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REFERENCES

1. Robson SC, Kirsch RE.National strategy for viral hepatitis: recommendations and guidelines for management in South Africa. *S Afr Med J* 1991; **80:** 347-356.
2. Abdool Karim SS, Thejpal R, Singh B. The prevalence of hepatitis B virus infection in rural black adults in Mseleni, South Africa. *Am J Public Health* 1989; **79:** 893-894.
3. Abdool Karim SS, Coovadia HM, Windsor IM, Thejpal R, Van den Ende J, Fouche A. The prevalence and transmission of hepatitis B virus infection in urban, rural and institutionalized black children of Natal/KwaZulu, South Africa. *Int J Epidemiol* 1988; **17:** 168-173.
4. Prozesky OW, Szmuness W, Stevens CE, Kew MC, Harley EJ, Hoyland JA, *et al*. Baseline epidemiological studies for a hepatitis B vaccine trial in Kangwane. *S Afr Med J* 1983; **64:** 891-893.
5. Tucker TJ, Maraisane M, Mtupie M, Kirsch RE, Moodie J, Kannemeyer J, Robson SC. Sero-prevalence of hepatitis E in rural and urban black communities in the Cape Province, South Africa. *Hepatology* 1994; **19:** 1351.
6. Robson S. Viral hepatitis. In: Kirsch RE, Robson S, Meissner P, eds. *Liver Update 1991*. Cape Town: Medical Research Council/University of Cape Town Liver Research Centre, 1991: 51-65.
7. Khuroo MS, Teli M, Skidmore S, Sofi MA, Khuroo MI. Incidence and severity of viral hepatitis in pregnancy. *Am J Med* 1981; **70:** 252-255.
8. Stevens CE, Beasley RP, Tsui J, Lee WC. Vertical transmission of hepatitis B antigen in Taiwan. *N Engl J Med* 1975; **292:** 771-774.
9. Schoub BD, Johnson S, McAnerny J, Blackburn NK, Padayachee GN. Exposure to hepatitis B virus among South African health care workers — implications for pre-immunisation screening. *S Afr Med J* 1991; **79:** 27-29
10. Hilleman MR, McAleer WJ, Buynak EB, McLean AA. The preparation and safety of hepatitis B vaccine. *J Infect* 1983; **7:** suppl 1, 3-8.
11. Andre FE, D'Hondt E, Delem A, Safary A. Clinical assessment of the safety and efficacy of an inactivated hepatitis A vaccine: rationale and summary of findings. *Vaccine* 1992; **10:** suppl 1: S160-S168.
12. Blumberg BS, Gerstley BJS, Hungerford DA, *et al*. A serum antigen (Australia antigen) in Down's syndrome, leukemia and hepatitis. *Ann Intern Med* 1967; **66:** 924-931.
13. Perrillo RP, Schiff ER, Davis GL, Bodenheimer HC, Lindsay K, Payne J, *et al*. A randomized, controlled trial of interferon alfa-2b alone and after prednisone withdrawal for the treatment of chronic hepatitis B. The Hepatitis Interventional Therapy Group. *N Engl J Med* 1990; **323:** 295-301.
14. Ncayiyana DJ. Coming to grips with the future of health care — the ANC National Health Plan. *S Afr Med J* 1994; **84:** 55-56.
15. Zwarenstein M, Barron PM. Managing primary health care in South Africa at district level — the MRC/IUPHC workshop. *S Afr Med J* 1993; **83:** 562-564.
16. Towards a National Health Information System for South Africa. Proceedings of the seminar organised by the Health Systems Trust, Broederstroom, March 1994.
17. Abdool Karim SS, Abdool Karim Q. Under-reporting in hepatitis B notifications. *S Afr Med J* 1991; **79:** 242-244.
18. Gerwel J, Shisana O, Zwarenstein M, Yach D. The western Cape School of Public Health — a declaration of intent. *S Afr Med J* 1991; **80:** 471-473.

ARTICLES

Clinical and biochemical features of acute viral hepatitis

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Viral hepatitis is a major cause of mortality and morbidity worldwide. Acute viral hepatitis, although a generalised systemic infection, presents with clinical manifestations relating directly to inflammation of the liver with hepatocellular dysfunction and jaundice.

