and there was no discharge or history of discharge of any kind. The patient was seen with me by Dr. Macdonald, to whose help I am indebted; he agreed that the condition might be an osteoma.

Operation.

On September 30th, 1921, an incision was made along the right eyebrow down to the periosteum. The supraorbital ridge was then felt to terminate in a sharp irregular ridge, and in attempting to separate the orbital periosteum a thick gelatinous substance the colour of very pale yolk of egg presented; this I swabbed and scooped away with a blunt spoon; it measured, perhaps, a tablespoonful. There was apparently a delicate envelope, and pieces of eroded floor of the frontal sinus adhered. After this removal none of the floor of the sinus remained. The cavity above was bounded by the roof of the sinus. Either there was no median raphe between the right and left sinuses or it had been eroded; an opening which would have admitted a pencil led to the left sinus. As the condition in the left sinus was obviously the same as the right, a further incision was made through the left eyebrow, the periosteum was reflected, and the floor of the sinus, which was thin and fragile, was chiselled through and the sinus emptied.

Both fronto-nasal ducts appeared to be occluded. Drainage was established by two thick gauze drains into the nose through openings made by a spoon in the position of both ducts. The incisions were sutured. The gauze drains were removed on the following day.

After-History.

A little blood-stained discharge continued to flow from the right nostril for some days.

Forty-eight hours after the operation I was called to the case, and in my absence Dr. Macdonald kindly saw the patient at about 10 p.m. He describes her condition as follows: "She was comatose, curled up in bed; could not be roused. Temperature 102°. Did not respond to any stimulus. Reflexes normal." By midnight her condition was improved in that she could be got to respond to vigorous stimulation, but in the circumstances the condition was alarming, indicating a possible onset of meningitis. On careful examination Dr. Macdonald came to the conclusion there were indications pointing to the condition being at least partly hysterical, and that this was probably so is borne out by immediate and uninterrupted improvement.

The following day she was so much improved as to be able to say her head ached. The temperature reached 100° in the evening, but from this date she rapidly got well, and three weeks after operation only complained of a little occipital headache and occasional diplopia after a quarter of an hour or so of reading or close work. The wounds healed with practically no disfigurement.

The gelatinous substance and lining was examined by the hospital pathologist. His report was as follows:

"I find the fluid contains no cells and is of a mucoid nature, whilst sections of the solid pieces show them to be the normal mucous lining of the tissues. These results lead me to think that the condition was probably due to accumulation of the normal secretion."

The Kettzomian Lectures

ON

AMOEBIC LIVER ABSCESS.

DELIVERED BEFORE THE MEDICAL SOCIETY OF LONDON *

BY

SIR LEONARD ROGERS, C.I.E., M.D., F.R.S.

[Abstract.]

LECTURE III.—THE PREVENTION OF AMOEBIC LIVER ABSCESS AND THE RECENT REDUCTION IN THE PREVALENCE AND MORTALITY.

In his final lecture Sir Leonard Rogers said that from what he had so far indicated with regard to the pathology and treatment of amoebic liver abscess, it would be sufficiently obvious that any simple method of preventing such a complication would be far more beneficial than even the most certain and established methods of cure. He wished, therefore, to devote himself in this third lecture to the measures which had enabled him to establish such prevention on a scientific basis. Ipecacuanha appeared to have been used at quite an early date in India in dysentery and hepatitis, but afterwards was superseded. In 1855, however, ipecacuanha was being used in large doses for dysentery among the British troops at Mauritius, and there were records of its reintroduction at a still earlier date. Maclean in 1854, in writing on hepatitis, did not mention ipecacuanha, but advised saline purges, strict dieting, and the cutting off of alcohol. In the same author's article in Reynolds's *System of Medicine* in 1871, however, he stated that for years past he had advised 20- to 25-grain doses of ipecacuanha in acute hepatitis, and remarked upon it

as a curious fact in the history of tropical medicine that in dysentery this drug should have been superseded by calomel and opium. It was now clear that such violent fluctuations in treatment were inevitable in India so long as amoebic dysentery remained undistinguished. Sir Patrick Manson had consistently advised large doses of ipecacuanha whenever hepatitis was associated with dysentery, and long before he recognized amoebic dysentery as a distinct disease he recommended ipecacuanha in cases invalided home from the tropics.

