Pre-meeting document

Hepatitis B vaccination: How to reach risk groups

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General background

Hepatitis B virus (HBV) is one of the world's most widespread infectious agents and the cause of millions of infections and deaths each year. Vaccination programmes aimed at risk groups are important for individual protection, but will not eliminate viral transmission in Europe, since 70% of acute hepatitis B cases are either acquired by sexual activity or are of unknown origin. In industrialised countries, HBV infection occurs mainly in young adults. However, when the virus is acquired during infancy it leads to extremely high rates of chronic carriership, contributing disproportionately to the overall pool of chronic hepatitis B surface antigen (HBsAg) carriers. The virus is transmitted by parenteral or mucosal exposure to HBsAg-positive body fluids from persons who are chronic carriers or have acute HBV infection. The highest concentrations of virus are in blood and serous fluids. Lower titres are found in other fluids, such as saliva and semen. Saliva can be a vehicle of transmission through bites; however, other types of exposure to saliva, including kissing, are unlikely modes of transmission. There appears to be no transmission of HBV via tears, sweat, urine, stool, or droplets.

In the United States and other industrialised countries, the most important route of transmission is by sexual contact, either heterosexual or homosexual, with an infected person. Faecal-oral transmission does not appear to occur. However, transmission among homosexual men occurs possibly via contamination from asymptomatic rectal mucosal lesions. Direct percutaneous inoculation of HBV by needles during injection drug use is an important mode of transmission. Transmission of HBV may also occur by other percutaneous exposure, including tattooing, ear piercing, and acupuncture, as well as needle-sticks or other injuries from sharp instruments sustained by medical personnel. These exposures account for only a small proportion of reported cases in low endemicity countries. Breaks in the skin without overt needle puncture, such as fresh cutaneous scratches, abrasions, burns, or other lesions, may also serve as routes for entry. Contamination of mucosal surfaces with infective serum or plasma may occur in mouth pipetting accidents, accidental eye splash, or other direct contact with mucous membranes of the eyes or mouth, such as hand-to-mouth or hand-to-eye when contaminated with infective blood or serum. Transfer of infective material to skin lesions or mucous membranes via inanimate environmental surfaces may occur by touching surfaces of various types of hospital equipment. Contamination of mucosal surfaces with infective secretions other than serum or plasma could occur with contact involving semen. (National Immunization Program, 2000).

Worldwide, most infections occur from infected mother to child, from child to child contact in household settings, and from reuse of unsterilised needles and syringes. In many developing countries, a vast majority of children becomes infected with the virus. In many industrialised countries (e.g., Western Europe and North America), the pattern of transmission is different. In these countries, mother-to-infant and child-to-child

transmission accounted for up to one third of chronic infections before childhood hepatitis B vaccination programmes were implemented. However, the majority of infections in these countries are acquired during young adulthood by sexual activity, and injecting drug use. In addition, hepatitis B virus used to be the major infectious occupational hazard of health workers, and, since more than ten years, most health care workers have received hepatitis B vaccine (WHO, 2000).

Control and the eventual elimination of transmission of HBV infection is possible with the appropriate use of hepatitis B vaccines. The prevention of chronic HBV infection has the potential of reducing the burden of chronic liver disease and primary hepatocellular carcinoma. Worldwide, strategies for the effective use of hepatitis B vaccine have been developed and are being implemented in those areas where childhood transmission is the predominant source of chronic HBV infections.

This explains why integrating universal hepatitis B (HB) vaccination into routine infant immunisation programmes is the best means for controlling hepatitis B in countries with intermediate to high levels of endemicity. In countries of low endemicity, universal immunisation of adolescents may be considered as an alternative to infant vaccination, as this strategy has a more rapid effect on the epidemiology of the infection. Where feasible, a double strategy (infant plus adolescent) is the optimal solution. With this strategy, adolescent immunisation is necessary only for the time required for the first cohort of immunised infants to reach adolescence. After universal vaccination programmes have been implemented, efforts must be made to sustain vaccine procurement, monitor coverage, check the incidence of acute disease, particularly in immunised cohorts and verify by seroepidemiological studies the progression made in the elimination of HBV transmission (Bonanni, 1998).

The World Health Organisation (WHO) recommended in 1992 that all countries should introduce universal hepatitis B vaccination into their immunisation schedules by December 1997. One hundred and sixteen countries, many of them in Western Europe, have complied with the recommendation.

The four main approaches to immunisation against hepatitis B are, in principle: (1) Vaccination of high-risk babies; (2) Universal adolescent immunisation; (3) Universal infant immunisation; (4) Vaccination of adults. Universal antenatal screening would permit identification of carrier mothers and immunisation of their babies. Vaccination of adolescents would provide protection close to the time when risk of exposure increases, and could be delivered as part of a wider package on health education. Universal vaccination of infants is the best option because it is known that vaccines can be delivered to babies at a very high coverage and it is more acceptable to parents (Zuckerman, 1996).

In countries such as the United Kingdom (UK), however, hepatitis B vaccine is offered to selected high-risk population groups only. Vaccination uptake in many of these groups is poor and transmission of hepatitis B remains a problem (Goldberg and McMenamin, 1998).

In the United States and other areas with 'low' rates of HBV infection, vaccination strategies have not been effective and have not fully taken into account the multifaceted epidemiology of HBV infection in those areas. Unfortunately, the majority of infections occur among adults who have been the most difficult to access, who acquire infection before they realise they are at risk, and where the changing epidemiology of HBV infections among the various risk groups only emphasises the problems of vaccine delivery. In addition, the majority of persons receiving vaccine as a result of the strategy to immunise adult high risk groups have been persons who acquire HBV infection through occupational exposure, a group that accounted for no more than 5% of cases even before vaccine was introduced. The failure of the immunisation strategy to prevent a disease with significant health care and economic consequences has stimulated a reevaluation of this approach. A comprehensive approach to eliminating HBV transmission must address infections acquired during early childhood as well as those acquired by teenagers and adults (Margolis *et al*., 1991).

The strategy to eliminate HBV transmission in the United States is now comprised of the following components: (1) Preventing perinatal transmission; (2) Routine infant vaccination; (3) Catch-up vaccination of children in high risk groups at any age; (4) Catch-up vaccination of all children at 11-12 years of age; (5) Vaccination of adolescents and adults in high risk groups. Current data indicate that implementing this strategy to eliminate HBV transmission is well progressing (Mast *et al*., 1998a). Substantial progress has been made in implementing routine infant hepatitis B vaccination. However, in 1996, an estimated 65,000 acute hepatitis B cases occurred, the majority of which were among young adults in high-risk groups. Recent surveys have found very low vaccination coverage among several high-risk groups, including men who have sex with men (MSM) and patients with sexually transmitted diseases (STD's). Targeted vaccination of persons with risk factors for hepatitis B virus infection can be provided in a variety of settings including family planning clinics, STD clinics, drug treatment centres, detention centres, jails, and prisons. However, vaccination programmes have been infrequently implemented in these settings and the majority of persons with acute hepatitis B cases have missed the opportunity to be vaccinated in the past. Thus, in order to accelerate elimination of HBV transmission in the United States, increased efforts are needed to implement effective hepatitis B vaccination programmes targeted to adolescents and adults in high risk groups (Mast *et al*., 1998b).

