almost the whole period. The only difference, then, was that during the second period the students were accompanied by a nurse-midwife. Miss Carter selected the occurrence of notifiable puerperal pyrexia as the test of the effect of this change, and she found that during the first period 5.22 per cent. of the cases were notifiable as puerperal pyrexia; during the second period the proportion fell to 2.19 per cent. There were no fatalities during the second period.

In comparing these results with those of the East End Hospital it must be remembered that the number of cases dealt with in the University College Hospital series is comparatively small, which to that extent invalidates comparison. It was, however, reported* that the puerperal pyrexia rate for the East End series was 1.1 per cent., while that for the University College Hospital series was 5.29 per cent. in the first half and 2.19 per cent. in the second half.

It would be wrong to look upon these minor complications of the puerperium as of no importance. It is probable that about 50 per cent. of them are due to minor degrees of uterine infection, either alone or in combination with injury, which may lead to long periods of suffering and invalidism. I would further call your attention to the fact that evidence is fast accumulating that chronic inflammatory changes in a cervix damaged in labour form a definite predisposing cause of cancer. Leucorrhoeal discharges in women who have been recently confined, therefore, call for careful local examination of the cervix, for the great majority of such discharges arise in fact from that part. The importance of prolapse and backward displacement of the uterus calls for no emphasis. Post-natal examination is essentially work for the man with practical experience: it does not demand a high degree of technical knowledge, and it could, with advantage, be entrusted to practitioners who will fit themselves to undertake it and to deal with it efficiently.

CONCLUSION

The outcome of all that I have been saying is this. I would suggest that the position of the general practitioner in relation to midwifery has already changed, and will probably change further, inasmuch as the bulk of the attendance upon confinements in the industrial classes is passing into the hands of midwives. With this change new opportunities are opening up for the doctor: in respect of the practice which is being taken out of his hands he may become, if he will, the consultant at first instance to the midwives. It is estimated that midwives already attend from 60 to 70 per cent. of the total births of the country, and in some areas the proportion is higher than that, and it appears to be rising year by year. The proportion of midwives' cases in which a doctor's services are called for is also steadily rising. Much of the ante-natal and post-natal work now being carried on could be efficiently done by general practitioners. If, however, he is to rise to this opportunity the practitioner must make himself efficient in practical knowledge, and he must try to keep himself abreast of progress in all departments of midwifery. He would then become a very important link in the chain of a national maternity service, and in my submission the work would be well worthy of the English doctor at his best.

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HEPATOMEGALY WITH PERSISTENT KETONURIA IN A CHILD

PROBABLY A CASE OF VON GIERKE'S "GLYCOGEN ACCUMULATION DISEASE" WITH FUNCTIONAL RECOVERY

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The following case was shown by me on March 23rd, 1923, at the Royal Society of Medicine (Section for the Study of Disease in Children, *Proceedings*, 1923, xvi, 56-60), under the heading "A case of enlarged liver with persistent acetonuria and diaceturia." The patient, a girl, was first seen at the age of 10, on June 10th, 1920.

HISTORY OF THE CASE

Father and mother were both alive; the former always had good health, but the mother was deaf (otosclerosis). The mother was the eldest of eight children; of the seven, three had died of phthisis, one had had a tuberculous wrist-joint, two had been epileptic, and one had been quite healthy. In the father's family there was nothing of note. Wassermann reaction (blood) in both the father and mother was negative. The patient had a sister, aged 7, who was said to have an "enlarged liver." On investigation the liver edge was found to be palpable two inches below the costal margin, but x-ray examination indicated ptosis of the organ rather than enlargement; the spleen was impalpable, and there were no other physical signs of importance. Wassermann reaction (blood) was negative.* The only other child had died twelve years before at the age of 3; he was said by a doctor to have had an "enlarged liver and spleen" and to have died of "kidney disease."

