Hepatitis B infection in the Pacific

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Introduction

Hepatitis B infection, a disease with propensity for chronicity and irreversible liver damage, is prevalent in the Pacific. In the past 25 years, significant advances have been made in scientific knowledge about this disease and in its prevention. Tests for detection of Hepatitis B (HBV) markers are now widely available and play a significant role in disease prevention. These tests have also helped in defining the epidemiology and natural history of the disease.[1,2] Development of an effective vaccine against HBV has perhaps been one of the most significant advances in preventive medicine. Plasma-derived vaccine has been available since 1982, and the recombinant vaccine since 1986. This article reviews some of the important aspects of HBV infection in general, and more specifically, highlights the situation in the Pacific.

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The Hepatitis B virus

Hepatitis B is caused by a DNA virus (HBV) belonging to the *Hepadna viridae*.[1,2] There are three morphological forms on electron microscopy : a 22 nm spherical particle, a tubular form of the same diameter and a 42 nm spherical particle (Dane particle). The first two are made up exclusively of HBV surface antigen (HBs Ag) while the third consists of the surface antigen enclosing the nucleocapsid core. The nucleocapsid core bears a second antigen, the 'c' antigen, which is found only within the virus and is not present in the circulation. A third antigen, the 'e' antigen is soluble and is found in the serum. In the virus, it is associated with the structural polypeptide. Detection of these viral antigens and corresponding antibodies help in establishing the diagnosis and clinical course of the infection.

The virus remains viable for at least one week at 25°C after drying.[2] It is destroyed by heating 100°C for one minute or to 60°C for 10 hours. Sodium hypochlorite (0.5%) destroys the virus within three minutes. Efficacy in destroying the virus may be reduced in the presence of high concentrations of proteins, such as pus and blood.

Transmission of HBV

The communicability of HBV is much greater than that of HIV. The virus is transmitted parenterally, through transfusion of blood and blood products and use of contaminated needles[1,2,3] It is also transmitted sexually and perinatally. HBs Ag has been demonstrated in blood, vaginal secretions, semen, saliva and milk. The groups at high risk for developing this infection are similar to those for HIV: those receiving contaminated blood transfusions, parenteral drug users, health care personnel, patient and staff of haemodialysis units, individuals with multiple sexual partners and babies born to infected mothers. In addition to these routes of horizontal transmission in social and household settings through close contact, particularly between children, is the most common type of HBV transmission worldwide. For example, prevalence of infection is high among family and institutional contacts, especially children, without any of the above recognised modes of exposure.

In areas of high endemicity, transmission occurs primarily during early childhood. This may occur during the perinatal period or later.[1,2] Only a small proportion of transmissions occur transplacentally and the risk increases in the third trimester. Perinatal transmission occurs mostly either during delivery or in the postpartum period. The likelihood of perinatal infection is increased if the mother is also Hepatitis 'e' antigen positive and corelates best with the presence of circulating maternal HBV viral DNA. Infants who become HBs Ag positive generally do so in the initial two months. However, in areas of high prevalence, the risk of being infected continues throughout childhood.

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Table 1. Serological markers in hepatitis B infection

Test	Self limiting infection	Persistent infection
Surface antigen (HBs Ag)	Positive during active infection. Disappears within 6 months	Remains positive
Anti HBs Ag	Appears after HBs Ag disappears. Indicates recovery and protection	Negative (occasionally low level positive)
e antigen (Hbe Ag)	Positive during acute infection. Disappears in 5 months	Positive if active infection continues. Also indicates higher risk of transmission. Negative in carrier states, usually without continuing liver damage
Anti Hbe	Appears after antigen clears	May be positive if e antigen is negative and vice versa
Anti HBc Ag Total	Persists (Usually for life)	Persists at high levels
Anti HBc Ag IgM	Positive in acute infection. Usually indicates recent infection. If positive in the absence of HBs Ag, indicates infection with Hepatitis B virus.	Occasionally positive