The Canadian Hepatitis B Working Group developed recommendations for the control of hepatitis B in Canada, including options for universal immunisation programmes. Despite

the availability of effective and safe vaccines in Canada since 1982, the reported incidence of acute hepatitis B and of death from HBV infections increased progressively during the 1980s. This increase reflects a failure of a selective vaccination strategy directed at identifiable high-risk groups to control virus transmission in the population. Health care workers are the one exception to this statement. Implementation of vaccination policies in hospitals has greatly reduced the incidence of acute HBV infection in health care workers, but this group has never accounted for a substantial proportion of cases in Canada. There are many reasons for the failure of the present selective immunisation strategy to affect disease incidence: (1) Cost of the vaccine; (2) Lack of physician awareness; (3) Difficulties in reaching members of high risk groups, who often do not perceive themselves as being at risk; (4) Concerns about vaccine safety; (5) Lack of compliance in completing vaccination schedules; (6) Absence of identified risk factors in 30% to 60% of recently infected individuals (Hepatitis B Working Group, 1994).

The Canadian Hepatitis B Working Group considered four options and developed pros and cons for each one. These options were the following: (a) Status quo (i.e., selective vaccination of high risk individuals); (b) Universal infant vaccination; (c) Universal vaccination of adolescents (i.e., 14 to 18 years of age); (d) Universal vaccination of children 9 to 13 years of age. Continuation of universal prenatal screening, provision of hepatitis B immune globulin (HBIG) and vaccine to newborns of carrier mothers, and continued vaccination of children at high risk would be recommended under all strategies.

Additionally, a specific Canadian recommendation concerning the option 'selected vaccination' includes the requirement for continued and improved targeted programmes for adults at high risk of exposure to hepatitis B. This is particularly important in the period before universal childhood vaccination is implemented in all jurisdictions, but it will also be necessary for the foreseeable future until those vaccinated under a universal programme reach middle age. The pros and cons for this option were summarised as follows. Pros: (1) There would be no added cost to the provinces and territories; (2) Current programs address those at highest risk. Cons: (1) The number of cases in Canada from 1980 to 1991 indicates that HBV infection has not been controlled through current programmes; (2) Incomplete coverage of target groups would continue; (3) Public concern over incidence of disease would not be addressed (Hepatitis B Working Group, 1994).

The Viral Hepatitis Prevention Board (VHPB) has also issued a number of guidelines relevant in this context. They include: (1) Consensus statement on universal hepatitis B vaccination programmes (Viral Hepatitis Prevention Board, 1996); (2) Recommendations on prevention of perinatal HBV transmission (Viral Hepatitis Prevention Board, 1998a); (3) Recommendations on injection safety and safe blood supply (Viral Hepatitis Prevention Board, 1998b); (4) Recommendations on prevention and control of hepatitis B

in the community (Grosheide and Van Damme, 1996). Their full text is included in this document as Appendices 1, 2, 3, and 4, respectively.

Universal infant and adolescent strategies have their own benefits and drawbacks; the VHPB has looked carefully into the rationale for and against these strategies. A combined infant and adolescent strategy emerges as having many of the advantages of the individual approach and fewer disadvantages. Universal vaccination is clearly the most effective strategy for preventing hepatitis B. Its timely and successful implementation, even in countries with medium and low prevalence, is a priority. There is no reason why hepatitis B should not follow the success of smallpox, polio, diphtheria, and measles vaccination (Hallauer, 1995).

Universal immunisation

Since 1991, WHO has called for all countries to add hepatitis B vaccine into their national immunisation programmes. As of March 2000, 116 countries had included hepatitis B vaccine in their national programmes including most countries in Eastern and Southeast Asia, the Pacific Islands, Australia, North and South America, Western Europe and the Middle East. However, many low-income countries in sub-Saharan Africa, on the Indian subcontinent and in the Newly Independent States do not use the vaccine. The price of the hepatitis B vaccine has been one of the main obstacles to its introduction in many of these countries (WHO, 2000).

The WHO hepatitis B vaccination policy can be summarised as follows. In 1991 EPI (Expanded Programme on Immunisation) set targets for the introduction of hepatitis B vaccine into national immunisation programmes. These targets, approved by the World Health Assembly in 1992, indicated that hepatitis B vaccine should be integrated into national immunisation programmes in all countries with a prevalence of chronic HBV infection (HBsAg) of 8% or greater by 1995 and in all countries by 1997. For all countries, the most effective strategy is incorporation of hepatitis B vaccine into the routine infant immunisation schedules. In 1994, the World Health Assembly, in its Ninth General Programme of Work added a disease reduction target for hepatitis B, calling for an 80% decrease in the incidence of new chronic HBV infections in children by the year 2001. Priorities should be (1) Routine infant hepatitis B vaccination; (2) Prevention of perinatal HBV transmission; (3) Catch-up vaccination of older persons (WHO, 2001).

Routine vaccination of all infants as an integral part of the national immunisation schedule should be the highest priority in all countries. In countries with a high endemicity of HBV infection (HBsAg prevalence >8%), routine infant hepatitis B vaccination can rapidly reduce transmission because most chronic infections are acquired from spread either from mother to baby or from child-to-child. In countries with lower

HBV endemicity, routine infant hepatitis B vaccination should also be the highest priority because a high proportion of chronic infections may be acquired during childhood in these countries; and many infections acquired during childhood occur among children born to mothers who are NOT infected with HBV. Thus, these infections would not be prevented by perinatal hepatitis B prevention programmes that screen pregnant women for HBsAg and provide post-exposure immunisation for infants of HBsAg-positive mothers (WHO, 2001).

In the United States, a number of recommendations have been prepared for universal vaccination of infants born to HBsAg-negative mothers (CDC, 1991a):

(1) Hepatitis B vaccination is recommended for all infants, regardless of the HBsAg status of the mother. Hepatitis B vaccine should be incorporated into vaccination schedules for children. The first dose can be administered during the newborn period, preferably before the infant is discharged from the hospital, but no later than when the infant is 2 months of age. Because the highest titres of anti-HBs are achieved when the last two doses of vaccine are spaced at least 4 months apart, schedules that achieve this spacing may be preferable. However, schedules with 2-month intervals between doses, which conform to schedules for other childhood vaccines, have been shown to produce a good antibody response and may be appropriate in populations in which it is difficult to ensure that infants will be brought back for all their vaccinations. The development of combination vaccines containing HBsAg may lead to other schedules that will allow optimal use of combined antigens.
(2) Special efforts should be made to ensure that high hepatitis B vaccination coverage is achieved in populations in which HBV infection occurs at high rates among children (Alaskan Natives, Pacific Islanders, and infants of immigrants from countries in which HBV is endemic).