The mother stated that pregnancy and labour had been normal, and that at birth the child had weighed 11 lb. She had been breast-fed, and had been perfectly well until 1 year old. From the age of 1 to 4 she had suffered from "fits" (description suggested epilepsy, with average frequency of one fit in two months), and between the ages of 3 and 5 had suffered from recurrent attacks of vomiting, strongly suggestive of cyclical vomiting. She had not appeared to grow during that period, and a medical man had said that "the liver was enlarged." She had not walked until she was 4 years and 3 months. Since that time her general health had been fairly good, and from the age of 5 she had grown steadily.

Photograph of the patient at the age of 12.

PHYSICAL EXAMINATION AND SPECIAL INVESTIGATIONS

The patient was very bright and intelligent, her mental capacity being fully up to her age standard. Physically she was rather undersized, and the development of the body was somewhat out of proportion to that of the limbs: height, 47 inches; spine from occipital protuberance to tip of coccyx, 20 inches; subcostal girth, 28 inches. The skull was normal. The teeth showed indentation on enamel of incisors, the margins of which were slightly irregular; other teeth were normal. The breath had a strong acetone odour. The liver edge was felt three inches below the costal margin, the edge being firm but not irregular. The spleen was impalpable and not enlarged to percussion. The heart, lungs, and nervous system were normal; brachial systolic blood pressure,

* This sister has since developed definite otosclerosis, but is otherwise well (January, 1933).

105 mm. Hg. X-ray examination confirmed the presence of an enlarged liver, but showed nothing else abnormal. The blood serum yielded a negative Wassermann reaction (three tests). Examination of urine showed: specific gravity 1022, acid reaction; acetone and diacetic acid both present, but no albumin and no sugar. Centrifugalized deposit showed a few epithelial cells, but no casts or crystals.

The complete blood picture was as follows: haemoglobin, 80 per cent.; colour index, 0.76; red blood cells, 5,200,000 per c.mm.; no vacuolation, but anisocytosis and poikilocytosis were marked; no nucleated red cells. White blood cells, 11,000 per c.mm. Differential count: polymorphonuclears, 54 per cent.; small lymphocytes, 26 per cent., large lymphocytes, 14 per cent.; eosinophils, 4 per cent.; basophils, 1 per cent.; myelocytes, 1 per cent.

During the two and a half years she was under observation she remained fairly well, was able to go to school, and to lead an ordinary life. The urine was examined on many occasions, and both acetone and diacetic acid were invariably present and sugar absent. As a rule, the breath had a strong acetone odour. Reaction to Wassermann test in June, 1922, was again negative. The blood picture showed no material change.

Liver Function Tests

Several hepatic efficiency tests were applied, all yielding negative results.

Straus's Laevulose Test.—The patient was given 60 grams laevulose and the urine was examined hourly for six hours; in no specimen was sugar found.

	Quantity	Specific Gravity	Sugar	Acetone
1	1½ oz.	1022	Nil	+
2	3½ oz.	1018	"	+
3	8 oz.	1014	"	+
4	3½ oz.	1018	"	—
5	3 oz.	1020	"	—
6	1½ oz.	1028	"	++

It is to be noted that in the specimens obtained four and five hours after taking the laevulose acetone was absent.

Blood Laevulose Test.—The blood sugar estimated by Benedict's method was found to be 0.109 per cent.* Twenty-five grams of laevulose were given by the mouth, and the blood sugar, estimated three-quarters of an hour later, was found to be 0.110 per cent. (Experimental error 0.005 per cent., certainly less than 0.01 per cent.)

Widal Haemoclastic Test.—Total white cell count, 8,700 per c.mm.; one hour after seven ounces of milk, 14,000 per c.mm.

Sulpho-conjugation Test (Foster and Kahn's test).—Ratio of ethereal sulphates to inorganic sulphates in urine (benzidine method): before thymol, 1:13; after half a gram of thymol, 1:4.4.