Blood Changes in the Early Recognition of Amoebic Hepatitis.

The lecturer continued his description of the researches which led up to the differentiation of the presuppurative stages of amoebic hepatitis, with prevention of abscess formation, rendering surgical interference unnecessary. Coincidentally with his studies in the etiology of amoebic liver disease he was working on blood changes in fever admissions. At the time he began this work (1901) it might safely be said that 90 per cent. of the fever cases were diagnosed and treated as malaria, although he found that only one seventh of them were really so, and among the fevers at that time nearly always confused with malaria were the more chronic forms of amoebic hepatitis, which were always treated with quinine. It was known that amoebic hepatitis produced a leucocytosis, but with no pathologist and a very small staff of overworked clinicians there was no detailed history of blood counts until he began his own investigations in Calcutta.

From his notes collected at that time he found that during nearly four years none of the hepatitis cases (including those going on to abscess formation) had been treated with ipecacuanha. It was clear, therefore, that at this time, in Calcutta at all events, the specific drug had been superseded by ammonium chloride in hepatitis. He showed some tables of cases to illustrate the leucocytosis which was found.

In a first series of five cases admitted for hepatitis and not going on to suppuration only two showed a very slight increase in the leucocytes. In sixteen other cases which went on to liver abscess all except one showed a leucocytosis, and even in that one there was a relative increase in leucocytes. The counts where there was leucocytosis varied from 12,750 to 38,500 leucocytes. The case which showed 38,500 leucocytes and another which showed 35,000 were cases of multiple small liver abscesses which rapidly proved fatal. In the more chronic and insidious forms leucocytosis was absent on admission, but developed later under ammonium chloride treatment.

At this stage in his investigation he had already proved that tropical liver abscess always contained amoebae, but rarely pathogenic bacteria. Therefore the abscesses were almost certainly caused by the amoebae, and were preceded by amoebic ulceration of the colon. He became convinced that ipecacuanha was a specific for the amoebic variety of dysentery, although useless for the bacillary form common in Indian gaois. Although cases in this presuppurative stage might or might not give a history of previous dysentery, he knew from his experience of the leucocytosis that latent amoebic ulcers must be present in some part of the large bowel which were healed by large doses of ipecacuanha.

Ipecacuanha in the Prevention of Amoebic Abscesses.

It was not, however, until 1907 that he was able to record a convincing series of successful cases. This included 15 cases of hepatitis he had met with among 1,350 consecutive fever admissions, or just over 1 per cent. It was not surprising that cases occurring in so small a proportion of the total number had not been differentiated by busy clinicians in the absence of blood examination.

The first three cases, which he showed in tabulated form, were cases of dysentery and hepatitis treated with ipecacuanha. The blood showed leucocytosis in all three. They had suffered from fever for eighteen, thirty-four, and forty-one days before they were put on ipecacuanha, and the fever ceased two, four, and three days after the full dose of this drug. The next eight cases were cases of hepatitis without dysentery: there was no previous history of dysentery, nor was there dysentery while in hospital; but one or two of them showed diarrhoea, and others constipation, and so on. In three of these cases, which were treated only with ammonium chloride, the fever went on for thirty-four, forty-four, and forty-nine days before the temperature came down. The others were treated with ipecacuanha, and the temperature quickly fell. Another group of four cases were cases without either dysentery or obvious liver symptoms; they were obscure cases of fever. Two of them showed leucocytosis on admission, and the other two developed it later, and on the strength of this all of them were put on ipecacuanha, and the temperatures came down quickly, in one case within two days.