In October 1997, the Advisory Committee on Immunization Practices (ACIP) expanded its hepatitis B vaccination recommendations for the United States to include all unvaccinated children aged 0-18 years and made hepatitis B vaccine available through the Vaccines for Children programme (VFC) for persons aged 0-18 years who are eligible for VFC. ACIP priorities for hepatitis B vaccination of children remain unchanged and include all infants; children in populations at high risk for hepatitis B virus (HBV) infection (e.g., Alaska Natives, Pacific Islanders, and children who reside in households of first-generation immigrants from countries where HBV infection is moderately or highly endemic); previously unvaccinated children aged 11-12 years; and older adolescents and adults in defined risk groups (CDC, 1999).

Prevention of perinatal hepatitis B virus infection

Neonatal infection with hepatitis B virus carries a very high risk of resulting in a persistent infection. Babies born to hepatitis B carrier mothers are at risk of infection through exposure to blood and body fluids during birth. These 'at risk' babies can only be identified through screening of all mothers during pregnancy. Prevention of infection in this group is a key element in any nation's strategy to reduce the incidence and eventually eliminate hepatitis B infection in its population, as the persistently infected infants are a reservoir of infection throughout their lives. The infected adult carries a relatively low risk of becoming a chronic carrier (< 10%). Various strategies for screening in pregnancy have been adopted. These include attempts to identify women with a history of 'risk behaviour', testing only women who were born in areas of high endemicity, pooling of sera and universal antenatal screening (Boxall, 1998).

If the mother is positive for both HBsAg and HBeAg, 70-90% of infants will become infected. Up to 90% of these infected infants will become HBV carriers. The risk of perinatal transmission drops to 20% if the mother is positive only for HBsAg. An estimated 25% of these carriers will ultimately die of liver failure secondary to chronic active hepatitis, cirrhosis, or primary hepatocellular carcinoma (HCC) (Grosheide and van Damme, 1996; National Immunization Program, 2000).

One of the priorities of the WHO hepatitis B vaccination policy concerns prevention of perinatal HBV transmission. Their points of view in this respect are, in summary (WHO, 2001):

(1) In order to prevent HBV transmission from mother to baby, the first dose of hepatitis B vaccine needs to be given as soon as possible after birth (preferably within 24 hours). In most countries, the most feasible strategy to prevent HBV transmission from mother to baby is to give a birth dose of hepatitis B vaccine to all infants. An alternative strategy is to screen all pregnant women for HBsAg and provide immunisation beginning at birth to infants of HBV-infected mothers. However, extensive resources are required to screen pregnant women and to track infants of infected mothers. Moreover, few countries have implemented programmes that have been successful in identifying all of the expected infants of HBV-infected mothers in the country, and in tracking these infants to assure completion of the hepatitis B vaccine series.
(2) The priority for incorporation of strategies to prevent perinatal HBV transmission in a particular country should take into account the relative contribution of perinatal transmission to the overall hepatitis B disease burden, and the feasibility of delivering the first dose of hepatitis B vaccine at birth. In general, it is most feasible to deliver hepatitis B vaccine at birth to infants who are born in health facilities. In addition, the availability of monovalent hepatitis B vaccine in pre-filled single dose injection

devices can facilitate administration of hepatitis B vaccine by birth attendants to infants delivered at home.

i. In all countries, achieving high vaccine series completion among all infants is the highest priority, and will have the greatest overall impact on the prevalence of chronic HBV infections in children, regardless of whether it is feasible to administer a birth dose.
ii. In countries where a high proportion of chronic HBV infections are acquired perinatally (e.g., Southeast Asia), a birth dose should be given to infants who are delivered in hospitals when hepatitis B vaccine is introduced. Efforts should also be made in these countries to give hepatitis B vaccine as soon as possible after birth to infants delivered at home.
iii. In countries where a lower proportion of chronic infections is acquired perinatally (e.g., Africa), use of a birth dose may also be considered after evaluating the relative contribution of perinatal HBV infections to the overall disease burden, and the feasibility and cost-effectiveness providing a birth dose to infants.

The following recommendations regarding the risk of perinatal HBV infection and its prevention were formulated by CDC (1991a):

(1) All pregnant women should be routinely tested for HBsAg during an early prenatal visit in each pregnancy, preferably at the same time other routine prenatal laboratory testing is done. HBsAg testing should be repeated late in the pregnancy for women who are HBsAg-negative but who are at high risk of HBV infection (e.g., injecting drug users, those with intercurrent sexually transmitted diseases) or who have had clinically apparent hepatitis. Tests for other HBV markers are not necessary for the purpose of maternal screening. However, HBsAg-positive women identified during screening may have HBV-related liver disease and should be evaluated (CDC, 1991b).
(2) Infants born to mothers who are HBsAg-positive should receive the appropriate doses of hepatitis B vaccine and HBIG (0.5 ml) within 12 hours of birth. Both should be administered by intramuscular injection. Hepatitis B vaccine should be administered concurrently with HBIG but at a different site. Subsequent doses of vaccine should be administered according to the recommended schedule.
(3) Women admitted for delivery who have not had prenatal HBsAg testing should have blood drawn for testing. While test results are pending, the infant should receive hepatitis B vaccine within 12 hours of birth, in a dose appropriate for infants born to HBsAg-positive mothers; (a) If the mother is later found to be HBsAg-positive, her infant should receive the additional protection of HBIG as soon as possible and within 7 days of birth, although the efficacy of HBIG administered after 48 hours of age is not known (Beasley, 1983). If HBIG has not been administered, it is important that the infant receive the second dose of hepatitis B vaccine at 1 month and not later than

2 months of age because of the high risk of infection. The last dose should be administered at age 6 months; (b) If the mother is found to be HBsAg-negative, her infant should continue to receive hepatitis B vaccine as part of his or her routine vaccinations, in the dose appropriate for infants born to HBsAg-negative mothers.

(4) In populations in which screening pregnant women for HBsAg is not feasible, all infants should receive their first dose of hepatitis B vaccine within 12 hours of birth, their second dose at 1-2 months of age, and their third dose at 6 months of age as a part of their childhood vaccinations and well-child care.

(5) Household contacts and sex partners of HBsAg-positive women identified through prenatal screening should be vaccinated. Hepatitis B vaccine should be administered at the age-appropriate dose to those determined to be susceptible or judged likely to be susceptible to infection.

Risk groups: general

WHO considers hepatitis B catch-up vaccination of persons older than one year of age as one of its priorities, besides routine infant vaccination and prevention of perinatal HBV transmission. This target group includes a number of risk groups for HBV infection. The need for catch-up vaccination of older persons varies depending on the endemicity of HBV infection in a particular country (WHO, 2001).

