LIVER DAMAGE IN GASTRO-ENTERITIS

BY

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Jaundice in gastro-enteritis is described as a rare terminal event (Sakula, 1943) and has been commonly regarded as a manifestation of septicaemia, as for instance in Buhl's disease (Capon, 1934). Recent advances in our knowledge of liver disease, particularly in relation to malnutrition, cast considerable doubt on this explanation, and Bonham-Carter (1947) has pointed out the significance of the various pathological changes which are found in the liver in fatal cases of gastro-enteritis. There is some reason to believe that the post-mortem appearances of cell damage, fatty infiltration, and early fibrosis which have been described, alone or in combination, depend to some degree on the severity and duration of the disease. This cannot be confirmed until the exact sequence of events is defined by a systematic study of liver biopsy material.

The purpose of this paper is to put forward further views regarding the cause of these liver complications, based chiefly on clinical observation, and to describe a method of treatment which has proved successful in a condition which up to the present has almost inevitably proved fatal.

In five of the six cases about to be presented, clinical evidence of severe liver damage was found. In the sixth some of the features which can be recognized as a syndrome were lacking, but as it compared so closely in other respects to the group as a whole it has been included in the series.

Potassium deficiency was the other striking change and was present in all six patients. The serious effect of loss of this salt from the system in gastro-enteritis and the reduction of mortality when it is made good have been described by Darrow (1946). We have confirmed this in many instances without obvious liver failure, but its association in the present series is noteworthy and calls for consideration of a possible relationship.

Clinical Picture and Incidence

Enlargement of the liver, which often appeared rapidly, jaundice, and haemorrhagic phenomena associated with a low prothrombin time were taken as evidence of liver damage. Oedema followed a

constant initial stage of dehydration and was considered to be closely related to the general metabolic disturbance. Speculation as to the cause and effect would be premature, since arguments can be deduced only from the beneficial results of combined therapy. The duration of gastro-enteritis before the onset of these complications was variable. In four infants profuse diarrhoea with some vomiting had been present from two to three weeks; in two others a much longer gastro-intestinal upset was reported. In all six the chance of any serious underlying defect is rendered unlikely by their after-history.

Severe pyogenic infections developed in four cases, but only in one was a focus present before the onset of liver damage. Polymorphonuclear leucocytosis was found at the height of the disturbance. It is a feature of acute liver failure in adults and need not, therefore, mean infection in our cases. There was no evidence of urinary infection except in Case 5, where it occurred late in the disease and was one of a number of secondary septic complications. An erythematous rash was present in two cases, both of whom were receiving various drugs at the time, including potassium, but it did not conform to the description of a diffuse erythema from potassium over dosage (Govan and Darrow, 1946), and the serum potassium was never abnormally raised. In all cases there was severe dehydration. Oedema was often gross at the worst stage of the illness.

Variations from the typical clinical picture just described were also encountered. Jaundice was absent in one instance (Case 3), a haemorrhagic tendency was lacking in another (Case 2), and in a third (Case 4) the only definite evidence of liver impairment was a raised serum bilirubin. Minor degrees of the condition undoubtedly occur, and in seventy consecutive cases of gastro-enteritis observed over the same period without obvious liver failure, three had a raised serum bilirubin (1 or 2 mg. per cent.) and three produced altered blood in the stool or vomit as special isolated features. In one other there was prolonged bleeding from an intravenous wound and a lowered prothrombin index. Considerable enlargement of the liver was also discovered in some severe cases with subsequent reversion to normal size without special treatment. It appears, therefore, that any idea of the incidence depends on the criteria used and the care with

which they are sought in the diagnosis of the disorder.

The cases presented in this paper had an easily recognizable clinical picture probably because they were extreme examples of the condition. Jaundice from our experience is a most ominous sign, and unless energetic treatment is undertaken is always liable to end fatally. Before its true significance was realized, this complication was noted in eight out of 300 cases of gastro-enteritis treated in the hospital during the last two years. Only two of the eight survived. In another series of 159, seven developed jaundice and died (Giles and Sangster, 1948). Of 216 cases described by Gairdner (1945), twenty-three became jaundiced, again with a uniformly fatal result.

