lation (storing) of glycogen in the hepatic parenchyma. The girl's kidneys also showed accumulation of glycogen. According to von Gierke, the disease is not in any way allied to diabetes mellitus.

During life the presence of von Gierke's glycogenic-accumulation disease is not likely to be absolutely established except by the microscopical examination of an excised piece of the liver or material obtained by liver puncture, but probably even without that a diagnosis of the disease (minor forms of which are perhaps not so extremely rare) can be sometimes arrived at. In this respect one of the latest articles on the subject may be consulted, especially that by L. Schall, which is founded on the observation of three children (not relations).² Schall concludes that the most important feature of the disease is an enormous enlargement of the liver (without splenomegaly), which has been present from earliest life and which is due to a heaping up of glycogen in the organ. The second feature to be noted is the presence of hypoglycaemia without the usual clinical signs of the condition, while a third is the fact that the glycogen cannot be mobilized by adrenaline. Fatness, ketonuria, and a certain weakness of the skeletal musculature may likewise be observed. According to Schall's observations the disease takes no acute course, and his earliest case—first seen in December, 1928, when the patient was 8 years and 6 months—in which the diagnosis was made certain by an exploratory laparotomy and microscopical examination of an excised piece of the liver, has been observed for almost four years without showing any change.

Although in the case which we have described examinations of the blood sugar (which was 0.075 per cent. in March, 1930) have not been carried out sufficiently often, it is difficult to explain the symptoms in any other way than to suppose the remarkable hepatomegaly to have been due to von Gierke's metabolic constitutional disease with heaping-up of glycogen in the liver.

Clinical Diagnosis.—Although Professor von Gierke* points out that during life the diagnosis of his "glycogen accumulation disease" can be made certain only by the examination of material obtained by puncture or excision of a piece of the liver, it seems to us that in all probability the disease will turn out to be, of all rare diseases, one of the easiest to diagnose with practical certainty during life. Picture a child of 5 to 12 years with an enormous uniform enlargement of the liver, which feels smooth and not especially hard, and is not tender to palpation. The child does not appear really ill, does not complain or look very weak, is not in the least jaundiced and has never been jaundiced, has no ascites, oedema, or thoracic disease, and tends to be rather fat than wasted, has no *enlargement of the spleen* or lymphatic glands, and no haematological sign of any kind of leukaemia, or indeed of any other disease. It is true that in a young child with evidence of rickets one might think of the possibility of fatty infiltration of the liver,* but in a case like the one we have described such a diagnosis could certainly not be entertained after watching the unaltered condition for a long time. Moreover, apart from starvation, wasting and vomiting, and a specially ketogenic diet, is there any disease in which, in the absence of an acute or infectious condition, the urine day after day, month after month, and year after year, nearly always contains acetone and diacetic acid, always without sugar? Is not the clinical diagnosis from both these considerations doubly probable? Possibly, in some cases, the ketonuria may not be so striking; but there are other clinical signs. There are, as pointed out by Schall, the presence of hypoglycaemia without the ordinary symptoms of hypoglycaemia, and

the adrenaline effect on the blood sugar to be taken into consideration. Surely a clinical diagnosis will sometimes be justified without liver puncture.

I wish to acknowledge my great indebtedness to those of my colleagues who from time to time have helped me in the examination of this case—Sir Humphry Rolleston, Dr. Clement Lovell, Dr. H. C. Lucey, and Dr. D. T. Davies.

REFERENCES

- ¹ von Gierke, E.: *Ziegler's Beiträge z. path. Anat. u. z. allg. Path.*, 1929, lxxxii, 497; *Med. Klinik.*, 1931, xxvii, 576, 611.
- ² Schall, L.: *Munch. med. Woch.*, 1932, lxxix, 2078 (with references to the literature after von Gierke's original paper).
- ³ von Gierke, E.: *Med. Klinik.*, 1931, loc cit.

ADDENDUM.—Just before the proofs were corrected a paper appeared in the *Lancet* for February 11th, 1933 (p. 297), by Dr. E. Bellingham Smith and Dr. Elizabeth O'Flynn, entitled "Familial hepatomegaly of uncertain pathology." The patient was a boy, aged 6 years, with enormous enlargement of the liver and chronic pulmonary fibrosis and bronchiectasis, who, whilst coughing, was seized with violent abdominal pain, and fatal collapse followed. During life a diagnosis of Gaucher's disease had been made because the left portion of the liver was taken to be an enlarged spleen, puncture of which had yielded large clear "Gaucher-like" cells. The necropsy and microscopical examination made the authors regard the case as probably of the same nature as Gierke's original case. The familial character of the hepatomegaly was more definitely evidenced than in the present case. On the other hand, there was no evidence of ketonuria. It may be repeated that the present case was shown as one of enlargement of the liver of uncertain nature with persistent ketonuria as long ago as March, 1923, and has since then almost completely recovered; but there was no associated severe infective disease present, such as bronchiectasis and pulmonary fibrosis.

