration in the corona radialis of the left hemisphere. This lesion began just anterior to the tip of the anterior horn of the left ventricle, extending posteriorly to the dorsal extremity of the caudate nucleus. The anterior limb of the internal capsule was also involved by this lesion. On examination of the brain of the second patient, there was discovered atrophy of both optic nerves and tracts, and the lateral geniculate bodies of each side were found to be about one-half normal size.—*Medical Record*, January 5, 1907.

# *School Hygiene.*

## SCHOOL LIFE VIEWED FROM THE STANDPOINT OF PSYCHOLOGICAL MEDICINE.

---

ONE of the most important papers presented at the Annual Meeting of the British Medical Association at Sheffield was upon the above-mentioned subject and was prepared by a well-known authority, Dr. Francis Warner, of London. The following are the headings of the discussion: Clinical Study in Schools: Mental and Physical Hygiene; the Children to be Educated. Constitutional Differences between Boys and Girls; Subnormal Children; Objective Study of the Child; Nerve-signs and Response. Types of Childhood; Healthy Children; Children with Some Degree of Defect in Physical Development; Neurotic Children; Children Showing Brain Disorderliness and Mental Dullness; Children Mentally Feeble. Training and Teaching: The School and the Staff.

---

## MEDICAL INSPECTION OF SCHOOLS.

---

A QUESTION was recently asked in the House of Commons as to what course the Government proposed to follow in dealing with school authorities who had neglected or postponed indefinitely the duty of providing for the medical inspection of schools. In reply, Mr. McKenna, President of the Board of Education, said that steps were being taken both by correspondence and by local investigation to ascertain the manner in which arrangements for medical inspection were being initiated, and a clause had been inserted into the code requiring as a condition of the payment of the annual grant in respect of any school that satisfactory provision should be made for the medical inspection of the children attending the school. Failure on the part of the local authority to comply with the requirements of the Act might therefore in addition to, and in substitution of, other statutory remedies result in the refusal of, or deduction from, the grant. Special attention had been called to this matter in the prefatory memorandum to the code, and he thought the publicity attaching

to the code could suffice to apprise the authorities of its requirements. The Board had no control over the salaries payable by local authorities to officers engaged in medical inspection, except in so far as inadequate remuneration might be found to result in the inefficiency of inspection; and until the various schemes were in working order and the Board had had opportunities of comparing the methods and efficiency of medical inspection in the various areas he should not be prepared to say whether any particular salaries could be regarded as insufficient. He had recently stated to a deputation that inquiries as to the methods or machinery of medical inspection should obviously be addressed to the Board in writing, and if made would receive prompt attention and as far as possible full replies. It was impossible to deal satisfactorily or completely with matters of detail within the limits of an answer in the House, and he should be exposing both the Board and local authorities to risk of misunderstanding if he attempted to do so.

