(Selzer, Parker & Sapeika, 1951). It is possible that children in Jamaica might be exposed to toxic factors of this kind, since from an early age they are given bush teas—that is, infusions of local plants. At the same time, Rhodes (1952) has shown that the children in whom this liver lesion develops present evidence of chronic and marginal malnutrition, and that their diet is very low in protein. Thus it seems possible that in these children ingested toxins are able to damage a malnourished but not a normal liver. This suggestion recalls the experimental work of Miller & Whipple (1940) some years ago.

These two examples illustrate the complexity of the problems with which we are faced in any attempt to disentangle the causes of hepatic fibrosis and cirrhosis in the tropics.

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Dietetic Aspects of the Treatment of Liver Disease

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General considerations

Rest. Regardless of dietetic considerations, there seems little doubt that one of the most important factors in the treatment of liver disease is adequate bed rest. It is now known that the circulation to the liver is decreased by the upright position

(Bradley, Ingelfinger & Bradley, 1952). This quite obviously would have an undesirable effect on the metabolic processes concerned with the recovery of a diseased organ. Similarly, after acute liver disease clinical experience also indicates the importance of graded exercise in the convalescent stages. Not infrequently, too sudden an assumption of activity will precipitate a relapse.

Carbohydrates. We know that liver cells are less susceptible to toxins when the glycogen reserves are good (Graham, 1915). Glucose is therefore administered freely to all patients with liver disease. Although it may be given by mouth, one should remember that the aim is to suppress hepatic glycogenolysis and for this purpose an appropriate level of the blood sugar must be maintained. Regardless, therefore, of the patient's ability to take food by mouth, glucose should be given intravenously if the disease seems sufficiently severe to merit it (Portis & Weinberg, 1952).

Protein. Patients should be adequately supplied with proteins rich in sulphur-amino-acids. Soluble casein is very satisfactory as a dietetic supplement. One aims at a total protein intake of some 200 g daily. In order to produce a protein-sparing effect, it is advisable to construct the diet so that it supplies more than 3000 Cal. This can be fairly easily done by adding carbohydrate foods. It is perhaps important to emphasize here that a good caloric intake can also be provided by fats and that it is probably erroneous to maintain a low-fat diet. Fried fats should be avoided since there seems little doubt that they tend to produce marked nausea and loss of appetite. Various attempts must be made to stimulate the patient's desire for food since anorexia is a very common accompaniment of liver disease. Meals should be presented in an attractive fashion. On occasion, crude-liver extracts injected intramuscularly increase the appetite quite remarkably.

In the acute stage of a severe liver disease, as in infective hepatitis, a large protein intake may well be an unnecessary strain on the capacity of a damaged organ. Usually the problem is solved by the fact that for some days the patient will not eat more than a fraction of what he is given. With return of the appetite it is best to increase the protein intake gradually.

Protein hydrolysates given intravenously have also been recommended. These often cause a good deal of trouble in the form of localized thrombophlebitis and thrombosis, which can sometimes be avoided by adding heparin to the infusion. I have never really convinced myself of the efficiency of hydrolysate treatment, especially since it is now known that the amino-acids of the blood are already much above normal in severe liver disease (Dent & Walshe, 1951).

Vitamins. Ample amounts of the vitamin B complex are usually prescribed because of the general importance of these substances in cellular oxidative mechanisms and their possible lipotropic effect. Not the least important is their effect in stimulating appetite. Ascorbic acid is said to protect against some hepatotoxins and is believed to improve the resistance of the liver cells. Folic acid is very useful in the treatment of the macrocytic anaemia often associated with severe liver disease. Cyanocobalamin has no therapeutic effect on this anaemia. Some authorities, however, recommend its administration in liver disease on the grounds of its well-known effects on nucleoprotein and protein metabolism as well as its possible lipotropic action.

