A British Medical Association Lecture

ON

HYPERTHYROIDISM.*

BY

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IN the great majority of chronic diseases we are called upon to recognize and remedy deficiencies of function resulting from morbid changes in individual organs. These structural changes may produce alterations in the size of the organ involved which may have mechanical effects—as, for example, retention of urine due to enlargement of the prostate gland. Mechanical effects of this kind are, however, in many cases of less importance than the functional disabilities. We have been apt in the past to pay great attention to both gross and minute changes in structure without fully appreciating their effects upon functional efficiency. We are learning by degrees to estimate more accurately the changes in function in a diseased organ and to realize their importance. Professor Hugh Maclean¹ has shown how this may be done in the case of the kidney by methods which are applicable in practice and, when taken into consideration along with the symptoms, afford valuable information as to the extent of impairment of function in cases of renal disease. In diseases of the endocrine glands we have to consider the results not only of changes in their size and shape, but also of alterations in their functional activity which may be either exalted or depressed. Enlargement of an endocrine gland may produce important effects owing to its anatomical position. Thus owing to its confined position a comparatively moderate enlargement of the pituitary gland may produce the serious pressure effects known as “neighbourhood” symptoms, which occur in some cases of acromegaly. In medicine we are more directly concerned with the results of changes in functional activity, which may be either greater or less than normal. The results of too great functional activity are, in the case of the thyroid gland, only too well seen in cases of Graves's disease. The dire results of loss of function in the case of the suprarenal glands are familiar to all in the form of Addison's disease.

In a former British Medical Association lecture² a general account was given both of the methods of ascertaining, as far as possible, the physical condition of the endocrine glands and of the symptoms which are due to changes in their functional activities. On this occasion the varieties and results of glandular overactivity, as illustrated by the thyroid gland, will be considered as well as the principles which should guide us in our endeavour to relieve them. Overaction of a secretory gland is in the first instance probably due to nervous influence. The effect of fear in arresting the action of the salivary glands is a familiar example of inhibition of secretion, whereas salivation at the sight of food illustrates the results of nervous stimulation. In the case of the thyroid gland hypersecretion in the first instance is probably due to nervous overstimulation, though stimulation by chemical messengers brought by the blood is also possible. Later on definite changes in size and structure enable the gland to maintain for months, or even years, the increased activity which is now generally known as hyperthyroidism.

The cases in which hyperthyroidism is a prominent feature may conveniently be divided into three groups:

1. Simple hyperthyroidism.
2. Toxic adenoma of the thyroid gland with hyperthyroidism.
3. Exophthalmic goitre or Graves's disease.

There is no hard and fast division between these groups, but the great majority of cases in which symptoms of hyperthyroidism are present fall into one or other of them. In hyperthyroidism there is an overproduction of the normal thyroidal secretion which contains its hormones. It is possible, though not yet proved, that the secretion in some cases is not only increased in quantity, but is also altered in quality, so that there may be dysthyroidism as well. There is good reason to believe that “thyroxin,” which has been isolated by Dr. Kendall, is the chief, if not the only active hormone secreted by the gland. This substance he has shown to be tri-hydro-tri-iodo-alpha-oxy-indol propionic acid

($C_{11}H_{10}O_3N_1I_3$). It is present in very small quantities, as two tons of fresh thyroid glands only yield 18 grams or 280 grains of thyroxin.

The most marked hyperthyroidism is seen in fully developed cases of Graves's disease. Here the microscopical changes in the gland are indicative of great secretory activity. The cells lining the alveoli are columnar instead of cubical, and the wall of the alveolus becomes plicated so that the secreting surface is increased while the colloid is changed in appearance. Similar but slighter changes in the gland can be produced experimentally. If part of the gland in the monkey is removed the remainder becomes more active as a compensatory change. A section of part of the right lobe of the thyroid gland of a rhesus monkey from which I removed the whole of the left lobe and part of the right lobe fourteen months before it was killed, shows similar changes in lesser degree, such as probably occur in the milder forms of hyperthyroidism in man.