The association of hepatic enlargement with the continued presence of acetone and diacetic acid in the urine, without glycosuria, was unusual. The history rather suggested a familial condition; the fact that both parents and the sister showed no signs of syphilitic disease, and all, including the patient, gave negative Wassermann reactions, excluded syphilis. The familial form of haemolytic jaundice was excluded by the absence of jaundice. As Sir Humphry Rolleston has pointed out (*Diseases of Liver*, first edition, p. 445), congenital cystic disease of the liver is known to occur in rare instances without the association of congenital cystic kidneys, and examples have been recorded by Borst, Dudgeon, W. Müller, and Batty Shaw. "Idiopathic" hepatic cirrhosis of children is also occasionally met with as a familial condition. Although either of the two last-mentioned disorders was a possible diagnosis, neither, as far as I was aware, was usually associated with persistence of acetone and diacetic acid in the urine. It was suggested in this case that these

substances might be of alimentary origin, and their persistence possibly due to interference with the metabolism of amino-acids in a liver embarrassed by the formation of fibrous tissue. Against this view, however, was the fact that none of the hepatic efficiency tests indicated any defect of liver function. Increasing the carbohydrates in the child's diet did not lead to a disappearance of the acetone (although it was absent for a very brief period following the administration of laevulose in the alimentary laevulose test), and her mother was emphatic in the opinion that the child was never as well when taking an increased amount of carbohydrate; she became listless and irritable, and developed a poor appetite.

None of the members present at the demonstration at the Royal Society of Medicine knew of any similar case. Dr. F. Parkes Weber, in the discussion, said that when he was shown the case in October, 1922, he was sceptical about the ketonuria always being present, but he was convinced by finding that the urine passed by the child at the time gave positive Gerhardt's and Legal's reactions.

SUBSEQUENT PROGRESS

The child remained for several years in much the same condition, and the urine continued generally to contain acetone and diacetic acid. In 1925 the liver seemed to be a little smaller. On March 4th, 1930, the fasting blood sugar was 0.075 per cent., and the blood sugar curve showed a delayed fall. In 1932 the patient, 22 years old, was bodily and mentally well developed, although puberty had been delayed till the age of 17. The liver could no longer be felt enlarged. Nevertheless her breath still often smelt of acetone, and she usually had acetone in the urine, but Gerhardt's reaction for diacetic acid was negative. Glycosuria had never been detected. The blood sugar, when tested in 1930, showed slight hypoglycaemia. The patient's height was 5 ft. 8½ in.; weight 9 st. 6 lb.; blood count: haemoglobin 90 per cent., erythrocytes 4,500,000 per c.mm., leucocytes 7,400 per c.mm. (nothing abnormal by differential count).

REMARKS

The patient seems to have practically "grown out" of her disease, which was clearly metabolic constitutional in origin. No one, however, could have suspected what was probably the exact nature of the metabolic defect in question till E. von Gierke in 1929 made a post-mortem examination in the case of a girl, aged nearly 8, who had died from influenza and was known to have had persistent enlargement of the liver of unknown origin. He found that the enlargement of the liver was due to excessive accumulation of glycogen. In an elaborate article, with coloured plates of microscopical findings,¹ he described the case under the heading "Hepato-nephromegalia glykogenica—Glykogenspeicherkrankheit der Leber und Nieren."

A similar glycogen accumulation was found in the liver of a boy aged 4 years and 10 months who died of pneumonia. The case was handed on to Professor von Gierke from Vienna. Both these children from their birth had had a strikingly full abdomen. In the girl a doctor had noted extreme enlargement of the liver five years before her death, but the nature of this hepatomegaly had never been settled. There had been no splenomegaly in either case, but in the girl the kidneys at the post-mortem examination were double their normal size. The other viscera seemed not to be involved in the chronic metabolic disease. In the liver of the girl Dr. Schönheimer, who undertook the chemical examination, found absence of the glycogen-splitting ferment which can be detected in normal livers. It seemed, therefore, that the enlargement of the liver was due to defective transformation of glycogen into sugar and to the resulting accumu-

* This may not have been the fasting blood sugar.

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.

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- ² Schall, L.: *Munch. med. Woch.*, 1932, lxxix, 2078 (with references to the literature after von Gierke's original paper).
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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

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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.