I will now mention some of the symptoms I observed in those cases in which the liver was enlarged: A coated tongue, a bitter taste in the mouth, nausea, perverted appetite, flatulence, constipation with pale clay-coloured stools; sallowness of the complexion and irritability of the skin; dull headaches, mental depression, lassitude, insomnia, irritability of temper, drowsiness after meals, and a disinclination for work; a sense of weight, or a feeling of discomfort in the right hypochondrium, and occasionally an aching in the tip of the right shoulder. The pulse was often slow.

It is my impression that when the liver is involved the tongue takes a longer time to become clean than in ordinary cases of dyspepsia. In support of this opinion I may relate a rather peculiar case:

The patient had taken alcohol to excess for some years. His tongue was covered with a thickish yellow fur. He told me it had been in the same condition for many years. He remembered a doctor drawing his attention to it twenty years ago. The liver was increased in size (6 in. of vertical dullness), and the organ was tender on pressure. He took strong sulphur water daily, and had liver packs every alternate day. At the end of six weeks he felt quite well, the liver dullness being $4\frac{1}{2}$ in., but there was no improvement in the condition of the tongue. As he was then leaving Harrogate I advised him to continue the liver packs during the winter, and I substituted iridin and colalin for the sulphur water. When I saw him in the following year his tongue had improved, and before he left it was perfectly clean.

Not uncommonly one meets with this type of case. The patient does not complain of anything very tangible. He has had a good deal of worry, but has led a healthy life. To use his own expression, he is somewhat "out of sorts." He feels a little depressed, is less energetic, and is inclined to take a pessimistic view of things in general. He does not suffer from indigestion or constipation. The liver may be found to be slightly enlarged, and in some instances slightly tender on pressure, but there is no other tangible sign. After a week of sulphur water and half a dozen liver packs the patient feels quite well, and the liver is normal in size. Two of my cases had liver packs only, without internal medication, and the result seemed to be equally good. I take it that these cases are examples of primary hepatic inadequacy.

The functions of the liver may be disturbed without any detectable enlargement of the organ.

I will cite a case in illustration. A lady was sent to Harrogate for recurring attacks of eczema of the face. The liver dullness measured 4 in. in the vertical diameter. She was a gouty subject. The treatment consisted of strong sulphur water and alkaline sulphur baths. At the end of a fortnight the eruption had disappeared. A few days later she was threatened with another attack, which she attributed to cold, but this quickly subsided under the influence of calamine lotion. Shortly after her return home she had a severe attack followed by others. Her medical adviser sent her again to me on May 30th, 1911. On this occasion I adopted a different line of treatment, namely, vigorous stimulation of the liver. She had liver packs daily, took colalin and podophyllin at bedtime, and strong sulphur water in the morning. In a week the eruption had vanished and has not reappeared.

It is an inference from this and other cases that in refractory irritative skin lesions functional disturbance of the liver ought to be taken into account.

The liver adapts itself to the extra functional demand made upon it with great celerity, and sometimes under stress displays sudden variation in size. I will briefly mention a case where the liver dullness became reduced 4 in. in ten days.

The patient suffered from sciatica. The liver dullness on July 8th, when I first saw him, was 5 in., and the organ was slightly tender on pressure. On July 17th he got ptomaine poisoning. I saw him on the 18th; the liver dullness was then $7\frac{1}{2}$ in.; on July 22nd it was $4\frac{1}{2}$ in., and on July 28th $3\frac{1}{2}$ in.

It has been suggested, and there is some evidence in support of the suggestion, that an increase of oxalic acid in the urine is an indication of hepatic insufficiency. Possibly alimentary glycosuria may also be an indication, but it is generally considered that this condition is associated with derangement of the pancreas.

The chief causes of functional derangement of the liver may be briefly summarized as follows: Dyspepsia, gastrointestinal disturbance, alcoholic excess, rich and highly-seasoned food, fevers, nervous influences, and residence in the tropics.

Treatment.

The best method of treatment is to diminish the amount of work the liver has to perform and to facilitate the circulation through it. The work of the liver depends chiefly upon the quantity and composition of the food; therefore, in order to restore normal hepatic function there must be a limitation of the food supply; but it must be borne in mind that too rigid a dietary may interfere with the nutrition of the liver cell, and thereby injuriously affect its activity. The restriction in the quantity of food should therefore be compatible with the maintenance of normal nutrition. A mixed diet is the best, the articles being of simple composition. Three meals a day are advised unless the gall bladder is involved. Carbohydrates and fats should be limited, as the former tend to ferment, and the latter are not easily absorbed if the quantity of bile excreted is diminished. Alcohol should be forbidden. Other irritants such as mustard, pepper, red pepper, horse-radish, ginger, cloves, strong meat broths, large quantities of salt, and the empyreumatic substances that are formed in baking and roasting should be avoided. In most cases it will not be necessary for the patient to exercise dietetic self-denial for more than a week. Rest after meals should be enjoined so that the functional hyperaemia of the organ is not disturbed. Exercise such as golf is very important. With increased, respiratory effort the liver is rhythmically compressed, and the venous blood flows more rapidly to the heart. For those unsatisfactory individuals who take little or no exercise massage, general and special, is desirable.