Clinical Investigations

A regular procedure was adopted in examining our cases and will be found incorporated in the charts which follow. Reference here will be made only to those clinical findings and investigations which presented some difficulty in accurate interpretation.

LIVER SIZE. This was measured in finger-breadths below the costal margin, changes being recorded only when they could be recognized as certain. A liver palpable at one finger's-breadth is generally regarded as normal for an infant. Though alterations within this limit may be significant, other factors such as the level of the diaphragm must be taken into account.

DEHYDRATION. The degree of dehydration is always difficult to estimate clinically. In our cases the notation +++ is reserved for the most severe examples of the condition, while a single + indicates a significant loss of skin elasticity.

OEDEMA. This is recorded only when its distribution was general.

DIARRHOEA. In diarrhoea the number of stools alone can be misleading; therefore definite alteration in their character is also mentioned in the protocols.

PLASMA PROTEIN. This was measured by the specific gravity method.

PROTHROMBIN TIME. This was calculated as a prothrombin index (Innes and Davidson, 1941) which has fallacies but was found a sufficiently reliable test when repeated for comparison in the course of the disease, and has obvious advantages in the simple technique and the small amount of blood required.

LIVER FUNCTION TESTS. No special liver function tests were carried out as a routine. In the earlier fatal cases, to which reference has been made, the alkaline phosphatase was only twice higher than twenty and the thymol turbidity normal more often than not.

Pathogenesis

LIVER DAMAGE. A parenteral pyogenic focus of infection can be excluded as it was present only in

one case in our series at the relevant stage. Bonham Carter's observations on post-mortem material give further support to the view that septic infection plays no major part in the cause of this complication, as in half his cases there was no evidence of such infection. Virus liver disease produces its own characteristic picture, quite unlike the syndrome we have described. The possible effect of toxic amines produced by abnormal enzyme activity of bowel flora (Gale, 1940) remains an open question.

Some nutritional deficiency seems to be the most likely factor and would fit in best with the course of the disorder and the limited histological investigations of the liver which have been made. If this were the pathological basis a good response might be expected to therapy which aims at restoring essential elements in the diet, since these, in common with all the food offered, have been largely lost through diarrhoea or vomiting.

As already stated, it is not possible as yet to present a clear picture of the morbid anatomy of the liver. In a few fatal cases in the past which we have studied the histological changes have not been constant and did not fall into one of the distinct groups so well defined by Himsworth (1947). In fact a number of changes have been found, not necessarily in association, namely fatty infiltration, dilation of sinusoids, parenchymal degeneration, and cellular necrosis with round cell infiltration. Early fibrosis was also occasionally present.

By analogy with experimental work and with the recent descriptions of fatty liver disease of infants in the tropics, lack of a lipotropic agent would appear to be the most likely cause of hepatic complications in gastro-enteritis. Fatty infiltration would well explain the slow return of the liver to its normal size under appropriate treatment. On the other hand it would not explain the acute onset of symptoms, rapid enlargement of the liver, and grave course of the disease, which are more in favour of a process resembling acute necrosis. Therefore, both on clinical grounds and from the post-mortem evidence, there is some reason to believe that the liver lesion in gastro-enteritis may combine features of the two main types of damage known to occur in experimental and human examples of hepatic disease.

DISTURBANCES OF FLUID BALANCE. In liver disease a high water content is characteristic of the lesion known as massive necrosis (Himsworth, 1947), and is thought to be a result of pathological change within the cell. In gastro-enteritis puzzling shifts of tissue fluid are related to electrolytic imbalance, where loss of intracellular potassium is the prime cause and transfer of sodium from the extra- to the intracellular compartment with reduction in the extracellular fluid an effect (Darrow et al., 1948). Although in most experimental procedures the change takes place chiefly in the muscles, its occurrence in the human liver in states of dehydration and shock is a possibility (Darrow, 1945).