Recent determinations of the basal metabolic rate, especially by Dr. W. M. Boothby³ of Rochester and by Dr. J. H. Means⁴ of Boston, have enabled the different degrees of hyperthyroidism to be measured in percentages, and it is claimed that the results are as valuable an indication of thyroidal activity as the readings of the thermometer are of the course of a fever. This determination takes a good deal of time, and has not as yet been extensively employed in this country. In hyperthyroidism there is an increased production of heat which may be estimated by indirect calorimetry. By this method the determination of the carbon dioxide production or of the consumption of oxygen gives information from which the basal metabolic rate can be calculated, and stated in percentages above or below an average normal rate. It has been found that in mild forms of myxoedema the basic metabolic rate is from -20 per cent. to -40 per cent. of the normal. Slight forms of hyperthyroidism have a metabolic rate from +20 per cent. to +40 per cent.; moderate cases of Graves's disease from +40 per cent. to +60 per cent., severe cases from +60 per cent. to +100 per cent.

As the result of more than 2,500 observations on about 1,200 subjects A. Peterson and W. Walter⁵ have shown that there is a general relationship between the pulse rate, taken in the resting and fasting condition required for determining basal metabolism, and the metabolic rate. As the basal metabolism increases from normal to +40 per cent. the pulse rate increases from 80 to 110. In determining this general relationship, cases in which there is cardio-vascular disease or other obvious cause of tachycardia are omitted.

The determination of the basal metabolism at regular intervals affords a useful indication of the progress of the patient under treatment. It has been shown by E. M. and D. Wilson that in a case of myxoedema under treatment the rate rises from -41 per cent. to -10.1 per cent., and in Graves's disease rest in bed for a month may cause a fall in the rate from +42 per cent. to +25 per cent. We are thus furnished with a method of measuring the severity of the malady and of recording the progress under treatment month by month on a chart, much in the same manner as the course of a fever is recorded day by day. In many cases these observations show that roughly the pulse rate varies directly, while the weight varies inversely with the metabolic rate. This is important, as it indicates that when the metabolic rate cannot be measured the variations in weight and pulse rate are useful indications as to the progress of a malady due to changes in the functional activity of the thyroid.

The changes in metabolism are still further illustrated by two of my cases of myxoedema and exophthalmic goitre in which a detailed analysis of the urine passed in twenty-four hours was made by Dr. C. Powell White before and after treatment. The patients were taking ordinary hospital diet, and the findings are of interest more in their comparative than their absolute values.

A woman, aged 39, was admitted to the Manchester Royal Infirmary suffering from well-marked myxoedema. A sample of the twenty-four hours' urine was taken for examination on March 17th, 1920, before treatment was commenced. The patient was then given one 2½ grain thyroid tabloid a day. On March 24th the dose was increased to 5 grains, on April 9th to 10 grains, and finally, on April 22nd, to 15 grains a day. The symptoms steadily diminished, and had practically disappeared when another sample of the urine was taken on May 7th, after treatment for fifty days.

Dr. White found the amount of nitrogen from urea was increased from 3,501 mg. a day in the first sample to 6,948 mg. a day in the second, or to almost exactly double the amount. The nitrogen from ammonia, creatinin, and uric acid was

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* Delivered to the Worcestershire and Herefordshire Branch.

also increased, the total nitrogen being increased from 5,208 to 8,444 mg. a day. This gives an indication of the increased metabolism under the stimulating effect of the thyroidal hormone.

The second case was that of a girl, aged 19, who was admitted to the Royal Infirmary on January 29th, 1920, with well-marked Graves's disease. The pulse rate varied from 98 to 120. She was kept at rest in bed and had two doses of x rays before the first sample of urine was collected on February 10th. Between this date and March 2nd, when the second sample of urine was taken, she received seven doses of x rays. The goitre and the exophthalmos both diminished a little, and the pulse rate fell to 96 but increased again to 108, and she lost 7 lb. in weight.

It is of interest to note that during this interval the urea nitrogen diminished from 7,550 to 2,744 mg. a day—that is, to nearly one-third of the former amount. The nitrogen from ammonia, creatinin, and uric acid had also diminished. The total nitrogen fell from 10,819 to 4,390 mg.—that is, to considerably less than one-half. As far as they go, these findings indicate the fall in metabolism which may occur in Graves's disease under the influence of rest and x-ray treatment.

The three clinical varieties of hyperthyroidism already mentioned will next be considered separately.