(1) In countries with a high endemicity of HBV infection (HBsAg prevalence >8%), most chronic HBV infections are acquired among children less than 5 years of age. Thus, routine infant vaccination will rapidly reduce transmission of HBV, and catch-up vaccination of older children is usually not warranted. In particular, catch-up vaccination efforts for older age groups should not detract from efforts to achieve high vaccination series completion among infants and efforts to prevent spread from mother to baby by giving the first dose of hepatitis B vaccine at birth.

(2) In countries with lower HBV endemicity, there may be a substantial disease burden from chronic infections acquired by older children, adolescents and adults. In these countries, vaccinating infants alone may not substantially lower disease incidence for decades, and catch-up strategies targeted to these older age groups may be desirable. Establishing surveillance for acute hepatitis B, and conducting seroprevalence studies of HBV infection, can assist in determining the groups at highest risk of acquiring HBV infection for whom vaccination and other prevention efforts may be targeted (e.g., health care workers, clients and staff of institutions for the developmentally disabled, injecting drug users, men who have sex with men, persons with multiple sex partners).

A number of risk groups have been described by the Centers for Disease Control and Prevention and include (CDC, 2000):

- Injection drug users.
- Sexually active heterosexuals.
- Men who have sex with men.
- Infants/children of immigrants from disease-endemic areas.
- Low socio-economic level.
- Sexual/household contacts of infected persons.
- Infants born to infected mothers.
- Health care workers.
- Haemodialysis patients.

The same organisation 'translates' these descriptions for a more general public as follows: You may be at risk if you: (1) Have a job that exposes you to human blood; (2) Live in the same house with someone who has lifelong hepatitis B virus infection; (3) Inject drugs; (4) Have sex with a person infected with hepatitis B virus; (5) Have sex with more than one partner; (6) Are a child whose parents were born in Southeast Asia, Africa, the Amazon Basin, the Pacific Islands, or the Middle East; (7) Are a patient or work in an institution for the developmentally disabled; (8) Have haemophilia; (9) Travel internationally to areas with a high prevalence of hepatitis B (CDC Wonder, 1996).

In the 2001 edition of its recommendations for adult immunisation, the Immunization Action Coalition (IAC) gives a definition of high-risk adults, adapted from the Advisory Committee on Immunization Practices (ACIP), as follows:

- Household contacts and sex partners of HBsAg-positive persons.
- Users of illicit injectable drugs.
- Heterosexuals with more than one sex partner in 6 months.
- Men who have sex with men.
- People with recently diagnosed STD's.
- Patients receiving haemodialysis or having renal disease that may result in dialysis.
- Recipients of certain blood products.
- Health care workers and public safety workers who are exposed to blood.
- Clients and staff of institutions for the developmentally disabled.
- Inmates of long-term correctional facilities.
- Certain international travellers.

IAC adds that prior serologic testing may be recommended depending on the specific level of risk and/or likelihood of previous exposure. Besides, the following is recommended for immigrants from highly endemic areas: (a) Provide serologic screening; (b) When HBsAg-positive persons are identified, offer appropriate disease

management; (c) In addition, screen their sex partners and household members and, if found susceptible, vaccinate (Immunization Action Coalition, 2001).

CDC (2000) states that a hepatitis B vaccine is available since 1982 and recommends routine vaccination of 0-18 year olds in the USA. Besides, it produces the following specific recommendations for prevention of hepatitis B in high risk groups: (1) Screening of pregnant women and treatment of infants born to infected women; (2) Screening of blood/organ/tissue donors; (3) Catch-up vaccination (after universal vaccination) of high risk groups of all ages.

Although HBV infection is uncommon among adults in the general population of industrialised countries, it is highly prevalent in certain groups. Risk for infection varies with occupation, lifestyle, or environment. Generally, the highest risk factor for HBV infection is associated with lifestyles, occupations, or environments in which contacts with blood from infected persons is frequent. In addition, the prevalence of HBV markers for acute or chronic infection increases with increasing numbers of years of high-risk behaviour. For instance, an estimated 40% of injection drug users become infected with HBV after 1 year of drug use, while over 80% are infected after 10 years. Based on the prevalence of HBsAg and other serological markers of HBV infection, various population groups are sometimes classified as high, intermediate, or low risk groups, in the following way (National Immunization Program, 2000):

(1) High risk:
- Immigrants/refugees from areas of high HBV endemicity.
- Clients in institutions for the developmentally disabled.
- Users of illicit parenteral drugs.
- Homosexually active men.
- Patients of haemodialysis units.
- Household contacts of HBV carriers.

(2) Intermediate risk:
- Male prisoners.
- Health care workers - frequent blood contact.
- Staff of institutions for the mentally retarded.
- Heterosexuals with multiple partners.

(3) Low risk:
- Health care workers - no or infrequent blood contact.
- Healthy adults (first-time volunteer blood donors).

A comprehensive strategy to prevent HBV infection, acute hepatitis B, and the sequelae of HBV infection in the United States must eliminate transmission that occurs during infancy and childhood, as well as during adolescence and adulthood. It has become evident that HBV transmission cannot be prevented through vaccinating only the groups

at high risk of infection. No current medical treatment will reliably eliminate chronic HBV infection and thus eliminate the source of new infections in susceptible persons (Perillo *et al*., 1990). Therefore, new infections can be prevented only by immunising susceptible persons with hepatitis B vaccine. Routine visits for prenatal and well-child care can be used to target hepatitis B prevention. A comprehensive prevention strategy includes: (1) Prenatal testing of pregnant women for HBsAg to identify newborns who require immunoprophylaxis for the prevention of perinatal infection and to identify household contacts who should be vaccinated; (2) Routine vaccination of children born to HBsAg-negative mothers; (3) Vaccination of certain adolescents; (4) Vaccination of adults at high risk of infection (CDC, 1991a).

Since most HBV infections in industrialised countries occur among adults, disease control could be accelerated by vaccinating emerging at-risk populations, such as adolescents and susceptible contacts of chronic HBV carriers. The recommendation for universal infant vaccination neither precludes vaccinating adults identified to be at high risk of infection nor alters previous recommendations for postexposure prophylaxis for hepatitis B (CDC, 1990).

The three major risk groups (heterosexuals with contact with infected persons or multiple partners, injection drug users, and men who have sex with men) are not reached effectively by targeted programmes. Deterrents to immunisation of these groups include lack of awareness of the risk of disease and its consequences, lack of effective public or private sector programmes, and vaccine cost. Difficulty in gaining access to these populations is also a problem. Further, there has been limited success in providing vaccine to persons in high risk groups due to rapid acquisition of infection after beginning high risk behaviours, low initial vaccine acceptance, and low completion rates (National Immunization Program, 2000).