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The most important causes of acute and chronic hepatitis are the five hepatotrophic viruses, hepatitis A, B, C, D and E. There are 2 other, as yet unidentified, hepatitis viruses, F and G.

The clinical features of acute hepatitis caused by these hepatotrophic viruses are similar and only minor features of the clinical disease, together with the incubation period and epidemiological history, help to distinguish the different acute hepatitides. Specific diagnosis requires serological testing.

The clinical severity of acute hepatitis varies. Most infections are asymptomatic, subclinical or anicteric with mild gastro-intestinal symptoms only. Occasionally infection results in acute fulminant hepatitis with an associated high mortality.

Clinical features of acute viral hepatitis

A full clinical history is important. Particular emphasis should be paid to a recent history of travel, high-risk sexual practices, blood transfusions and the use of drugs.

Symptoms

The most common symptoms experienced during the prodromal phase include: malaise and fatigue, myalgia, anorexia, nausea and vomiting, right upper quadrant discomfort and fever.[1] Between 5% and 15% of patients with hepatitis B may develop a serum-sickness-like syndrome. Other extrahepatic manifestations, which may occur in acute viral hepatitis, include urticaria and angioneurotic oedema, arthritis, vasculitic and renal lesions, myocarditis and cardiomyopathy, pancreatitis and CSF abnormalities.[2] The prodromal symptoms usually last a few days to 2 weeks and are followed by the development of jaundice. However, jaundice may occur in the absence of any prodromal symptoms. Frequently, the systemic symptoms improve with the development of jaundice. Occasionally there is a prolonged cholestatic phase with associated pruritus. If there are minimal prodromal symptoms it is often difficult clinically to distinguish this form of viral hepatitis from extrahepatic cholestasis or drug-induced cholestasis.

During recovery, the nausea improves and the appetite returns. General malaise may persist for some time and relapses associated with an exacerbation of symptoms and of jaundice occur in up to 5% of patients. These may be precipitated by too early a return to work or vigorous exercise programmes.

Signs

The most common physical signs in acute hepatitis are jaundice, right upper quadrant tenderness and mild hepatomegaly. Splenomegaly occurs in 5 - 10% of patients and lymphadenopathy is occasionally seen.[1] Skin rashes may be present and in children with acute hepatitis B, a papular acrodermatitis involving the arms, legs and face may be found.

Fulminant viral hepatitis occurs in a small proportion of patients. This is associated with the development of

worsening jaundice and fulminant liver failure. Occasionally the onset is so rapid that coma and death occur in the absence of marked jaundice. The clinical signs are those of fulminant liver failure: hepatic encephalopathy (deteriorating level of consciousness, foetor hepaticus, asterixis and constructional apraxia), gastro-intestinal bleeding due to gastric erosions, coagulopathy, renal failure and development of portal hypertension. Decreasing liver size together with the development of ascites and oedema are poor prognostic signs. It is important to stage the degree of encephalopathy as, without transplantation, patients with stage 4 coma have a less than 20% survival rate. Patients with fulminant viral hepatitis and a deteriorating level of consciousness should be managed at a centre experienced in the multidisciplinary intensive care required; ideally, a liver transplant programme should be available.

Biochemical features

The serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities are sensitive indices of hepatocellular damage.[3] The rise in transaminase activity begins in the prodromal phase, preceding the onset of jaundice, and also occurs in those patients who remain anicteric. There is usually an eight-fold or greater increase in transaminase activities with the ALT being higher than the AST. In uncomplicated cases the transaminase activities decrease rapidly. Normal values are usually found by the third week of the illness. The persistence of elevated transaminase levels for longer than 6 months may imply ongoing activity and progression of the disease. Although transaminases are sensitive markers of hepatocellular damage, they are not specific and cannot be used to predict the outcome. There is no relationship between the degree of transaminase activity and the severity of the disease. A falling transaminase level together with clinical deterioration and increasing coagulopathy may be found in extensive hepatocyte necrosis and be associated with impending fulminant liver failure.