1. Simple Hyperthyroidism.

In this condition there is a slight uniform enlargement of the thyroid gland similar to that which occurs in the simple parenchymatous goitre of puberty, but it is accompanied by symptoms of hyperthyroidism. The pulse rate is accelerated and may be from 90 to 120 a minute. There is mental alertness, with agitation in some cases, and a fine tremor of the extended hands is visible. The skin is warm, and may be moist. There are no eye symptoms. This condition corresponds to what used to be described by French writers as the *formes frustes* of Graves's disease. Fatigue is easily induced, but many patients are still able to carry on their usual occupation. The metabolic rate may be increased to over + 60 per cent. In these cases early and prompt treatment is most important. Untreated, the symptoms are apt to become more marked, and some of the cases pass on into fully developed Graves's disease.

Surgical treatment is not required. Rest in bed for a week or two or longer according to the severity of the symptoms is followed by marked improvement and a fall takes place in the metabolic rate. Prolonged rest in bed is not required in these cases, and in the milder forms of the malady it is sufficient to ensure that ten to twelve hours are spent lying down. Medicinal treatment is useful and a prolonged course of arsenic in small doses of from 3 to 5 minims of Fowler's solution is often beneficial. If there is much excitability bromides may be given with the arsenic in small doses. Quinine hydrobromide in doses of 3 to 5 grains is also valuable and may be given alone or with arsenic. X-ray treatment is more reliable than any medicinal treatment in these cases. Details of this vary according to circumstances. A full dose may be given twice a week for the first few weeks and then once a week, the amount and frequency of the dosage being regulated by the progress, and it is advisable to give a few doses at lengthened intervals at the end of the course rather than to end it abruptly.

2. Toxic Goitre with Hyperthyroidism.

In this condition a goitre which may be either parenchymatous or adenoparenchymatous has usually been present for several years without causing any general symptoms. At the end of this quiescent period, which may be as long as ten years, the gland begins to show signs of overactivity. This may be the result of some sudden emotional shock or accident, or it may follow a prolonged period of nervous strain. The goitre may or may not be further increased in size. The symptoms of hyperthyroidism are those we have already considered, but they may become severe and all the symptoms of Graves's disease may appear—a variety of the malady which has also been described as secondary Graves's disease.

If such an increase in the size of the goitre takes place as to cause pressure on the trachea, clearly operative treatment must be adopted. In cases in which there are no pressure signs the indications are not so clear. My own view is that these cases of toxic adenoma should be treated by operation if the goitre is large, and especially if it is an adenoparenchymatous or cystic goitre, as soon as marked symptoms of hyperthyroidism appear. The extent and character of the operation must be adapted to the needs of the case. Removal

of one lobe is apt to leave displacement of the trachea by the lobe which is left. Bilateral partial resection seems best to meet the needs of these cases. If operation is declined, or the condition of the patient prevents operation, treatment of the hyperthyroidism must be carried out on the lines already described. Improvement will take place, but the goitre is not appreciably diminished in size and the results are not very satisfactory.

3. Exophthalmic Goitre.

The symptoms of this malady are so well known that no description is necessary. In the treatment of fully developed Graves's disease we are faced by a difficult problem. Opinions differ widely as to the relative merits of medical and surgical treatment. I shall therefore endeavour to give shortly the results of personal experience. With regard to medical treatment all that I have already said about the treatment of simple hyperthyroidism holds good in the case of Graves's disease, though the greater severity of the symptoms entails a stricter régime. At first complete rest in bed in moderate and severe cases is essential, and may have to be continued for several weeks or even months.

The question of the influence of diet in the treatment of this malady is of importance owing to the work of Chalmers Watson, McCarrison, and Professor and Mrs. Mellanby. It has been shown by Chalmers Watson that a meat diet produces changes in the thyroid gland in animals suggestive of hyperthyroidism. Colonel McCarrison⁶ has shown that excess of fats or of unsaturated oleic acid in the diet may cause a relative deficiency of iodine and enlargement of the thyroid gland, and it has been suggested that fats should be reduced in these cases. Professor and Mrs. Mellanby⁷ found in their work on experimental rickets that when butter was included in the diet a fivefold increase in the size of the thyroid took place, the hyperplasia in some cases affecting chiefly the secretory cells of the alveoli, and in others the intervascular cells. Increasing the fat in the diet of puppies from 10 to 20 grams intensified the change, and on a diet containing 20 to 25 grams of butter the weight of the thyroid gland was found to be fourteen times the weight of the gland in puppies which were fed on cod-liver oil instead of butter, and in which no increase in the size of the gland took place. They have found that in cases of Graves's disease the addition of butter intensified the tachycardia and nervousness, and was followed by loss of weight. They advocate, therefore, a diet of separated milk powder, porridge, bread, green vegetables, eggs, and lean meat, with 15 c.cm. of cod-liver oil each day. I have usually advised the exclusion of red meat and their extractives from the diet. On the other hand, I have given fats, especially if there is loss of weight, in the form of milk (up to three or four pints), cream, butter, and animal fats. I also allow fish, eggs, bread, vegetables, and fruit. It is evident that further investigations are required to ascertain the most suitable diet in these cases, as it does not necessarily follow that a diet which induces hypertrophy of the gland in healthy animals is unsuitable for the treatment of Graves's disease in man.

