Viral Hepatitis
— Some Current Concepts

By Dr. P. P. Mathew*

FOR A meaningful programme of surveillance and control of Viral Hepatitis, Laboratory confirmation of clinical diagnosis is essential. Given necessary funds and safe facilities, serological confirmation is possible in Bahrain in the near future.

A. LABORATORY TESTS :-

I Serological Techniques for Hepatitis A

a) Immune electron microscopy. This is a technique whereby interaction between virus particles and specific antibody is visualized by electron microscopy. As few as 10^4-10^6 particles per millilitre may be detected (which is 1000 times more sensitive than routine electron microscopy).

b) Complement fixation and immune adherence haemagglutination. The latter is 10 - 100 times more sensitive than the former.

c) Solid-phase radioimmunoassay. It is hoped that it would be possible in future to perform these tests in Bahrain. With a modified technique it is possible to assay the IgM antibody (anti-HAV) fraction denoting current infection. Radio-immunoassay test (Havab-Abott Laboratories) is commercially available.

Note : Complement fixation is the least sensitive of the 4 techniques for the detection of anti HAV. Immune electron miscroscopy and radio-immuneassay are apparently of equal sensitivity. Immune adherence haemagglutination is intermediate.

II Serological Techniques for Hepatitis B

a) Agar gel immunodiffusion
b) Counter-immunoelectrophoresis
c) Complement fixation
d) Rheophoresis
e) Reversed passive latex agglutination
f) Passive haemagglutination (+ +)
g) Immune adherence haemagglutination (+ + +)
h) Immune electron microscopy (+ + +)
i) Immunofluorescence microscopy
j) Reversed passive haemagglutination (+ + +)
k) Solid-phase radioimmunoassay (+ + + +)
l) Radioimmunoprecipitation (+ + + +)
m) Enzyme immunoassay (+ + + +)

In general terms g, h, j, k, l & m are more sensitive than the rest for detection of HBsAg. One or more of these tests can be used for detecting Anti HBs, HBcAg, Anti-HBc, HBeAg and Anti HBe with differing sensitivity. Passive haemagglutination and Radio-immunoassay are the only 2 commercial tests available at present for Anti HBs detection.

Note : Patients with acute Hepatitis B usually have detectable HBsAg in their blood for a period ranging from a few days to several months. The interval between exposure and appearance of detectable serum HBsAg may vary from 2 or 3 weeks to 3 or 4 months. Abnormal liver function tests and clinical signs and symptoms appear some days or weeks after initial appearance of HBsAg. In most cases, the disappearance of HBsAg and subsequent appearance of anti HBs signal recovery. In about 5 to 10% of adults with Hepatitis B, infection with HBV persists and HBsAg remains detectable for many months or years.

Anti HBc appears very often in carriers.

B. EPIDEMIOLOGY AND CONTROL :-

I Hepatitis A

Geographical distribution : World wide

Age distribution :

In developed countries infections occur at all ages with about 50% of clinical cases in children less than 15 years. In tropical and subtropical areas, most infections are probably acquired in childhood, and many are subclinical. By adult age most people would have had the disease, either clinically or subclinically.

Modes of Spread :

1. Intestinal-oral, more readily under conditions of poor sanitation and over crowding. The period of maximal infectivity in a case is during the 2 week period before onset of jaundice.

2. Water-bone and food borne. The ingestion of undercooked shell fish grown in polluted waters is attended

* Public Health Department,
Ministry of Health,
State of Bahrain.

by a risk of acquiring hepatitis A.

3. Other modes of spread: Serum containing HAV has been shown to be infective. Syringe-transmitted Hepatitis A has been reported. Possibility of spread by the respiratory route, by infected urine and by sexual contact exists.

Control :

Good personal hygiene, sanitary disposal of excreta, and sterilisation of eating utensils and body and bed linen of patients with Hepatitis A reduces spread. In the home situation the washing of hands before eating or handling foods is probably the single most important preventive measure. The intra-muscular administration of normal pooled human immunoglobulin (a 16% solution, in a dose of 0.02 - 0.12 ml/kg body weight) before exposure to the virus or early in the incubation period will prevent or attenuate a clinical illness, while not always preventing infection. In apparent or subclinical Hepatitis may develop. This may be followed by passive-active immunity which could confer prolonged immunity on the individual.

