REFRESHER COURSE FOR GENERAL PRACTITIONERS

INFECTIVE HEPATITIS

BY

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It is now generally accepted that infective hepatitis is an infectious disease due to a virus. The condition designated "catarrhal jaundice" since the time when Virchow described a plug of mucus obstructing the lower end of the common bile duct in a fatal case is now recognized as being identical with infective hepatitis. Biopsy and necropsy studies, in many cases conforming exactly to the clinical picture of catarrhal jaundice, have shown without doubt that the underlying lesion is a hepatitis with necrosis of liver cells, especially in the centrilobular zones, disruption of the liver cell columns, and considerable cellular infiltration mainly in the portal tracts.

A closely related disease, apparently identical in its clinical and pathological manifestations, is known to follow the injection of blood or serum from certain donors. This condition, known as homologous serum jaundice, has a longer incubation period than ordinary infective hepatitis—50–140 days compared with 25–36 days—and often has a more severe clinical course and a somewhat worse prognosis.

Epidemiology

In civilian practice large epidemics are rare, though apparently isolated cases and small epidemics are by no means uncommon. Conditions in war, however, especially among the armed Forces, seem to provide ideal conditions for epidemic spread, and in both the recent world wars epidemics of crippling proportions occurred, particularly in the Mediterranean theatres.

Extensive epidemiological studies have suggested two possible routes of infection—by droplet inhalation from infected pharyngeal secretions, or by ingestion of contaminated food or water. The ability to transmit the disease to human volunteers by spraying the throat with nasopharyngeal washings provides confirmatory evidence for droplet infection. On the other hand F. O. MacCallum found in some cases that nasopharyngeal washings were not infectious, but he succeeded in transmitting the disease with faeces given in capsules. These observations suggest that transmission by ingestion of faecal contaminated material is a distinct possibility, since the virus is shown to be present in faeces. The discordant results of different epidemiologists may perhaps be explained by strain variations in different epidemics, some being excreted into the nasopharyngeal secretions and giving rise to droplet infections, while in others excretion is mainly via the faeces, transmission in such epidemics being mainly by ingestion. For adequate epidemic control both routes of infection should be anticipated and prevented so far as is possible.

Owing to the minute quantity of blood or serum that may convey homologous serum jaundice, the most stringent aseptic precautions must be taken to prevent large outbreaks of this type of hepatitis. The use of one syringe and a different needle for each subject in a series of mass injections of any kind has been shown to be inadequate to prevent cross-infection. The only sure technique in such cases is to provide a heat-sterilized

needle and syringe for each subject. Owing to the great increase in the number of blood and plasma transfusions, cases of homologous serum jaundice must be expected to arise fairly often until some satisfactory means of sterilizing the blood and plasma is developed; ultra-violet irradiation has unfortunately been found unreliable.

Symptomatology

It is convenient to consider the clinical manifestations in two stages determined by the appearance of jaundice.

Pre-icteric Stage

In almost every case the appearance of jaundice is preceded by a prodromal phase characterized by gastrointestinal symptoms, particularly nausea and loss of appetite. Fever is often present with its usual accompaniments of headache, malaise, and some general aches and pains. It is rarely severe, though in some cases it dominates the prodromal picture. In most cases the temperature falls with the appearance of jaundice some one to six days after the onset of symptoms. In some cases, however, fever persists for a few days with the jaundice. In a small proportion of cases a period of several days of normal temperature and comparative well-being may intervene between the prodrome and the appearance of jaundice, which in these cases is usually accompanied by a recurrence of the fever for a few days.

The most characteristic and suggestive features at this stage are upper abdominal pain, usually on the right side, and loss of appetite associated with nausea. Vomiting and diarrhoea also occur in about one-fifth of the cases and may result in dehydration. Physical signs are not very helpful. The liver may be enlarged and tender and the spleen just palpable, but the incidence of splenomegaly varies considerably in different epidemics. A useful sign is the development of an acute epigastric pain on sharply punching the lower ribs in the right axillary line.