The oedema of malnutrition can no longer be

regarded as a simple osmotic effect of hypoproteinaemia (Denz, 1947; Henschel et al., 1947), and this is in general borne out by the inconstant relationship of plasma protein level to the occurrence of oedema in our cases. All of them were given oral or intravenous fluid but seldom more than was adequate for their needs and to make good their continued losses. Therapeutic over-hydration cannot, therefore, be accepted as a cause of the oedema. There was never any clinical suggestion of cardiac failure.

A low serum potassium was present in all cases and it should be stressed that a normal serum level does not necessarily exclude cellular deficiency (Miller and Darrow, 1940). Exactly how potassium loss occurs in gastro-enteritis is not fully understood; certainly it is out of proportion to the degree of tissue destruction and quantity passed in the stools (Darrow, 1946). We have observed two effects in all forms of gastro-enteritis when such a deficit is not made good: difficulty in rehydration despite massive quantities of fluid by any route, and a tendency to oedema. Administration of potassium orally or in urgent cases intravenously, brings about a rapid return to normal and points to potassium as an important determining factor in the proper distribution of water.

HAEMORRHAGE. Except in Case 3, in which the bleeding time was prolonged, investigation was confined to the prothrombin time. Haemorrhage from the bowel or stomach mucosa was clearly related to hypoprothrombinaemia and was quickly controlled soon after treatment began. Hypocalcaemia was not found.

To summarize our ideas of the pathogenesis, we believe that infants who survive the acute period of severe dehydration have necessarily passed through a severe state of malnutrition and may thus readily suffer from liver failure later in the course of their disorder. Should they succumb, histological evidence of liver damage might be expected and has in fact been found. Clinically, minor degrees of this complication have been mentioned, where presumably the process had taken a milder course as a result of a more favourable balance of intake over loss, and had spontaneously been arrested as the diarrhoea ceased. The same argument applies to potassium deficit, since cow's milk contains 1.54 g. of this electrolyte per litre and if re-alimentation is not long delayed is sufficient to supply the child's needs.

Treatment

The decision to treat these cases with large doses of protein was first taken on the supposition that fatty infiltration was the main pathological change in the liver and with the knowledge that methionine has a strong lipotropic action. Protein, it was argued, would also supply badly needed nitrogen

and calories. Later, when the lesion was suspected to be of a more complex nature, justification for this form of therapy appeared even greater, since more than one of the amino-acid constituents of the protein molecule might be required (Witts, 1947).

There is some reason to believe that intravenous human serum in adequate amounts would prevent this complication of gastro-enteritis (Alexander), but regular parenteral alimentionation in all cases has its restrictions and disadvantages. The oral route was favoured on general principles and casein hydrolysate chosen in the belief that it would be the most readily absorbed of any form of orally administered protein. Large amounts were given, as it had been shown that these could be taken without ill effect (Palacky, 1947). On the rare occasions where persistent vomiting precluded oral administration, casein hydrolysate was given intravenously. For various reasons this form of protein was preferred to serum. The main object was to present the liver immediately with all the essential amino-acids. If this depended on the breakdown of serum protein it was thought there would necessarily be some delay in their supply (Eckhardt et al., 1948). Nevertheless in analysing the results any serum given has been taken into account, the protein content being reckoned as 6 g. per cent., and in one case this proved highly significant.

The preparation used was 'casydrol' (Genatosan) which the makers claim contains all essential amino-acids, with peptides in the proportion of about 40 per cent. Analysis revealed methionine in a concentration of 3 per cent. in the intravenous preparation, that is 0.075 per cent. in the solution as administered, and 1 to 2 per cent. in the oral powder, with cystine in considerable amounts. Oral 'casydrol' consists of equal parts of hydrolysed protein and lactose. It was given diluted in water or in breast milk in concentrations up to 15 per cent. (that is 7.5 per cent. casein hydrolysate). Beginning with small amounts, the quantity of 'casydrol' was gradually increased to 60 to 80 g. a day, and the largest amount given was 120 g. a day. Breast milk was used in the belief that it is the most easily digestible, and was introduced early in most cases. Intravenous 'casydrol' was administered in 2.5 per cent. solution with 5 per cent. glucose. These sugar additions are valuable in supplying calories, sparing protein, and overcoming ketosis. Intravenous 'amigen,' which was used in one case, has the same proportions of casein hydrolysate and glucose as the intravenous preparations of 'casydrol.'