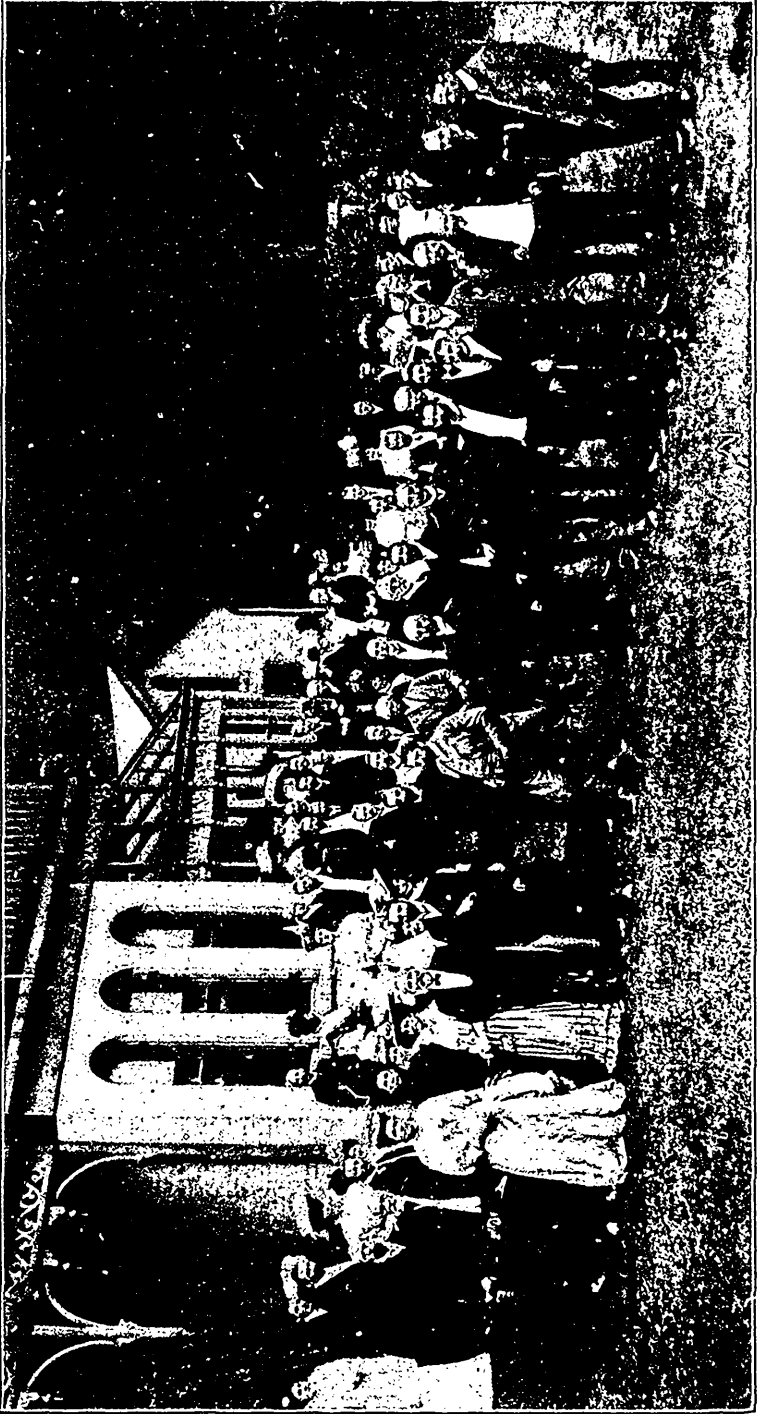
---

#### TUBERCULOSIS AMONG SCHOOL CHILDREN.

THE subject of school hygiene has not been overlooked in connection with the International Congress on Tuberculosis. A series of papers is being prepared, which will deal with Medical Inspection of Schools, School Nursing, Prophylaxis of Tuberculosis in School, etc. Dr. Elliott, of Toronto and Gravenhurst, has charge of the paper describing what Canada is doing in the matter.

It may well be recalled in this connection that the discussion upon Dr. W. J. Dobbie's paper at the last meeting of the Canadian Hospital Association on Tuberculosis brought out the importance of carrying the anti-tuberculosis campaign right into our schools. Dr. Gordon's contribution to the discussion was an eloquent and convincing address on this subject, and a resolution was forwarded to the Ontario Educational Association, then in session.

The Government of Newfoundland also appreciates the importance of fighting tuberculosis in the schools. They have given a grant sufficient to defray the expenses of all the teachers in the colony, some two hundred and fifty in number, in connection with a Teachers' Anti-Tuberculosis meeting in St. John's, Nfld. This is part of the aggressive warfare now being waged by the Newfoundland Society for the Prevention of Tuberculosis. This work is badly needed, as the mortality from tuberculosis is said to have increased 50 per cent. in the last six years in Newfoundland.



Garden Party given by the Academy of Medicine Toronto, on Friday, September 18th, 1908, in honor of the French Physicians.

# The Canadian Journal of Medicine and Surgery

J. J. CASSIDY, M.D.,

Editor.

43 BLOOR STREET EAST, TORONTO.

W. A. YOUNG, M.D., L.R.C.P. Lond.,

MANAGING EDITOR

145 COLLEGE STREET, TORONTO.

**Surgery**—F. N. G. STARR, M.B., Toronto, Associate Professor of Clinical Surgery, Toronto University; Senior Surgical Assistant, Toronto General Hospital; N. A. POWELL, M.D., C.M., Prof. of Medical Jurisprudence, Toronto University; Consulting Surgeon Toronto General Hospital, etc.

**Clinical Surgery**—ALEX. PHIMROSE, M.B., C.M. Edinburgh University; Professor of Anatomy and Director of the Anatomical Department, Toronto University; Associate Professor of Clinical Surgery, Toronto University; Secretary Medical Faculty, Toronto University.

**Orthopedic Surgery**—B. E. MCKENZIE, B.A., M.D., Toronto, Surgeon to the Toronto Orthopedic Hospital; ex-President of the American Orthopedic Association; and H. P. H. GALLOWAY, M.D., Windsor, Man., Member of the American Orthopedic Association.

**Gynecology and Obstetrics**—GEO. T. MCKEUGH, M.D., M.R.C.S. Eng., Chatham, Ont.; and J. H. LOWE, M.D., Toronto.

**Medical Jurisprudence and Toxicology**—ARTHUR JUKES JOHNSON, M.B., M.R.C.S. Eng., Coroner for the City of Toronto; Surgeon Toronto Railway Co., Toronto; W. A. YOUNG, M.D., L.R.C.P. Lond., Associate Coroner, City of Toronto.

**Physiotherapy**—CHAS. R. DICKSON, M.D., C.M., Queen's University; M.D., University of the City of New York; Electrologist Toronto General Hospital, Hospital for Sick Children; and St. Michael's Hospital.

**Pharmacology and Therapeutics**—A. J. HARRINGTON M.D., M.R.C.S. Eng., Toronto.

**Pediatrics**—ALLEN BAINE, M.D., Toronto; A. R. GORDON, M.D., Toronto; HELEN MAOMURCHY, M.D., Toronto.

**Oral Surgery**—E. H. ADAMS, M.D., D.D.S., Toronto.

**Dermatology**—D. KING SMITH, M.B. Tor., Toronto.

**Medicine**—J. J. CASSIDY, M.D., Toronto, ex-Member Ontario Provincial Board of Health; Consulting Surgeon, Toronto General Hospital; W. J. WILSON, M.D., Toronto, Physician Toronto Western Hospital; and Dr. J. H. ELLIOTT, ex-Medical Superintendent, Gavenhurst Sanatorium, Ont., 611 Spadina Ave., Toronto.

**Clinical Medicine**—ALEXANDER MCPHEDRAN, M.D., Professor of Medicine and Clinical Medicine Toronto University; Physician Toronto General Hospital, St. Michael's Hospital, and Victoria Hospital for Sick Children.

**Mental and Nervous Diseases**—N. H. BEMEK, M.D., Minko Insane Asylum; CAMPBELL MEYERS, M.D., M.R.C.S., L.R.C.P. (London, Eng.), Private Hospital, Deer Park, Toronto.

**Public Health and Hygiene**—J. J. CASSIDY, M.D., Toronto, ex-Member Ontario Provincial Board of Health; Consulting Surgeon Toronto General Hospital; and E. H. ADAMS, M.D., Toronto.