II Hepatitis B

1. The carrier state : The survival of HBV in man is ensured by the existance of a reservoir of persistent carriers, estimated to number 120 million. The prevalence of HBsAg in apparently healthy adults varies from 0.1% in parts of Europe, North America and Australia to 15% in several tropical countries. The decline in HBsAg carriage rates with age suggests that the carrier state is not life long. HBeAg has been found more commonly in young than in adult carriers, while the prevalence anti HBe appears to increase with age. These findings suggest that young carriers may be the most infective.

Modes of spread :

a) Blood : In low prevalence areas a major mode of spread continues to be the inoculation of blood and some blood products as in transfusion, or by accidental inoculation of minute quantities of blood such as may occur during surgical and dental procedures, intravenous drug abuse, mass immunisation, tattooing, acu-puncture and laboratory accidents. Accidental percutaneous inoculation by communally used razors, tooth brushes, bath brushes etc have been occasionally implicated. Mosquitoes and other blood sucking insects can theoretically effect mechanical transmission, although convincing evidence is lacking.

b) Perinatal transmission : Transmission of infection from carrier mothers to their babies can occur during the perinatal period. Mothers with high titre of HBsAg and or presence of HBeAg or suffering from acute Hepatitis B (particulary in the third trimester or early peurperal period) pose greater risk to the baby. Most children infected at this time become persistent carriers. The mechanism of perinatal infection is uncertain. Although HBV can infect the foetus in utero, this would appear to happen rarely. The value of giving hyper immunoglobulin to these infants at birth has not been conclusively proven.

c) Other modes of spread : Mouth to mouth transmission may be important. Cohabitation with an acutely or chronically infected person is attended by significant risk. HBsAg has been detected in saliva, semen, vaginal secretions, menstrual blood, breast milk and faeces and it is possible that the infection can be transmitted through mucocal surfaces. Even-though no Hepatitis B epidemics due to contaminated food or water have been observed, faecal oral route of transmission is possible according to evidence.

III Hepatitis associated with transfusion

Major risk factors in post-transfusion hepatitis : The risk of post transfusion hepatitis increases with the number of units transfused.

Studies in the U.S.A. have shown that the risk of post-transfusion Hepatitis is higher with blood from commercial sources than with blood from voluntary donors (about 6 times)

Post-transfusion Hepatitis not caused by Hepatitis A or B virus : Whereas 30% of the cases of post-transfusion Hepatitis used to be caused by HBV before the introduction of HBsAg testing, that virus now causes only about 10% of cases following transfusion of blood in which HBsAg is not detectable by a sensitive method. As for the remaining 90% of cases, only a diagnosis of exclusion is yet possible.

In the United States of Amercia where post-transfusion

hepatitis (PTH) was studied, some salient features were observed viz. (1) In USA, the majority of PTH cases are not caused by Hepatitis B, but rather by an agent or agents not yet identified. (2) There is continuing risk of PTH when blood from paid donors is used, even if appropriate screening techniques show the blood to be HBsAg negative. Prospective studies indicate that routine screening for HBsAg by sensitive third generation tests would decrease the risk of PTH by only 20%. A large percentage (around 75% according to large scale prospective studies in the USA) is not caused by Hepatitis B virus, but by some other agent or agents. Only 50% of the PTH cases were found to be positive for HBsAg when tested. Moreover, the non B PTH cases were found to be not caused by other known hepatitis viruses such as Hepatitis A virus, cytomegalo virus or Epstein-Barr virus.

Hepatitis risk from Plasma derivatives : Certain plasma derivatives prepared from large pools of plasma have been known to carry a very high risk of contamination with HBV. Althoguh the risk has not been well quantified, in the past most batches of fibrinogen, anti-haemophilic factor and factor IX complex were believed likely to contain HBV.

Immunoglobulin and albumin products prepared by the cold ethanol fractionation method of Cohn and heated for 10 hours at 60°C have a well established reputation of being free from contamination with infective HBV.

Possible ways of improving the safety of the high risk plasma derivatives include the use of small plasma pools from voluntary donors, the elimination of all HBsAg reactive units after testing by a sensitive method among other measures.

Until manufacturing methods are developed that will yield uniformly safe batches of these plasma derivatives, the potential benefit of their use should be carefully weighed against the risk on an individual basis.