Intravenous fluid except where otherwise stated was supplied as half-strength Hartmann's solution with 5 per cent. glucose. Routine intravenous treatment in this hospital has for some time been alternate bottles of this solution and half-strength serum or plasma. Though not always regularly

followed for various reasons, it was in general applied to these cases, some of which received considerable amounts of whole protein. In the discussion which follows it is referred to as serum.

Potassium chloride was given intravenously when urgently required, as indicated by persistent fluid imbalance and low serum potassium levels. A 1 to 2 g. dose was added to the total amount of intravenous fluid given over the twenty-four hours, and this dosage was continued by mouth as soon as adequate absorption seemed likely until full feeding was established. Reference to the records shows that the intravenous route was used with caution and with frequent checks on the serum potassium. Our usual practice is to give the salt by mouth in the absence of severe vomiting or unless an intravenous has been set up to meet fluid needs. In the present series the oral route, even when relied upon from the start (Case 1) was quickly effective and quite adequate for maintenance purposes in all cases.

Extra sodium was supplied as 1/6th molar lactate, orally or intravenously, where required (Cases 2, 3, and 5).

Vitamins were administered as indicated on the records. Special importance was attached to the B-group for its possible lipotropic action (Himsworth, 1947) as well as its general value. Beminal* was chosen for injection, later replaced by Benervat† tablets by mouth.

Choline was given as an additional lipotropic agent at the suggestion of Dr. Elgood, who has since reported on its value (Elgood, 1948), but the dosage and upper limits of tolerance in human disease are unknown (Leading article, *British Medical Journal*, 1945). If a weight for weight comparison is made with experiments on growing rats, approximately 1 g. per day would be necessary to cure fatty infiltration in an infant.

Chemotherapy was employed for specific infection and on occasion empirically.

Results

All six infants recovered from the dangerous condition with which we are concerned; one died later from a septic complication. The haemorrhagic diathesis was the first to clear up in a few days; fading of the jaundice and disappearance of the oedema followed next, but it usually required some weeks before the liver returned to its normal size. Cases 1, 2, and 4 were satisfactory from the first. Recovery in Case 6 was slower, and though full investigations were not carried out and late sepsis complicated the picture, the prolonged course and failure to restore fluid balance was probably related to potassium deficiency which was not

specifically corrected. Protein in this case was supplied at a rate that proved adequate in others. In two (Cases 3 and 5) the hepatic and metabolic disturbance cleared up rapidly with replacement therapy, but severe gastro-intestinal symptoms continued for some time.

Casein hydrolysate was generally well tolerated by mouth, in keeping with the experience of others (Lewes, 1944; Shohl, 1943; Hartmann et al., 1944), but the number of cases is too few to permit a final opinion on this point. It was certainly encouraging to find the digestion settling well at the height of treatment (Cases 1, 2, and 4). In Case 3 overdosage of casein hydrolysate is a possibility, and although the azotaemia (Jan. 19 to 24) was probably the result of dehydration and oliguria, the amount of protein offered (7 to 10 g. per kilo) at the time might well have proved too great a tax on the kidneys of an infant suffering from a reduced blood volume. In this patient, also, the adequate store of protein derived from intravenous serum previously given and proper correction of electrolytic balance had already begun to promote recovery before oral casein hydrolysate was started.

No previous records existed from which the optimum dosage of casein hydrolysate could be deduced: 10 g. per kilo had been estimated as the upper limit of assimilation (Elman, 1947). In our cases the result of intravenous treatment gives perhaps the clearest guide, and 1 g. per lb. per day was associated with good recovery (Case 5). With the wastage that is bound to occur in diarrhoea, the daily dosage of casein hydrolysate required by mouth is likely to be higher and more in the region of 2 to 4 g. per lb. body weight per day (Cases 1 and 2).