Selected risk groups

Persons with occupational risk

HBV infection is an occupational hazard for health care workers and for public safety workers who have exposure to blood in the workplace (US Dept of Labor and US Dept of Health and Human Services, 1987; CDC, 1989). The risk of acquiring HBV infections from occupational exposures depends on the frequency of percutaneous and permucosal exposure to blood or blood-contaminated body fluids. Any health care or public safety worker may be at risk for HBV exposure, depending on the tasks he or she performs. Workers who perform tasks involving contact with blood or blood-contaminated body fluid should be vaccinated (US Dept of Labor and US Dept of Health and Human Services, 1987; CDC, 1989; US Dept of Labor, 1989). For public safety workers whose exposure to blood is infrequent, timely postexposure prophylaxis should be considered

rather than routine preexposure vaccination. For persons in health care fields, vaccination should be completed during training in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions, before trainees have their first contact with blood (CDC, 1991a; National Immunization Program, 2000).

The occupational health of surgeons and other health care workers has been examined and evaluated. Surgeons routinely work with potentially infectious materials. The risk of acquiring a disease from one percutaneous exposure is 0.3-0.4% for human immunodeficiency virus (HIV), 6-30% for HBV, and 2.7-10% for hepatitis C virus (HCV). Rates of blood contacts vary but may reach up to 11.9 per 100 h in the operating room. Residents are at highest risk, and obstetrics and gynaecology surgeons suffered the highest rate of exposures (10%) as a group. Contributing risk factors include trauma or emergency orthopaedic procedures, high patient blood loss, long procedures and holding tissue by hand while suturing. However, across occupations, nurses and other health workers experience greater risks than surgeons regarding potentially infectious exposures do. Preventive measures such as the HBV vaccine and protective devices (i.e., self-capping needles, needle-free iv systems and improved barrier materials) have reduced the occupational risk of acquiring a blood-borne infection (Patz and Jodrey, 1995).

Clients and staff of institutions for the developmentally disabled

The special behavioural and medical problems encountered in institutions for the developmentally disabled make this a high risk setting for clients and staff. The risk of HBV infection in these institutions is related to bites and contact with blood, skin lesions, and body fluids that contain HBV (National Immunization Program, 2000).

Susceptible clients in institutions for the developmentally disabled, as well as staff who work closely with clients, should be vaccinated. Susceptible clients and staff who live or work in smaller residential settings with known HBV carriers should also receive hepatitis B vaccine. Clients discharged from residential institutions into community programmes should be screened for HBsAg so that appropriate measures can be taken to prevent HBV transmission. These measures should include both environmental controls and appropriate use of vaccine.

Staff of non-residential day-care programmes for the developmentally disabled (e.g., schools, sheltered workshops) attended by known HBV carriers have a risk of infection comparable with that of health care workers and therefore should be vaccinated (Breuer *et al*. 1985). The risk of infection for other clients appears to be lower than the risk for staff. Vaccination of clients in day-care programmes may be considered (CDC, 1991a).

Haemodialysis patients

Haemodialysis patients are one of the high-risk groups for blood-borne viral infection due to their need of blood transfusions for renal anaemia. In addition, the haemodialysis

procedure itself is a risk factor for blood-borne viral infection. Therefore, prevention of blood-borne infection in haemodialysis units is highly important. Although the hepatitis B vaccine is less effective in these patients, it is recommended for all susceptible haemodialysis patients (National Immunization Program, 2000).

Vaccinating patients early in the course of their renal disease is encouraged because patients with uraemia who are vaccinated before they require dialysis are more likely to respond to the vaccine (Seaworth *et al*., 1988). Although their seroconversion rates and anti-HBs titres are lower than those of healthy persons, patients who respond to vaccination will be protected from infection, and the need for frequent serologic testing will be reduced (Moyer *et al*., 1990; CDC, 1991a).

In studies performed on blood-borne infections in haemodialysis units in Fukuoka, Japan, it was shown that the HBsAg prevalence did not differ with experiencing or not experiencing blood transfusion, nor did it increase with the duration of haemodialysis therapy. These findings suggest that infectious control of hepatitis B virus such as isolation of carriers and screening of blood donors may be effective for the prevention of blood-borne viral infection among haemodialysis patients (Washio, 1998).

In an American report published in 1994, it was stated that hepatitis B vaccine has been recommended for all susceptible haemodialysis patients since it became available in 1982. However, by 1993 only 29% of haemodialysis patients in the United States had been vaccinated. In 1993, vaccination coverage among patients in the southern California region was 13%, lower than in northern California or any other state in the United States.

Among immunocompetent persons, a protective antibody response develops in 90-95% of vaccine recipients, protection against HBV infection persists even when antibody titres subsequently decline, and booster doses are unnecessary. In contrast, the proportion of vaccinated haemodialysis patients who develop a protective antibody response is lower (50-60%), and booster doses are necessary to maintain protection against hepatitis B when antibody titres decline below protective levels (Stevens *et al*., 1984; CDC, 1991a; CDC, 1996).

Recipients of certain blood products

Patients who receive clotting-factor concentrates, such as haemophilia patients, are at high risk of infection. Subcutaneous vaccination should be initiated as soon as their specific clotting disorder is identified. Prevaccination testing is recommended for patients who have already received multiple infusions of these products (CDC, 1991a).

Conventional treatment of beta thalassaemia major is based on regular blood transfusion from early childhood. Maximum effectiveness of transfusion therapy depends, among other factors, on the following: (1) Availability of safe blood. Donation programmes

should aim at retaining repeat donors, who carry decreased risk of transmitting blood-borne infections. Donors should be screened with laboratory tests performed to the highest possible standard of quality. Selection of safe donors can be improved by the adoption of questionnaires containing direct questions on risk factors for transfusion transmissible infections; (2) Continuous monitoring of transfusion transmissible infections; (3) Vaccination against hepatitis B of all suitable patients (Rebulla, 1995).

Household contacts and sex partners of HBV carriers

All household and sexual contacts of persons identified as HBsAg-positive should be vaccinated. Hepatitis B vaccine should be administered at the age-appropriate dose to those determined to be susceptible or judged likely to be susceptible to infection (CDC, 1991a).

Household contacts of persons with acute hepatitis B virus infection

Since infants have close contact with primary care-givers and they have a higher risk of becoming HBV carriers after acute HBV infection, prophylaxis of an infant less than 12 months of age with HBIG (0.5 ml) and hepatitis B vaccine is indicated if the mother or primary care-giver has acute HBV infection. Prophylaxis for other household contacts of persons with acute HBV infection is not indicated unless they have had identifiable blood exposure to the index patient, such as by sharing toothbrushes or razors. Such exposures should be treated like sexual exposures. If the index patient becomes an HBV carrier, all household contacts should receive hepatitis B vaccine (CDC, 1991a).

