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HEPATIC INSUFFICIENCY

Extensive damage to the liver, as, for example, in portal cirrhosis, is compatible with normal function of liver cells: the disease is then called "well-compensated." Hepatic insufficiency, or hepatocellular failure,[1] results when liver-cell function is impaired and is associated with a number of clinical features resulting from widespread disturbances of physiological mechanisms. The most important of these are jaundice, ascites, fetor hepaticus, and endocrine, circulatory, and neurological changes. Portal cirrhosis is not the only cause of hepatic insufficiency; the syndrome can occur in infective hepatitis and in other forms of cirrhosis. It may be associated with the terminal stages of obstructive jaundice, though it is remarkable how long a patient can tolerate bile-duct obstruction without deterioration in the function of the liver. Interference with the arterial blood supply and occlusion of the hepatic veins (Chiari's syndrome) both lead to liver failure, though portal-vein obstruction does not impair the function of the liver. Bleeding from oesophageal varices is not in itself a sign of hepatic insufficiency, and in patients with extrahepatic portal obstruction the liver is normal. Liver failure may arise insidiously or may be precipitated by alcohol, gastrointestinal bleeding, infections, and operations.

The various forms of hepatic insufficiency are best illustrated by the patient with portal cirrhosis. Ascites in liver disease always implies hepatic insufficiency, and is often accompanied by oedema, oliguria, and jaundice. The serum bilirubin is raised, serum albumin is lowered, and flocculation tests are positive. The lowered serum albumin leads to a fall in colloid osmotic pressure and this appears to be the principal factor in the onset of ascites in certain types of hepatitis.[2] Attempts have been made to determine the critical level of serum albumin in patients with cirrhosis, and J. Post and A. J. Patek[3] give a figure of 3.1 g. per 100 ml. It is well known, however, that ascites may be present at concentrations greater than this, and other factors, such as an increase in portal venous pressure and even in hepatic venous pressure[4] are probably equally important. Whatever the ultimate mechanism, there is little doubt that, as in heart failure, salt retention is responsible for the perpetuation of ascites. The sodium concentration in urine, sweat, saliva, and faeces is negligible, and increased amounts of salt-retaining corticoids, such as aldosterone, have been reported.[5] This abnormality of salt retention provides a basis for the treatment of these patients.

Endocrine changes are also a feature of hepatic insufficiency. These are only partially explained by the theory that the damaged liver fails to inactivate steroid hormones and especially oestrogens.[6] Spider naevi and palmar erythema are perhaps the best known of these signs of liver disease, though they can occur in normal people as well as in pregnant women and in patients with rheumatoid arthritis. For some reason spider naevi are rarely found below the nipple line except on the arms, and this characteristic distribution is difficult to explain on an endocrine basis. Other endocrine changes are gynaecomastia, testicular atrophy, loss of body hair, and menstrual disturbances. The young female with cirrhosis is almost always infertile. Pigmentation and clubbing also result from severe liver disease, though their aetiology is obscure. Patients with cirrhosis may have warm extremities, but do not sweat because of salt retention. A bounding pulse and the presence of capillary pulsation have led to measurements of cardiac output,[7] and this is sometimes increased. The reason for this is not known, but a similar "high output state" may be seen in patients during hepatic coma.

The neurological manifestations of hepatic insufficiency have received more attention recently.[8] They may occur in acute or chronic forms and are characterized by mental and motor disturbances. Changes in behaviour, with confusion and disorientation, may progress to stupor and coma. The coma fluctuates, and it is unwise to give a poor prognosis. A characteristic "flapping tremor" of the outstretched hands may be observed, and this may spread to involve the whole body so that the patient is completely incoordinate. Rigidity and exaggeration of the tendon reflexes are seen, and meningism and epileptiform convulsions can occur. There is often a sweet, musty odour in the breath, which is known as fetor hepaticus and may be a useful sign when the patient is first seen in coma. Fetor hepaticus used to be considered a grave sign, but it is now known to occur

[1] Sherlock, S., *Diseases of the Liver and Biliary System*, 1955, Oxford.
[2] Bjørneboe, M., *et al.*, *Arch. intern. Med.*, 1949, **83**, 539.
[3] Post, J., and Patek, A. J., jun., ibid., 1942, **69**, 67.
[4] Madden, J. L., *et al.*, *Surg. Gynec. Obstet.*, 1955, **99**, 385.
[5] Luetscher, J. A., and Johnson, B. B., *J. clin. Invest.*, 1954, **33**, 1441.
[6] Dohan, F. C., *et al.*, ibid., 1952, **31**, 481.
[7] Kowalski, H. J., and Abelmann, W. H., ibid., 1953, **32**, 1025.
[8] Sherlock, S., *et al.*, *Lancet*, 1954, **2**, 453.
[9] Challenger, F., and Walshe, J. M., ibid., 1955, **1**, 1239.
[10] Walshe, J. M., ibid., 1955, **1**, 1235.
[11] Riddell, A. G., *Postgrad. med. J.*, 1955, **31**, 389.
[12] Atkinson, M., *et al.*, ibid., 1954, **1**, 128.

as a transient feature in patients who are not in coma. The odour is thought to be due to methyl mercaptan and related substances.[9] "Hepatic coma" is believed to be due to poisoning by nitrogenous compounds absorbed from the gut, which either by-pass the liver through extensive portal-systemic anastomoses or are not detoxicated by the damaged liver. The biochemical disturbance is complex, though ammonia appears to play a part, and J. M. Walshe[10] has suggested that there is an interference with ammonia-binding mechanisms in the brain. A. G. Riddell[11] has recently reviewed the mechanism of hepatic coma and made useful suggestions about the management of patients with this condition.