Icteric Stage

The appearance of jaundice is usually accompanied by some improvement in the subjective well-being of the patient. In severe cases the jaundice is frankly obstructive, the stools are clay-coloured, and constipation is troublesome. In mild cases the stools may remain normal in colour, but in every case the obstructive nature of the jaundice declares itself by the appearance of bile pigment in the urine.

Nearly all cases run a benign course, the jaundice and symptoms gradually subsiding in one to three weeks. When the jaundice has completely cleared and the patient is becoming convalescent there is a well-recognized tendency to relapse and the reappearance of the jaundice. These patients usually make a complete recovery after a further period of rest in bed. A more serious variation from the usual course is for the jaundice to persist for several weeks or months. This is often associated with progressive and permanent liver damage, culminating in hepatic cirrhosis. This sequence

of events occurs in about 0.5 to 1% of cases. A somewhat greater proportion, some 1-2%, after making an apparently complete recovery, relapse some months later. The clinical course in relapse tends to be more severe than in the first attack, and permanent sequelae are probably more frequent.

The most serious, and often fatal, deviation from the common benign course is the onset of acute yellow atrophy. This complication is usually heralded by evidence of cerebral disturbance with delirium subsequently declining into coma and often followed by death. Reduction in the area of hepatic dullness is commonly described, and sometimes the appearance of a haemorrhagic tendency, with bleeding particularly from the mucous membranes. These most serious symptoms are strongly suggestive of massive hepatic necrosis, and call for strenuous therapeutic measures if death is to be averted.

Differential Diagnosis

In the midst of an epidemic diagnosis in the icteric phase is fairly obvious. In the pre-icteric phase the diagnostic problem is that of pyrexia of unknown origin. At this stage the pronounced loss of appetite, abdominal pain and tenderness in the right upper quadrant, and the appearance of urobilin in the urine are points of greatest significance.

Once jaundice has appeared the chief problem of the physician is to distinguish infective hepatitis from other causes of jaundice associated with biliuria. Toxic jaundice resulting from exposure to liver poisons such as carbon tetrachloride or T.N.T. can usually be excluded on the history. Weil's disease, or spirochaetal jaundice, is usually associated with a rat-infected environment; and, clinically, severe conjunctival injection, herpes labialis, and albuminuria are characteristic. Moreover, excellent laboratory diagnostic methods are available—namely, the isolation of the causative spirochaete from the blood or urine in the early stages, and the serum-agglutination tests later on. Infectious mononucleosis, or glandular fever, may also be associated with jaundice and a clinical picture much like that of infective hepatitis. A blood count is not very helpful, as a moderate lymphocytosis and mononucleosis is also common in hepatitis. A positive Paul-Bunnell heterophil agglutination test will, however, readily identify the cases of glandular fever after the first week.

Jaundice due to obstruction of the extrahepatic bile ducts may prove extremely difficult to differentiate from infective hepatitis, especially those cases of hepatitis in which the jaundice persists for more than three to four weeks. This differentiation between obstructive and parenchymal jaundice is a major diagnostic problem, as the treatment of obstruction is mainly surgical and that of hepatitis entirely medical. It is mainly for this type of case that the large variety of so-called liver-function tests have been developed. It must, however, be emphasized that no single laboratory test is infallible, and when one considers the damage to the hepatic parenchyma that must inevitably result from several weeks of biliary obstruction it is hardly surprising that cases of biliary obstruction may show evidence by these tests of parenchymal change. Nevertheless their diagnostic usefulness has been amply demonstrated, and when combined with the clinical data and history a correct diagnosis may be reached in well over 90% of cases. As most liver-function tests require adequate laboratory facilities, and since, moreover, surgical inter-

vention is required for nearly all cases of obstructive jaundice, it is advisable that all suspected cases of hepatitis that remain jaundiced for longer than one month should be transferred to hospital for further investigation.

