PREOPERATIVE ASSESSMENT OF THE PATIENT WITH LIVER DYSFUNCTION

L. STRUNIN

The preoperative assessment of liver function is important, but often neglected. All anaesthetic techniques reduce liver blood flow and many anaesthetic drugs are metabolized and excreted by the liver. Liver dysfunction may be accompanied by renal dysfunction and impairment of the blood clotting mechanism. Certain liver problems may be amenable to treatment before operation and others may require steps to be taken during anaesthesia. The presence of viral hepatitis may imply personal risk for the anaesthetist. It can be seen, therefore, that a number of factors are relevant in the assessment of liver function before operation. The first steps are a careful history and examination of the patient.

Although many liver function tests are available, it should be remembered that these are rarely specific in their own right, and the tests are often somewhat crude and inaccurate. Abnormalities are only seen when considerable liver damage has already occurred. Too much reliance should not be placed on a single value of any test, but, where possible, serial estimations should be carried out so that a trend may be detected. However, from all the evidence it should be possible to categorize the patient, so that problems relating to anaesthesia and surgery may be minimized.

The surgical procedure proposed is relevant since detrimental postoperative changes in liver function occur which are related to the extent of surgery. In the patient with a pre-existing liver problem surgery may be a major factor in determining outcome. Although it may be difficult to distinguish the interaction between anaesthesia and surgery in patients with severe liver problems, it seems clear that major surgery is not well tolerated.

Five categories of liver dysfunction are: previous history of jaundice; jaundice as the presenting symptom; chronic liver disease; viral hepatitis; acute liver failure. These should not be considered as water-tight compartments, indeed there is obvious overlap, but they form a useful guide for the anaesthetist when determining what steps to take for patients with liver dysfunction in relation to their presenting symptoms.

PREVIOUS HISTORY OF JAUNDICE

This is a common problem. The patient gives a history of jaundice, usually many years previously, but is now well and has apparently normal liver function. The most likely diagnosis is viral hepatitis. If liver function tests such as serum bilirubin, proteins, aspartate aminotransferase (AST), alkaline phosphatase (ALP) and prothrombin activity are within normal limits and the surface antigen for hepatitis B virus (HBsAg) and e-antigen (see below) are absent, then it is unlikely that any problem will be encountered during anaesthesia and surgery in such a patient. If antibodies to HBsAg are detected, this would confirm that the patient has had a previous attack of viral B hepatitis and is now immune. On the other hand, if abnormalities in liver function tests are detected, such as increased AST, bilirubin and globulin concentrations, with reduced serum albumin concentration, and particularly if HBsAg or e-antigen is detected, this might imply that the patient has developed chronic liver disease as a result of a previous infection with hepatitis B virus. In this instance the precautions outlined below should be followed.

In the patient with a history of previous jaundice, specific questions should be asked concerning anaesthesia and surgery. If jaundice relates to a previous anaesthetic every effort should be made to ascertain which anaesthetic drugs were used and the exact sequence of events concerning the occurrence of the liver dysfunction. It is obviously important to ascertain whether it was felt that any particular drug given during a previous anaesthetic was responsible for the jaundice after operation. Although in many instances there will have been a clearly identifiable cause of the postoperative jaundice, such as blood transfusion or infection, since it is assumed that a further anaesthetic is now contemplated the role of anaesthetic or other drugs in the previous episode will obviously have a bearing on the choice of anaesthesia on the present occasion. It is beyond the
scope of the present article to discuss in detail the problems related to repeated anaesthesia, particularly at close intervals, where unexplained liver dysfunction has occurred after a previous anaesthetic. The reader is referred to a recent Editorial in this Journal which gives the relevant references (Strunin, 1976).

**Jaundice as the Presenting Symptom**

Jaundice is a clinical observation characterized by yellow pigmentation, seen first in the sclera and then in the skin and other tissues, and occurs when serum bilirubin exceeds 20 \( \text{\mu mol litre}^{-1} \). Such an increase may be associated with disorders of bilirubin metabolism or may be evidence of cellular liver disease. Many causes of jaundice are not amenable to surgical treatment and unnecessary diagnostic laparotomies are still carried out too frequently merely because of a lack of careful questioning of the patient concerning drug history, alcohol intake, evidence of chronic liver disease or viral infection. On the other hand, unnecessary delay in the patient with obstructive jaundice, amenable to surgical treatment, may lead to cholangitis and renal failure.