With regard to medicinal treatment, the special organic preparations such as rodagen, antithyroidin, or thyroidectin, have not given any specially good results. Milk of a thyroidless goat has, however, been helpful in some cases, but it is difficult to obtain and hardly worth the trouble and expense entailed. Of drugs, arsenic, bromides, belladonna, convallaria, and quinine hydrobromide are the most useful.

X-ray treatment has proved to be of great value, and there can be no doubt as to its power to reduce the activity of the gland. This was clearly shown in a case recently recorded by Mr. H. Stratford,⁸ in which radiation of the scar and supraclavicular region for a year after removal of the breast for carcinoma had induced such extensive atrophy in a previously healthy thyroid gland that the patient developed myxoedema. The amount and frequency of the dose and the total duration of the treatment must be adapted to the needs of each case. The treatment may be continued for six months or a year, or even longer if improvement is taking place. As a fair example the following case may be mentioned:

Miss W., aged 36. When seen on January 18th, 1918, she had a slight goitre which had been present for about three months. There was exophthalmos, with tremors and loss of hair, and the pulse rate was 140. X-ray treatment, which had been given twice a week from December 14th, 1917, was continued till September, 1918. It was then continued once weekly till May, 1919. Steady improvement took place, as is shown by the increase in weight

from 8 st. 10 lb. on March 2nd, 1918, to 12 st. 11 lb. in May, 1919, and to 13 st. 2 lb. in October, 1920—a gain of 4 st. 6 lb. When seen last, on February 3rd, 1922, she had been steadily at work as a school teacher since May, 1919. She occasionally has palpitation, but is otherwise well, the pulse rate being 88.

In this case the treatment occupied seventeen months, during which she received about 100 doses of x rays. Dr. Barclay informs me that on an average some twenty-five doses are sufficient to produce a good result. It is, however, quite worth while to continue the treatment up to one hundred doses if necessary.

Dr. A. E. Barclay and Dr. Woodburn Morrison have treated many of my cases, and by the kindness of Dr. Morrison I am able to give you the general results which followed this treatment in one hundred consecutive cases of exophthalmic goitre treated by them with x rays. In some seventy of these cases this treatment was carried out on my advice. Of these cases, 82 were women and 18 men. In 4 men and in 17 women the symptoms were mild; in 9 men and in 34 women they were of medium severity; and in 5 men and in 31 women severe. In the men the duration of treatment was from five months to two years in the mild cases, from three months to three years in the medium cases, and from one to four years in the severe cases. In the women the treatment lasted from five months to two years in the mild cases, from six months to four and a half years in the medium cases, and from six months to five years in the severe cases. The condition of these cases after treatment is briefly shown by dividing them into three classes. In the first class are placed only those in whom complete recovery has taken place; thus 2 mild and 2 medium cases in men, 8 mild, 7 medium, and 8 severe cases in women, or 27 per cent. in all, completely recovered. In the second class are grouped all the cases in which a good functional result was obtained—that is to say, those cases in which, although some symptoms still persisted, such marked improvement had taken place that a living could be earned and a normal life could be lived. This result was obtained in 11 men, 2 being mild cases, 6 of medium severity, and 3 severe cases; 38 women were placed in this class—8 slight cases, 20 of moderate severity, and 10 severe cases; so that altogether a good functional result was obtained in 49 per cent. The third class contained those who continued the treatment but only showed slight improvement: two men, one being a medium case and the other a mild one, and 17 women—1 mild, 6 medium, and 10 severe cases—came into this group, making 19 per cent. The remaining four women gave up the treatment without showing any improvement.