The lecturer showed temperature charts obtained in these various cases. In one case the fever had lasted fifty-eight days

* Abstracts of Lectures I and II appeared in the BRITISH MEDICAL JOURNAL of February 11th and 18th, 1922.

before the ipecacuanha was given, yet after it was given the temperature came down in two days. Taking the whole of this series, it was noteworthy that 12 out of 15 cases were unassociated with dysentery, yet he was able to recognize them as amoebic in origin, and treat them with ipecacuanha. Of 21 other cases admitted with hepatitis and treated with quinine and ammonium chloride, 16 went on to suppuration, while of 12 cases treated with ipecacuanha, 11 of them showing well-marked leucocytosis, every one rapidly cleared up without going on to suppuration. There could be no doubt, therefore, that suppuration was averted by the use of ipecacuanha. When one got a very high leucocyte count in such a case as multiple liver abscess the polynuclear percentages were usually between 80 and 90, and the total leucocytes might range above 30,000, which carried a very serious prognosis. But he had seen a case of severe hepatitis, with a count of 20,000 or 25,000, cured by ipecacuanha without going on to suppuration.

Chronic Amoebic Hepatitis as a Common Cause of Cirrhosis of Liver in the Tropics.

The lecturer then turned to consider chronic amoebic hepatitis as a common cause of cirrhosis of the liver in the tropics. In an analysis which he had made of the records of nearly 5,000 *post-mortem* examinations in Calcutta, extending over a period of thirty-seven years, he found 6.9 per cent. of cases of well-marked cirrhosis of the liver. As this disease was common among Mohammedans, who were prohibited by their religion from taking alcohol, some other cause than alcoholism had to be looked for. On working out the percentages of the principal complications, he found granular kidney in 28 per cent. of the fatal cirrhosis cases and 13 per cent. of the latent cases, and dysentery in 25.6 per cent. of the fatal cases and 30.1 per cent. of the latent cases. Further investigation confirmed the intimate relationship between cirrhosis and dysentery, but the question remained as to the form of dysentery to which these cirrhosis cases related. Fortunately, he was able to complement his study of the *post-mortem* records by eight years of actual experience of necropsies in Calcutta, and he could testify that he found evidence of former chronic amoebic dysentery in three-fourths of the cirrhosis of liver cases; it was always of the amoebic variety. It was not difficult to account for the close relationship between these two diseases; he ascribed the cirrhosis to the long-continued amoebic irritation of the portal branches in amoebic dysentery, leading eventually to increased interlobular fibrous tissue.

Was there such an entity as "tropical liver" apart from amoebic hepatitis? The latest edition of Sir Patrick Manson's book introduced a graphic description of tropical liver, but the lecturer himself believed that the survival of the term "tropical liver" from the writings of nearly a century ago was fraught with danger. It was very interesting to note that such a warm advocate of ipecacuanha as Norman Chevers had said that he knew nothing of the mysterious disease called tropical liver. The abuse of alcohol doubtless did affect the liver in the tropics as elsewhere, while the remarkable immunity of women and children to liver abscess might be explained by their non-addiction to alcohol, though he thought there were other factors. But he urged that the so-called "tropical liver" should never be put on ammonium chloride treatment until amoebic disease had been definitely excluded.

He related the case of a patient admitted for dysentery which subsided in ten days after a castor-oil mixture had been given; but seven days later the patient developed an acute hepatitis, with high fever, pain in the right shoulder, and a slight shadow in the liver as seen under *x* rays. The surgeon diagnosed abscess, and was only persuaded by the lecturer to give ipecacuanha treatment before proceeding to operation, owing to the fact that the man had had dysentery before. Within two days after the administration of the ipecacuanha the pain ceased, within three more the temperature fell to normal, all signs of liver abscess disappeared, and there was a complete recovery without recourse to operation.

The Decline in Incidence of Amoebic Disease.