Complications

Except for some soreness of the buttocks, no complications occurred from oral administration of 'casydrol.' Vomiting, unless already a feature of the case, did not occur. The intravenous route on the other hand had disastrous complications. Even with careful precautions the prolonged period of slow administration of such a suitable culture medium carries the continual danger of chance bacterial contamination. Septic complications of the severest kind were encountered (Cases 5 and 6). We have since found that 1/20,000 merthiolate is an effective sterilizing agent, and no ill effects have been noted from its use.

Prognosis

The grave danger of hepatic failure in gastro-enteritis has been stressed and the good response to special treatment demonstrated. Late development of hepatic fibrosis cannot be excluded, but the return of the liver to its normal size, usually within a month of clinical recovery, makes this unlikely. No such complication has been found in the follow-up of our cases to date.

* Beminal contains 10 mg. of thiamine, 25 mg. of nicotinic acid, and 0.5 mg. of riboflavin, pyridoxine, and pantothenic acid.

† Benervat tablets contain 1 mg. of thiamine, 15 mg. of nicotinic acid, and 1 mg. of riboflavin.

Conclusion

Jaundice is an uncommon but well recognized complication of gastro-enteritis, and a very serious condition. Evidence has been produced that liver damage may arise from severe metabolic disturbances which follow acute states of nutritional failure. Extreme examples of the condition are recognized by jaundice, enlargement of the liver, and a haemorrhagic diathesis. Oedema is often present. Variations have been observed in the clinical picture, and milder forms are mentioned. Post-mortem investigations so far undertaken reveal two main pathological features: cell damage, and necrosis or fatty infiltration; but further studies are needed to elucidate the exact nature and order of events in the liver.

It is suggested that protein deprivation is chiefly responsible for the pathological changes in the liver, and the excellent clinical response obtained where it is supplied in an assimilable form is in favour of this theory. Dehydration and loss of potassium are

also thought to play their part in the pathogenesis, and restoration of fluid, electrolytes, and this salt in particular is an essential part of the treatment.

Casein hydrolysate by mouth has proved an efficient method of providing the necessary protein when other forms requiring digestion were not tolerated. On occasion recourse had to be made to the intravenous route. This has the serious danger of infection, and a method has been described to prevent such an occurrence.

We are indebted to Sister Knapman and her nursing staff for their indefatigable care of these patients, for it is largely due to them that these children's lives were saved.

We should also like to thank Dr. Martin Bodian for his interpretation of the histology in the fatal cases.

Appendix: Case Histories

In the charts which follow, the line for weight is broken at the addition or removal of a splint.

FIG. 1.—Chart of Case 1.

COMMENT. There was no focus of pyogenic infection and the urine was sterile on admission. Penicillin and sulphadiazine were given to cover the risk of possible infection from previous intravenous treatment, the wounds being very dirty, but there was no phlebitis. The absence of any haemorrhage is thought to be related to prompt treatment.

Case 3 (W.M.), Aged 5 months

GASTRO-ENTERITIS; SEVERE HAEMATEMESIS AND PURPURA; PRO- LONGED DIARRHOEA; RECOVERY

A healthy baby weighing 14 lb. 8 oz. developed severe enteritis fourteen days after admission to hospital for dilatation of

anal stricture. On the seventh day of illness and while still on an intravenous drip he developed mild generalized oedema to which an excess fluid intake contributed. Its subsidence by the next day coincided with a deceptive appearance of general improvement which, though not apparent on the chart, was sufficient to persuade observers that he had turned the corner, and the first intravenous drip was completed with a blood transfusion. Watery diarrhoea continued, and progress is recorded on the chart from the eighth day of his illness.