ACUTE OBSTRUCTION OF THE COLON

BY

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Acute obstruction of the bowel is certainly one of the most serious surgical emergencies that we as doctors are called upon to deal with, and the patient's life will depend upon prompt recognition of the nature of the case and the taking of such steps as will adequately relieve the condition with the least possible delay. The mortality from acute obstruction is still much higher than it should be.

The patient, with very few exceptions, will be suffering from two, and possibly three, distinct conditions. (1) An obstruction to the lumen of the bowel, which prevents any of the contents from passing along the lumen. (2) A toxæmia due to the absorption of poisons generated in the obstructed bowel; this toxæmia, while often not very evident—or at least often obscured by the more obvious results of the obstruction—is a very real source of danger to the patient, and has to be taken very seriously into account in the treatment of the case. (3) If the bowel is strangulated from bands, adhesions, or twists, or any other condition which in addition to causing obstruction of the lumen also causes obstruction to the blood supply of the affected portion of bowel, then serious damage to part of the bowel wall will be a third factor causing danger to the patient. In a case of hernia or volvulus all these three factors will be present in varying degrees, but in the more usual forms of obstruction, such as stricture, only two of these factors are present.

DIAGNOSIS

The necessity of making a diagnosis between a case of obstruction of the small and one of the large bowel always arises, but should as a rule not present any serious

* Smooth symmetrical enlargement of the liver due to fatty infiltration (retention and heaping-up of fat in the glandular cells of the liver) was formerly not rarely found at post-mortem examinations on rachitic infants.

difficulty. In the first place some 75 per cent. of all cases of obstruction of the small bowel are the result of external hernia, and if looked for, as they always should be, will be easily detected, but apart from this the symptoms are usually very different. In small bowel obstruction the symptoms are most acute, and vomiting of the characteristic faecal type occurs almost from the onset of the crisis. Pain is usually well marked and often severe, and there is little distension in the early stages. Such distension as is present will be in the central part of the abdomen. The appearance of the abdomen in a case of obstruction is often alone sufficient to enable one to distinguish between an obstruction of the small and of the large bowel. In obstruction of the large bowel distension is usually the chief symptom, and vomiting only occurs late and is never so severe or frequent as in obstruction of the small bowel.

Having arrived at the conclusion that the case is one of obstruction of the large bowel, it is advisable to diagnose, if possible, the cause of the obstruction, or at any rate the probable nature and whereabouts of the obstructing lesion. This is often a matter of very considerable difficulty, but there are a number of factors which will assist us, and the possibility of error, though always present, can usually be reduced to a comparatively small fraction.

In the first place the law of probabilities, which is just as useful in medical practice as it is in playing bridge, will be a great help. If we see a bird on a telegraph wire in a London street it may be a canary, but the probabilities are very great indeed that it is a sparrow. Now by far the commonest cause of obstruction of the large bowel in people over middle age is cancer, and there will therefore be a probability of at least two to one that a tumour is the cause of the trouble. After this the commonest cause is diverticulitis, which probably accounts for more than one-half of the remaining cases. Thus the probabilities offer a very big chance that cancer of some part of the colon is the cause, a considerably smaller chance of diverticulitis, and quite a small chance that some other condition is responsible. This small chance is probably not more than about 10 per cent. If we continue to use the law of probability it will assist us further, as we know that the commonest situation for a cancer of the large bowel is in the rectum or pelvic colon, which accounts for some two-thirds of all cases. The next commonest site is in the caecum, and after that the splenic angle. We also know that very much the most usual situation for an obstruction due to diverticulitis is in the pelvic colon. We may therefore conclude, before we look for any other evidence, that the chances are very considerable that we have to deal with a cancer of the bowel, probably at the lower end of the colon.