Regarding drugs, I would suggest a pill containing colalin and iridin, or podophyllin and colalin, at bedtime, followed by a dose of sulphate of soda or Carlsbad salts in the morning for a week or longer. If the stools are clay coloured, calomel may be substituted for either of the pills.

CONGENITAL ABSENCE OF THE COLON.

BY

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In reporting the following case I have in view not so much the interest due to the tuberculous lesions in the abdomen, with symptoms simulating recurrent appendicitis, as the rare abnormality of an entire absence of the colon, which was revealed, so to speak, accidentally in the course of operation. While congenital absence of the colon can be very easily explained on developmental grounds, I have not been able to find any clinical record of such a case. Neither can I recollect having come across an example of this condition in the dissecting-room during the years when I was a demonstrator of anatomy in the University of Glasgow.

The patient, a man aged 23 years, was admitted to the Western Infirmary, Glasgow, on September 7th, 1910, as a case of recurrent appendicitis, with a view to operation. During the previous two months he had had several attacks of pain in the right iliac region, lasting for a few days and then passing off. At the time of admission he was just recovering from one of these attacks. There was slight tenderness and rigidity in the iliac fossa, and a distinct mass could be felt, which certainly gave me the impression that we had to do with a lesion of the appendix with adhesions. The pulse and temperature were normal.

Five days later I operated with a view to removal of the appendix. On opening the abdomen by the usual gridiron incision I found a portion of the small intestine bound down by adhesions in the right iliac fossa, forming the mass which had been felt through the abdominal wall, but no trace of caecum or appendix. Having enlarged the incision in order to get free access to the abdominal cavity, further evidence of tuberculous disease was found. There was quite a variety of lesions exhibited. In addition to the adherent bowel above mentioned several distinct bands were present, under one of which a loop of intestine was caught and constricted almost to the point of strangulation. Having freed these bands, a number of enlarged glands were next observed in the mesentery, in the upper part of which one large glandular mass had softened and formed a tuberculous abscess as big as a hen's egg. This was incised and scraped out thoroughly, then closed by carefully suturing the edges of the peritoneum over it. Further examination of the bowel revealed several softened tuberculous patches on the surface of the gut, which were also scraped and covered in by Lembert sutures.

Finally I made a careful examination of the whole intestine and satisfied myself that the colon was entirely absent. The

small intestine could be traced into the rectum at the pelvic brim, with no apparent trace of caecum or appendix.

The abdominal wound was closed in layers, and united by primary union. The patient made an uneventful recovery and left the hospital at the end of sixteen days. Quite recently I had a note from him to say that he went to work a fortnight after leaving the ward and has remained perfectly well since.

A SIMPLE HAEMOGLOBINIZED SALINE CULTURE MEDIUM

FOR THE GROWTH OF LEISHMANIA AND
ALLIED PROTOZOA.*

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ROGERS, to whom belongs the credit of the discovery of *Leishmania donovani* of kala-azar going into fully formed flagellates in culture, made use of a saline solution containing a certain proportion of sodium citrate, to which he added the parasite-laden blood derived from the splenic puncture. Later the same author recommended the addition of a little citric acid, as this medium gave more abundant cultures. I believe a similar medium was used by workers who subsequently confirmed Rogers's discovery in India and in England: 'Nicolle' of Tunis made use of Novy-McNeal medium in his early cultures of *Leishmania infantum* of Algeria. This medium consists of the water of condensation of ordinary peptone agar slopes, into which, while yet fluid at 55° C., is incorporated 25 to 33 per cent. of defibrinated rabbit's blood. This medium was utilized also by Leishman and his collaborators in their culture work. Nicolle simplified the classical Novy-McNeal medium by using only agar and NaCl without peptone or meat extract. It is this medium which is now generally used in *Leishmania* culture work, and it goes by the name of Nicolle-Novy-McNeal or N.N.N. medium. It is also in this medium that Nicolle grew and demonstrated for the first time the cultural forms of *L. tropica* of the Tunisian oriental sore. Row of Bombay utilized dilute human blood (in saline) for his first cultures of *L. tropica* of the oriental sore of Cambay. Later, Carter used a similar medium for his cultures of *L. tropica* of the oriental sores of Northern India. Carter's formula consists of 4 parts of heated serum, 4 parts of red blood cells of the rabbit, and 3 parts of 10 per cent. sodium citrate in saline.

While working out the comparative merits of all these media, two things forced themselves on attention.

1. That haemoglobin seems to be essential for the growth and development of *Leishmania*.
2. That any changes in the character of the growth of these bodies seem to depend entirely on the way in which haemoglobin is present in the culture fluid, namely, according as it is free in solution or only in the red blood corpuscles unhaemolyzed.