**Physiology**—A. B. EADIE, M.D., Toronto, Professor of Physiology Woman's Medical College, Toronto.

**Pathology**—W. H. PEPPER, M.D., C.M., Trinity University, Pathologist Hospital for Sick Children, Toronto, Associate Demonstrator of Pathology Toronto University; Surgeon Canadian Pacific R.R., Toronto, and J. J. MACKENZIE, B.A., M.B., Professor of Pathology and Bacteriology, Toronto University Medical Faculty.

**Ophthalmology**—J. M. MACCALLUM, M.D., Toronto, Professor of Materia Medica Toronto University; Senior Assistant Eye Department Toronto General Hospital, Oculist and Aurist, Victoria Hospital for Sick Children, Toronto.

**Nose, Throat and Ear**—PERRY G. GOLDSMITH, M.D., 84 Carlton St., Toronto, Laryngologist and Aurist; Provincial Institution for the Deaf and Dumb; Senior Assistant Ear, Nose and Throat Department Toronto General Hospital.

**Address all Communications, Correspondence, Books, Matter Regarding Advertising, and make all Cheques, Drafts and Post-office Orders payable to "The Canadian Journal of Medicine and Surgery," 145 College St., Toronto, Canada.**

Doctors will confer a favor by sending news, reports and papers of interest from any section of the country. Individual experience and theories are also solicited. Contributors must kindly remember that all papers, reports, correspondence, etc., must be in our hands by the first of the month previous to publication.

Advertisements to insure insertion in the issue of any month, should be sent not later than the fifth of the preceding month, London, Eng. Reprint via W. Hamilton Mill, Thanet House, 231 Strand, W.C. Agents for Germany, Starbuck's News Exchange, Mainz, Germany.

Reprints supplied Authors at Cost.

VOL. XXIV.

TORONTO, OCTOBER, 1908.

No. 4.

## Editorials.

### L'ENTENTE CORDIALE MEDICALE.

As one entered into the spirit of cordiality extended to the French Gentlemen, distinguished in the world of medical science, recently visiting Toronto for a day and hours *en route* to Washington, D.C., to attend the great Congress on Tuberculosis, one again regretted the little mix-up that occurred at the Tower of Babel, and wished a long, long wish for a universal language (with respect to Esper-

auto), universally spoken. Fortunately, a number of our doctors are fluent linguists, and they fittingly expressed the sentiments of all, namely an admiration for the French physicians and their achievements, and for their beautiful and beloved France. Was it not a Frenchman who voiced the sentiment we all know so well:

"It is when we are far from our country that we feel, above all, the instinct which attaches us to it."

After an auto ride around the city, Dr. R. A. Reeve (Dean of the Medical Faculty of Toronto University) was first, as ever, to invite the visitors to take luncheon with him, and also extend his hospitality as far as possible to local members of the profession, thereby conferring a great privilege, as well as pleasure, only possible by an informal meeting. The few toasts were fittingly phrased, and the Dean's guests expressed themselves as charmed with the fine University buildings. In the afternoon the "Academy of Medicine," in its present delightful quarters, opened wide its doors and windows to the "pic, pic" of the birds of passage, of both plumage sombre and plumage gay, and over the teacups an hour soon sped away, adding its laughter to pleasant memories.

From another page, by permission, the faces of the distinguished guests of the Academy of Medicine greet our readers.

The medical men of Canada owe, indeed, a debt of gratitude to Dr. J. F. W. Ross and his associates for their herculean efforts in planning and carrying out their idea of an Academy of Medicine in Toronto; its possibilities and scope are only beginning to be fully realized.

In the evening a brilliant dinner party was the farewell tendered the French doctors by Dr. J. F. W. Ross and Dr. W. H. B. Aikins. It is not a passing compliment, but the whole truth, to say that Toronto men feel deeply grateful to those who, through personal kindness and hospitality, made not only for themselves but in a large measure for our Canadian city a delightful and lasting impression upon the strangers within our gates. Medical Gentlemen of the *savoir faire*, do not be too proud to disdain your success.

W. A. Y.

### EXOPHTHALMIC GOITER.

IN this issue of our journal we publish several papers on exophthalmic goiter. These papers first appeared in the *Journal of the American Medical Association*, and we are indebted to that journal for the pleasure of being able to place them before our readers. The physiology of the thyroid gland in its relation to exophthalmic goiter is discussed by S. P. Beebe, M.D., New York City; the pathology of exophthalmic goiter by W. G. MacCallum, M.D., Associate Professor of Pathology, Johns Hopkins University, Baltimore; the diagnosis by Lewellyn F. Barker, M.D., Baltimore; the medical treatment by Robert B. Preble, M.D., Chicago; the surgical treatment by Albert Kocher, M.D., Berne, Switzerland. These papers are all of a high type and show what is actually known of this somewhat recondite subject. The etiology of the disease is obscure. In some cases goiters which appear to be of the simple kind, under excitement or other unknown cause, begin to pulsate and are attended with some protrusion of the eyeballs, these symptoms disappearing by rest and time, the case subsequently reassuming the clinical features of a simple goiter. Such cases as these stand as a kind of link between the simple goiter and that known as the exophthalmic goiter, Graves' or Basedow's disease, and yet between the two affections there must be some wide difference, for the simple goiter appears to be a local affection, whereas the exophthalmic form is probably part of a more general disease, marked by the enlargement of the thyroid body, often prominence of the eyeballs, always palpitation of the heart, a peculiar thrill in the blood-vessels, and a general want of muscular and brain power.

Dr. Beebe says that we know little of what the thyroid secretion does when confined to physiologic limits; but we do know that animals overdosed with thyroid preparations exhibit symptoms characteristic of exophthalmic goiter, viz., exophthalmus, tachycardia, tremor, gastro-intestinal disturbance, profuse sweating, increase in temperature, rapid loss in body weight, severe mental disturbance. Granting that the hyper-secretion theory explains the origin of the signs and symptoms of exophthalmic goiter, no adequate explanation of the hyperactivity of the thyroid can be given. Two commonly accepted possibilities are offered: (1) This disease

is the result of a nervous shock; or (2) it is a compensatory hypertrophy occurring during a toxemia.