It is extremely difficult to assess fairly the results of medical treatment in a disease such as exophthalmic goitre. In the opposite condition of myxoedema the value of treatment is at once evident because we are dealing with a malady which, before I first suggested and introduced the treatment by thyroid extract thirty-one years ago, inevitably got worse and ended in death; whereas under treatment health is now regained and life can be prolonged to its normal limit. Exophthalmic goitre in a certain proportion of cases tends to improve and even disappear under any rational line of treatment or even without it. Different series of cases have shown the following results. The course of exophthalmic goitre under medicinal treatment has been described by several writers. Dr. H. Mackenzie⁹ gives a table of 33 cases combined with 24 cases recorded by Dr. R. T. Williamson, in the Manchester Royal Infirmary. Of these 57 cases, 14 died and 10 recovered completely, which gives a complete recovery of 17.5 per cent. and a mortality of 24.5 per cent. Of 169 cases admitted into Guy's Hospital during 1888–1907 (both inclusive) collected by Sir William Hale-White,¹⁰ 75 were accounted for. Of these, excluding cases which were operated on, there were 67, of whom 26 were dead, whereas among 53 private patients only 7 died. Dr. J. H. Campbell,¹¹ who collected the cases treated at the same hospital between 1908 and 1917, was able to trace 89 out of 127. Dr. Campbell gives his results in round figures as: almost cured, 40 per cent.; very much improved, 30 per cent. (these 70 per cent. would correspond to the two first classes of Drs. Barclay and Morrison's tables); died, 15 per cent.; not much improved or worse, 15 per cent.

Broadly speaking, then, under the influence of rest and medicinal treatment some 25 per cent. of cases are fatal, a similar percentage recover, and the remaining 50 per cent. improve to a greater or less extent. Returning to the group of 100 cases treated by x rays, as far as I know, all are living, and we see that 76 per cent. either recovered completely or regained good functional activity suitable for ordinary life.

It may fairly be claimed that more cases recover and that the period of disease or invalidism is materially shortened under x -ray treatment than without it. The risk of causing myxoedema by too much radiation is small, but it has occurred in one case which I have seen. I have, however, seen myxoedema follow recovery from exophthalmic goitre without the use of x rays, and other similar cases have been recorded.

In some of my cases, and especially in those residing at a distance, radium has been used, the applications being usually made once every six weeks. This treatment appears to be unsuitable for very severe or acute cases, as the primary effect may be to temporarily increase the hyperthyroidism. In one acute case which was under my care in the Manchester Royal Infirmary the first application of radium was followed by a rapid exacerbation of the symptoms and the patient died. Dr. E. S. Reynolds informs me that he knows of two sisters who both died under similar circumstances. In many cases good results are obtained, and the following may be given as a fair example of the effects of this treatment.

A man of 25 was seen in June, 1919. He had a small goitre, slight exophthalmos, tremors, nervousness, and a pulse rate of 136. He had seven or eight doses of radium in the course of a year. When last seen in February, 1922, he was feeling well, and had been able to undertake the work of a secretary to a company. He had gained 2 st. in weight. The pulse was 70 in bed, 80 when up at home, but it was 120 when he came to see me.

Dr. A. Burrows¹² has recently tabulated the cases of exophthalmic goitre treated with radium at the Manchester and District Radium Institute during the years 1915–19. During this period 180 cases were treated. His conclusions are as follows: "Fifty-two of these cases are recorded as cured—that is to say, all symptoms and signs of disease have disappeared, except sometimes some slight exophthalmos, for over two years, and only one recurrence is recorded. Many cases have already when they come for treatment definite myocardial failure, which may persist, and although the hyperthyroidism is cured they cannot be recorded as cured cases. The application of radium is a prolonged process, and much patience is needed because the treatment may last from two to three years." Five cases were well for six months or more, but had not been recently traced. If these cases are included we find that 31.6 per cent. recovered under radium treatment. The remaining 122 cases are all returned in one group as improved, not improved, or died, so that we are unable to compare the results, as far as improvement is concerned, with those obtained by x -ray treatment, and the number of deaths is not recorded.

Surgical Treatment.

In adopting surgical treatment in exophthalmic goitre we endeavour to effect a rapid reduction of the overactivity of the gland to a normal level by the removal of a sufficiently large amount of the secreting tissue. This may be achieved by ligation of the superior arteries, followed by a subtotal thyroidectomy at a later stage, or the thyroidectomy may be done forthwith. My early experience of operation was unfortunate, as the first three cases all died. The mortality is now stated to be from 2 to 5 per cent. In mild cases operation is not required; in cases in which the trachea is compressed it is essential. It is in moderate and in severe cases that opinion is divided. In any case, medical treatment should have a full trial for six months; if no improvement has then taken place operation should be considered. The most suitable cases are those in which the goitre is of considerable size, as they do not do well under medical or radiological treatment.