If all that had been claimed with regard to the prevention and treatment of liver abscess was true, some results ought by this time to be reflected in the statistics of cases, taking a wide area and a considerable period of years. Several years ago he published certain figures relating to the liver abscess cases occurring at the European General Hospital at Calcutta during the five years previous to his reintroduction of the ipecacuanha treatment and during the six years following. He had now brought the figures up to date (1921), and they showed a reduction of nearly one-half in the annual admissions during the later period as compared with the former, and a fall in the mortality from 43.5 to 23.3 per cent. He also gave the figures for hepatitis and liver abscess cases at the

London School of Tropical Medicine during the period before the use of ipecacuanha was established as a means of preventing suppuration, during the period after ipecacuanha, but before emetine treatment was established, and during the period for which both treatments had been in vogue. In the first period the number of cures of liver abscess was 5 out of 13 cases, in the second 10 out of 15 cases, and in the third the whole of the 14 cases admitted had been cured.

The most convincing demonstration, however, was afforded by a chart which he had carefully plotted to show the incidence of amoebic hepatitis and liver abscess, and their relationship to dysentery and diarrhoea, in the British army in India during the last fifty years. The number of British soldiers in India during this period varied from 50,000 to 80,000. The incidence of hepatitis during the fifty years from 1869 onwards showed a steady fall. Dysentery showed a general decline broken by a number of epidemic rises, and diarrhoea showed the same features, the epidemic peaks occurring in the same years as in dysentery. When there was an epidemic rise in dysentery, the ratio of liver abscess to dysentery fell, thereby suggesting that the great majority of cases of epidemic dysentery were not that form of dysentery which was related to amoebic liver abscess and hepatitis—that is to say, not the amoebic form but the bacillary form; and it was known that the bacillary form was the one which gave rise to these epidemics. The close relationship between diarrhoea and dysentery which the chart demonstrated was of great importance. Diarrhoea was just as closely related to hepatitis as dysentery. There were two cases of hepatitis to every three cases of dysentery, and also to every three cases of diarrhoea. The correlation was extraordinarily close. A large number of cases of diarrhoea in India were really cases of amoebic disease, and would be better called amoebic colitis, for the grouping of them as diarrhoea rendered them liable not to be treated with ipecacuanha, and accordingly many of them went on to amoebic abscess. Another important fact in this connexion was that in an analysis of 1,000 *post-mortem* examinations, correlated with clinical findings, 50 per cent. of the fatal amoebic dysenteries were found not to have been recognized as dysentery at all in hospital; the diagnosis was almost invariably chronic or tuberculous diarrhoea, so that many fatal dysentery cases only gave rise to the symptoms of diarrhoea, and a large number might have been readily cleared up with ipecacuanha. In the earlier period to which the chart related there was a decline in the case-incidence of amoebic abscess, but a less marked decline in the mortality, and this, the lecturer suggested, was due to the fact that open operation about this time came into general favour and aspiration was relegated to the background. The decline in liver abscess went parallel with the somewhat similar course of hepatitis. Between 1896 and 1902 there was a rise in the number of cases of liver abscess, the high level continuing until about 1907, and the incidence of hepatitis meanwhile fell at first and afterwards remained practically stationary, so that there appeared to be nothing to account for this extraordinary rise in liver abscess. The maximum year for liver abscess cases was 1902, and this was the time when, immediately after the Boer war, a large number of army medical officers returned to India from South Africa, where they had had to deal almost entirely with the bacillary form of dysentery, and had found saline treatment of great value. Even previous to this the saline treatment had been boomed in India, owing to the successful use of it in gaol dysentery, which was of the bacillary type. The marked rise in the prevalence of liver abscess in the British army at that time was obviously due to the neglect of ipecacuanha in favour of the then popular saline treatment. The ratio of liver abscess cases to dysentery suggested the same conclusion; during this rise in the prevalence of liver abscess the ratio of liver abscess cases to dysentery was doubled.