A macular rash which appeared soon after admission and lasted a few days was thought to be caused by a barbiturate. The profuse watery diarrhoea was unaffected by two twenty-four-hour periods of starvation. On the thirteenth day there was bilateral suppurative otitis media, the drums

FIG. 3.—Chart of Case 3.

having been normal three days before. On the fourteenth day there was extensive purpura and haematemesis, sudden gross enlargement of the liver, and slight puffiness of the face, but no generalized oedema. Oral casydrol was begun. Intravenous treatment included potassium chloride, 1/6 molar lactate, blood, and much serum. After seventy-two hours the purpura had gone and there was no more haematemesis or melaena. The liver returned to normal size quickly, although profuse diarrhoea continued, needing further prolonged treatment. There was no jaundice. The urine was sterile (fig. 3).

COMMENT. Though initial doses of casydrol were small, the intravenous serum must be taken into account as a source of protein. In the six days before symptoms of liver damage developed, daily protein intake by mouth was at the rate of 1 g. per lb., much of which must have been lost, and 0.6 g. per lb. intravenously. In the first three days after the onset of these symptoms 0.3 g. per lb. was supplied orally as hydrolysate and 0.8 g. per lb. intravenously as serum. In this case high oral dosage of casein hydrolysate later was associated with continued diarrhoea.

FIG. 4.—Chart of Case 4.

Case 4 (J.P.), Aged 4 months

GASTRO-ENTERITIS; SCANTY PURPURA AND LIVER ENLARGEMENT OF UNCERTAIN SIGNIFICANCE; SEVERE DEHYDRATION; RECOVERY

This baby, with a history of twenty-seven days' diarrhoea and vomiting, was treated for fourteen days in a local hospital with two three-day intravenous infusions of normal saline and a blood transfusion (no intravenous fluid was given for the last five days), and a dried milk mixture supplying an average fluid intake of 3 oz. per lb. The stools improved but hydration became inexplicably worse. On March 2 the liver was found to be palpable at one finger breadth, and it was firm; there were petechial haemorrhages on the palate, conjunctivae, and skin flexures, and also slight generalized oedema which had gone by the next day. The baby was admitted to the Hospital for Sick Children on March 3, and progress is recorded on the chart from that time. The urine was sterile. There was no focus of pyogenic infection (fig. 4).

COMMENT. This case did not present the full clinical picture described in the other five. Bleeding was confined to small haemorrhages in flexures and palate. Prothrombin index was normal. Liver enlargement was not remarkable, but did subside slightly. There was no jaundice, though serum bilirubin was raised. Serum potassium was very low. She was at the time of her transfer in a phase where hydration was obviously difficult to achieve despite a good oral intake and the development of slight oedema. Uninterrupted oral feeding throughout her period of treatment in the local hospital is noteworthy. Her state at the time of transfer is to be compared with Case 2 on Jan. 28 to 29, with Case 5 on March 7 and with Case 1 on March 29 to 30. Oral casydrol was well tolerated in large doses. Chemotherapy was given to cover the risk of a blood-stream infection from previous intravenous infusions.

Case No. 5 (R.P.), Aged 8 months

GASTRO-ENTERITIS; JAUNDICE AND HAEMORRHAGE; SEPTIC COMPLICATIONS; RECOVERY

This baby was sent to hospital for investigation of vomiting. He had a history of 'vomiting' since birth, and of passing two or three stools a day, sometimes green and slimy, from the age of five months. Some degree of mismanagement, including over-feeding, was partly responsible for these symptoms. He was weaned, vomiting ceased, and in ten days he went home weighing 17 lb., having brief pyrexia on Feb. 23 and 24. After three days he vomited, refused feeds, had offensive stools, and became collapsed. On re-admission on Feb. 29 he was having frequent effortless vomits and was put on an

intravenous drip. Progress is recorded on the chart from this time.