Clinical features

Subclinical and asymptomatic infections are common. When symptomatic, acute hepatitis usually follows an incubation period of 50 - 180 days and is not distinguishable from viral hepatitis due to other agents. However extra-hepatic manifestations, such as rashes, often critical, and arthiritis are more common in HBV infection compared to other types of viral hepatitis. More than 90% of infected adults recover with complete clearing of HBs Ag and without sequelag in less than 10 weeks. Chronic infection develops in about 10% of adults with icteric hepatitis.[1,2] Nearly half of these patients have normal liver tests and are considered to be healthy carriers. The remaining show evidence of hepatitis like elevated transaminase levels. Chronically infected individuals can have histological abnormalities in the liver, with varying degrees of activity and fibrosis, which may progress to the end stage of cirrhosis. Generally, patients with more active disease have a greater propensity to develop cirrhosis. Hepatocellular carcinoma is also strongly associated with chronic infection. Chronicity is more likely to develop in those individuals with insidious, mild or subclinical infections. During the acute disease, 1-2% of patients develop fulminant hepatitis with mortality rates of up to 90%. These patients, if they recover, are unlikely to develop chronic disease.[1,2]

Clinical manifestations of acute hepatitis are often absent among infected newborns and children.[1,2] Persistence of the virus is more common in this group compared to adults.[1,2] About 90% of the infants infected at birth become chronic carriers. The risk decreases steadily with age, to about 10% in those infected in adulthood.

The disease also progresses to chronicity in males more than in females.[1,2] Other factors that contribute to chronicity are immunosuppression at the time of infection, corticosteroid therapy during acute infection, and repeated exposures as occurs in health care workers and drug addicts. There also appears to be a genetic predilection for chronicity.

Table 3. Seropositivety for Hepatitis B in blood donors of Pacific countries*

Country	% Positivity
Cook Islands	11.6
Fiji	7.6
French Polynesia	1.2
Guam	1.2
Kiribati	12
Marshall Islands	9.3
Micronesia	4.3
Palau	1
Papua New Guinea	16.7
Samoa	3.4
Solomon Islands	19.5
Tonga	16.5
Vanuatu	10.9

