small tumor formation and without involvement of the lymph-nodes.

In three cases a very interesting experiment was made. The tests were made in the ordinary way with blood-serum and found positive. The cancerous tissue from these cases, procured at operation, was ground in a mortar with powdered glass, emulsified with a small amount of salt solution and placed in an incubator for an hour. The suspension was then centrifuged and the supernatant fluid injected into guinea-pigs sensitized in the usual way. In all three cases the typical positive cancer reaction was obtained. Although no final conclusion can be drawn from these experiments, they certainly seem to indicate that the substance in the blood-serum in reality originate from the cancer tissue itself.

The twenty negative cases may be divided into the following classes: tuberculosis, 3; normal, 3; syphilis, 3; hypertrophic cirrhosis of liver, 1; myocarditis, 1; sarcoma, 1; gall-stones, 1; cirrhosis of the liver, 2; anemia, 1; jaundice, 1; acute intestinal obstruction, 1; intestinal stasis, 1; papilloma of the bladder, 1.

The most interesting classes of cases are the tuberculous, syphilitic and sarcomatous. There were three cases of tuberculosis; one of the peritoneum with tumor formation, one of the lung with enlarged bronchial glands, and one chronic suppurative cervical adenitis. The syphilitic cases were all of the tertiary type one syphilitic leukoplakia of the tongue, one syphilitic inflammation of the mouth and nose, one ulcer of the soft palate. The latter two cases gave positive Wassermann tests and yielded to salvarsan. The leukoplakia of the tongue gave a negative Wassermann. The leukoplakic patches were removed and microscopically showed the typical evidences of chronic inflammation.

CONCLUSIONS

1. From these tests it seems possible that the anaphylactic test may prove an aid in the early diagnosis of cancer. The five early cases, which gave positive tests, seem particularly significant.

2. The margin of error (8 per cent.) is not large enough to invalidate the test.

3. The most valuable single factor is the uniformity of negative tests in non-malignant cases. There seems no possibility of making a diagnosis of cancer, when cancer is not present.

4. A positive diagnosis seems absolute evidence of the presence of cancer.

5. This test needs further trial by other workers.
19 West Seventh Street.

ABSTRACT OF DISCUSSION

DR. OSCAR BERGHAUSEN, Cincinnati: In the ordinary case of cancer in which the tissue is accessible, the microscopic examination is sufficient, but when that is not the case some other means of diagnosis must be sought, such as the method described by Dr. Ransohoff. This method gives some promise of being a valuable means of diagnosis. The fact that 87.7 per cent. of accurate diagnoses were made in cancer cases is indeed most encouraging. It is very seldom that any method of diagnosis by clinical or specific means reaches that high rate. The change following the injection is very marked, as in a case at which I had the pleasure of being present. The experiments were all made at the laboratory of the Cincinnati Hospital, and several men made the observations to confirm those of Dr. Ransohoff. The test differs from previous tests along anaphylactic lines in that normal serum, as well as cancer serum, was used.

SURGERY OF THE THYROID

OBSERVATIONS ON FIVE THOUSAND OPERATIONS *

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During the twenty-five years ending May 14, 1913, 5,000 operations were performed on the thyroid in the clinic at St. Mary's Hospital. These operations were done on various types of goiters and may be classified as follows:

Simple goiters.....	2,306
Including	
Transplantations in cretins.....	11
Operations for malignancy: carcinoma, 52; sarcoma, 7..	59
Operations on syphilitic thyroids.....	1
Exophthalmic goiters, including double and single ligation, extirpation, partial thyroidectomy.....	2,295
Early operations not classified, majority simple goiter....	309
Total	5,000

An increase in the size of the thyroid may be physiologic or pathologic. In the higher invertebrates the gland has a marked sexual relationship, and through this association we have a suggestion that the thyroid may be a factor in the manifest disturbances which occur at certain periods, especially in the female, as the well-known goiter of adolescence, the congestion of the thyroid during menstruation and its not infrequent enlargement during pregnancy.