**Classification of Jaundice**

The causes of jaundice may be classified according to mechanism: increased bile pigment production, defective uptake and transport within the hepatocyte, defective conjugation, or defective excretion. In practice, however, there may be difficulty in attributing jaundice specifically to any of these mechanisms, since all may be involved (Sherlock, 1975). The capacity of the liver to handle bile pigment may increase considerably, so that even in chronic haemolytic diseases serum bilirubin is rarely increased above 50 \( \text{\mu mol litre}^{-1} \). In Gilbert's disease, which is the commonest variety of familial, unconjugated, non-haemolytic hyperbilirubinaemia, where bilirubin transport is defective serum bilirubin is also not usually greater than 50 \( \text{\mu mol litre}^{-1} \). The i.v. nicotinic acid test (Fromke and Miller, 1972) may be used to establish the diagnosis and obviate the need for a liver biopsy. Patients with Gilbert's disease may develop jaundice following anaesthesia and surgery and the nicotinic acid test may be helpful in distinguishing such jaundice from more serious liver damage.

Defective excretion of bilirubin, that is obstructive jaundice, may occur either within the bile canaliculi and small ducts within the liver, that is intrahepatic cholestasis, and may be associated with widespread hepatocellular damage such as is seen in cirrhosis and in conditions where there is conjugated hyperbilirubinaemia (for example Dubin–Johnson syndrome), or as a result of drug sensitivity, for example the phenothiazine groups of drugs. Extra-hepatic obstruction may result from gall-stones, strictures, carcinoma of the biliary tree or carcinoma of the head of the pancreas. The differentiation of intrahepatic cholestasis from extrahepatic obstruction is obviously crucial in determining whether surgery is indicated.

**Deciding factors for surgery in jaundiced patients**

The differential diagnosis of medical or surgical jaundice is not always straightforward. However, a careful history and examination of the patient, with the results of various liver function tests and diagnostic aids, may be helpful (table I). Measurements of aminotransferase (AST) and alkaline phosphatase (ALP) have often been used to distinguish obstructive jaundice from jaundice associated with hepatocellular disease. It is traditional to consider high aminotransferase concentrations and a modest increase in alkaline phosphatase concentrations as being more likely to be the result of hepatocellular damage, whereas when alkaline phosphatase is grossly increased with only a small increase in aminotransferase this is often taken to indicate an obstructive lesion. However, the pattern of change is often
not clear and, in addition, patients with severe obstructive jaundice may have been treated with steroids (Williams and Billing, 1961) as a diagnostic test to attempt to distinguish hepatitis from extrahepatic obstruction. The former may resolve during steroid therapy.

Other biochemical investigation is rarely rewarding unless some specific disease is suspected, for example the measurement of caeruloplasmin in Wilson's disease, or measurement of α-fetoprotein (AFP) which is grossly increased in patients with hepatocellular carcinoma (hepatoma). Screening for HBsAg may be helpful in distinguishing patients with either acute or chronic liver disease associated with viral infection, and tests for cytomegalovirus or the EB virus of glandular fever may be helpful in distinguishing these causes of jaundice. Auto-antibody testing should be carried out to eliminate other chronic liver diseases associated with auto-immune disorders.

Needle biopsy of the liver is one of the main diagnostic methods of determining the causes of jaundice. Infusion of fresh frozen plasma before biopsy will reduce the risk of haemorrhage even in patients whose prothrombin time is prolonged as a result of their jaundice (Gazzard et al., 1974). Although liver biopsy is usually carried out in the conscious patient perhaps sedated with diazepam, in children general anaesthesia is sometimes required. A needle biopsy is of necessity a blind procedure and, as an alternative, needle biopsy via a laparoscope enables samples to be taken from specific areas of the liver; general anaesthesia may be required.