The latest period of this inquiry, from about 1907 onwards, showed, as regards liver abscess, a rapid fall until the frequency of cases was diminished to less than one-third of what it had been in the early period, and there was also a marked fall in the death rate. During this same period both dysentery and diarrhoea rose for a time to double their ordinary numbers, but the incidence of liver abscess still remained very low, and the death rate reached the lowest point of all. It was still more remarkable that the curve representing hepatitis actually fell to its lowest point at the very time when dysentery and diarrhoea were rising. The year 1907, which was the last year of high incidence of liver abscess, was the year in which he demonstrated the great

value of ipecacuanha in preventing abscess formation. The fall in the mortality had begun a year earlier, and this coincided with the adoption of the treatment by aspiration and injection of amoeba-destroying drugs. Altogether the death rate in cases of liver abscess declined from 56 per cent. in the earlier period covered by the chart down to 28 per cent. in the end period. He concluded that the great reduction both in the prevalence and the mortality of liver abscess was due to preventive measures by means of ipecacuanha and to treatment by the aspiration and injection method. The decline in hepatitis as related to dysentery was also marked after the establishment of emetine treatment.

The Medical Cure of Multiple Small Amoebic Liver Abscesses.

The final question to which the lecturer addressed himself was the possibility of cure by medical means alone of already formed amoebic liver abscess. He had long thought that such cure was possible, and he now felt assured that this could take place under emetine treatment. He thought also that the small early acute multiple liver abscesses should prove very amenable to the specific action of ipecacuanha and emetine. It was wonderful what emetine treatment of a week's duration could do in the way of removing the extensive gelatinous infiltration characteristic of this condition. Emetine was probably the most definite specific drug known to medicine. Some day it would gain a place in the *British Pharmacopoeia*, even if some hoary remedy had to be sacrificed to make room for it.

In concluding his series of lectures, Sir Leonard Rogers referred to the foundation in Calcutta of a post-graduate research school of tropical medicine. He had long been convinced that, in the absence of post-graduate teaching, a new generation of medical men must arise before the general public could reap the benefit of the conclusions of the research worker. In the particular province with which he had had to deal in these lectures, he could say that amoebic disease was easily preventable in the great majority of cases, and that the development of amoebic suppuration in the liver should cause serious questioning to arise in the mind of the medical man in whose hands it had occurred; while in the case of patients who came under observation with an already formed liver abscess the treatment of election should be aspiration and emetine, with some form of sterile siphon drainage if necessary. He was convinced that with the more general adoption of the measures for which he had pleaded, whose rationale he had established as the result of careful observation extending over many years, this particular tropical disease might be almost completely abolished, thereby rendering tropical and subtropical countries safer and easing the white man's burden.

Memoranda :

MEDICAL, SURGICAL, OBSTETRICAL.

EXOPHTHALMIC GOITRE IN CONGENITAL SYPHILIS.

CONGENITAL syphilitic affections of the endocrine glands are of much interest, and so I venture to think that the following case of exophthalmic goitre in a child suffering from congenital syphilis is worth recording. The adrenals, pituitary gland, and the testes are said to be the endocrine glands most often structurally damaged in congenital syphilis, and affections of the thyroid are rare, especially myxoedema and exophthalmic goitre, although hypothyroidism is not so uncommon.¹

The patient is a fairly well nourished girl, aged 4½ months. The mother states that the child has abscesses of the buttocks. The mother had one child in 1914, which is stated to be quite well. In 1917 the mother was found to be suffering from late secondary syphilis, and her Wassermann reaction was positive. She received galy 0.25 gram intramuscularly, kharsivan 2.1 grams intravenously, and 7 grains of mercury intramuscularly. She then discontinued treatment. She states that in 1918 she had a stillbirth at full time.