Naturally, a patient who has this disease requires rest of mind and body and a carefully regulated dietary. Baths, massage, electro-therapy have all been used with advantage, probably in proportion to the belief the patient entertains of their efficacy. Drugs have been employed in its treatment with more or less success, namely, iron, if there is anemia, arsenic, digitalis, the bromides of sodium and potassium, opium, quinine, antipyrin, salicylates,aconite, sodium phosphate, and strychnia. Dr. Preble thinks that bodies prepared from various glands, having an internal secretion, such as the thyroid, the thymus, the suprarenals, the ovaries and testicles, are useless, with the exception of the thyroid preparations, which are positively harmful, unless in cases in which exophthalmic goiter is associated with myxedema.

That a number of antitoxic or cytotoxic preparations have been used in the treatment of this disease would seem to best fit in with the current idea, that an excessive or perverted activity on the part of the thyroid gland is the essential factor of this disease. These preparations are of two sorts: (1) Those derived from animals which have suffered thyroidectomy; (2) those derived from animals to which normal or pathologic thyroid glands have been administered. The milk, either natural or desiccated, from thyroidectomised animals has been extensively used. Moebius' thyroïdin (a preparation of the blood of a sheep from which the thyroid gland has been removed some time previously) has given good results. The dose is from 2 to 12 drops daily, given for a period of twenty days. Recently a serum has been used, which is prepared by Rogers and Beebe by the use of nucleoproteid and thyroglobulin from normal and pathologic glands.

Dr. Preble attaches little importance to any form of medicinal therapy in exophthalmic goiter, and expresses the opinion that the cures and improvements apparently resulting from any kind of medical treatment are to be referred to rest, to hygiene, and the healing effects of time, rather than to the material administered.

This leaves a large part of the therapeutic field open to the surgeon. Dr. Kocher, who writes on the surgical side of exophthalmic goiter, believes that increased vascularisation in a part of the thyroid, or in several areas of that gland, is the essential patho-



logical feature, which calls for surgical treatment in this disease. His admirable paper is worthy of the closest perusal. We shall close this editorial notice of these papers with a citation from Dr. Kocher's paper, which at once exhibits the current theories of the etiology of exophthalmic goiter and a sufficient reason for treating this disease by a surgical operation. Dr. Kocher says: "Whether we admit a primary irritation of the sympathetic nerve, and, therefore, an increased irritation of the gland, or a primary increase of thyroid material and from it an irritation of the sympathetic system, or both, it amounts to the same thing, so far as the thyroid operation is concerned. By reducing the hypertrophic thyroid tissue, or reducing its blood supply, we reduce the possibility of too extensive a reaction to the primary cause, and also enable the gland to counteract new outbreaks of primary causes, which a nervous subject can easily show."

J. J. C.

#### MUZZLE THE DOGS.

It would seem as if the authorities of Toronto did not understand the grave aspect of the situation of having dogs running about our streets unmuzzled. One of their duties toward the public is to place some kind of a safeguard between them and danger. In the streets of our celebrated "Ward," curs of all degrees of lineage disport themselves, small children are as thick as flies, and as friendly as can be with the dogs, often sharing "bite about." Of course, the "dog wagon" calls sometimes, but certainly not often enough.

In the East End, where the child population is large, also, the number of dogs is alarming. In one street near Parliament, we counted twenty-two dogs, one brute nearly as large as a Shetland pony, and none of them wore a muzzle. If the threatened epidemic of Rabies, which has given us a forewarning recently in Toronto, should break out, more children would be bitten in a short time than many Pasteur Institutes could give treatment to, and the parents possibly could not afford even to send them for treatment.

Why not make a law that all licensed dogs *must be muzzled*, and not allowed to roam unaccompanied by their owners, and vigorously enforce the law that all tramp dogs be charged with vagrancy and sent painlessly to a happier hunting ground?

W. A. Y.

## EDITORIAL NOTES.

**Dietetic Treatment of Gastric Ulcers.**—W. Sternberg (*Be-handlung des Ulcus Ventriculi Mittels Rationeller Küche*) believes that mechanical conditions, rather than chemical ones, are of the greatest importance in the treatment of gastric ulcer. Food may be so prepared that it is extremely easy to digest, not in the sense of chemical predigestion, but in the physical direction. This physico-mechanical preparation of food is most important for the stomach and upper part of the intestine. He gives illustrations of 13 improved kitchen utensils, which allow the food to be ground and strained, while yet retaining a consistency which permits of mastication. He would banish the spoon for stirring and use only the pestle. For hospitals he recommends a marble mortar, worked by power, or by hand, for grinding the food, raw or cooked, passing it then through a hair sieve, working it through the sieve with a broad masher, not a spoon. Still more effective is the passing of the food through a cloth. Two men hold the ends of a large cloth, and force the substance through it with two heavy wooden ladles, with great force. The substance then is smooth as velvet and melts in the mouth. This renders the food exceptionally digestible in the stomach. In this way the famous French dishes, "Crème de Gibier" and "Crème de Volaille," are made.