The usual method of visualizing the biliary tree is by an oral or i.v. cholangiogram. However, if the serum bilirubin is greater than 34 μmol litre⁻¹ these techniques are unsatisfactory because the radio-opaque dye is not excreted into the biliary tract. Percutaneous transhepatic cholangiography may be performed by passing a thin (skinny) needle directly through the abdominal wall into the liver until bile is aspirated, then radio-opaque dye is injected and serial radiographs taken. The technique may be associated with haemorrhage, biliary peritonitis and the occurrence of acute cardiovascular collapse. The latter is probably as a result of septicaemia associated with leakage from the biliary tree; in longstanding-biliary obstruction the bile is almost invariably infected. Percutaneous cholangiography is usually carried out without a general anaesthetic, often under diazepam sedation, but as a precaution a large-bore i.v. infusion should be set up before the procedure so that, in the event of cardiovascular collapse, the circulating blood volume may be rapidly restored by transfusion.

Disorders of blood coagulation

A prolonged prothrombin time is commonly found in the jaundiced patient. Prothrombin is synthesized by the liver but requires the presence of vitamin K. In obstructive jaundice vitamin K is not absorbed in the intestine as bile salts are absent. Several other clotting factors also require the presence of vitamin K and therefore complex blood coagulation problems may occur in the jaundiced patient. Furthermore, if there is hepatocellular disease, defective synthesis may also lead to a lack of clotting factors. Such defective synthesis is associated with a low serum albumin concentration.

All jaundiced patients should receive a course of parenteral vitamin K therapy before anaesthesia and surgery. If prothrombin activity does not return to normal, it is indicative of hepatocellular damage, and fresh frozen plasma infusion may be helpful in reducing the risk of severe haemorrhage during surgery or diagnostic procedures (Gazzard et al., 1974).

Renal failure after operation

It has been known for some time that there is an increased incidence of renal failure following anaesthesia and surgery in patients with obstructive jaundice (Zollinger and Williams, 1956; Dawson, 1965a). Such renal failure has been attributed to anoxia (Dawson, 1964) associated with the normal decrease in renal blood flow during anaesthesia and surgery, and the possible toxic effects of bilirubin (Baum, Sterling and Dawson, 1969). More recently Bailey (1976) has suggested that renal failure after surgery may be caused by excess endotoxin produced from the patient's own bowel flora, caused by the reduction in bile salts resulting from biliary obstruction. In the patients studied by Bailey (1976) endotoxin was found in portal blood when serum bilirubin was in excess of 140 μmol litre⁻¹. The finding of endotoxin in portal blood correlated with a decrease in creatinine clearance, indicating renal damage.

Dawson (1965b) showed that renal failure following surgery could be prevented in the jaundiced patient by inducing a diuresis before operation, and maintaining it during operation and in the period immediately after operation with mannitol i.v. Mannitol 5% or 10% is all that is required; mannitol 20% is excessively hypertonic and is not necessary. In
addition, antibiotics should be administered before operation to reduce the gut flora and thus the amount of endotoxin produced, and further antibiotics may be necessary i.v. during surgery to prevent the occurrence of septicaemia associated with surgical manipulations of the biliary tree.

CHRONIC LIVER DISEASE

Chronic liver disease, hepatocellular disease or cirrhosis are often used interchangeably to describe the same thing. Cirrhosis is a pathological term and describes the changes which occur in the liver, produced by a number of aetiological factors. Chronic liver disease may produce little alteration in liver function and only when some additional insult, often iatrogenic, produces further deterioration in liver function does the underlying disease state become clinically obvious as jaundice, ascites or encephalopathy. In most instances the aetiology of cirrhosis cannot be established and the disease is known as cryptogenic cirrhosis. Some 30% of the cases in the United Kingdom (Stone, Islam and Paton, 1968) are associated with alcohol. The immunologically based diseases, such as chronic active hepatitis and primary biliary cirrhosis, also account for a significant number of patients with cirrhosis. Infection with hepatitis B virus is another aetiological factor.

