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# Hepatocellular Jaundice

**SHRIKANT Y. WAGH, SHARAD C. SHAH**

**Introduction :**

If examined in good daylight, jaundice is a layman's diagnosis. It means yellow discolouration of sclera, skin and mucous membranes. Excess of vitamin A also causes yellow discolouration but this is very rare. Mepacrine causes yellow discolouration of skin and not that of the sclera, and this is again a very very rare cause. Whenever one sees a yellow discolouration of sclera, he must say that this is jaundice and nothing else.

*Types* :

Jaundice is just a feature of some disease process, and it is not a diagnosis. The cause of every jaundice must be known. According to the steps in bilirubin metabolism, the cause may be at three levels and hence jaundice is of 3 types :-

1) Prehepatic or Haemolytic.
2) Hepatic or Hepatocellular.
3) Posthepatic or Cholestatic (Obstructive).

*Causes* :

At the outset it must be stated that hepatocellular jaundice is by far the most common variety found in practice and that this is the main problem which a physician is required to handle. Hence hepatocellular jaundice is considered in detail with particular attention towards viral hepatitis. Damage to parenchymal liver cells causes hepatocellular jaundice. The most frequent cause of this damage is infective hepatitis In India, whenever one sees a case of jaundice he must first think of an infective hepatitis. Other causes, however, are not uncommon. These include :-

1) Serum hepatitis, Chronic active hepatitis.

2) Poisons : Alcohol, Carbon tetrachloride, Arsenic. Chlorpromazine Testosterone, Isoniazid, Hydantoin, Phenylbutazone, etc.

3) Bacterial infections : Septicaemia, Typhoid, etc.

4) Congenital defects.

*Viral Hepatitis* :

Viral hepatitis includes infective hepatitis (virus A) and serum hepatitis (virus B).

A) The virus of infective hepatitis is transmitted by faecal-oral route. This transmission is encouraged by improper water supply, inadequate environmental sanitation and faulty personal hygiene. Contamination of water supply has caused major epidemics in various parts of India. Flies and food-handlers also help in transmission. Clinical cases and incubatory and convalescent carriers are the source of infection.

B) Transfusion of infected blood, plasma and blood products causes serum hepatitis. Injection by infected needle, tatooing, sexual contact, parenteral injections and venepunctures can also spread it.

*Clinical features of viral hepatitis*

A severe anorexia and distaste for smoking and tobacco chewing are the commonest early symptoms. 4-10 days prior to the development of jaundice. Other symptoms such as malaise, fever, nausea, and vomiting are seen. Occasionally noncolicky upper abdominal pain occurs.

Then the sclerae become yellow and bile appears in urine. As jaundice deepens the urine becomes darker and liver becomes palpable. The stools are pale due to intrahepatic cholestasis caused by inflammation. The spleen may be palpable. Jaundice and liver enlargement regress after an icteric phase of 1-4 weeks and urine and stools regain their normal colour. Occasionally the hepatitis may be nonicteric.

Except in fulminant varieties, immediate prognosis is always good in infective hepatitis. Females, especially middle aged and elderly, have a worse prognosis than males. In epidemics, mortality rates are 1-2%. Serum hepatitis has a higher mortality.

*Differentiating features of infective and serum hepatitis* :

These are given in the following table.

TABLE I

| | Infective hepatitis | Serum hepatitis |
|---|---|---|
| Incubation period | Short (15—50 days) | Long (50—150 days) |
| Onset | Acute | Insidious |
| Age | Children, young adults | Any-usually older |
| Occurrence | Epidemic | Sporadic |
| Severity | Usually mild | Often severe |
| Australia antigen | Absent | Present |
| Abnormal SGPT | Brief (30 days) | Prolonged (35—200 days) |
| Value of Gamma-globulin prophylaxis | Good | Uncertain |

*Differential diagnosis* :

The diagnosis of viral hepatitis is "historical". The word historical has got two meanings. Since times immemorial i.e. historical days, doctors diagnose viral hepatitis by way of natural history or evolution of this disease. Nothing else is required for diagnosis. Similar affection of other members of the society is a strong positive evidence of infective hepatitis. In fact in epidemics, in every case, an infective hepatitis must be suspected. Results of biochemical tests form a definite supportive evidence. In the preicteric phase a real diagnostic difficulty can arise and it can be mistaken for any acute viral or bacterial infection, particularly influenzial fever and common upper respiratory infections. Urinary bilirubin then comes to the rescue of the physician and solves the dilemma. If serum bilirubin can be performed, well and good. If further facilities are available ask for SGPT which will definitely indicate hepatocellular damage. Hepatic amoebiasis, so common in this country can be easily confused with preicteric infective hepatitis. Fever with pain and tenderness in right hypochondrium are common. SGPT is only marginally raised in this condition. Always look for lymph nodes. They are enlarged in infectious mononucleosis which can be diagnosed by a positive Paul Bunnel reaction. In the icteric phase, diagnostic problem may arise if viral hepatitis is followed by a prolonged cholestatic phase. Drug induced or alcoholic hepatitis can be diagnosed only by a history of consumption of these drugs or alcohol. Weil's disease can be diagnosed by history of exposure to rats, a polymorphonuclear leucocytosis, myositis and renal involvement. An acute exacerbation of haemolytic jaundice may present with abdominal pain, jaundice and mild fever. A distinctive lemon-yellow jaundice and absence of bile pigment in urine defferentiates this condition.