Vitamin A deficiency is common in liver disease. It is due largely to impaired absorption owing to deficiency of bile and possibly, in man, to impaired conversion of carotene. There is also defective absorption of vitamin D, as well as the possibility that additional amounts of this vitamin are required in hepatic dysfunction. For these reasons, 5000 i.u. vitamin A and 1000 i.u. vitamin D are given once or twice daily. Vitamin K and α-tocopherol have a more specific application. The former given intramuscularly is important in restoring the lowered plasma prothrombin of patients with obstructive liver disorders. There is also a growing clinical impression that, though its administration to patients with hepatocellular disorders does not affect the level of the plasma prothrombin, it does act as a deterrent to the haemorrhagic tendency. The explanation of this phenomenon is not known (Lichtman, 1949). α-Tocopherol plays a significant part in relation to the sulphur-amino-acid requirements of the liver cell and for this reason it is wise to administer it quite freely to patients with hepatic disorders, especially since plasma levels are low in cirrhosis. These are believed to indicate depleted stores (Klatskin & Molander, 1952).

Lipotropic agents. There are several reports of improvement in patients with cirrhosis and other liver disorders treated with choline or methionine or both (Franklin, Salk, Steigmann & Popper, 1948). The administration of these substances is based on the concept that liver failure in this condition is at least in part due to the accumulation of fat in the surviving cells. Removal of the lipid material could be expected to improve intracellular metabolic conditions. Methionine has also been found useful for prophylaxis in workers coming into frequent contact with hepatotoxins used in industry.

Electrolytes. It is now becoming increasingly recognized that liver disease may be associated with profound disturbances of the body electrolytes. In severe liver failure the blood potassium tends to fall to low levels (Latner, 1950; Artman & Wise, 1953). This may in part be due to the glucose therapy, as well as to more direct effects of the disease itself possibly related to the frequent association of a kidney tubular defect.

There is also a marked tendency for retention of sodium in cirrhosis especially if accompanied by ascites (Layne & Schemm, 1947). It is probable that this retention is in some way connected with the low levels of serum albumin. It is interesting to note that the serum sodium tends to be diminished (Schwarz, Siegmiller, Phillips, Gabuzda & Davidson, 1953).

Thus in all conditions of severe liver disease the electrolyte content of the blood should be estimated fairly frequently and the necessary salts administered or withheld in order to restore normality.

Severe and acute liver disease

When liver disease is very severe the patient is often comatose. Even when consciousness is not unduly affected, there is very profound anorexia, so nutriment must be given intravenously.

A number of authorities have advocated the use of amino-acids intravenously in addition to glucose. I have never obtained much success with such a régime.

In a group of cases with 'acute yellow atrophy' as well as in cases which would be more accurately described as severe infective hepatitis, good results have been obtained with an intravenous régime consisting of glucose, saline, potassium chloride and massive doses of thiamine, nicotinamide and riboflavin (Latner, 1950). α-Tocopherol is given intramuscularly in addition to vitamin K. Large doses of antibiotics are also administered. It is interesting to note that the latter have been amply justified in the light of more recent research related to the nutritional production of liver necrosis.

The following is a description of a case treated in this way. A young doctor was admitted to hospital intensely jaundiced and in a stuporous condition. He had been suffering from infective hepatitis with demonstrable hepatomegaly. On the day of admission clinical examination had demonstrated a sudden marked diminution in the size of the liver. He lapsed into coma half an hour after admission and remained in this condition for 2 weeks. The intravenous régime had been instituted immediately and it became necessary to carry out feeding by stomach tube on the 10th day. He recovered from the coma and in spite of the fact that he developed generalized serous effusions, a mild hemiparesis and haemorrhagic phenomena, he eventually made a complete recovery. He is now in good health, 2 years after his attack.

In a fairly large group of cases, the survival rate is now approximately 80%. There has been a remarkable absence of *sequelae* after recovery.

Surgical aspects. The regime just outlined has been found very useful in combatting liver failure occurring after cholecystectomy as well as in the preparation for operation of severely ill patients with biliary-tract disorders. On several occasions the plasma prothrombin has returned to normal levels in spite of the fact that vitamin K alone over a period of a week had previously had no effect. Similar successful uses of the regime in surgery have been reported by others, for example in the treatment of coma occurring after porto-caval anastomosis performed for portal thrombosis complicating cirrhosis (Hunt & Whittard, 1954).