Briefly, the advantages of operation are:

1. The saving of time by the rapid reduction of the hyperthyroidism and relief of the symptoms.
2. The diminution of the risk of irreparable damage to the heart in the form of the chronic myocarditis which develops in severe and in prolonged cases.
3. The complete and rapid recovery in some cases.

The disadvantages are:

1. The risk to life.
2. The uncertainty of the ultimate result owing to the difficulty in determining the right amount of the gland which should be removed in each case. For example, one of my cases had two partial thyroidectomies performed, but at the end of ten years still showed marked symptoms of the malady, which finally subsided under x -ray treatment.
3. The tendency to recurrence at the end of a year.

As an example of a successful operation advised under special circumstances the following case may be mentioned:

Mrs. M., aged 27, seen on February 14th, 1921. A goitre had first appeared eighteen months before; this was followed by dyspnoea on exertion and occasional palpitation. She had a moderate uniform enlargement of the thyroid gland with tremors of the hands. The pulse rate was 150 and the cardiac impulse extended two fingerbreadths outside the left nipple line. There was exophthalmos. As this patient wished to go to China as soon as possible with her husband to reside in a district some 7,000ft. above sea-level, and was about to visit relations in Minnesota, I advised her to go to the Mayo clinic for operation. In June last the basal metabolic rate was *plus* 40, when Dr. Verne C. Hunt of Rochester did a ligation of both superior thyroid vessels. After this she gained 20 lb. in weight and improved in general condition, but the basal metabolic rate was *plus* 45. Dr. Hunt has kindly informed me that on September 6th a double resection of the gland with removal of the isthmus was done. She had an uneventful convalescence and was able to go to Japan in November. The latest report received from Mrs. M. in Japan stated that she was perfectly well. I advised early operation in this case owing to the special circumstances already mentioned, and the result has been most satisfactory.

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A PULMONARY SIGN IN ACUTE INFECTIONS OF THE BILIARY TRACT.

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Most medical men are familiar with the deceptive abdominal symptoms and signs which may sometimes dominate the clinical picture in the early stages of pleuropneumonia. Most can recall mistaken diagnoses as well as the feeling of satisfaction which has followed a successful detection of the trouble above the diaphragm and the sparing of the patient an abdominal exploration both unnecessary and fraught with risk. On the other hand, I find that very few are familiar with the converse picture—namely, the case presenting pulmonary symptoms and signs in which the primary and focal lesion is in the upper abdomen.

That acute infections of the gall bladder and bile ducts are frequently associated with definite physical signs at the base of the right lung is a fact I have repeatedly observed; in a number of cases it has led to an incorrect diagnosis, a primary lung lesion being suspected and the pain in the right hypochondrium being regarded as referred from the pleura.

My attention was first directed to this sign some ten years ago by the case of a gentleman on whom I had operated for inguinal hernia:

Mr. T. D., aged 65, was operated on (December 12th, 1912) for a right inguinal hernia. Four days later (December 16th) he complained of severe pain on the right side of his chest and in the right hypochondriac region of the abdomen; temperature 100°, pulse 90, respirations 26. There were very definite tenderness and rigidity just below the right costal margin, and a deep inspiration caused great pain in this region. I made a diagnosis of acute cholecystitis probably associated with gall stones, and recommended the local application of heat. At the request of his relatives a physician was called in to see him, and he discovered that there were numerous crepitations at the base of the right lung, and diagnosed congestion of the right base with referred abdominal pain. Two days later a definite tinge of jaundice appeared, and the original diagnosis received strong support. In a week the infra-costal pain and tenderness had subsided.

In January, 1914, I was called to see the patient again. He had had three attacks similar to that described above, and in this, the fourth, attack the symptoms were much more urgent than ever before. I operated and found a partially gangrenous gall bladder, containing pus and over 100 calculi.