*Differentiating clinical features of the 3 types of jaundice* :

These are briefly given in the following table (Table 2).

TABLE II

| Feature | Hepatocellular | Haemolytic | Cholestatic |
|---|---|---|---|
| Colour | Orange yellow | Lemon yellow | Yellow green |
| Pruritus | Present & Non-persistant | Absent | Severe & Persistant |
| Urine | Dark | Normal | Dark |
| Faaces | Pale | Normal/Dark | Clay-White |
| Liver size | +— | Normal | ++ |
| Spleen | +— | ++ | +— |

**Investigations :**

a) Bile in urine :- Excretion of bile in urine occurs even before the appearance of clinical jaundice so that in an undiagnosed febrile illness a viral hepatitis can be detected at an early stage by a very simple testing of urine for bile. This test is positive in every hepatobiliary disease and negative in haemolytic jaundice. The test is very simple, inexpensive and a sensitive quantitative index for detecting bilirubin in urine.

1) *Fouchet's test* : Take 10 ml. of urine in a test tube and add 5 ml. of barium chloride to it. The urine turns milky. This is filtered through a filter paper. After filteration, take out the filter paper and allow it to dry a little. The paper shows a yellow precipitate. Two drops of Fouchet's reagent are dropped over this precipitate. A positive reaction is indicated by a blue green precipitate; the intensity of the colour is directly dependant upon the amount of bilirubin present in urine.

2) *Foam test* :- A still simpler test consisting of vigorously shaking a test tube containing urine. A profound and persistent foam indicates bile in urine. This test is definitely useful but probably less specific and has got no quantitative significance.

b) If there are no facilities for other investigations, do not worry, because the clinical diagnosis of viral hepatitis is quite certain on history and examination. If there are facilities and if the patient can afford, ask for serum bilirubin and SGPT only. For God's sake, please specify. High bilirubin gives a quantitative index of level of jaundice. Clinical jaundice appears when serum bilirubin is about 2mgm%. This means that its estimation helps in detecting a "preclinical" jaundice. SGPT is normally upto 30 i.u. It rises to several hundred units in hepato-cellular jaundice but does not exceed 100 units in cholestatic types. SGPT levels are high very early in the disease and it forms the best diagnostic evidence in the preicteric phase. Serum alkaline phosphatase need not be carried out unless a cholestatic jaundice is really suspected. It is only moderately raised in viral hepatitis.

*Management* :

1) Although an infectious disease, isolation is not required. Cases of mild jaundice can be managed at home. Others require hospitalisation. Great care must be taken in handling and disposal of blood samples, faeces and urine.

2) Bed rest is imperative during acute phase. Return to activity during convalescent phase should be gradual.

3) Diet should be nutritious and of a high protein content (provided that there is no evidence of acute hepatic failure). Plentiful supply of carbohydrates is essential. Glucose, fruits and fruit juices provide these carbohydrates. Intake of fats is to be restricted due to patient's aversion to them.

4) Alcohol and other hepatotixic drugs are strictly prohibited.

5) Corticosteroids are not indicated at all.

6) All of us know that this is a viral disease and safe antiviral agents are yet to be found out. This further implies that there is no specific drug for this particular disease. Using Liv-52 or Livomyn and such other proprietary indigenous products give a false sense of security. If you use them, be aware that they are not of much help. In recent controlled trial consisting of over 200 patients, it has been shown that AROGYAWARDHINI, an Ayurvedic counterpart of these products, does not alter the course of the disease although the course may be milder in some cases.