Clinical findings

Compensated chronic liver disease is compatible with a complete feeling of well being, and when symptoms do occur they are usually vague, such as malaise, dyspepsia, weight loss, loss of libido and menstrual disturbances. One of the most useful signs of cirrhosis is the presence of spider naevi on the skin of the face, arms and upper torso. There is evidence of a high output circulatory state, with flushed extremities, dilated veins, capillary pulsation and a collapsing pulse. The size of the liver is very variable, ranging from shrunken to very large, and may change during the course of the disease. Clinical examination of the size of the liver may be misleading and the only accurate method is by liver scintiscan using 99mTc-sulphur colloid (Sullivan, Krasner and Williams, 1976).

A constant feature of cirrhosis is increased resistance to flow of blood in the portal venous system, resulting eventually in congestive splenomegaly and collateral venous channels — portasystemic shunts. These latter are found most commonly around the umbilicus, at the lower end of the oesophagus and in the rectum. The increase in portal venous pressure is usually described as portal hypertension. In the later stages of chronic liver disease there may be progressive water retention, hyponatraemia, azotaemia and oliguria as a result of reduced renal plasma flow. Other signs which suggest that chronic liver disease has become decompensated include jaundice, oedema, ascites, a flapping tremor of the hands and changes in the neurological state progressing to coma. A sudden change in size or shape of the liver may indicate that a hepatoma has developed. Three major complications may occur in the cirrhotic patient—encephalopathy, ascites and gastrointestinal haemorrhage. Other problems include infection, jaundice and vitamin deficiency. Drug metabolism is related to liver cell function, and, although considerable liver damage is necessary before drug metabolism is interfered with significantly, this factor should be taken into account. Recently, Forrest and colleagues (1977) showed that the plasma half-lives of antipyrine, paracetamol and lignocaine are correlated significantly in terms of prolongation of action with an increase of the vitamin K1 corrected prothrombin time ratio and a reduction in serum albumin concentration in patients with chronic liver disease. There was no correlation with serum bilirubin concentration or serum AST activity. These findings suggest that impaired drug elimination is related to depressed hepatic protein synthesis.

Patients with chronic liver disease may present for anaesthesia and surgery either for procedures unrelated to their liver dysfunction or as a result of complications such as gastrointestinal bleeding. As has already been indicated, liver function tests may not be of great help in estimating the amount of liver damage that has occurred, but a number of schemes have been devised to attempt to estimate hepatic reserve. The multifactorial system described by Child (1964) combined two laboratory and three clinical observations and is a reasonably reliable indication of the risk of surgery and of long-term prognosis, particularly following portasystemic shunting (table II). More recently, Pugh and colleagues (1973) have modified Child's system to include other tests (table III). Using this system patients who score 5–6 points are considered to be good operative risks (grade A); 7, 8 or 9 moderate (grade B); and patients with 10–15, poor operative risks (grade C). Allowance should be made in the grading for patients with primary biliary cirrhosis in whom the concentration of bilirubin is usually out of
Table II. Clinical and laboratory classification of patients with cirrhosis in terms of hepatic functional reserve (data from Child (1964))

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum bilirubin (µmol litre⁻¹)</td>
<td>&lt;40</td>
<td>40–50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Serum albumin (g litre⁻¹)</td>
<td>&gt;35</td>
<td>30–35</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Easily controlled</td>
<td>Poorly controlled</td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>None</td>
<td>Minimal</td>
<td>Advanced coma</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Excellent</td>
<td>Good</td>
<td>Poor-wasting</td>
</tr>
<tr>
<td>Risk of operation</td>
<td>Good</td>
<td>Moderate</td>
<td>Poor</td>
</tr>
</tbody>
</table>

Table III. Grading of severity of liver disease (data from Pugh and others (1973))

<table>
<thead>
<tr>
<th>Clinical and biochemical measurement</th>
<th>Points scored for increasing abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy (grade)</td>
<td>None, 1 and 2, 3 and 4</td>
</tr>
<tr>
<td>Bilirubin (µmol litre⁻¹)</td>
<td>&lt;25, 25–40, &gt;40</td>
</tr>
<tr>
<td>Albumin (g litre⁻¹)</td>
<td>35, 28–35, &lt;28</td>
</tr>
<tr>
<td>Prothrombin time (seconds prolonged)</td>
<td>1–4, 4–6, &gt;6</td>
</tr>
</tbody>
</table>