Prognosis

In most cases the prognosis is excellent, complete recovery without sequelae occurring in over 90%. The immediate mortality among the otherwise healthy and well-nourished is approximately 0.2%. But in 1-2% there is chronic liver damage, with persistence of hepatic enlargement, slight jaundice, which waxes and wanes, and permanent impairment of health usually terminating months or years later in hepatic cirrhosis with ascites. Clinical evidence of chronic parenchymal damage may usually be found in these patients. Pulsating spider naevi on the face, hands, and arms and a mottled erythema of the palms and soles may be seen in cases of either sex. In men, loss of hair on the chest, gynaecomastia, and testicular atrophy with loss of libido may also occur, while in women menstrual disturbance, especially menorrhagia, is not uncommon. All these disturbances are thought to result from an excess of circulating oestrogens owing to impairment of the liver's normal capacity to inactivate these hormones. Slight oedema of the ankles, with hypoproteinaemia and reversal of the albumin/globulin ratios, and a moderate degree of anaemia, sometimes of macrocytic type, are also indicative of the progressive failure of the liver in these chronic cases.

Certain factors seem to predispose the individual to a severe attack. Malnutrition is probably a major factor in the high mortality observed in outbreaks among the native populations in less well nourished communities of the world; mortality rates up to fifteen times those occurring in healthy European communities have been reported. Previous severe injury or burns also appear to affect the prognosis adversely, and were probably responsible for the unusually high mortality rates in some of the published reports on Service personnel in the last war. Pregnancy also seems to impose considerably increased risk of acute yellow atrophy in patients with infective hepatitis.

Malnutrition, recent injury, and pregnancy all have in common a considerable disturbance of protein metabolism, and, in the light of recent experimental work on the production of massive hepatic necrosis by diets deficient in protein, it has been suggested that a similar metabolic disturbance may be at work in these hyper-susceptible cases.

Treatment

There is at present no specific chemotherapeutic agent operative against the virus of infective hepatitis. The extensive epidemics of recent years, however, have provided excellent opportunities for therapeutic trials of several regimes, and have resulted in considerable uniformity of opinion about the best methods of reducing the duration of disease and the likelihood of sequelae.

Rest in bed for as long as the jaundice persists is probably the most important of all the therapeutic measures. With the disappearance of bile from the urine the patient may be allowed to leave his bed for purposes of toilet, but rest in bed should otherwise be maintained until any hepatic enlargement and tenderness have virtually disappeared. Return to full activity should be gradual, as many cases relapse if this precaution is ignored. After

a period of two to three weeks in bed, at least a fortnight should be allowed for convalescence.

Recent experimental work has emphasized the importance of protein in maintaining the integrity and function of the liver. Fatty diets, however, have been shown to enhance the toxicity of several liver poisons. There is therefore general agreement that the patient's diet should be rich in protein and carbohydrate, but poor in fat. If, however, fat be too severely restricted, the meals become unpalatable. A daily diet containing 150 g. of protein, 350 g. of carbohydrate, and 50 g. of fat will provide about 2,500 calories, which is ample for a patient confined to bed. As the appetite is impaired and nausea and vomiting are common, meals should be small but be given at frequent intervals. If dehydration occurs from excessive vomiting parenteral fluid and even parenteral feeding may have to be used.

There is little evidence that supplements of methionine, cystine, or choline will affect the duration of the disease in subjects who were previously healthy. It is, however, possible that, in the previously malnourished, supplements of the sulphur-containing amino-acids may reduce the mortality from acute yellow atrophy. These are most conveniently given as methionine in tablet form in a daily dosage of 3-5 g.

Patients in whom little bile is reaching the intestine may have difficulty in their absorption of fats. Such patients on a low-fat diet may suffer from deficiency of fat-soluble vitamins. This is unlikely to become manifest in acute cases, but in those in which the symptoms persist for several weeks vitamins A and E should be given, and vitamin K also if the plasma-prothrombin level is low. Vitamin A may be given in daily doses of 25,000 to 50,000 units, and vitamin E in a daily dose of 100 mg.

Of the water-soluble vitamins, ascorbic acid will probably be adequate provided the diet contains, as it should, a reasonable amount of fresh vegetables and fruit. The water-soluble vitamins of the B complex are very intimately associated with liver metabolism. Since an imbalance of these vitamins may well result from supplementation with the known pure preparations, a cheaper and more satisfactory means of achieving the same end may be obtained by giving a crude liver or yeast extract.