An examination of the rectum is the next procedure, as it will tell us whether there is a tumour in the rectum, and in a normal individual we shall be able to feel whether there is any tumour or swelling in the pelvis. If an examination can be made with a sigmoidoscope it will enable us to confirm or exclude the presence of an obstructive lesion at the extreme lower end of the colon, which is the commonest site. An examination of the abdomen will be of some assistance, as we should be able to feel a tumour, if present, in the caecal region, though it is very unlikely that it will be palpable anywhere else. If, however, diverticulitis is the cause of the obstruction it is most probable that a hard tender swelling will be detectable in the left iliac fossa. The patient's previous symptoms, if any, before the onset of the obstruction will also be of value. In cases of cancer there are almost always symptoms of irregularity of the stools and evidence of blood for some weeks or months. In diverticulitis there will be a history of attacks of pain in the abdomen,

usually accompanied by temperature often extending over a considerable period, it may be for some years.

SOME DIFFICULTIES

In at least two-thirds of the cases of obstruction of the large bowel it should be possible to diagnose both the nature and the site of the lesion, but there will always remain a residue where an exact diagnosis cannot be established, and these cases call for further consideration. In looking through my case books I find quite a number of cases of obstruction of the colon, of which many were not diagnosable with certainty previous to operation. In two cases a previously undetected megacolon was the cause of an acute obstruction. In one case a correct diagnosis was made and the patient relieved without operation, in the other the patient was put on the operating table and an anaesthetic administered, but the relaxation produced by the latter caused a copious evacuation and relieved the obstruction, and a subsequent examination with a sigmoidoscope established the diagnosis. In two cases the obstruction was caused by adhesions from a chronic appendix abscess, deep in the pelvis, which had not been detected and was not even suspected until discovered at the operation for obstruction of the colon. In three cases the obstruction was caused by acute cellulositis inflammation of a section of the pelvic colon due to diverticulitis. In one case an almost complete fibrous stenosis of the pelvic colon from the same cause was present, and in a number of cases diverticulitis of the pelvic colon was the cause. In some of these the lumen had become so narrow as to get blocked, and in others the colon had become acutely kinked as the result of adhesions to neighbouring structures. Adhesions or bands were the cause of obstruction in several cases. These were mostly due to some previous operation on the abdominal cavity performed many years previously. Hypertrophic tuberculosis was the cause in two cases, and in three cases tuberculous peritonitis in childhood had caused almost complete obliteration of the abdominal cavity, which must have been present for many years without causing serious trouble, but had finally, from the contraction of some particular band of fibrous tissue, caused a complete obstruction. Five cases were due to volvulus. Two of them were cases of volvulus of the pelvic colon; two were due to volvulus of the whole caecal angle, the twist occurring around the superior mesenteric artery and involving almost the whole of the small intestine and half the colon. These cases are almost invariably fatal owing to the enormous mass of gut involved and the difficulty of untwisting it, but one of these patients survived and is alive to-day. The other case of volvulus was one of the splenic angle. This must be a very rare occurrence, as I have never seen any other case where the splenic angle was loose enough to be able to twist at all. In this case it was quite loose and had a long mesentery.

There was also one case due to a large stercolith stuck in the lower end of the pelvic colon. It could not be diagnosed, as there was so much oedema below it that it was not possible to feel it, or see it with the sigmoidoscope, although, of course, a swelling could be felt which was thought to be a growth. In one case the obstruction was due to a large submucous lipoma in the pelvic colon.

TREATMENT

Immediate operation is called for in all cases, although there is no harm in administering an enema, which may possibly relieve the immediate symptoms, and, in a few cases such as megacolon, may relieve the obstruction entirely. The operation will always be an anxious and dangerous one, owing to the patient's condition. The chief dangers are vomiting while the patient is under the anaesthetic, and toxic shock. It often happens that when

the abdomen is opened there is sudden faecal vomiting, and if the patient is deeply under the anaesthetic some of the vomit gets into the lungs and causes a fatal broncho-pneumonia. This can be guarded against by passing a stomach tube directly the patient is unconscious, and before commencing the operation. The stomach may be either washed out or allowed to drain during the operation, and washed out before the patient leaves the table. A still better method is to do the operation under local or spinal anaesthesia, so that the coughing reflex is not abolished. The prevention of toxic shock is more difficult. The administration of large quantities of water or saline so as to dilute the poisons and encourage their elimination is most important, but this is not easy. If the patient is not being sick it can be administered by the mouth, but if there is sickness this is impossible, and if the obstruction is low down rectal salines will probably not be retained. It is often necessary to give subcutaneous, or intravenous, saline, and this should always be done in a bad case before or during the operation. Glucose, or some other form of sugar, should also be given by the most convenient route.