Culture fluids containing red blood corpuscles unhaemolyzed offer a distinct resistance to a vigorous growth of flagellates, while those containing free haemoglobin in solution offer no such resistance. This is one of the reasons why it is difficult to obtain a series of successive cultures by using culture fluids containing unhaemolyzed red blood corpuscles, while vigorous cultures and subcultures are obtained indefinitely by the use of N.N.N. medium which contains free haemoglobin in abundance. The better results obtained in his later experiments by Rogers in the acidified citrate medium are perhaps to be accounted for by the haemoglobin set free by the citric acid. The presence of free haemoglobin in the alimentary canal of blood-sucking insects like the mosquito, the flea, or the bug (which retain the ingested blood for several days), explains the cultural forms of the parasites found in these, after they have been made to suck blood rich in the parasites.

Further, it may be of interest to note that while free haemoglobin in the saline medium of a certain density is eminently favourable for a rapid and vigorous growth of flagellates, the presence of unhaemolyzed red blood corpuscles seems to favour the multiplication of the original parasites as such. This is what takes place in Nature—for example, at the seat of disease, namely, the spleen or

liver in kala-azar, or the lesion in oriental sore—as well as *in vitro*. It is easy to demonstrate this by planting a clot, say, from the needle of a kala-azar splenic puncture in a saline solution, when an examination of the clot, even at the end of four days, will reveal an enormous number of $\odot$ bodies which have apparently multiplied in the meshes of the clot. A similar result is observed in an N.N.N. culture, as this becomes concentrated by age. Thus a culture containing vigorous flagellates about the fifth day shows about the twelfth to fifteenth day a large number and masses of $\odot$ bodies resulting from the post-flagellate growth of the parasite. This was referred to in another communication, and will form the subject of a separate memoir.

From the foregoing it is clear that the condensation fluid of Nicolle-Novy-McNeal medium fulfils all the conditions for a vigorous growth and multiplication of flagellates. But in practice in tropical laboratories the following difficulties present themselves:

1. The quality of blood available from a rabbit, even by a direct cardiac tapping, is so small that one cannot expect to obtain more than a dozen tubes for one rabbit sacrificed.
2. The quantity of condensation fluid obtained is not more than 1 to 1.5 c.cm.
3. This fluid gets concentrated in the course of a few days, owing to the tropical heat, but chiefly owing to the large surface of the agar slopes exposed to evaporation, so that the culture tubes are available from three to four days after they are prepared and before they are ten to twelve days old.

This gives an interval of only six days or so for subculturing. Further, it entails an enormous sacrifice of rabbits on the one hand, and on the other hand a great deal of labour in preparing the culture medium freshly every week.

It is to meet these difficulties that an attempt was made to simplify the process of making a suitable culture fluid, which would be like the condensation fluid of the N.N.N. medium in composition and be at the same time available readily and in larger quantity.

Details of Technique.

1. With the usual antiseptic and aseptic precautions about 5 c.cm. of blood are collected from the punctured marginal vein of a rabbit (blood can be aspirated easily to the extent of 5 to 8 c.cm. from one of the superficial veins of the forearm in man—thanks to Major Glen Lister's advice—when human blood is required) and poured into a sterile test tube containing a few glass beads. The tube is shaken to defibrinate the blood.
2. The defibrinated blood is now rendered laky by the addition of sterile distilled water in quantity requisite to dissolve all the haemoglobin available (1 in 8 to 10 of distilled water is found sufficient for the rabbit's blood in Bombay). The haemolysis may be also induced by repeated freezing and thawing, and is perhaps preferable when a stronger solution of haemoglobin is required.
3. The next step is to utilize the laky blood to dilute the NaCl solution so as to ultimately have a strength of 0.8 to 0.9 per cent. NaCl with a fair colour of the haemoglobin (after a great many experiments this strength has been found to be the best), and for this final admixture I follow the following routine:

From a stock solution of 1.2 per cent. NaCl two portions are sucked up with a sterile pipette and nipple and transferred to empty sterile test tubes of about $\frac{3}{8}$ in. diameter.

These tubes are kept in a water bath at 56° C., and when they are at this temperature one portion of the laky blood is added to each saline tube. This gives a strength of about 0.85 to 0.9 per cent. NaCl. The heating of the saline previously is done with the double object of ensuring sterility and of destroying any complement that may be present in the defibrinated blood.

By this method, with about 5 c.cm. of blood, as many or more culture tubes are made as can be prepared with the sacrifice of a rabbit, and the quantity of the culture fluid is at least 5 c.cm. in each tube, instead of being only 1 c.cm. to 1.5 c.cm. of the N.N.N. medium. The tubes thus prepared are ready for immediate use (after cooling), and from start to finish take twenty to thirty minutes to prepare.

In this culture fluid flagellates flourish and multiply even after five to six weeks, so that subcultures can be made at leisure any time during this period, as the fluid does not get so easily concentrated, as does the condensation water of the N.N.N. medium, which by this time completely dries up owing to the large surface exposed to evaporation by the agar slope.

The following advantages may in brief be claimed for the haemoglobinized saline medium:

1. The culture medium can be made at once when

* Communicated to the Bombay Branch of the British Medical Association.