The first stool was virtually normal, but with resumption of oral feeds diarrhoea became profuse and watery. Haematemesis began on March 7 and jaundice with enlargement of the liver appeared soon afterwards. Vomiting was copious, and little given by mouth was retained. An attempt to combine oral feeding with intermittent gastric drainage was unsuccessful. He was given by the intravenous route casydrol 2.5 per cent. glucose 5 per cent., electrolytes, including potassium and extra saline, serum, and blood. The parenteral supply at the critical stage, March 7 to 16, was at an average daily rate of 1.2 g. of protein and 18 calories per lb. (1 g. casein hydrolysate and 0.2 g. serum per lb. body weight). Oral feeding was tried with casydrol in approximately 12 per cent. solution (6 per cent. casein hydrolysate) reduced to 3 per cent. (1.5 per cent.) and omitted after a week as dilute breast milk was introduced. On March 12 there were the first signs of left otitis media, which on March 13 yielded pus. On March 13 there was a general maculo-papular rash. On March 14 pus and *B. coli* were found in the urine and a blood culture grew *Staphylococcus aureus*. The worst of the metabolic disturbance was not over, but watery diarrhoea continued for some days, with some substance in the stool on March 17 and the first formed stool on March 21. Subsequent illness was prolonged, with the development of multiple abscesses, and on April 5 meningitis (no organisms cultured), from which recovery after treatment with penicillin and streptomycin was complete. The liver was one finger breadth on April 4 (fig. 5).

COMMENT. Jaundice, a grossly enlarged liver, and haematemesis developed after a thirteen-day illness in which vomiting of unusual severity had been a feature. At this stage there was no pyogenic infection. Evidence of liver damage regressed quickly under treatment. There were two phases of moderately severe dehydration. Oedema was present, but not gross. At first potassium was not supplied adequately. In addition a queer electrolytic disturbance developed, which has been seen since in other

cases, consisting of continued loss of chloride in the urine despite low serum chloride and sodium. It may in part explain the lack of any gross oedema. No adrenal cortical extract was given. Suppurative phlebitis developed at some of the intravenous sites, and though the bottles were not cultured, there is good reason to suppose it was the result of contamination during the long period of suspension. Chemical irritation did not seem to play any part, as only a proportion of the veins used were affected.

Our thanks are due to Dr. Wilfrid Sheldon for permission to publish this case.

Case No. 6 (L.W.), Aged 1 month

GASTRO-ENTERITIS; PROLONGED JAUNDICE WITH RECOVERY; LATER DEATH FROM SEPSIS

This baby's birth weight was 7 lb. She was breast fed. She was born in a nursing home, where she had diarrhoea as part of a small epidemic. Stools 'improved' but vomiting and difficulty in feeding continued, with failure to gain weight. There was severe diarrhoea and vomiting for one week before

FIG. 5.—Chart of Case 5.

admission, and jaundice for two days. The urine was sterile. Progress is recorded on the chart from admission on Oct. 3, with jaundice and enlargement of the liver as marked features.

Phlebitis developed on Oct. 8 proceeding to cellulitis, with *B. coli* on culture, the same organism being grown from a bottle of 'amigen'. On Oct. 20 she was found to have *B. coli* meningitis, successfully treated with streptomycin. From about this time the stools, though frequent, were minute in quantity and semi-formed. On Nov. 8 there was a low-grade staphylococcal abscess at the site of a previous intravenous injection, and on Nov. 20 she was found dead. At autopsy an unsuspected staphylococcus lung abscess was found. Histologically the liver showed no fatty infiltration or fibrosis (fig. 6).

COMMENT. Close inquiry into the history revealed that the stools were never normal from the time of the first diarrhoea. There was no infective focus when liver symptoms developed. Signs of liver damage slowly subsided over two weeks. Protein was supplied during this time at an average daily rate of 2.1 g. per lb., of which 0.8 g. per lb. was intravenous as serum and casein hydrolysate and the rest oral, for the most part as breast milk. Severe diarrhoea continued. No extra potassium was given. Hydration was never satisfactory and, despite a fluid intake that was not excessive, pronounced oedema developed, clearing rapidly as subsidence of diarrhoea permitted resumption of normal feeding. Meningitis was a complication of treatment. Death was from a later and unrecognized similar pyaemic complication.

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FIG. 6.—Chart of Case 6.

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