Cirrhosis. The most effective treatment of uncomplicated cirrhosis is the high-protein diet already discussed. Some authorities combine it with lipotropic agents. There should also be an ample supply of vitamins. There is still some disagreement on the question of consumption of alcohol. Drinking is important, since it deprives the patient of money he needs to afford a high-protein diet, and may also necessitate a greater intake of protein to cover the caloric effect of the alcohol (Best, Hartroft, Lucas & Ridout, 1949).

Ascites. Good results in the long-term therapy of ascites are obtained by a regime in which the patient is given large amounts of protein and also mercurial diuretics. These are administered in an attempt to induce diuresis and remove some of the sodium and water retained by the body. Over a number of years, we have had quite good results following therapy of this nature. I can well remember two cases both of which did remarkably well.

Case 1: The patient, an accomplished pianist, aged 70, had been bedridden for a year. Paracentesis had to be performed at 10-day intervals. Within a few months of

commencing therapy it was no longer necessary to carry out frequent removal of the ascitic fluid and the patient was easily able to leave his bed. He returned home from hospital, the interval periods between paracenteses gradually became longer, and he lived a more or less normal life for a man of his age. Throughout therapy, his appetite was stimulated with a crude-liver extract. He died at the age of 74.

Case 2: This patient, a man aged 47 years, was first seen in 1950. His abdomen was widely distended and he had become bed-ridden. The therapeutic régime was instituted. At first, frequent paracenteses had to be carried out, these gradually became less and less frequent and were no longer necessary after 2 years of therapy. He was then living a more or less normal life. His liver-function tests were also normal. He developed urinary symptoms in 1954, and whilst under investigation in hospital he vomited and unfortunately developed an inhalation bronchopneumonia from which he died.

The question of limiting the dietary salt intake is somewhat debatable. There is a tendency for development of the low-salt syndrome. On the other hand, quite good results have been obtained with a low-sodium régime combined with the therapy already outlined (Atkinson, Paton & Sherlock, 1954).

It is interesting to note that the low sodium intake can be relaxed when the serum albumin has returned to normal levels as a result of therapy, and after 10–40 months an unrestricted sodium intake may be allowed (Eisenmenger, 1952).

In spite of the good results of long-term therapy, paracentesis is still unfortunately the most effective immediate form of treatment. It must be remembered, however, that the ascitic fluid contains fairly large quantities of protein which the liver will have to regenerate.

Portal hypertension with severe haemorrhage. The treatment of this condition is undoubtedly surgical and involves the production of some form of vascular anastomosis between the portal and systemic systems. Diet, however, plays a large part in preparing the patient for operation and also in aiding recovery after operation.

Coma in liver disease

It is important to differentiate coma accompanying acute severe liver disease from that resulting from a long-standing cirrhosis (Anonymous, 1953). In the former instance there is some chance that the liver cells may regenerate after they recover from the acute noxa. With well-developed Laennec's cirrhosis, even when the patient is comatose, there are relatively few necrotic cells; the parenchymal cells have for long been subject to ischaemia which must obviously diminish their powers of regeneration.

As already pointed out, my own régime has given satisfactory results in the acute cases, but it is not nearly so successful with the coma of cirrhosis. Recently it has been claimed that the latter can be reversed by large doses of sodium glutamate (Walshe, 1953). This has been confirmed by a number of other observers. It is claimed that hepatic coma is at least in part due to ammonia intoxication and that glutamate will often overcome it by conversion of ammonia to glutamine. In my

own experience, this type of therapy has not been successful in the treatment of the acute cases, in fact, I formed the opinion that in three cases death was apparently accelerated.

In both types of coma, undesirable serum-electrolyte changes should be corrected.

The cases described were seen in consultation with Professor F. J. Nattrass, Dr R. Mowbray and Dr H. G. Miller.

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