Persons who have casual contact with carriers at schools and offices are at little risk of catching HBV infection, and vaccine is not recommended for them. Unless special circumstances exist, such as behaviour problems (biting or scratching) or medical conditions (severe skin disease) that might facilitate transmission, vaccination of contacts of carriers in child care centres is not indicated (National Immunization Program, 2000).

Sex partners of persons with acute hepatitis B virus infection

All susceptible persons whose sex partners have acute hepatitis B infection should receive a single dose of HBIG (0.06 ml/kg) and should begin the hepatitis B vaccine series if prophylaxis can be started within 14 days of the last sexual contact or if sexual contact with the infected person will continue. Administering the vaccine with HBIG may improve the efficacy of postexposure treatment. The vaccine has the added advantage of conferring long-lasting protection. Counselling and encouraging condom use can be considered as well.

Adoptees from countries where HBV infection is endemic

Adopted or fostered orphans or unaccompanied minors from countries where HBV infection is endemic should be screened for HBsAg (Margolis *et al*., 1991). If the

children are HBsAg-positive, other family members should be vaccinated (Hershow *et al.*, 1987; CDC, 1991a).

International travellers

Viral hepatitis is one of the commonest illnesses to afflict travellers. Hepatitis B is less common than hepatitis A and particularly affects those who engage in sexual activity abroad or who are exposed occupationally. It can be prevented through vaccination of the appropriate groups of travellers (Hall, 1993).

Vaccination should be considered for persons who plan to spend more than six months in areas with high rates of HBV infection and who will have close contact with the local population. Short-term travellers who are likely to have contact with blood or sexual contact with residents of areas with high or intermediate HBV endemicity should be vaccinated. Persons travelling abroad who will perform medical procedures in areas where HBV infection is common are at very high risk. Vaccination should begin at least 6 months before travel to allow for completion of the full vaccine series, although a partial series will offer some protection. The alternate four-dose schedule should provide protection if the first three doses can be delivered before departure (CDC, 1991a; (National Immunization Program, 2000). Rapid schedules can also be considered for last minute travellers (0, 7, 21, and 360 days) (Bock *et al.*, 1995).

A survey was made to determine the risks of infection with hepatitis B among European travellers and to compare this with the immunisation status in various risk groups. The conclusions were that a significant proportion of travellers surveyed unwittingly exposed themselves to the risk of hepatitis B infection while at medium/high risk destinations. The majority of at-risk travellers had not been vaccinated, regardless of their destination. Improved advice and clear recommendations to avoid transmission are needed (Zuckerman and Steffen, 2000).

Injecting drug users

Injecting drug users who share equipment may transmit and acquire blood-borne virus infections, including HIV, HBV, and HCV. Estimates of the number of people who are at risk of infection from injecting drug use are needed in order to plan services and care, and to interpret surveillance data. In a British study performed in 1995, the data were examined from registries of drug use and two surveys of the general population from which estimates of the number of injecting drug users in England and Wales have been derived. Drug registries included only those whose drug use was identified during contact with drug or medical services, so these sources provide minimum estimates but may be used to monitor trends: 25,706 drug users in England and Wales were notified to the Home Office in 1993, 12,253 of whom were current injectors. Estimates derived from surveys of the general population suggest, however, that between 51,900 (95% confidence interval (CI): 33,000-71,600) and 77,700 (95% CI: 4100-151,200) people in

England and Wales were at risk of infection from current injecting drug use, of whom between 10,400 (95% CI: 7200-13,800) and 15,500 (95% CI: 800-30,200) were at risk of blood-borne virus infections as a result of sharing injecting equipment. In the 16 to 34-year age group about one in 200 men and one in 400 to 500 women might have been injectors (Durance and Hepstonstall, 1995).

All injecting drug users who are susceptible to HBV should be vaccinated as soon as their drug use begins. Because of the high rate of HBV infection in this population, prevaccination screening should be considered. Injecting drug users known to have HIV infection should be tested for anti-HBs response after completion of the vaccine series. Those who do not respond to vaccination should be counselled accordingly (CDC, 1991a).

The National Immunization Program (2000) states that injection drug users are at extremely high risk for HBV infection. All injection drug users who are susceptible to HBV should be vaccinated as soon as possible after their drug use begins.

Sexually active homosexual and bisexual men

Homosexual men are at increased risk for infection with hepatitis B virus (HBV). Both plasma-derived and recombinant vaccines have been shown to induce long-standing protective immunity in this population. However, non-responders and weak responders to HBV vaccine have become a problem because of an impaired antibody response due to previous infection with human immunodeficiency virus. In addition, human immunodeficiency virus infection predisposes persons to the development of a HBV carrier state following HBV infection. Vaccination remains the most effective tool for preventing hepatitis B in homosexual men (Goilav and Piot, 1989).

Susceptible sexually active homosexual and bisexual men should be vaccinated. Because of the high rate of HBV infection in this population, prevaccination screening should be considered. Men known to have HIV infection should be tested for anti-HBs response after completion of the vaccine series. Those who do not respond to vaccination should be counselled accordingly (CDC, 1991a).

To audit hepatitis B immunisation in a genitourinary medicine clinic in the UK, a retrospective case note review of all homosexual and bisexual men presenting as new patients during 12 months in 1988 and follow up review of notes to May 1990 were performed. Twenty-five men had been previously tested for hepatitis markers; of the 732 not previously tested, 440 (60.1%) were screened for hepatitis B markers. 207 (69%) of the 300 patients without hepatitis B serological markers started the vaccine course, and 141 (68%) completed it, with 75 (84%) of the 89 tested after immunisation being immune. An estimated 24% of susceptible new patients were rendered immune as a result of the immunisation policy. Patients who presented with a further episode of a sexually

transmitted disease were more likely to have been screened (25% v 12%, p less than 0.0001) and immunised (31% v 18% p = 0.02); those known or found to be positive for HIV antibody were more likely to have been screened (23% v 14%, p = 0.047) but less likely to have been immunised (6% v 17%, p = 0.004). So the major failure was that in not screening. Failure to immunise patients found to be susceptible and failure of compliance with the vaccine course contributed. Non-response to the vaccine was of minor importance. The authors concluded that improvements in vaccine delivery were required (Bhatti *et al*., 1991).

Sexually active heterosexual men and women

Vaccination is recommended for men and women who are diagnosed as having recently acquired other sexually transmitted diseases, for prostitutes, and for persons who have a history of sexual activity with more than one partner in the previous six months (Alter *et al*., 1990). Most patients seen in clinics for sexually transmitted diseases should be considered candidates for hepatitis B vaccination (CDC, 1991a).

