

# EPIDEMIOLOGY BULLETIN

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## INACTIVATED HEPATITIS B VIRUS VACCINE

(Recommendations of the Immunization Practices Advisory Committee (ACIP))

### Introduction

Worldwide, recommendations for using hepatitis B virus (HBV) vaccine will vary in accordance with local patterns of HBV transmission. In the United States, an area of low HBV prevalence, certain groups are at substantially greater risk than the general population of acquiring infection. It is for these higher-risk groups that the vaccine is currently recommended. To date, 12,000 individuals have been given this vaccine, and no untoward effects have been observed over periods of time extending up to 3 years. The recommendations that follow are intended as initial guides for immunization practice, and will be modified as additional data and experience are accumulated. Because the cost of this vaccine is high, a discussion of the cost effectiveness of prevaccination susceptibility testing is included.

### Hepatitis B Virus Infection in the United States

The estimated lifetime risk of HBV infection in the United States varies from almost 100% for the highest-risk groups to approximately 5% for the population as a whole. An estimated 200,000 persons, primarily young adults, are infected each year. One-quarter of them become ill with jaundice. More than 10,000 patients are hospitalized with hepatitis B each year, and an average of 250 die of fulminant disease. Between 6% and 10% of young adults with HBV infection become carriers. The United States currently contains an estimated pool of 400,000-800,000 infectious carriers. Chronic active hepatitis develops in over 25% of carriers (100,000-200,000), and often progresses to cirrhosis. Furthermore, recent studies have demonstrated an association between the HBV carrier state and the occurrence of liver cancer. It is estimated that 4,000 persons die from hepatitis B-related cirrhosis each year in this country, and that more than 800 die from hepatitis B-related liver cancer.

The role of the HBV carrier is basic to the epidemiology of HBV transmission. A carrier is defined as a person who is HBsAg positive on at least 2 occasions, at least 6 months apart. Although the degree of infectivity is best correlated with HBeAg positivity, any person with a positive test for HBsAg is potentially infectious. The likelihood of developing the carrier state varies inversely with the age at which infection occurs. During the perinatal period, HBV transmitted from HBeAg-positive mothers results in HBV carriage in up to 90% infected infants, whereas 6%-10% of acutely infected adults become carriers.

Carriers and persons with acute cases have highest concentrations of HBV in the blood and serous fluids; less is present in other body fluids, such as saliva and semen. Transmission is via percutaneous or permucosal routes. Infective blood or body fluids can be introduced by means of contaminated needles or through sexual contact. Close personal contacts such as those that occur among household contacts of HBV carriers or among children in institutions for the mentally retarded can also spread infection. Transmission of infection by transfusion of contaminated blood or blood products has been greatly reduced since the advent of routine screening with highly sensitive tests for HBsAg.

Although subtypes of HBV exist, infection or immunization with 1 subtype confers immunity to all subtypes.

Serologic surveys demonstrate that although HBV infection is uncommon among adults in the general population, it is highly prevalent in certain groups. Those at risk, based on the presence of serologic markers of infection, are described in Table 1. Immigrants/refugees and their descendants from areas of high HBV endemicity are at high risk of HBV infection. Homosexually active males and users of illicit injectable drugs are among the highest-risk groups, acquiring infection soon (10%-20%/year) after adopting these lifestyles. Inmates of prisons also appear to be at high risk, possibly as a consequence of drug abuse or homosexual practices. Patients and staff in custodial institutions for the mentally retarded are also at increased risk of having HBV infection. Classroom contacts of some deinstitutionalized carriers may also be at higher risk than the general population. Intimate household and sexual contact with HBV carriers increases risk, as does receiving certain pooled plasma products and undergoing hemodialysis.

There is increased risk for certain medical and dental workers, and related laboratory and support personnel, who have frequent contact with blood from infective patients. Employment in a hospital without exposure to blood carries no greater risk than that for the general population.

TABLE 1: EXPECTED HEPATITIS B VIRUS PREVALENCE IN VARIOUS POPULATION GROUPS

|   | Prevalence of serologic markers of HBV infection |                |
|---|--|----------------|
|   | HBsAg(%)   | All markers(%) |
| <b>High risk</b>                                      |  |                |
| Immigrants/refugees from areas of high HBV endemicity | 13   | 70-85          |
| Clients in institutions for the mentally retarded     | 10-20  | 35-80          |
| Users of illicit parenteral drugs                     | 7  | 60-80          |
| Homosexually active males                             | 6  | 35-80          |
| Household contacts of HBV carriers                    | 3-6  | 30-60          |
| Patients of hemodialysis units                        | 3-10   | 20-80          |
| <b>Intermediate risk</b>                              |  |                |
| Prisoners (male)                                      | 1-8  | 10-80          |
| Staff of institutions for the mentally retarded       | 1  | 10-25          |
| Health-care workers                                   |  |                |
| Frequent blood contact                                | 1-2  | 15-30          |
| <b>Low risk</b>                                       |  |                |
| Health-care workers                                   |  |                |
| No or infrequent blood contact                        | 0.3  | 3-10           |
| Healthy Adults (first-time volunteer blood donors)    | 0.3  | 3-5            |

## Vaccine

Hepatitis B virus vaccine is a suspension of inactivated, alum-adsorbed 22-nm surface antigen particles that have been purified from human plasma by a combination of biophysical (ultracentrifugation) and biochemical procedures. Inactivation is a 3-fold process using 8-M urea, pepsin at pH2, and 1:4,000 formalin. Each of these processes has been shown to inactivate HBV and representative viruses from all known groups, and thus should inactivate any viruses potentially contaminating the vaccine. HBV vaccine contains 20 ug/ml of HBsAg protein.