Since then I have made a habit of examining the bases of the lungs in cases of acute biliary infections, and have found that crepitations at the right base occur in quite a fair percentage of cases. The following case illustrates the importance of recognizing the significance of this physical sign:

Mrs. F., aged 53, was operated on for gall stones on November 10th, 1920. She gave a typical history of recurrent attacks of gall-stone colic extending over a period of five years. At the operation ten gall stones were removed from the gall bladder, which was

drained. She left hospital at the end of four weeks with the wound healed. Five days after leaving hospital she had an attack of pain round the right side of the chest. Her doctor found crepitations and some pleural friction at the right base, and gave the opinion that this was a chest condition and not connected with the biliary tract. The patient, however, insisted that the pain was the same as she had had before operation. At intervals of a few weeks the attacks recurred, always accompanied by the basal pulmonary signs, and she had poultices applied round the right side of the chest.

On January 16th, 1921, she had a very severe attack, again with crepitations, but this time also with very acute tenderness in the right hypochondrium. Poultices over the right base gave no relief, and after a few days she had a definite tinge of jaundice. Her doctor diagnosed cholecystitis and sent her into hospital. A swelling was found in the right hypochondrium and great tenderness on pressure in this region. Over the base of the right lung numerous fine crepitations could be heard, and there was slight dullness on percussion. On January 19th, 1921, she was again operated on. The gall bladder, greatly enlarged and thickened, containing muco-pus and one faceted calculus plugging the cystic duct, was removed. Since the second operation she has been entirely free from biliary and pulmonary symptoms.

This pulmonary sign may also be found where the infection is located in the ducts and where the gall bladder is not the chief seat of trouble, as the following case shows in a most instructive manner:

Mr. D., aged 67, had suffered for over a year from frequently recurring attacks of pain and discomfort in the epigastrium, accompanied by rigors and always followed by a faint tinge of jaundice. The pain was never very severe, but in each attack he felt ill, had a temperature of 100° to 101° F., and was confined to bed for several days—the latter mainly because his doctor always found signs of congestion at the base of the right lung. On several occasions the question of operation was discussed, but it was doubted whether it was justifiable on account of the pulmonary symptoms. Latterly the attacks recurred so frequently, and the jaundice though slight became so constant, that he consented to operation. His doctor noted in each attack crepitations at the right base, none at the left.

Operation (January 9th, 1921).—A very large and somewhat thickened gall bladder was found. It contained no calculi. The common duct was very dilated and thick-walled, the head of the pancreas was hard—the seat of chronic interstitial pancreatitis. The common duct was opened and a large quantity of granular debris and bile-sand scooped out. No calculi of any size were present. A probe passed readily into the duodenum. The common duct was drained, and in view of the sclerosing pancreatitis a cholecysto-duodenostomy was performed. The patient made an uneventful recovery, rapidly put on weight, and a year later reported that he had been entirely free from all biliary and pulmonary trouble.

The interesting point in regard to this case was the fact that the pulmonary signs accompanying his recurring attacks of cholangitis were for a time regarded as a contraindication to operation, and had no jaundice been present even more emphasis would certainly have been laid on the pulmonary as opposed to the biliary symptoms.

Etiology of the Pulmonary Congestion.

Three possible explanations for this must be considered:

(1) The infection in the gall bladder or bile ducts spreads by way of the peritoneum through the lymphatics of the diaphragm and so reaches the pleura and the base of the lung. Facts which favour this theory are that in two cases, besides the crepitations, pleural friction was detected over the right base, and in another case a well-marked pleurisy with effusion was present within twenty-four hours of the operation for removal of the infected gall bladder.

(2) That reflexly, from irritation of the sensory fibres of the phrenic nerve, the diaphragmatic excursion on the right side is diminished, the expansion of the base of the right lung is restricted, and some hypostatic congestion results. There can be no doubt that this factor of impaired movement of the diaphragm plays a considerable part, and whether it be a phrenic reflex or a mechanical difficulty owing to the boarding of the abdominal muscles and the plastic adhesions so frequently present about the lower border of the liver, or both, is of little moment. It is of interest, however, in this connexion to note that over 50 per cent. of those patients showing pulmonary signs complained of acute shoulder pain, usually attributed to a phrenic reflex.

(3) That the lung condition is a blood infection settling in a part of the lung the expansion of which is restricted by the factors mentioned in (2).

The work of Else and of Rosenow has shown how liable the gall bladder is to infection through the blood stream. It is therefore perfectly feasible that the blood-borne infection which settled in the gall bladder might secondarily light on a part of a lung crippled by deficient expansion.