Apart from rest and careful dietary supervision, the treatment of infective hepatitis is largely symptomatic. Constipation, which may be troublesome, especially when very little bile is reaching the intestines, is best dealt with by saline laxatives. If a sedative is required barbiturates and opium alkaloids are best avoided, as their detoxication and excretion are largely dependent upon normal liver function. Chloral hydrate and paraldehyde are undoubtedly the safest. Nausea and vomiting may be very resistant to treatment, but small meals and attention to the bowels are usually sufficient to avoid the necessity for more drastic measures. In extreme cases it may be necessary to feed the patient parenterally. Alcohol should be strictly avoided, both during the disease and preferably for several months afterwards.

Relapses and remissions should be treated in the same way as first attacks, but return to full activity should be slower, as such relapses considerably increase the risk of permanent hepatic damage. Pre-coma and coma require treatment that is quite beyond that usually attainable in the home. If it is thought that coma is likely to develop the patient should be transferred to hospital as soon as possible.

PUBLIC HEALTH ON SHOW

The art or craft of exhibiting, which has been brought to a new high level in the Festival of Britain, is well exemplified in a display which is open for this summer at the London School of Hygiene and Tropical Medicine. Here, superimposed on the interesting permanent museum of the school, on the second and third floors at Keppel Street, there has been arranged a display which advertises some of the achievements in public health and social welfare of the last 100 years, and particularly of the last 50. In its arrangement, in the way the story is told, it is wholly admirable. All the means available to the modern exhibitor have been used—attractive text, catchy slogans, pointed cartoons, comparative photographs, telling diagrams and charts, and ingeniously designed models. Sometimes no text is necessary; the pictures themselves are enough. In the section concerned with child health, for example, two photographs are shown side by side. One of them is of a group of boys in a Southwark school in the 'nineties, the other of a similar group in the same area 50 years later. The contrast is impressive. It is evident that the boys in the earlier picture are ill nourished; they appear dull, listless, vacant in expression; some are obviously defective; a number appear to be adenoidal, whereas in the other photograph almost all the boys are bright and alert, well nourished, and well clad. But many of the exhibits in this section take one back to an earlier period, when large numbers of children, especially in industrial areas, had no childhood—the time of W. P. Frith's "Crossing Sweeper" and Shaftesbury's ragged schools. When the Great Exhibition was opened, infant mortality in this country was something like 158 per 1,000 births; in the last quinquennium it was below 40 per 1,000. Other photographs trace the evolution of welfare centres from the early shacks in which some of them were housed to the modern well-equipped building. They also tell the story of the beginnings of school medical inspection and the school dental service.

The National Health Service

One large exhibit of many panels introduces us to the ramifications and interrelations of all that is comprised in the National Health Service. The chart of the services and administrations and how they are derived and the relation they bear to one another looks rather like a map of London underground transport. One of the panels is devoted to the family doctor. Here we are told that circumstances will not allow the general building of health centres for many years to come, but that there is urgent need to improve the conditions under which general medical practice is carried on. The encouragement of group practice, it is pointed out, could foster such improvement. "The family doctor is the basis of the National Health Service." The work of the medical officer of health is also well depicted in his relation to the health, welfare, education, and children's committees of his local authority, and photographs illustrate his manifold activities. Some attempt is also made to indicate the organization of the hospital services in a region. Then there are the ancillary services, each with its appropriate pictures—the Public Health Laboratory Service, organized by the Medical Research Council; the immunization service, carried out by the local authority and family doctors; the transfusion service, for which regional hospital boards are responsible; and, finally, mass miniature radiography.

Nutrition in West Africa

Some experimental researches in public health are portrayed with an ingenuity which fastens them on the lay mind. These include comparative studies of health and of ages at death of people of tropical and of temperate climates, and the difference which the conquest of malaria has made in the Tropics (Ceylon). A large section is devoted to setting out graphically what is called an experiment in human nutrition. During the last few years an effort has been made to raise the standard of life of the