Present Condition of the Patient.—The weight of the child is 11½ lb. Both lobes of the thyroid are enlarged. This is very noticeable when the child draws its head backwards or cries. The eyes are prominent, and show the "thyroid stare." Von Graefe's sign is present, Moebius's sign absent. The heart is apparently normal; the pulse rate before examination is 134, after examination of the child, 160. There are no nervous symptoms. A few papulo-

squamous spots are present on the face, several pustules on the trunk. Saddle-nose is present. On the right buttock is an undermined ulcer, on the left buttock one pustule. The glands, mouth, pharynx, tongue, are all apparently normal. The Wassermann reaction is positive.

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PNEUMOCOCCAL PERITONITIS SIMULATING ACUTE GANGRENOUS APPENDICITIS.

It has been my unfortunate experience during some years of practice to come across several cases of pneumococcal peritonitis in which the diagnosis of acute appendicitis was made and an operation for its removal undertaken. In all cases similar conditions were noticed. The abdomen was filled with pus, like thin cream, with a faint yellow-green colour, but without faecal smell. The appendix was easily found— injected externally, but healthy internally. The bowels had the same appearance.

To all intents and purposes, at the operation these cases are looked upon as a favourable variety, but if only the precaution of rapidly making a blood count, before deciding upon operation, were taken it would be found that most of these cases have a leucocyte count of over 30,000 per cubic millimetre, some 45,000 per cubic millimetre. The gravest prognosis must be given; all the cases I have seen have died within four days after the operation.

The previous symptoms in these cases, as seen in children from 3 to 12 years of age, are interesting, for the patients rarely complain of abdominal pain; the abdomen is quite supple, and there is no rigidity in the appendix region, nor of the lumbar muscles. The abdomen does not move with the respirations.

Acute appendicitis due to the streptococcus must not be confounded with these cases, for here we usually have the classical appendix symptoms and an acutely inflamed appendix with thin serum. The prognosis depends upon the blood count, and if it is 30,000 leucocytes per cubic millimetre or over, one may safely say that the case is hopeless; the fact that we now have many antistreptococcal serums to use may alter the outlook in an otherwise desperate condition, if heroically administered. The usual favourable acute appendicitis has, as a rule, a blood count of 14,000 to 20,000 leucocytes per cubic millimetre.

Bognor.

J. F. REV.

INTESTINAL OBSTRUCTION DUE TO PARALYTIC ILEUS.

A. B., a woman aged 55, was under the care of my partner, Dr. T. Murray Newton, and myself for five months suffering from vomiting. This occurred two or three times during the day, it had no relation to meals and no distinctive features. She had no pain; the pulse and temperature were normal, and the tongue was clean. She was thin and very sallow. The examination of the abdomen was negative. Constipation was a salient symptom throughout, and aperients were continually required. Dieting and rest in bed for two months relieved her condition so that she was able to go about. She, however, vomited occasionally, and retained a very sallow colour. Generally she had lost weight.

During August her condition became much worse. On the 25th there was very frequent vomiting, a rising pulse rate, and the abdomen was slightly distended. The next morning the vomiting had become continuous, the abdominal distension was much more marked, and there was very marked peristalsis. Dr. Denyer, physician to Hull Royal Infirmary, agreed that she had intestinal obstruction, and that immediate operation was necessary.

I opened the abdomen the same evening, and found all the colon immensely distended, but there was no obstruction in the rectum nor any part of the colon. Examination for other causes proved negative. The central incision was closed and a temporary colostomy made. The vomiting stopped immediately, and she has never vomited since. Full-sized motions were passed by the rectum after the fifth day, and some faeces through the colostomy wound. The sallow colour has disappeared. She has gained weight, and is obviously in better health than she has been for years. The weight, which at operation was 5 st. 10 lb., was 7 st. 1 lb. on February 18th.

The case seems to fall into the group of cases of intestinal atony following stasis and bacterial toxæmia well described in Nothnagel's *Encyclopaedia*.

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¹ Rolleston: *Proc. Roy. Soc. Med.*, February, 1921.