While as yet we have no knowledge of a specific causative factor in the production of goiter, nevertheless a great deal has been learned during the past quarter of a century concerning the physiology and pathology of the gland. Among its several functions the thyroid has been shown to be a *defense gland* and that it has much to do with physical and mental development. It is evident that increased activity of the gland is required during infections in different organs of the body. Several observers, among them McCarrison, believe this demand to be occasioned by intestinal toxemia, and that this may play an important part is undoubtedly true. The work of various goiter commissions and the reports of those observers who have made a study of the etiology of goiter make it quite apparent that, whatever the agent, it seems to be more readily conveyed by water than by any other medium, although water is probably not the sole carrier. The so-called goitrogenous water, when boiled, is not infective. Evidence varies as regards intestinal toxemia. Boiled water contaminated with the feces of an individual having recently developed goiter has produced goiter in goats, while the filtered residue of goitrogenous water from districts in which goiters prevail has also produced the same result in man and the goat. This does not necessarily prove a specific agent; it may indicate a demand on the system for increased resistance and greater elimination of toxic material. Repeated tonsillitis is another disease in which an infection may have a bearing on the hyperactivity of the thyroid.

The thymus gland and the thyroid are undoubtedly intimately associated in the growth and development of early life. We now know that the thymus is much more regularly persistent throughout life than it was formerly supposed to be and that not infrequently the gland may be of great size in advanced middle age, compressing the trachea at or just above its bifurcation. Such a complication is more common and more grave in late goiters of the serious hyperplastic type.

* Read in the Section on Surgery of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

The occasional large goiter observed in the cretin has but little active parenchyma. If these goiters cause distress they should be removed. We have repeatedly transplanted gland from the mother, and also from fresh simple and exophthalmic goiter. In none of these cases did the transplanted gland functionate, though for a short time it furnished secretion by absorption.

Changes in the voice are often caused by the presence of goiter. Large right-sided goiters quite frequently produce paresis of the left recurrent laryngeal nerve. It is therefore advisable to make a laryngoscopic examination before doing a thyroidectomy, which otherwise may be blamed for the paresis discovered later. Loss of voice through injury of the recurrent laryngeal nerve during operation is not a rare occurrence. Possibly 10 per cent. of patients have some temporary hoarseness, and about 5 per cent. a permanent difficulty with one cord, but without loss of voice. This percentage is small compared with the number of cases of paresis or paralysis due to the pressure of a goiter.

The left recurrent nerve, which is more frequently affected, lies slightly deeper than the right and has received more stretching during embryonic life. This may account in some measure for its greater susceptibility to injury from pressure. Extensive exposure of the nerve, as is done in some clinics, is necessary only in an operator's early experience, or in operating on nodular thyroids which extend beneath the trachea and which may have displaced the nerve. The scar tissue resulting from the traumatism of a too free exposure of a nerve may lead to secondary paresis.

Intrathoracic goiters and deep substernal goiters are of serious import and are found about once in fifty operations for simple goiter. Slight substernal projections are much more frequent. The diagnosis rests on (1) dull area on percussion, (2) the roentgenograph, and (3) evidences of substernal pressure (dilated veins, obstructive dyspnea and palpation of the upper pole of the gland just above the clavicle).

A special histology of the parathyroid glands was described by Sandstrom in 1880, and they have been the subject of much investigation and experimentation from a surgical point of view during the past few years.

While a great deal has been attributed erroneously to the parathyroids, they are worthy of serious consideration by the surgeon operating on the thyroid. There are four parathyroids in the human being normally and, since the veins of these bodies have no valves, they are quite liable to imperfect development through congestive conditions occurring during birth. Inasmuch as but one or two of them may be active and their injury during operation may cause tetany, their location must be avoided by preserving the posterior capsule, especially when both sides of the thyroid are operated on. Because of the difficulty in identifying the parathyroids, it is best also to preserve all small gland-like bodies beneath or connected with the posterior capsule. Treatment, however, of operative tetany with calcium lactate and also beebes' parathyroid with thyroid extract has been very effectual. Our experience with this disease and treatment is limited to one mild case of temporary duration.