Hepatitis as an Occupational Hazard

Viral Hepatitis is an occupational risk among health workers. Where specific studies have been undertaken, it has been shown that the major risk is from HBV and not from HAV. Rare instances of transmission of Hepatitis B from health care workers to their patients (eg. HVB carrier dentists) have been reported, but the available information shows that health care personnel are at greater risk of contracting Hepatitis B from their patients than vice versa. Higher risk of hepatitis B has been identified for physicians, dentitsts, nurses and laboratory and dialysis technicians. High risk work areas include haemodialysis and oncology units, hospital laboratories, blood banks and surgical intensive care units.

A seroepidemiologic survey of practicing physicians done in the USA in 1975-76 concluded that HBV acquisition risk in physicians involved in patient care is at least 5 times that for a comparable non-physician population. Of the specialities, surgery and pathology were associated with the highest prevalence rates. Physicians with no clinical duties such as research scientists and administrators had the lowest prevalence rates.

Hospital employees who come in contact with blood or other secretions of patients have ample opportunity to be repeatedly exposed to HBV. The risk of recurrent exposure is higher for employees working in Hospitals located in areas of high HBV prevalence.

The prevention of occupational Hepatitis B is extremely important. An appropriate environmental hygiene measure is to minimise the frequency of contact of susceptible persons with blood and potentially infective secretions from patients.

Health workers outside haemodialysis and oncology units who routinely handle blood and other secretions should adhere scrupulously to sound hygienic measures for all specimen handling. They should for example avoid touching their mouth or eyes with their hands.

An unusually high incidence of Hepatitis B has been noted both among patients and among medical staff in haemodialysis and oncology units. In haemodialysis and oncology units the transmission of HBV may be reduced by implementing the following measures :-

1. Continuous screening of patients and staff for HBsAg from time of entry to the units, and the avoidance of contact between HBsAg positive staff and susceptible patients.
2. Segregation of HBsAg positive patients from susceptible patients.
3. Employment of staff with anti HBs for care of HBs positive patients.
4. Segregation of all dialysing equipment used for HBsAg positive patients.

Passive Immunization Against Hepatitis B

The availability of tests for anti HBs has made it possible to select high titre plasma for the manufacture of Hepatitis B immunoglobulin.

In one of the field (1) studies, Hepatitis B immunoglobulin was significantly more effective than ordinary immunoglobulin when attack rates were compared after 4—6 months, but no difference between the two types of immunoglobulin was found when attack rates were compared after 8—12 months because of a number of late cases in the recipients of Hepatitis B immunoglobulin. In (2) another field study there was a significant lowering of the attack rate in recipients treated with Hepatitis B immunoglobulin as compared with the group given the ordinary immunoglobulin and these results were not altered by the appearance of late cases.

The widespread use of Hepatitis B immunoglobulin might not be advisable in endemic situations where repeated or chronic exposure is the rule. In these situations it may be possible to achieve passive-active immunity with immunoglobulin containing a relatively low anti HBs titre.

Guidelines for passive Immunisation Against Hepatitis B

1. The major indication for Hepatitis B immunoglobulin is post-exposure prophylaxis for a single acute exposure to HBV such as when blood known or strongly suspected to contain HBsAg is accidently inoculated ("needle stick") ingested orally (as in a pipetting accident), or splashed on to mucous membranes. Hepatitis B immunoglobulin with a high anti HBs titre, standardised against a reference preparation, should be administered in a dose of approximately 5 ml for adults as soon as possible after such exposure.
2. In endemic settings such as haemodialysis units where HBV transmission is known to occur and where preventive hygiene measures cannot be implemented, prophylaxis with immunoglobulin containing anti HBs may be considered on a continuing basis. There is contraversy as to high-titre or low-titre immunoglobulin is preferable in these circumstances.
3. Individuals with a significant titre of anti HBs are generally resistent to HBV infection and usually require no passive immunisation.
4. Passive immunisation with Hepatitis B immunoglobulin does not appear to be indicated after blood transfusion, provided that HBsAg positive blood has been excluded by sensitive methods, because under such circumstances most cases of post-transfusion hepatitis are not due to HBV infection.

Active Immunisation Against Hepatitis B

A number of experimental vaccines have been tested for safety and effectiveness, and it is hoped that in the not too distant future a safe and effective vaccine will become available for use.

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