As regards the operation itself, all surgeons are agreed that "to get in quick and get out quicker"—the famous motto of the late Professor Murphy of Chicago—is even sounder in cases of acute obstruction than it is in cases of acute peritonitis, for which it was originally invented. One should do the least possible that will relieve the obstruction and leave direct interference with the lesion to a subsequent operation when the patient has got over the toxæmia which has been produced by the obstruction. Some years ago, at Bristol, Mr. Burgess and I advocated blind caecostomy in these cases as the best treatment, and there is still considerable difference of opinion on this question. The advantages of blind caecostomy are that it can be performed under local anaesthesia through a small incision with the absolute minimum of interference with the abdominal cavity, and that it completely drains the whole of the colon above the obstruction and rapidly gets rid of the toxæmia. The opening, if made by the tube method, which I suggested in 1922 (*Lancet*, 1922, ii, 1117), will remain open for ten days to a fortnight and will close itself without a secondary operation. This gives time enough to perform a second operation to deal with the obstructing lesion. It has been urged against blind caecostomy that it does not enable a diagnosis to be made of the obstructing lesion, but this is not a serious objection, as it is not the lack of an exact diagnosis that is threatening the patient's life, but the obstruction. It has also been pointed out that if the obstructing lesion is a volvulus it will not be relieved by a blind caecostomy. This is a more serious objection, but volvulus only accounts for about 1 per cent. of cases of obstruction, and in any case it is generally fatal. It was pointed out by Mr. Burgess that if it can be proved that the mortality from acute obstruction of the colon can be reduced materially and as a whole by blind caecostomy, this is sufficient justification for its adoption.

While surgeons still hold different views as to the advantages of blind caecostomy in cases of colonic obstruction they all agree that a colostomy or caecostomy should be performed above the site of obstruction, and the actual obstructing lesion should not be dealt with at the time, but be left till after the obstruction has been relieved. On no account should any attempt be made to resect the obstruction or to short-circuit it. An occasional successful result from such a procedure is no justification for the very serious risk involved. The subsequent treatment of the patient should aim at getting rid of the toxæmia by freely administering water in some way or another and relieving the overloaded bowel. It is

generally better to evacuate the bowel by means of enemata given through the artificial opening rather than by administering purgatives by the mouth.

CONCLUSIONS

1. It should not be difficult to diagnose obstruction of the large bowel from that of the small.
2. The commonest cause of obstruction of the colon is a growth in the pelvic portion, and the next commonest diverticulitis in the same region. It should be possible to diagnose the cause of the obstruction with only a small percentage of error.
3. The chief danger and the most frequent cause of death is the toxæmia which results from the obstruction. This can be best dealt with by the free administration of fluids.
4. The best operation for relieving the condition is blind caecostomy or colostomy performed under local anaesthesia.

A QUANTITATIVE MODIFICATION OF THE BENDIEN REACTION IN SERO- DIAGNOSIS OF MALIGNANCY*

BY

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In 1931 Dr. S. G. T. Bendien of Holland published his observations in "Specific changes in the blood serum," and introduced a flocculation test which he claims, with certain reservations, differentiates between normal and pathological serums by variations in the reaction. Although he details many reaction changes which occur with malignant serums, the test is not primarily put forward as specific for cancer. The Bendien test consists of two parts: the first, a chemical precipitation of proteins from a serum by a specially arranged series of acetic acid sodium vanadate mixtures, and secondly, the spectrographic examination of the precipitated protein. The observations and conclusions of the second part of the test are based upon technical findings of a specialized kind, and have been criticized by Smith, Holiday, and Marrack (1931), whose findings have so far not been refuted. The first (precipitation) part of the test has also been questioned by Fine (1932), but this adverse criticism is tenable only so long as the reaction is restricted to the use of unheated serum, which, as will be shown later, is an insufficient employment of the test.

After carrying out over two hundred tests upon various serums, nearly all Bendien's flocculation reaction observations upon human serums, and several upon animal serums, have been confirmed. The delicacy of the precipitation reaction is striking, and necessitates a carefully standardized technique; but this gives to it a degree of differentiation between serums, and of variations from time to time in the serum of the same case, which suggest that the test has a definite clinical value.

Several of the difficulties which were met with, and observations which were made in doing the precipitation test, suggested that a quantitative estimation of the deposits would give more concise findings than the qualitative readings suggested by Bendien, and the following is a brief description of the modified quantitative method that has been employed, and upon which the subsequent findings are based.

The Reagents.—The first eight mixtures of N/10 acetic acid and N/10 ortho-sodium vanadate are prepared accord-

* Paper read before the Liverpool Medical Institution on November 24th, 1932.