*Prophylaxis* :

a) In infective hepatitis, high standards of personal hygiene are imperative. Contamination of food and milk should be prevented. Education especially regarding fly control and food hygiene is possibly our responsibility. Boiling of water for 10 minutes or superchlorination( (1.2 — 1.6 ppm x 30 mins) help in safeguarding against infective hepatitis. The filters are useful but very costly for most of our population. 5 ml. of human gamma-globulin given intramuscularly during early incubation pe-

riod affords protection against infective hepatitis for about 6 months. Notification of cases is desirable and its importance has been grossly understimated as a preventive measure.

b) Serum hepatitis is controlled by limiting the use of blood products and transfusions. Syringes, needles dental equipment, etc. should be either disposable or well sterilised. Routine screening of blood donors for Australia antigen helps in reducing incidence of serum hepatitis.

*Fulminant Hepatitis* :

This is a hyperacute course of viral hepatitis and carries more than 75% mortality. Hence it is essential to be alert in any early diagnosis of this dreadful situation. Patients with poor nutritional status and especially those who continue to consume alcohol and other hepatotoxic agents are more likely to take fulminant course but it must be remembered that one can never predict as to which patient would go for a fulminant course. This type of course may be at the onset—this may be very difficult to diagnose and carries a very bad prognosis.

a) *Features* :- In an apparently established case of viral hepatitis if the patient starts behaving oddly, becomes apathetic and mentally confused, shows purperic patches or if his urine becomes scanty, one must think in terms of a fulminant hepatitis which demands for an expert's help and skilled management. Leucocytosis, high serum bilirubin and a prolonged prothrombin time are positive investigations. A markedly dry tongue, foetar hepaticus (a disagreeable sweetish odour), a flapping tremor, flexor plantars and brisk reflexes aid further in diagnosis. Liver size rapidly decreases and ascites may be present. The patient is then in danger of lapsing into hepatic coma and peripheral circulatory failure.

b) *Management* :- This consists of the following :-

Strict bed-rest.
No proteins.
Fluid and electrolytic balance.
Oral Neomycin/Streptomycin 1 gm 6 hourly.
Inj. Calcium gluconate.
Corticosteroids.
Levodopa.
Exchange transfusion (?).
Extracorporeal exchange transfusion (baboon) (?)
Charcoal catridge.

*Chronic active hepatitis* :

This is a chronic liver disease existing for more than 6 months. Relapses and remissions occur and multisystem manifestations may be present. Liver biopsy is essential for diagnosis. This shows disturbed architecture and piecemeal necrosis. These changes lead to or are accompanied by cirrhosis. Prednisolone (20-60 mgm/day) and Azathioprine (75-150 mgm/day) over prolonged period help in this condition.

*Congenital hyperbilirubinaemias* :

The hepatic metabolism of bilirubin consists of (1) uptake of unconjugated bilirubin, (ii) its conjugation and (iii) its excretion into bile ducts. According to congenital defects at these stages four syndromes have been described (Gilbert, Criggler-Najjar, Dubin-Johnson, Rotor). All of them except the Criggler-Najjar syndrome, carry an excellent prognosis. If you see a patient who has jaundice for many years, please do not bother too much about him, because he will turn out to be a case of congenital hyperbilirubinaemia and will have an excellent prognosis.

*Intrahepatic cholestasis* :

Cholestatic jaundice is of 2 types. The obstruction may be outside or within the liver. The extrahepatic variety caused by stones, strictures and malignancy is the "surgical" jaundice. Viral hepatitis causes intrahepatic cholestasis due to swelling of the cells whereas cirrhosis causes irregular intrahepatic fibrosis leading to cholestasis. Hepatic malignancy and drug sensitivity (e.g. Chlorpromazine) also cause intrahepatic cholestasis. General features of cholestatic jaundice have already been mentioned. Differentiating features between extrahepatic and intrahepatic cholestasis

are tabulated below. (Table 3). It must be stressed that in diagnosis of intrahepatic cholestasis, natural history or evolution is again the most important consideration.

Management of intrahepatic cholestasis is mainly medical. Withdrawal of the offensive drug is essential. The protein-calorie intake must be maintained. Coconut oil or

TABLE III

*Differentiating clinical features of extra-hepatic and intrahepatic cholestasis*

| | Extrahepatic | Intrahepatic |
|---|---|---|
| Age | Usually middle age | Usually younger |
| Previous history | May have antecedant attacks of pain in abdomen antecedent weight loss | 1) Exposure to drugs or hepatitis virus<br>2) Preicteric stage |
| Pruritus | Severe | + |
| Pain | Frequent | Usually absent |
| Hepatic tenderness | Rare | Often present early |
| Splenomegaly | Rare | Common |
| Palpable gall bladder | + | Absent |

Exposure to virus or a particular drug and a typical history of the preicteric stage form the basis of diagnosis.

Safflower oil should be used instead. Fat soluble vitamins must be supplemented. Pruritus if annoying can be managed by zinc-calamine lotion.