**Overfeeding and Improper Feeding are Causes of Infantile Diarrhea.**—Reports for July, 1908, turned in by seventy-five physicians who attended the poor in the congested areas of Chicago under the direction of the Department of Health of that city, show that by far the greater part of sickness among babies has been due to lack of proper care. Improper food, *overfeeding*, overdressing, lack of personal cleanliness, and want of fresh air are factors that produce most of the illnesses that kill the babies in hot weather. The most frequently reported abuse is *overfeeding*. The temptation to feed the baby every time it cries is too often yielded to. The feeding of improper food is another very common and frequently disastrous practice. Hundreds of little babies have been found eating rich, heavy foods—such as pastries, cakes, sausages, etc. Not a few have been observed feeding on soured milk. Among the overfed and the improperly fed diarrheal diseases are most preva-

lent. When these diseases develop, home treatment is resorted to and, in the majority of cases, proper medical attention is called for too late. Overdressing, lack of bathing, and want of fresh air are also mentioned in the physicians' reports as contributing factors to infantile mortality in hot weather. An interesting observation is made relative to the rates of mortality noted among the babies in the poorer sections of Chicago and babies on the boulevards of that city: "It has been observed that fully 75 per cent. of the babies in the poorer section of the city are breast-fed—a much larger proportion than among the boulevard babies. And yet, under existing conditions, the baby of the poorer sections of the city has less chance of surviving his first year than the baby of the better residence districts. Correct the existing conditions, however, and give the baby of the poorer sections the intelligent care it should have and we will soon see a death rate among them lower than among the boulevard babies. Other things being equal, the breast-fed baby has a much better chance of living than the artificially-fed one." The observations of the Chicago physicians go to prove that unsanitary premises and the general milk supply have less to do with the high infantile mortality in that city than is commonly supposed. The personal habits of the people are believed to be productive of the trouble. The mothers require to be taught how to care properly for their children. The physicians of the Chicago Health Department are carrying on a campaign of instruction by teaching the poorer people of the city how they should raise the young, and especially how they should avoid hot-weather diseases.

**Urotropin (Hexamethylene-tetramine).**—This drug, formed by the action of formaldehyde on ammonia, was introduced in 1894 by Nicolaier, as a urinary antiseptic, and still holds the first place among drugs used for that purpose. Regarding the prevention of bacteriuria, J. W. Churchman (Johns Hopkins Hospital Reports, Vol. 13, pp. 139-207), says: "In no cystoscopy done in the practice of Dr. Young on patients whose urine was uninfected and who had received urotropin internally did the subsequent examination of the urine by centrifugalization reveal organisms. But, in one case, in which the patient had not received this preventive medication, an infection did develop. Incipient bacteriuria without cystitis can, in the majority of cases, be inhibited by internal medication. In exceptional cases the bacteriuria will persist, despite

treatment. In the majority of bacteriurias associated with cystitis, it is practically impossible to wholly remove the organisms which have produced cystitis. Pus may diminish in amount, symptoms be relieved, and the urine cleared, but only occasionally will the infections disappear completely. From a series of bacteriological experiments with the urines of patients who took urotropin, methylene blue or salol by mouth, Churchman concludes: (1) Administration of urotropin, methylene blue or salol renders the urine inhibitive of the growth of the staphylococcus pyogenes, streptococcus pyogenes, B. typhosis, B. coli communis, and B. proteus vulgaris. (2) Urotropin and methylene blue are more inhibitive than salol; the choice lies with the first. (3) These drugs effect inhibition of bacterial development, rather than destruction of bacterial life. They render urine an uncongenial medium for growth, but not an environment necessitating death. (4) Their effect is weakest on the staphylococcus pyogenes and strongest on B. typhosus and streptococcus pyogenes. S. J. Crow (*Johns Hopkins Hospital Bulletin*, April, 1908) says: "In four cases, in which gall bladder operations were done at the Johns Hopkins Hospital, urotropin was given immediately afterwards in large doses (60-75 grains daily). The material aspirated from the sinus, before the administration of the drug, contained large amounts of various bacteria; that aspirated from the sinus subsequent to its administration was entirely free from bacteria, and chemical tests showed the presence of large quantities of urotropin, or its decomposition product, formaldehyde. In the case of the typhoid bacillus, the rapid disappearance of the organisms was especially evident. In a case of gonorrhoeal arthritis, treated with large doses of urotropin (80 grains a day), aspiration showed that the gonococcus had completely disappeared from the aspirated pus. The clinical condition of the joint improved markedly. Crow finds that the presence of urotropin has been demonstrated in bile, cerebrospinal fluid, synovial fluid, pleural effusion and the blood of man. When given in sufficiently large doses (75 grains per diem), it appears in the bile in quantities which suffice to exercise a decided bactericidal action.

**Some of the Uses of Chloretone.**—Chloretone, made by adding caustic potash to chloroform and acetone, is a white camphoraceous compound. It is an anaesthetic, general and local and hyp-

notic—dose gr. ii—x. It resembles chloral in its hypnotic action; in its combined analgesic and antiseptic action it resembles a combination of cocaine and menthol. It produces regular and deep sleep in doses of from 4½ to 9 grains, and may be given in powders, capsules or in an alcoholic menstruum. It is only sparingly soluble in cold water, but dissolves readily in hot water, alcohol, ether and chloroform. It produces a longer sleep than chloral, chloralamide, or the well-known combination of chloral and bromide of potassium. Its local analgesic action on the mucous membrane of the stomach causes it to be indicated in seasickness and in the stomach aches of nervous patients. It is also useful in premenstrual pains and the vomiting of pregnancy in doses of 2½ to 3 grains for two or three doses, at half-hour intervals. In dental caries a portion of a mixture made after the following formula may be applied with advantage to the aching tooth on a bit of absorbent cotton:

R. Chloretone,	
Camphor.....aa	ʒss
Tr. cinnamomi.....	℥viii
Ol. cajuput.....	gr. lxxvii

In acute diseases of the nose and throat and of the larynx, sprays of the following mixture exercise sedative, vaso-constrictive and decongestive effects:

R. Chloretone.....	gr. 15
Camphor.....	gr. 33
Menthol.....	gr. 33
Tr. cinnamomi.....	℥viii
Liq. vasoline.....	ʒiij

Warbrick has successfully used the above formula, combined with adrenalin, in sprays and inhalations, for the treatment of acute and chronic rhinitis. In tonsillitis and in hay-fever, when the painful areas can be reached, he applies the mixture to the affected parts, by means of an applicator tipped with cotton; in cases of laryngitis he uses sprays of the same mixture. Lubet-Barbon and Fiocro employ it as an analgesic to overcome the obstinate dysphagia of patients who have large tubercular infiltrations of the larynx or to relieve the pains, which follow the application of the galvano cautery. The analgesia lasts two or three hours. They also comment favorably on its not inconsiderable antiseptic and microbicidal power.