Viral hepatitis is of most concern, since infection with this virus may be followed by chronic liver disease. This is most probably the result of an immune-mediated response to the virus (Eddlestone and Williams, 1974). Patients may become long-term carriers of the virus and constitute a potential risk for infecting others. In 1967, Blumberg and his colleagues described an antigen (Australia antigen) which has been shown to be the surface antigen (Hb₅Ag) of the hepatitis B virus. A further antigen, the e-antigen which is derived from the core of the hepatitis B virus, has been found in up to 67% of cases of Hb₅Ag-positive chronic active hepatitis (El Sheik et al., 1975). Therefore e-antigen testing may prove to be one of the most useful ways of indicating potential infectivity of sera and it has been suggested that if e-antigen is absent in Hb₅Ag-positive individuals it may be that they do not constitute a risk to others (Lancet, 1976). Nevertheless, patients who are Hb₅Ag positive should be treated as potentially infective and appropriate precautions taken during the course of an anaesthetic. It should be recognized that patients with liver disease associated with hepatitis B virus are not usually as potentially infective as the
patient with renal disease who acquires hepatitis B infection. In the patient with liver disease, circulating concentrations of Hb$_B$Ag are relatively low, whereas patients with chronic renal failure who have depressed immune responses cannot generate antibodies to neutralize their circulating Hb$_B$Ag.

When anaesthetizing the Hb$_B$Ag-positive patient it is essential that a routine is followed and this should begin from the time when the patient is sent for from the ward (Waterson, 1976). The number of personnel in the operating theatre should be kept to a minimum and all should wear disposable caps, masks, gowns, gloves and overshoes. For the anaesthetist the wearing of gloves (some prefer two pairs) is mandatory but may make the placement of i.v. needles more difficult. Unnecessary injections and blood sampling should be avoided. Clearly marked rubbish bags should be available so that every disposable item that comes into contact with the patient may be incinerated. Non-disposable anaesthetic items may be sterilized where appropriate by heating, ethylene oxide or the use of Diversol BX (Diversey Limited) which is a crystalline blend of chlorinated trisodium phosphate, mixed with a bromine salt.

Dykes and Bunker (1970) estimated that in the United States some 200–300 patients per year will present for anaesthesia and surgery whilst incubating viral hepatitis. Several studies after anaesthesia and surgery in such patients have suggested that liver function tends to deteriorate (Harville and Summerskill, 1963; Hardy and Hughes, 1968; Marx et al., 1968). In general it seems undesirable to anaesthetize such patients and the advent of immunological tests for both hepatitis A and B should reduce the incidence of these unnecessary events. Experience of anaesthetizing patients with chronic liver disease, who are carriers of Hb$_B$Ag, does not suggest that any “activation of virus” occurs following uneventful anaesthesia and surgery (Dykes, 1977).

**ACUTE LIVER FAILURE**

The clinical manifestations of acute liver failure are many and, as well as those directly related to hepatic damage, include neurological, acid–base, cardiac, renal, metabolic and haematological disturbances. The most outstanding feature is the development of coma. The coma seen in liver disease is usually termed “hepatic encephalopathy”, and Sherlock and her colleagues (1954) demonstrated that patients with hepatic encephalopathy had a circulatory pathway which allowed products of bacterial action on protein in the colon to reach the brain without being metabolized by the liver. Acute liver failure with hepatic encephalopathy occurs in two groups of patients: those with chronic liver disease (cirrhosis with some precipitating cause), and as a complication of fulminant hepatic failure. This was defined by Trey and Davidson (1970) as coma developing within 8 weeks of the onset of symptoms in patients whose liver function before the illness was presumed to have been normal.

Although acute liver failure is a rare event, it is a diagnosis which the anaesthetist should consider when encountering a comatose patient, perhaps in the intensive care unit. The characteristic features of hepatic coma include hyperventilation, fluctuating level of consciousness and haemorrhage, usually from the gastrointestinal tract. The more obvious signs of liver disease may not necessarily be immediately apparent. Since one of the commonest causes of fulminant hepatic failure is virus infection with either hepatitis A or B, precautions, as outlined above, may be necessary. The signs and symptoms and management of acute liver failure have recently been reviewed by Ward and his colleagues (1977).

**REFERENCES**