As regards the non-surgical treatment of goiter, there is no question but that many cases of simple goiter, especially of the adolescent type, undergo a natural resolution, which is also true of congestions and enlargements occasionally observed during pregnancy. In the hyperemic goiters of adolescence some form of iodine treatment may have a favorable effect. In encapsulated adenomas the use of iodine may manifest a temporary

favorable effect on the surrounding gland, but the effect on the encapsulated tissue is uncertain. Its use between the ages of 35 and 60 seems to stimulate the activity of the thyroid and to cause degenerative changes. More recent experience in the non-surgical treatment seems to indicate the use of thymol, salol and iodine as intestinal antiseptics. The administration of thyroid gland has rather an uncertain effect, yet apparently produces favorable results in the early treatment of simple goiters. In a considerable percentage of cases, hyperthyroidism unquestionably is checked at various stages of the disease by natural or therapeutic measures. In exophthalmic goiters temporary improvement has been obtained by the use of the Roentgen ray, which seems also to be of value in carrying serious cases through exacerbations. The cytolytic serums for specific action on the thyroid have not borne out in their results the early expectations of the medical profession.

In operating on the thyroid, the best exposure to be obtained is through a transverse incision low in the neck, the skin and platysma turned together each way from the incision. Should further exposure be necessary, the sternohyoid may be sectioned high in the exposed area to prevent movement of the cutaneous scar and preserve a working muscle. In simple goiters it is best to extirpate a greatly enlarged lobe. If both lobes are symmetrically enlarged, division of the isthmus with double resection of the gland is indicated for the best cosmetic results. Midline encapsulated adenomas should be enucleated with division of the isthmus. Lateral encapsulated adenomas may be enucleated or the whole lobe extirpated.

If symptoms of hyperthyroidism are present, extirpation is indicated. In severe cases of hyperthyroidism, in acute attacks and relapses or exacerbations, the condition should be considered medical until improvement takes place. If no improvement proves manifest under such care, injections of boiling water into the lobes (Porter) may give relief.

During the first three or four months of the symptoms extirpation can safely be made since the heart then is not dilated. If dilated to exceed 1 inch, primary ligation of the superior thyroid vessels is indicated, followed in four months by extirpation. After the first year a much smaller percentage of cases requires primary ligation. A single test ligation on one side may be made in doubtful cases, to be followed in a week by a second ligation or partial extirpation according to the degree of reaction.

The records of a large number of patients in this series show an average gain of 22 pounds within four months after ligation. These patients were then operated on, a partial thyroidectomy being done with safety. Following these methods of safety, we have performed 278 operations on cases of hyperthyroidism between deaths. Long-standing cases of simple goiter and adenoma may, by degeneration or chronic slow thyrotoxicosis, cause serious disturbances in the heart, kidneys and blood-vessels. Especially is this true of patients in middle and advanced middle life. When such complications are present operations are made with considerable risk.

Excluding malignancy, the mortality in operating on goiters is very low. It varies but little at present in the cases of so-called simple goiter, in which class are included occasional complications, from the cases of so-called exophthalmic goiter with hyperplastic glands. In the early development of surgery, operations on exophthalmic goiters were delayed until serious complications arose with the heart, kidneys or nervous system. This led to a high mortality, which naturally deterred physicians from sending patients to surgeons for early

operation. The greater the delay the greater the mortality—hence a surgical vicious circle. Our mortality in the first sixteen cases (which were, of course, advanced) was 25 per cent.—about the average percentage in other clinics at that time. The mortality at present varies from 1 to 3 per cent. This great reduction in mortality is probably due less to operative skill and technic than to better judgment as to the time and extent of the operative procedure instituted, as well as to the skilled use and rational choice of an anesthetic. The various causes of mortality are hyperthyroidism, embolism, pneumonia, hemorrhage, sepsis, etc.