J. J. C.

**PERSONALS.**

---

DR. IRVING CAMERON returned from Great Britain on the 20th of September.

DR. A. J. JOHNSON was elected Director of the Confederation Life Association last month.

DR. SKINNER GORDON announces her removal to 467 Spadina Avenue, south-east corner of the Knox College Crescent.

DR. R. D. RUDOLF has been appointed Professor of Therapeutics in the Medical Faculty of the University of Toronto.

DR. NORMAN K. WILSON, one of the recent Council graduates, is practising with his father, Dr. W. J. Wilson, at 159 College St.

DR. F. C. TREBLCOCK, 722 Spadina Avenue, announces to the profession that in future he will confine his attention entirely to ophthalmic practice.

DR. CRAWFORD SCADDING returned from a delightful honeymoon trip to England about a month ago. Needless to say, he looks to be in the pink of condition.

DR. E. A. MCCULLOCH, partner of Dr. N. A. Powell, is progressing. His condition, however, is not altogether what his friends would like. We wish him speedy restoration to health.

DR. CHARLES M. STEWART, 142 Carlton Street, late Senior Resident Surgeon the Throat Hospital, Golden Square, London, desires to announce that he will confine his practice entirely to diseases of the ear, nose and throat.

DR. HARRY MORELL, of Regina, on July 22nd, while driving to the Indian School, after the Government House reception given to the Saskatchewan Medical Association, in company with Dr. and Mrs. Bingham, Toronto, took quite ill, necessitating operative interference on the part of Dr. Bingham. The outcome of the case was all right, as Morell writes, as "My friend Bingham did a good job, and I want you and my friends to know this."

DR. HAMILL, Medical Broker, Janes Building, Toronto, who conducts the Canadian Medical Exchange, for the purchase and sale of medical practices and properties, desires us to say to physicians

thinking of disposing of their practices or properties that this is an unusually desirable time for them to list their offers with him, as he has the best list of buyers registered with him that he has had for many months and is in a position to quickly and quietly sell any inviting medical practice anywhere in Canada.

WE are glad to be able to report that Dr. Bruce L. Riordan, who went down for treatment to the Pasteur Institute, New York, two weeks ago, is getting along nicely. Dr. Riordan was bitten by a family pet dog, and on the cadaver being examined the animal was found to have contracted rabies in a most acute form. The doctor considered that an ounce of prevention was worth a pound of cure, and placed himself promptly under treatment, with the result that he has almost entirely recovered.

WE had the pleasure of having a call recently from Dr. A. R. Avison, of Seoul Korea. A great many Toronto physicians will remember Dr. Avison, who practised on Carlton Street for many years, but who gave himself up to medical missionary work in Korea in 1895. The doctor is now Medical Superintendent of Severance Hospital at Seoul, Korea, and is doing magnificent work there, not only saving souls, but attending to the bodily ills and infirmities of that Eastern race. Dr. Avison is spending the early autumn in Canada, and returns to his home in the East before Christmas.

## Correspondence.

*The Editor cannot hold himself responsible for any views expressed in this Department.*

### A VALUABLE DISCOVERY—A NEW HYPNOTIC.

EDITOR OF CANADIAN JOURNAL OF MEDICINE AND SURGERY:

Sir,—Please allow me to call attention to the discovery that apomorphine hydrochloride, when administered hypodermically in doses just short of the emetic dose, is an ideal hypnotic. In doses of the 1-30th of a grain, it may be used with safety in all cases in which a hypnotic or antispasmodic is indicated, but is of special value in the treatment of acute alcoholism and delirium tremens. This valuable discovery was made by Dr. C. J. Douglas, of Boston, in 1899, but, strangely enough, the discovery remains almost unknown, and the boon, of course, not taken advantage of, as it doubtless will be when this important property of apomorphine becomes fully realized. We know how promptly this drug acts when administered as an emetic in emetic doses of the 1-10th or the 1-8th of a grain. With almost equal promptness is its action when administered as a hypnotic. The alcoholic, however wild or noisy, will, as a rule, be peacefully sleeping in ten or twelve minutes after the 1-20th or the 1-30th of a grain is administered subcutaneously. This sleep may last several hours, when the patient awakens refreshed and sober. Douglas employed the remedy, with these doses, in over 200 cases, mostly alcoholics, including cases of delirium tremens, and with gratifying results. Drs. Coleman and Polk, of Bellevue Hospital, New York, used it in over 300 cases of alcoholism, also with gratifying results. Dr. Rosenwaser, inebriatist to Newark Dispensary, Newark, N.J., has also used apomorphine in the same manner, and for the same purpose, and with equally satisfactory results. The dose administered was from 1-30th to 1-20th of a grain. With these doses, the hypnotic effect is secured in 67 per cent. of the cases. Even the 1-40th of a grain, in my experience, is effective with some patients.

There are vagaries in the conduct of apomorphine that should be noted, viz., it is inert when administered in a solution of boracic acid; it is almost inert as a hypnotic or centric emetic when administered by the mouth. It should also be noted that the crystalline form only should be used, and also that, in cases in which the pulse is feeble, strychnine should be given in association with the apomorphine.