Street youths are at high risk for many health problems, including sexually transmitted diseases and blood-borne infections. In a cross-sectional anonymous study conducted in Canada from December 1995 to September 1996 and involving street youths in Montreal, the prevalence of risk behaviours for HBV infection and of markers of past and present HBV infection were estimated. The results indicated that the mean age of the subjects was 19.5 years; 69.3% (303/437) were males. Many subjects had high-risk behaviours: 45.8% (200/437) had injected drugs, 24.5% (107/436) had engaged in prostitution, and 8.7% (38/437) reported having a sexual partner with a history of unspecified hepatitis. The prevalence rate for one or both HBV markers was 9.2% (40/434) (95% confidence interval [CI] 6.7-12.3%). Multivariate logistic regression analysis showed that being over 18 years of age (adjusted odds ratio [OR] 4.5, 95% CI 1.8-11.7), having injected drugs (adjusted OR 3.5, 95% CI 1.5-8.3) and having had a sexual partner who had unspecified hepatitis (adjusted OR 3.2, 95% CI 1.3-7.5) were all associated with HBV infection. The study documents the importance of HBV infection in the street youth population: 9.2% of the subjects in our study had markers of infection. Sexual and drug use risk behaviours of street youths should be evaluated by health professionals caring for them so that harm reduction counselling can be offered. The authors conclude that hepatitis B vaccination clearly needs to be promoted as a preventive intervention; only 12% of the subjects in the study had completed the three-dose vaccination schedule despite the availability of free vaccine (Roy *et al*., 1999).

Inmates of long-term correctional facilities

Prison officials should consider undertaking screening and vaccination programmes directed at inmates with histories of high risk behaviours (CDC, 1991a).

The prevalence of HBV and HCV infection among inmates entering the New South Wales (NSW), Australia, correctional system was determined and risk factors for infection examined in a cross-sectional survey. The results suggested that about a third of adult male prisoners entering the NSW correctional system might have been infected with HBV or HCV. Measures such as education about hepatitis risk factors and HBV vaccination are needed to reduce hepatitis transmission in this population. The reported high prevalence of hepatitis B and C in prison populations is attributed to the disproportionate number of people in prisons who engage in risk behaviours, particularly injecting illicit drugs. It is estimated that up to 60% of inmates are committed for drug-related offences. Further, an Australian study estimated that during their incarceration 25-44% of inmates occasionally injected illicit drugs, 14-34% engaged in occasional anal intercourse and 5%-18% did both. Few inmates were knowledgeable about risk factors, with injecting drug use nominated by only 20% and tattooing by only 2%. However, those who had been imprisoned previously were significantly more likely to identify injecting drug use as a risk factor than those new to the correctional system, and significantly less likely to answer 'no idea' about risk factors. NSW prison inmates are offered hepatitis B vaccination if their sentences exceed six months and they are considered 'at risk'. However, inmates with shorter sentences may also be at risk. The authors believe that all inmates have the right to be protected from possible infection and that all should start a course of hepatitis B vaccination on entry to the correctional system. It may be appropriate to use recently described accelerated vaccination schedules, which provide protective levels of anti-hepatitis B surface antibody relatively quickly (Butler *et al*., 1997).

HIV-infected inmates are often co-infected with HBV and/or HCV. HIV may dramatically modify the course of viral hepatitis infection, especially chronic hepatitis C. The converse is uncertain: chronic hepatitis does not seem to accelerate HIV disease progression. For those infected with HIV alone, avoiding exposure to hepatitis viruses is important, given the poor outcome of co-infected patients. Availability of drug rehabilitation services in correctional facilities is paramount. The hepatitis B vaccine is recommended for those at high risk for contracting HBV, including HIV-infected persons who do not have evidence of prior HBV infection. It appears to be preferable that those who are at high risk for HBV infection be vaccinated before they become infected with HIV, since the hepatitis B vaccine is less effective in those who are HIV-infected. Also, the vaccine may increase the risk of chronic HBV infection in those who are HIV-infected and who become HBV-infected while they are receiving HBV vaccinations. Hepatitis B vaccination is feasible within a correctional system. In fact, if incarceration represents a period of forced sobriety and lower risk of HBV exposure for those who use drugs or engage in risky sexual behaviour, prisons may be the ideal setting for hepatitis B vaccination. Current guidelines recommend that institutionalised persons should receive vaccination. However, without additional funding, correctional facilities may be unable to afford this public health measure (Spaulding *et al*., 1999).

The National Immunization Program (2000) summarises its points of view as follows. Long-term male prison inmates are at increased risk of HBV infection because of injection drug use, homosexual activity, or other factors. The prison setting provides an access point for vaccination of inmates with histories of high-risk behaviour.

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Appendix 1 VHPB consensus statement on universal hepatitis B vaccination programmes (Viral Hepatitis Prevention Board, 1996)

- VHPB supports the 1991 WHO target of implementing universal hepatitis B prevention programmes in all countries by 1997.
- Hepatitis B vaccination should be integrated into existing national programmes (where they exist) for the immunisation of infants and adolescents.
- Strategies aimed at vaccinating and changing behaviour in high-risk groups must continue.
- The universal screening for HBV makers in pregnant women should be encouraged, taking into account country-specific economic status technical infrastructure. Where effective maternal screening does not exist, resources may be better directed towards a universal vaccination programme.
- The hepatitis B prevention programmes must be carefully monitored and evaluated. Updates need to be available at regular intervals.
- The VHPB recognises the importance of raising the awareness of health care providers, policy makers and the general public about the dangers of hepatitis B as a community health risk. The board aims to reduce iatrogenic transmission through education and training.

Appendix 2 VHPB recommendations on prevention of perinatal HBV transmission (Viral Hepatitis Prevention Board, 1998a)

Perinatal transmission is one of the most efficient and devastating modes of transmitting hepatitis B virus because 60 to 90% of infected newborns become chronic carriers of the virus. The main objective of maternal screening is to identify HB carrier women and to prevent hepatitis B carriage in their infants; this can be achieved by screening all pregnant women for HBsAg and vaccinating newborns of carrier mothers. Control of perinatal transmission can also be achieved by universal newborn vaccination starting at birth.

Where screening of pregnant women for HBsAg exist, countries may wish to continue screening programmes. If this is the case, any screening programme should include all pregnant women, as selective screening of pregnant women (focused on risk groups) misses a significant proportion of carrier mothers. Screening for HBsAg should be part of routine antenatal care.

Women who present for delivery without having been screened for HBsAg should be tested immediately. Their newborns should be vaccinated within 12 hours of birth, irrespective of the results of the screening test.

Most industrial countries have carried out universal screening of pregnant women for many years.

- It allows identification of newborns that require immediate vaccination.
- It allows identification of carrier mothers and prevention of further secondary spread of HBV, as well as representing a health benefit to the mothers.
- In infants of carrier mothers, it offers the option to implement universal infant immunisation in combination with other infant vaccination programmes.