The results of operating on simple goiters are well known to be exceedingly satisfactory. Severe myxedema is but a rare complication following such operations, especially if the area of the gland nearest the capsule be preserved. The large colloid masses in the interior of these glands represent the great bulk of the tumor but the least amount of the working area of thyroid tissue.

Operation in cases of hyperthyroidism appears to give about 75 per cent. of cures, while the remaining 25 per cent. are more or less benefited, according to the degree of complication and the stage of the disease. Probably 10 per cent. have some degree of relapse in from one to three years after operation, usually manifested by the return of symptoms. In these rare cases further operation by ligating the vessels, and in most cases by removal of a portion of the remaining lobe, improves the condition of the patient by reducing the amount of thyroid secretion. Exophthalmos of marked degree and long standing may still be present when other symptoms are cured. This is due to the gradual contraction of the non-striated muscle which sustains the globe to the anterior supporting orbital fascia (Landstrom). In some cases we have greatly improved this condition by removing the superior and middle sympathetic ganglions.

If the patient is in a good general condition without complicating conditions, a general anesthetic, for instance, ether by the drop method, is preferred. Ordinarily patients receive 1/6 grain of morphin and 1/150 grain of atropin half an hour before the operation. Nervous patients having exophthalmic goiter may receive 1/200 grain of scopolamin one hour before operation, but without the atropin unless a general anesthetic is also to be given. Scopolamin is uncertain in its effects, some patients being made worse by its use. Patients suffering from grave complications rendering general anesthesia inadvisable can be carried through extensive operations by free local injections of novocain, 0.5 per cent.; and a combined local and general anesthesia, as advocated by Crile, may be of advantage in many cases. Intratracheal anesthesia is indicated in those cases of scabbard or distorted trachea in which the patient is already suffering from dyspnea, or more especially in those suffering from malignant disease of the thyroid, and complications due to enlarged thymus.

ABSTRACT OF DISCUSSION

DR. GEORGE W. CRILE, Cleveland: I can confirm Dr. Mayo's conclusions by my own experience, having operated in over 800 cases of goiter of all types and varieties. I have never seen a single case in which cancer of the thyroid diagnosed before operation was cured by operation. I have seen a few cases in which cancer of the thyroid, not suspected before operation, but found by the pathologist, was cured. The safety of the operation for colloid goiter is so great at the present time that, if the patient demands operation, one is justified in removing the gland for cosmetic reasons. The care Dr. Mayo suggested in the preservation of the voice is

excellent. I have found that one may take out the entire lobe, carrying the dissection right to the edge of the capsule, using very small hemostats, keeping a bloodless field so that one can see from the beginning to the end of the operation the lymph-vessels as they run out of the gland. In this way it would be impossible to remove either a parathyroid or to injure the recurrent laryngeal nerve. Passing to another subject, I wish that a commission might be appointed for the purpose of investigating the adolescent period of children living in goitrous districts. I believe that the syrup of ferrous iodid in 5-minim doses, three times daily, for periods of a month during every year, will control nearly all cases of simple hypertrophy. One of the factors in the production of adolescent goiter lies in the geologic change in the constituents of the earth where iron is not found in the food as once it was. I find that clinically one can make a very accurate prediction of the pathologic condition to be found in the gland. There is no more doubt in my mind as to the benefits of operation for exophthalmic goiter than of opening an abscess. Patients confirm that view, and our clinics have grown not through reference by physicians but through reference by patients. Nowadays, I believe that there is a general feeling not only among surgeons but also among patients that exophthalmic goiter is a disease that should not be allowed to go on until the stage of degeneration is reached. I believe that the late results of the disease are largely under control. One can operate now and control the hyperthyroidism by the principle of anoci-association, and not have a single change for the worse at the end of the operation, no matter how severe the case, how large the gland or how rapid the pulse-beat.