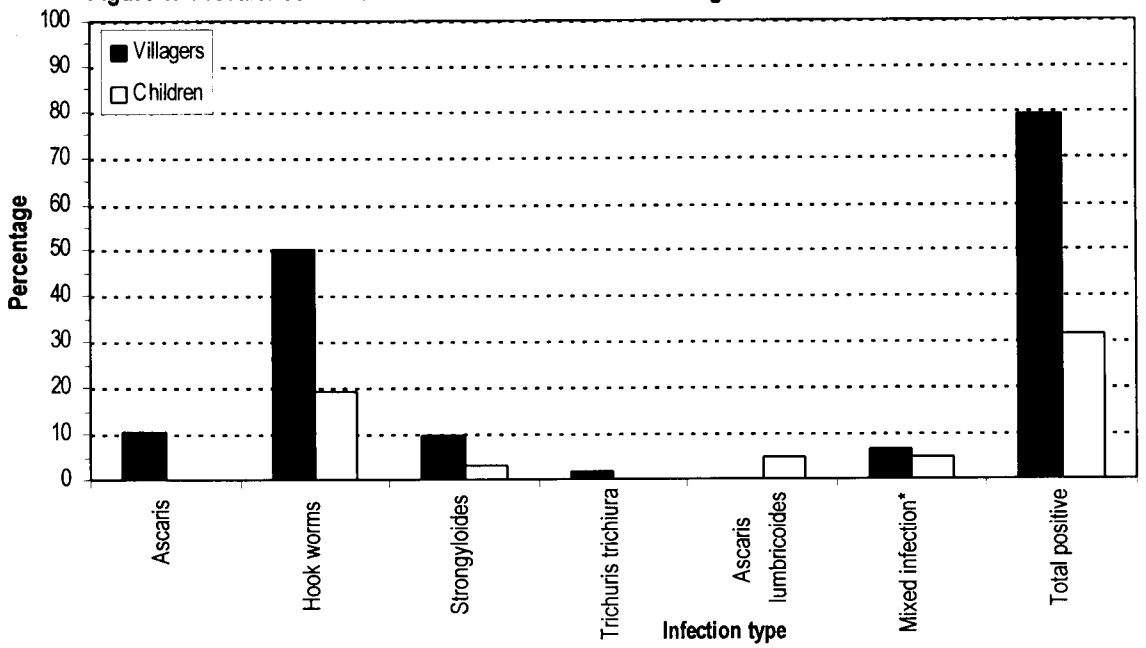
* *Source: Reference 7*

Diagnosis

Specific diagnosis of HBV infection requires testing for serological markers.[1,2] HBs Ag is positive in more than 95% of infected individuals. This remains the most sensitive and specific marker for the diagnosis of hepatitis B infection. Serological events following hepatitis B infection are depicted in Table 1. HBs Ag is detectable during all stages of the infection including late in the incubation period and chronic infection. Persistence of HBs Ag for more than 6 months defines chronic infection.

Another antigen likely to be positive in early disease is the 'e' antigen. Presence of 'e' antigen indicates *active* HBV infection, acute or chronic. The risk of transmission is higher if the source individual is 'e' antigen positive. The best test of level of viral re[lication and infectiv-

Figure 1. Prevalence of intestinal helminth infection in villagers and school children



Note: Villagers (123): all ages. School children (130): 7-14 years

ity is circulating HB viral DNA, but this is less readily available than tests for e Ag and anti Hbe. The antibodies that can be detected are the anti-HBc, anti-HBS antibodies. The anti-HBc antibodies are frequently detected at the onset of clinical illness, a few weeks after HBs Ag becomes detectable. Presence of anti-HBc IgM indicates that the infection is acquired recently. However low titres of this antibody may be present in chronic infections also. The test is positive in infected but HBs Ag negative individuals. Anti HBs appears only after the disappearance of HBs Ag and indicates protection against reinfection. Similarly, anti-Hbe appears only after the corresponding antigen is cleared and indicates less infectively in a HBs Ag positive individual. Only anti-HBs antibody indicates protection; anti HBc indicates exposure.

Treatment

Interferon alpha has been found to be effective in clearing the virus from 30-40% of selected patients with chronic infection[3,4,5] but therapy is complex, must be given by injection, is prolonged and costly. In those who respond, transaminases return to normal, liver histology improves and recurrences are not very common. Anti viral drugs like penciclovir, famciclovir and lamivudine undergoing clinical trials for the treatment of chronic infection, appear to be promising.[5]

Prevention and control

HBV infection can be prevented by preventing transmission and also by protecting individuals at risk. Procedures adopted include routine screening of all donated blood and blood products for HBV, pre exposure vaccination of individuals at risk, providing immunoglobulin and vaccines as post prophylaxis to unprotected persons, practising universal precautions and safe sex.

Vaccine. Vaccines contain HBs AG and two types are available for routine use.[1,2] These are the plasma derived vaccine and the recombinant vaccine. The safety and efficacy

Table 2. Prevalence of HBs Ag among blood donors and pregnant women in Suva, Fiji

		1994	1995	1996
Pregnant women	Number tested	4371	5228	5514
	Number positive	209	236	279
	Percentage positive	4.8	4.5	5.1
Blood donors	Number tested	4510	5003	4808
	Number positive	268	291	205
	Percentage positive	5.9	5.8	4.3

of these vaccines have been proven in large field studies and are similar. Both are useful for pre and post exposure prophylaxis. Protection lasts for at least 10-15 years.

Immunoglobulin. High titre specific HBV immunoglobulin (HBIG) is available in limited supply and at high cost. This was shown to be effective in preventing infection in children exposed to infectious serum. Prevention of transfusion associated hepatitis using specific immunoglobulin however has not been proven conclusively. Imunoglobulin is recommended as an adjunct to vaccine for post exposure prophylaxis.