This important discovery will surely mark the commencement of a new era in the management of cases of acute alcoholism and delirium tremens. In many hospitals, at present, these troublesome cases are far from being welcome guests; but when it becomes generally known that we have at command an hypnotic, safe and prompt in its action, and peculiarly adapted to the management of these perplexing cases, this reluctance to their reception should be entirely removed. It is doubtless pretty generally known to the members of the medical profession of this Province that a bill was prepared several years ago for the Ontario Government for the economic treatment of indigent inebriates. This bill was drafted by a joint committee, representing the Ontario Medical Association and the Prisoners' Aid Association, respectively. From various causes this bill has never been presented to the Ontario Legislature, but a special effort will be made to have it introduced at the next session. In this bill, as will be remembered, it is proposed, with a view to economy, to utilize the wards of the general hospitals of the Province for the reception and treatment of indigent inebriates of the more hopeful class. This discovery of the hypnotic property of apomorphine, and the facility with which it brings alcoholic patients under control, will, doubtless, help very materially in clearing the way for the introduction of the bill; and when the bill is adopted, and its provisions faithfully carried out, it should go a long way in cutting off the supply of recruits for the jails of the Province, as well as for the combined reformatory and farm colony about to be established by the Ontario Government.

In this connection, I would add that, in the proposed bill, provision is also made for combining the Massachusetts probation system of prolonged supervision, with medical treatment, and this medical treatment may be carried out, according to the nature of the case, either in a hospital or in the form of dispensary or home treatment. This system of combining the probation system with medical treatment has been in operation in Toronto by the Ontario Society for the Reformation of Inebriates for over two years, on a small scale, with encouraging results. Yours, truly,

A. M. ROSEBRUGH,

Secretary Ontario Society for the Reformation of Inebriates.  
Toronto, August 22, 1908.

# Obituary

## DEATH OF DR. HODGE, OF LONDON.

Dr. Geo. Hodge, of London, Ont., Professor of Clinical Medicine in the Western Medical School, and one of the best-known physicians in Ontario, died at St. Joseph's Hospital, in London, on August 26th, from pneumonia. Dr. Hodge was 68 years old, and graduated from Queen's University in 1870.

## DR. WILLIAM NATTRESS SUCCEUMBS TO PLEURISY.

THE illness of Lieut.-Col. Dr. William Nattress had a fatal termination on September 14th, shortly before 5 o'clock, at the residence, 42 Carlton Street. The deceased was a native of Woodbridge, Ont., and was in his 56th year. He was in rather poor health when as Chief Medical Officer of the Western Ontario Command of the Permanent Army Medical Corps he left for the tercentenary celebration at Quebec. During the wet spell there Dr. Nattress was seized with pleurisy and had to undergo an operation for empyaema. He rallied sufficiently to be brought home, but continued seriously ill. The deceased was married in 1890 to Miss Denison, daughter of Col. G. T. Denison. The bereaved widow is the recipient of sympathy from a wide circle of friends. Dr. Nattress was a member of Holy Trinity Church, of which his brother, Rev. George Nattress, of Boston, Mass., was at one time one of the clergy. Dr. Nattress was widely known in military and medical circles, and attained recognition in the literary sphere by his authorship of the school-text-book, "Temperance and Hygiene." The funeral took place on Wednesday, September 16th, at 1.30 p.m., from the family residence to Weston, where the interment was made in St. John's Cemetery. The service at the house was conducted by Rev. Dr. Pearson, of Holy Trinity Church, and at the grave by Rev. T. C. Street Macklem, of Trinity College. Lieut.-Col. Septimus Denison, C.M.G., S.O.; Col. F. L. Lessard, C.B., A.G.; John Galloway, D.A.A.G., and Major J. T. Clarke, A.M.C., were pall-bearers. The chief mourners included his brothers, Isaac Nattress, Leonard Nattress, Rev. George Nattress, Joseph Nattress and Thomas Nattress; his nephews, Rev. Thomas Nattress, Dr. John Lawson, Dr. Joseph

Lawson; Col. G. T. Denison, father-in-law; Major G. T. Denison, brother-in-law; A. M. M. Kirkpatrick, brother-in-law, and Douglas Kirkpatrick, nephew. There was a large attendance of citizens, which included military men and members of the medical profession.

---

#### DEATH OF DR. GEORGE HUNT, OF NEW LOWELL.

---

SELDOM has death removed a member of the community and left such widespread sorrow as is felt by the passing away at New Lowell, Ont., of Dr. George Hunt on September 5th. Although only forty-three years of age, he had endeared himself to hundreds of families, and among the poor especially, where he ministered cheerfully and often without hope of reward. On all sides expressions of sympathy are heard for those he leaves behind, a wife and son, a mother and a sister.

The late Dr. Hunt was born at Thornton on November 29, 1865. He graduated from Victoria University and Toronto Medical School in 1886, and after practising for two years with Dr. R. L. Island at Rosemount removed to New Lowell, where he has lived ever since. He was the first Medical Health Officer of the Township of Sunnidale, and held the position to the end. In 1899-1900 he was elected to the County Council, where he was the chief mover in organizing a House of Refuge for Simcoe County. As a politician Dr. Hunt was becoming widely known, and did effective service. He had been chosen as President of the Conservative Association for Centre Simcoe, and held that office at the time of his death.

## *News of the Month.*

### FURTHER APPOINTMENTS TO THE MEDICAL FACULTY OF THE UNIVERSITY OF TORONTO.

THE Board of Governors of Varsity have made two additions to the medical faculty.

Dr. Graham Chambers, B.A., M.D., becomes Associate Professor in Clinical Medicine, and Dr. Walter McKeown, B.A., M.R.C.S. (Eng.), Associate Professor in Clinical Surgery. Both are Arts graduates of Toronto University, as well as men who received their first medical training in the city of Toronto.