DR. A. J. OCISNER, Chicago: The enlargement of the thyroid is primarily a physiologic condition. There seems to exist a certain balance between the amount of thyroid secretion and the amount of secretion that is needed by the human organism for the purpose of carrying on its physiologic work. The thyroid seems to work ahead and, when there is an unusual strain on the physiologic activity of the body, the thyroid seems to prepare for it. This occurs especially when there is to be produced a large amount of new tissue of a highly organized character, or of the bony framework, as for instance during pregnancy. There may be a physiologic increase in size of the thyroid or an increase in weight. The same may be true during the period of puberty. There is an increase in the size of the pelvic bones, and other changes in the anatomy of the girl are followed by an increase of the thyroid. We have another interesting example brought out by Professor Wilms, who found that the students coming to the university from hyperthyroid countries developed hyperthyroidism a short time after their arrival at the university. It seemed as if the thyroid had to produce an additional amount of secretion so as to make it possible for the person to get his growth under the handicap placed on him by the presence of certain substances in the water which he drank. When the young man goes to the university where the water does not contain these, where the thyroid must supply the substances and overcome this handicap, he develops hyperthyroidism. As soon as the boy goes home and drinks the water there, the hyperthyroidism promptly disappears. Some of the water from a town where 70 per cent. of all the inhabitants had goiter was given to rats. Every normal rat which drank this water for a period of weeks developed goiter. This water was boiled and given to other rats and did not produce enlargement of the thyroid. Something in the water had been changed. One of Wilms' assistants, who came from this town, gave water from across the valley to children there; these children did not have large thyroids. The children born on a certain farm did not have enlargement of the thyroid, but those who were born later into the same family, on a new farm, all had enlargement of the thyroid. The water was boiled and there was no more enlargement of the gland. Instead of giving iron or iodids, I would boil the water.

We must not lose sight of the physiologic side of this question. When the calamity has occurred, we must relieve

the condition surgically before it has been destructive in its action, because, as Lundstrom demonstrated in the examination of all his cases, once the destruction has occurred, it is permanent.

DR. CHARLES H. MAYO, Rochester, Minn.: Dr. Crile called attention to a very valuable point, namely, that we have enough cases of goiter now all over the country to warrant the appointment of a goiter commission. In carrying on that work we ought to have the active cooperation of surgeons, internists, physiologic chemists and serologists, to see whether this question cannot be threshed out by having such a group of men at work on it, each one working on a series of cases, so that we could get something before this Section to guide us in our further work. Switzerland has had two or three such commissions, and the Indian government also has such a commission, which has already done an enormous amount of work. There is no doubt that goiter is toxic, but toxic as alcohol is toxic to the blood-vessels and to the heart. When a patient (usually a woman) has suffered for twenty or thirty years from colloid goiter, she begins to think about the goiter. She consults a physician and he starts to treat her with iodine, and in six weeks or three months she thinks that the goiter is smaller, but the doctor will change his indication for treatment from goiter to myocarditis or endocarditis. That can be done by treatment in overstimulating the gland which for twenty or more years could not give the necessary secretion. Nature has fortunately endowed us with enough glands so that we can spare a few. Take out one kidney or even half of the remaining kidney and still half a kidney will do the work. We can get along with one tenth of a pancreas, but that does not mean that we have too much kidney substance or too much pancreas substance. It simply means that Nature can accommodate herself to a certain extent so that a part of a gland can do the work of a whole gland. Take the high-school girl who is overworked, whose general condition is bad from overexcitement. She is very nervous; she receives a sudden shock. She has been struggling with an oversecretion of the gland, trying to neutralize certain poisons, and following the shock she develops in a few weeks a severe grade of exophthalmic goiter. Due to what? To overthrow or upsetting of the balance which had existed and which prevented any untoward effect on the sympathetic nervous system. It did not come on suddenly. It suddenly became acute. That is all. It had been there for a long time. It made her nervous and the shock made it acute.