Usually by the time the patient becomes overtly jaundiced, the transaminase levels have peaked and are beginning to fall. Serum bilirubin levels are variable and are dependent on the degree of cholestasis. Most of the bilirubin is conjugated. Fulminant hepatitis can occur in the absence of significant hyperbilirubinaemia.

Urobilinogenuria may occur before the serum bilirubin levels are elevated. Urobilinogen disappears from the urine during the cholestatic phase and reappears during recovery. Bilirubinuria may precede the onset of clinical jaundice and persist during the cholestatic phase.

A small amount of circulating conjugated bilirubin usually becomes covalently linked to albumin. This linkage is irreversible and the bilirubin will persist in the circulation until the albumin to which it is bound is degraded. This hyperbilirubinaemia, which is not associated with bilirubinuria, is of no clinical significance.

Serum alkaline phosphatase (ALP) levels are usually only mildly elevated in acute viral hepatitis. However, where cholestasis is marked, high levels of serum ALP activity may be found. The increase in serum ALP usually parallels that of the bilirubin.

Serum albumin concentrations are usually normal in mild acute viral hepatitis. Low levels may be found in fulminant hepatitis. Serum globulin levels frequently rise if the viral hepatitis follows a prolonged course. Cryoglobulinaemia may occasionally be seen. Serum α-fetoprotein concentrations are usually raised during the acute illness[4] and tend to rise as the serum transaminase levels fall, suggesting that α-fetoprotein may be a marker of regeneration.

There is some evidence that gluconeogenesis is reduced in uncomplicated hepatitis. However, blood glucose levels are usually maintained in these cases and the finding of hypoglycaemia should suggest progression to fulminant hepatitis.

Haematological changes

The haemoglobin concentration, white cell and platelet counts and prothrombin international normalised ratio are usually normal in uncomplicated viral hepatitis.

Early on in the illness, however, as in other viral infections, a leukopenia, specifically a lymphocytopenia often with atypical lymphocytes, may occur. Later, relative lymphocytosis, macrocytosis, reduced red cell survival[5] and low serum haptoglobin levels may be seen. Occasionally, thrombocytopenia, agranulocytosis, pancytopenia and transient red cell aplasia may occur.[6]

The erythrocyte sedimentation rate is usually elevated during the prodromal phase but decreases with the onset of jaundice. Serum vitamin B_{12} levels are raised in acute viral hepatitis as are serum iron levels. Fulminant viral hepatitis is usually associated with a coagulopathy.

Frequency of investigations

While the initial biochemical tests allow the diagnosis of hepatitis in general, serological tests are essential to establish the aetiological diagnosis. The progress of any patient with hepatitis is best monitored clinically and repeated biochemical tests should only be used when clinically indicated. Thus in uncomplicated cases of viral hepatitis there may be no need to repeat the serum biochemical tests. On the other hand, clinical deterioration may suggest the need for further testing. In practice it should seldom be necessary to repeat the biochemical tests more than twice unless the disease is complicated by acute liver failure or proceeds to chronic hepatitis.

REFERENCES

1. Lavine JE, Bull FG, Millward-Sadler GH, Arthur MJP. Acute viral hepatitis. In: Millward-Sadler GH, Wright R, Arthur MJP, eds. *Wright's Liver and Biliary Disease*. London: WB Saunders, 1992: 679-786.
2. Gocke DJ. Extrahepatic manifestations of viral hepatitis. *Am J Med Sci* 1975; **270:** 49-52.
3. Stolz A, Kaplowitz N. Biochemical tests for liver disease. In: Zahim D, Boyer T, eds. Hepatology. *A Textbook of Liver Disease*. Philadelphia: WB Saunders, 1990: 637-666.
5. Kivel RM. Hematological aspects of acute viral hepatitis. *Am J Dig Dis* 1961; **6:** 1017-1031.
6. Hagler L, Pastore RA, Bergin JJ. Aplastic anaemia following viral hepatitis: report of 2 fatal cases and literature review. *Medicine* 1975; **54**(2): 139-164.
4. Kew MC, Purves L, Bershon I. Serum alpha-fetoprotein levels in acute viral hepatitis. *Gut* 1973; **14:** 939-942.