Pre exposure prophylaxis with vaccine is currently recommended for all susceptible and at risk groups.[6] It is recommended for all infants in all countries by WHO, which set 1997 as the target year for all countries to establish HBV control programs. WHO has also set a target of 80% reduction in new childhood HBV infection by the year 2000. The HBV vaccine has been included as part of routine childhood immunisation in many Pacific countries. The high risk groups for whom vaccination is recommended are health care personnel including laboratory workers, homosexual males, heterosexuals with multiple sex partners, intravenous drug users, institutionalised individuals babies born to infected mothers, dialysis patients and emergency service personnel.

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Babies of mothers with HBs Ag should receive the vaccine immediately after birth. If the vaccine is not available at the time of birth, it should be given as early as possible during the first week. A second dose of vaccine is given after one month and a third dose at 6 months of age. These infants may derive a small additional increment in protection if HBIG is also given within a few hours of birth.

Guidelines for **post occupational exposure prophylaxis** have been established. Susceptible persons exposed to HBV percutaneously or through mucosal splashes, should receive both the vaccine and HBIG, administered at different sites, as soon as possible. Both these products have no proven efficacy in the treatment of HBs Ag positive individuals. Since delta virus infection is always associated with HBV infection, prevention of HBV also prevents delta viral infection.

Blood banking. Sensitive methods of detecting HBs Ag are being employed by most blood banks to screen out infected blood. Nevertheless transfusion induced HBV continues to occur, although at a reduced frequency. This problem should further decrease with proper donor selection, mandatory testing for hepatitis, using blood only when indicated, and universal infant HB immunisation.

Adopting good practices, including universal precautions, will prevent transmission occurring during patient care. Spouses and family contacts of hepatitis B-infected individuals should be educated on modes of transmission and methods of prevention and all unsusceptible household contacts and sexual partners should be immunised.

HBV situation in the Pacific

The prevalence of chronic infection is particularly high in the Pacific. Prevalence rates among the blood donors from different countries, are shown in Figure 1.[7] These figures, are representative of the problem in adult population in these countries.[7] In such areas with high prevalence, most infections are transmitted perinatally or in early childhood. Therefore routine neonatal immunisation against HBV was introduced in many of these countries.[8,9,10] Although data collected from children before immunisation programs were introduced showed high prevalence rates, current figures are significantly lower.[8,9,10]

There is paucity of data on the prevalence of chronic infection and its complications in Fiji. A survey done in 1982 showed that 11% of adult Melanesian population had chronic infection with HBV and 60-90% had evidence of past infection.[11] There was no major difference between rural and urban population.

Current prevalence can only be estimated from rates obtained from screening two groups of apparently normal population : blood donors and pregnant women. Data from these two groups tested at CWM hospital, Suva, are shown in Table 2. The overall prevalence of HBV in Fiji in these two groups is about 5-6%. It is higher among blood donors, a group which mostly comprises of men. Infection rates were at least two times higher in the Fijian population (approximately 7%) compared with the Indian population (approximately 3%). In 1982, Fijians had a prevalence of 11% and Indians 2%.

Individuals with chronic HBV infection have a 200 fold greater risk of developing hepatocellular carcinoma compared with an uninfected persons. In 1995, liver cancers were

reported in 38 cases (28 Fijians, eight Indians and two belonging to other races).

Measures are being implemented for the control of this infection in Fiji. In addition to routine screening in blood banks, all newborn babies receive vaccination. Vaccine coverage was 82% in 1996.[12] HBs Ag screening tests are being offered to all pregnant women attending hospital clinics.

In summary, HBV is a global problem, with higher prevalence rates in certain parts of the world, including the Pacific. It is a highly transmissible and causes significant morbidity and mortality. Effective screening and control programs together with increased community awareness regarding transmission, should reduce the burden of this infection in future.

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When I look upon the past, I can only dispel the sadness which falls upon me by gazing into the happy future when infection will be banished ... The conviction that such a time must inevitably sooner or later arrive will cheer my dying hour.

Ignaz Semmelweis (1818-1865)

'Etiology'