LANGE'S COLLOIDAL GOLD CHLORID TEST ON THE CEREBROSPINAL FLUID IN CONGENITAL SYPHILIS*

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AND

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CHICAGO

Anyone who has had much experience with the Wassermann reaction and other laboratory tests as applied to the diagnosis of congenital syphilis must feel that such reactions are entirely inadequate, and this especially applies to those cases in which they are most needed, that is, in very young infants.

Zsigmondy¹ has shown that certain albuminous bodies when brought in contact with a solution of colloidal gold in the presence of an electrolyte, would, in certain concentrations, cause a clumping together of the small colloidal particles producing various changes in color and even precipitation. He also found that when these albuminous substances were in less dilute solutions they possessed a protecting power which prevented precipitation.

Furthermore, it was noted that the point at which protection ceased and precipitation began was different for each albumin. Lange, therefore, concluded to try the effect of spinal fluids on colloidal gold solutions.

Very shortly Lange found that when he used a certain amount of cerebrospinal fluid from a patient with general paresis, in the presence of 0.4 per cent. sodium chlorid and added the colloidal gold solution he got a certain change of color. He tried this again with spinal fluid from a similar case and got the same kind of a reaction. These tests were repeated always with the same result.

Tabetic spinal fluid was then tried with a resulting reaction approaching somewhat that of general paresis cases. Continuing in this way he found that all cerebrospinal syphilis cases reacted in about the same dilutions; and that those cases not due to syphilis either gave no reaction at all or reacted at different dilutions. He was thus, by the gold test alone, able to differentiate the luetic cases from those due to other diseases.

As Lange's experiments and studies continued he found that general paresis had an absolutely typical reaction; that, knowing nothing about the history of the case, one could say, from the gold test alone, whether or not the fluid in question was from a case of general paresis. The reaction for tabes, although quite characteristic, is not pathognomonic. One can, however, say that it is undoubtedly syphilis. Syphilitic meningitis gives a definite reaction for syphilis. On the other hand, Lange found that tuberculous meningitis, suppurating meningitis and other forms of meningeal inflammations, whenever the spinal fluid gave a positive Nonne (ammonium sulphate test), would give a positive gold reaction, lower down the scale of dilutions.

It can now be seen that Lange found something in the gold test which was much finer than anything in the tests heretofore in use. The Nonne simply told him that he had a pathologic fluid. With the gold test he could in some cases diagnose, and in all cases he could say with a high degree of certainty whether or not the case was one of syphilis.

Lange himself is extremely conservative and, in order to make a definite diagnosis, he still advises the use of the clinical history, the Wassermann, cell-count, and the Nonne in addition to the colloidal gold-precipitation test.

Materials Needed for the Test.—

- 1 per cent. solution of gold chlorid (Merek's Yellow Crystals).
- 2 per cent. solution of potassium carbonate.
- 1 per cent. dilution of liquor formaldehydi.
- 10 per cent. solution of sodium chlorid.
- Jena glass beaker, 1,000 to 1,500 c.c.

It is of the greatest importance that one have a good indicator with which to work in order to get accurate results with Lange's gold test. In order to make up such an indicator the following technic should be followed out in the minutest detail:

1. All glassware used must first be cleaned with acid, then washed in distilled water and dried with heat. Pipets may be dried out with alcohol and ether.

2. To make 500 c.c. of indicator (a) take 500 c.c. of freshly double distilled water in a Jena glass beaker (1,000 to 1,500 c.c.), and heat slowly over wire gauze; (b) when the water is approximately 60 C., add, while still heating, 5 c.c. of 1 per cent. solution of gold chlorid and then follow immediately with 5 c.c. of 2 per cent. solution of potassium carbonate; (c) heat rapidly to boiling; (d) turn out flame as soon as first steam bub-

* From the Laboratory of the Presbyterian Hospital, Chicago.
1. Zsigmondy: Ztschr. f. Chemotherapie, 1912, 1, 44.