Dr. Chambers is one of the chiefs of the medical staff of the Toronto General Hospital, and Dr. McKeown is one of the surgeons of St. Michael's Hospital staff.

### TORONTO'S NEW MORGUE:

As soon as \$1,500 worth of furniture is installed, the new city morgue in Lombard Street will be ready for use. It is just as handsome and complete as \$40,000 can make it.

A long apartment on the ground floor, to the west, is finished in oak, with a high wainscoting. It is divided in the middle by the receptacles for bodies. There are two tiers of seven receptacles each, and the bodies are placed on carriers, which pull outward on rollers. The tiers are iced from above, and the entire outfit resembles a huge refrigerator. The icing is done through an opening on the west side of the building, eliminating the necessity of entering the building to place the ice in the receptacle. The morgue accommodates fourteen bodies, and is a replica of the morgue attached to the Bellevue Hospital in New York City.

On the right of the entrance is the office, where a girl is in attendance from 8 a.m. until 5 in the afternoon. After that hour the caretaker takes over the management of the place until 2 a.m.

On the second storey, to the front, and running the entire width of the building, is the apartment set aside for the hearing of inquests. A retiring room has been placed at the disposal of the coroners. It includes a very complete lavatory. In the rear is a room for lawyers. To the west are apartments for male and female witnesses, each equipped with lavatories. In fact, every official or person whose business takes them to an inquest has been

well looked after. There is one apartment there to which as yet no use has been assigned, and it was doubtfully dubbed the Press Room. The city fathers will be put to it to even name the many apartments which they have incorporated in the new morgue.

Stables and carriage houses have been provided for the ambulances which handle cases of infectious diseases. The stable accommodates three horses and the house two ambulances. Above are sleeping apartments for the man on duty.

A citizen who was of a cynical and doubting turn of mind suggested that far less expensive quarters could have been secured which would have answered the purposes of the new morgue just as well. One of the old but solidly built residences in the downtown section could have been secured and alterations made at an expenditure, say, of \$2,000. There are many such buildings in Richmond, Church, or Jarvis streets, and one could have been turned into a morgue without offending the neighborhood or eliminating one of the facilities now possessed by the new one. Three bodies at one time constituted a record for the old morgue, and four made a great exception. Whether the fourteen shelves will ever be called into use or not is a matter which depends upon the city's growth, but from past records they will suffer dire neglect.

The entire building is handsome, commodious, and possesses every facility for which it was erected.

---

#### DRS. J. N. E. BROWN AND BRUCE SMITH RETURN AFTER VISITING BRITISH HOSPITALS.

Dr. J. N. E. Brown and Dr. R. W. Bruce Smith returned on August 26th from their six weeks' visit to England and Scotland, where they were, on behalf of the Ontario Government, looking into the construction and administration of hospitals and asylums. Dr. Smith gave his attention especially to sanitarium, jail farms and poorhouses. Dr. Brown looked more particularly into the administration of hospitals. They visited London, Edinburgh, Glasgow, Paisley, Belfast, Birmingham, and other cities, and also looked at out-of-town institutions. Everywhere they were cordially received, and they gathered much useful information. Their formal report is in preparation. Dr. Brown mentioned that he had observed quite a number of features in the systems of building and equipping hospitals that were quite different from anything he had seen in the United States, and some things entirely new in Great Britain. He learned some valuable facts about the unit system of buildings, and a new system of ventilation, about which he expects to make some recommendations looking to the new General Hospital buildings in this city.

### STAFF REORGANIZATION AT ST. MICHAEL'S HOSPITAL.

---

A COMPLETE reorganization of the medical staff of St. Michael's Hospital has been announced. There are a number of reasons for the changes, chief among which may be mentioned the fact that when the General Hospital was reorganized, a rule was passed allowing no medical man on the special or department staffs of that institution who was connected with those of another hospital. This rule, however, does not apply to consulting staffs. Another reason is that St. Michael's has a great amount of clinical work, of which Toronto University wished to have the benefit. A system which will work in with these conditions has been adopted. There will now be two services in surgery, of which the chiefs are Dr. I. H. Cameron and Dr. Walter McKeown, and two services in medicine, with Dr. R. J. Dwyer and Dr. H. B. Anderson presiding. The heads of the department of obstetrics and gynecology are Dr. T. Fenton, Dr. A. H. Garrett and Dr. M. Crawford, while Dr. G. H. Burnham is chief of the department having to do with diseases of the eye. A list of the complete staff will shortly be announced. Doctors who are debarred, by the new rule referred to, from acting on departmental staffs, are still retained upon the consulting staff.

Plans are partly ready for a large addition to St. Michael's Hospital, to be built on the property directly to the north of the present building.

---

### THE INTERNATIONAL MEDICAL CONGRESS AT BUDAPEST.

---

THE sixteenth International Medical Congress will be held at Budapest, Hungary, under the distinguished patronage of the aged Emperor of Austria, from the 29th of August to the 4th of September, inclusive, 1909.

A strong Canadian Committee has been formed to represent the medical profession of Canada at this conference. The following is the Committee: Drs. H. S. Birkett and F. Shepherd, of Montreal; Dr. J. D. Courtenay, of Ottawa; Dr. J. Third, of Kingston, Dr. Ingersoll Olmsted, of Hamilton; Dr. J. D. Wilson, London, Dr. Halpenny, of Winnipeg; Dr. S. T. Tunstall, of Vancouver, and Dr. O. M. Jones, of Victoria; and Drs. W. H. B. Aikins, A. H. Garratt, E. E. King, J. S. MacCallum, G. R. McDonagh, A. McPhedran, G. S. Ryerson and A. H. Wright, Toronto.

The Secretary of the Committee is Dr. W. H. B. Aikins, 50 College Street, Toronto.