Patients with liver disease must avoid sustaining further damage to the liver. They usually tolerate operations badly, and anaemia and malnutrition must be combated by haematinics and a well-balanced diet. Recent work suggests that high-protein diets, ammonium compounds, and substances such as choline and methionine may precipitate hepatic coma. It is therefore probably both unwise and unnecessary to give excess protein, and methionine and choline should no longer be used in the treatment of liver disease. Alcohol must be forbidden, and sedatives should be used sparingly and in small doses. Infections usually respond best to the newer antibiotics. Regimes based on salt-free diets and mercurial diuretics are often beneficial to patients with ascites,[12] but ammonium chloride should be prescribed with caution. Repeated paracenteses are a drain on protein. Intravenous glucose is useful supportive therapy for the patient in hepatic coma, and Walshe uses large doses of glutamic acid for its ammonia-binding capacity. This drug is valuable in the coma of chronic hepatic insufficiency, but fails to influence the course of massive hepatic necrosis due to infective hepatitis. Although rare, it is this form of hepatic insufficiency which still remains a challenge to the physician's skill in therapy.

EMPLOYMENT OF THE ELDERLY

One of the most interesting of the many problems raised by the ageing of our population turns on the employment of middle-aged and old people. In 1954 a study carried out under the auspices of the Ministry of Pensions and National Insurance[1] showed that six out of every ten men decided not to take their minimum pension at age 65, but to continue at work; and 45% of those who continued said they did so because of financial necessity. For reasons that are obvious enough, official policy tends to welcome the continuation of old people in employment; they may help to expand output in a time of full employment, and, by postponing the age at which they begin to draw retirement allowances, may ease the strain on insurance funds. Some men on reaching the age of 65 are disposed to take their pensions, feeling that they have earned them; some, who might have liked to continue in employment, find the work in which they are engaged to be taxing them too heavily and see little prospect of being able to change to something more suitable. Although under 4% of the men in the Ministry of Pensions study gave "heaviness of work" or "strain" as the reason for retirement, men whose work entailed a possible cause of strain were apt to retire earlier than other men. Unskilled men are usually at a disadvantage. Not for them the sheltered life of the old craftsman, who, in his own time, may well be able to continue to turn out work of a quality and individuality that command a ready market. In heavy industry, such as shipbuilding, some of the more demanding jobs virtually impose a schedule of retirement which, for ordinary mortals, begins to operate long before the age of 65: the skilled men of the yards, no longer able to follow their trade, may be given jobs as gatekeepers, storekeepers, and the like, which at least preserve their contact with the only working life they have known; but there are never enough jobs of the kind to meet the demand, and the unskilled, regarded as having less claim, are unlikely to be able to secure them.

In his study of men engaged in foundry work I. M. Richardson[2] found they were apt to move from heavy to lighter work in their fifties and sixties. More recently, on the other hand, in a study of the job changes of men of different age groups between light and heavy work in a factory making electrical batteries, R. M. Belbin[3] found that the heaviest work was often carried out by the older workers and the lightest by the younger. But, as Belbin himself points out, his results are not altogether comparable with Richardson's. It must be very difficult to establish criteria that will make possible an accurate comparison of jobs by "heaviness." Changes of job in which ill-health was a factor were excluded from Belbin's series but included in Richardson's; and it must often be wellnigh impossible to draw a line, in the case of a man past middle age whose background is heavy industry, between incapacity for work born of, or aggravated by, the aftermath of illness or injury

[1] *National Insurance Retirement Pensions: Reasons given for retiring or continuing at work*, November, 1954, London.
[2] Richardson, I. M., *Brit. J. industr. Med.*, 1953, **10**, 269.
[3] Belbin, R. M., ibid., 1955, **12**, 309.
[4] Thomas, G., and Osborne, B., *Older People and their Employment*, an inquiry made by the Social Survey for the Ministry of Labour and National Service, 1950, London.
[5] MacPhail, A. N., and Ferguson, T., *Glasg. med. J.*, 1955, **36**, 319.
[6] Clark, F. le Gros, and Dunne, A., *Ageing in Industry*, 1955, The Nuffield Foundation, London.
[7] Grant, I. D., *British Medical Journal*, 1955, **2**, 1181.
[8] *Second Report of the National Advisory Committee on the Employment of Older Men and Women*, 1955 (H.M.S.O., 1s. 9d.).