Most countries currently administer HBIG and vaccine to infants of carrier mothers, although recent evidence suggests that vaccine alone may be just as effective. Vaccine should be given within 12 hours of birth. In cases where HBIG is given, it should be administered within 12 hours of birth at another injection site than the vaccine. The schedules most widely used are 0, 1, 6 and 0, 1, 2, 12 months, both of which are shown to be effective.

Effective programmes for the prevention of perinatal transmission require transfer of information to the mother, and among the antenatal care centre, the delivery unit and the infant immunisation provider. An organisational framework should be in place and responsibility for co-ordination of HBsAg screening and follow-up of vaccination of newborns should be well defined. Countries should systematically monitor and evaluate prevention programmes.

Where maternal screening programmes do not exist, resources may be better directed towards universal neonatal immunisation programmes. Control of perinatal transmission can be achieved if the first dose of vaccine is delivered at birth. HBsAg-positive mothers should not be discouraged from breast-feeding.

Appendix 3 VHPB recommendations on injection safety and safe blood supply (Viral Hepatitis Prevention Board, 1998b)

Injection safety

- Education of health care providers and the public about the dangers of unsafe injections;
- Education of healthcare providers and the public on appropriate and inappropriate use of injections;
- Insistence that a separate sterile needle and a separate sterile syringe be used for each injection, and then properly disposed of;
- Use, wherever possible, of auto-destruct syringes and the provision of adequate supplies of sterile needles and syringes and sterilising equipment as appropriate;
- Routine evaluation of the effectiveness of prevention programmes;

- Research into the extent of the problem of unsafe injections in central and Eastern Europe (CEE) and the Newly Independent States (NIS).

Safe blood supply

- All countries should develop a structured blood transfusion service to ensure the safety of blood through proper donor selection, blood collection and testing, and appropriate use. All donations should be screened for HBsAg, anti-HCV and anti-HIV.
- Although the most recent and technologically advanced screening assays may not be available in many countries because of financial, logistical or technical constraints, this should not prevent the development of an effective blood-screening programme. The undisputed benefit of screening all blood donations far outweighs concerns over the absolute sensitivity of the available assays.
- The international community should ensure that countries in greatest need receive resources necessary to achieve safe blood use. Manufacturers of reagents are urged to make affordable screening tests available to developing countries.

Appendix 4 VHPB recommendations on prevention and control of hepatitis B in the community (Grosheide and Van Damme, 1996)

1. Universal vaccination: the need for early cover

Universal childhood and early adolescent vaccination protects individuals from infection later in life, whether because of occupational risk, sexual activity illnesses or other behaviour such as intravenous drug use which poses a hepatitis B risk. The sooner individuals are vaccinated against hepatitis B the better. Early vaccination protects individuals from childhood infection, which results in high carrier rates and chronic disease. Chronic disease is associated with serious and fatal liver cancer.

Infant vaccination programmes

The VHPB endorses the 1991 statement of the WHO Working Group on the control of Viral Hepatitis in Europe, which stated: "The routine immunisation of infants and adolescents should receive the highest priority. Hepatitis B vaccination should be integrated into the routine infant immunisation programme in all countries".

Adolescent vaccination programmes

The Board also supports recommendation made by the WHO Global Advisory Group of the Expanded Programme on Immunisation endorsed by the World Health Assembly in 1992: "Hepatitis B vaccine should be integrated into the national immunisation programmes ... in all countries by 1997. Countries with a low prevalence may consider immunisation of all adolescents as an addition or alternative to infant immunisation".

Adolescent programmes should be directed at young adolescents before the age of 13, and are appropriate in countries where there are structures and resources for delivery of vaccines to young adolescents such as school health services.

Infant plus adolescent vaccination programmes

Combined universal early adolescent and infant vaccination programmes have been shown to have the fastest impact on reducing levels of hepatitis B infection. Vaccination of young adolescents can of course stop once the first group of individuals vaccinated as infants reaches early adolescence.

High risk strategies plus universal vaccination

High-risk group approaches have failed to control hepatitis B infection in the general population. But it is good medical practice to protect individuals in these groups. Strategies aimed at vaccinating and changing behaviour in high-risk groups should therefore continue. However, universal vaccination programmes are also needed to eliminate hepatitis B infection, even in areas of low endemicity, because high-risk strategies alone are clearly failing. Public health officials, healthcare providers and the public need to be aware of this and take action.

2. Recommendations for maternal screening

Where screening of pregnant women for hepatitis B marker exists, it should continue, but any screening programme should cover all women rather than selected groups. Selective screening has been shown to miss many cases of hepatitis B. The VHPB recommends that, within 12 hours of birth, babies born to carrier mothers should receive specific hepatitis B immune globulin (HBIG) and the first dose of vaccine at another injection site. Where effective maternal screening programmes do not exist, the VHPB feels that resources may be better directed towards a universal vaccination programme aimed at adolescents or infants or both.

3. Combined vaccines

The VHPB supports efforts to add hepatitis B vaccination to existing infant and adolescent vaccination programmes. Hepatitis B vaccines can and should be integrated into any existing schedule. In addition, combination vaccines would be useful in hepatitis B control programmes. The VHPB advocates the development and use of combination vaccines, which contain the hepatitis B component. These vaccines require fewer injections, thus making them more acceptable to the public and the health care provider, and representing savings on syringes, storage, transportation, record keeping, and training. In addition, it could possibly reduce the number of medical visits required. The implementation of universal hepatitis B vaccination, however, should not be delayed until such combined vaccines are available.

4. Raising awareness about the dangers of hepatitis B

The VHPB seeks to raise the awareness of health care providers about the dangers of HBV as a community health risk and about the need for hepatitis B immunisation, both for themselves and for their patients. The VHPB also realises the importance of understanding the attitudes, believes and behaviours of health care providers, health policy makers and the general public (especially the parents) when working to improve the success of universal hepatitis B vaccination programmes. The VHPB aims to produce and support educational initiatives targeted at these groups.

5. Monitoring and evaluation

The hepatitis B prevention programmes must be carefully monitored and evaluated. Updates need to be available at regular intervals.

6. Booster strategies

There are no reported cases of clinical hepatitis B or HBV carrier state in individuals who have been vaccinated successfully (> 10 IU/l anti-HBs) in more than 10 years follow-up, despite the loss of detectable antibody in many individuals. Immunological memory induces a rapid anamnestic response in exposed individuals. This can abort clinical hepatitis B or the development of the carrier state. However, some clinically insignificant breakthrough infections have been reported in vaccinated individuals in whom only anti-HBc seroconversion occurred. Given these data, routine administration of booster doses in universal vaccination programmes is not recommended by the VHPB.

7. Contraindications to vaccination

There are few absolute contraindications to vaccination. Still, withholding vaccination for inappropriate contraindications has been identified as an important cause of under-immunisation. For hepatitis B vaccination only severe reactions to previous doses, hypersensitivity to one of the vaccine components, and fever above 38.5°C are considered contraindications.