After a series of 3 intramuscular doses of HBV vaccine, an average of over 90% of healthy adults developed protective antibody (1,2). A course of 3 10-ug doses induces antibody in virtually all infants and children 3 months through 9 years of age tested to date. Protective antibody titers have persisted during 3 years of observation, although a gradually declining titer has been observed.

Field trials of the United States-manufactured vaccine have shown 80%-95% efficacy in preventing infection or hepatitis among susceptible persons (3,4). Protection against illness was complete for persons who developed antibodies after vaccination but before exposure. The duration of protection and the consequent need for booster doses are not yet known.

Studies are planned or are under way in various settings to assess the value of vaccination after HBV exposure. For post-exposure prophylaxis, see the ACIP recommendations for the use of immune globulin (5); see below for recommendations regarding infants born to mothers who are HBV carriers and for sexual contacts of patients with acute hepatitis B.

## Vaccine Usage

Primary adult vaccination consists of 3 intramuscular doses of 1.0 ml of vaccine (20 ug/1.0 ml) each. The second and third doses should be given 1 and 6 months, respectively, after the first. For patients undergoing hemodialysis, and for other immunosuppressed patients, 3 2-ml doses (40 ug) should be used. For children under 10 years of age, 3 similarly spaced doses of 0.5 ml (10 ug) are sufficient. Vaccine doses administered at longer intervals than those stipulated provide equally satisfactory protection, but optimal protection is not conferred until after the third dose. Since HBV vaccine is an inactivated (non-infective) product, it is presumed that there will be no interference with other simultaneously administered vaccine(s). The duration of protection and the need for booster doses have not yet been determined.

## Vaccine Storage

Vaccine should be stored at 2C-8C but not frozen. Freezing destroys the potency of the vaccine.

## Side Effects and Adverse Reactions

Side effects among 12,000 recipients of HBV vaccine observed to date have been limited to soreness and redness at the injection site (3,4).

Data are not available on the safety of the vaccine for the developing fetus, but because it contains only non-infectious HBsAg particles, the risk to the fetus from the vaccine should be negligible. In contrast, HBV infection in a pregnant woman may result in severe disease for the mother and chronic infection for the newborn. Pregnancy should not be considered a contraindication to the use of this vaccine for persons who are otherwise eligible.

### Effect of Vaccination on Carriers

The vaccine produces neither therapeutic nor adverse effects in HBV carriers (6).

### Vaccination of Immune Persons

Vaccination of individuals who possess antibodies against HBV from a previous infection is not necessary but will not cause adverse effects. Such individuals will have a post-vaccination increase in their anti-HBs levels. Passively acquired antibody, whether from hepatitis B immune globulin (HBIG) administration or from the transplacental route, will not interfere with active immunization (7).

### Prevaccination Serologic Screening for Susceptibility

HBV carriers and those having antibody from previous infection need not be vaccinated, but serologic screening to detect such individuals before vaccination may or may not be cost effective. The decision to screen potential vaccine recipients is an economic one that depends on 3 variables: 1) the cost of vaccination, 2) the cost of testing for susceptibility, and 3) the prevalence of immune individuals in the group. All are important in estimating whether routine, selective, or no screening will be most economical in an HBV vaccination program.

Figure 1 shows the relative cost effectiveness of screening, given different costs of screening tests and the expected prevalence of immunity. In constructing the figure, the assumption was made that the cost of 3 doses of vaccine is \$100 and that there are additional costs for administration. For any combination of screening costs and immunity to hepatitis, the cost effectiveness can be estimated. For example, if the expected prevalence of serologic markers for HBV is over 20%, screening is cost effective if costs of screening are no greater than \$30/person. If the expected prevalence of markers is less than 8%, and if the costs of screening are greater than \$10 per person, vaccination without screening is cost effective.

Screening in groups with the highest risk of HBV infection (e.g., users of illicit injectable drugs, homosexually active males, and institutionalized mentally retarded persons) will be cost effective unless testing costs are extremely high. For groups at intermediate risk (e.g., health-care workers with an expected prevalence of 8%-20%), cost effectiveness of screening may be marginal, and vaccination programs may or may not utilize screening. For groups with a low expected prevalence of HBV serologic markers (e.g., entering health professionals) screening will not be cost effective.

For routine screening, only 1 antibody test, either anti-HBc or anti-HBs, need be used. Anti-HBc will identify all previously infected persons, both carriers and those who are not carriers, but will not discriminate between members of the 2 groups. Anti-HBs will identify those previously infected except for carriers. For groups expected to have carrier rates of <2%, such as health-care workers, neither test has a particular advantage. For groups with higher carrier rates, anti-HBc may be preferred to avoid unnecessary vaccination of carriers. If a radioimmunoassay (RIA) anti-HBs test is used for screening, a minimum of 10 RIA sample ratio units should be used to designate immunity (2.1 is the usual designation of a positive test) (4).

### Serologic Confirmation of Post-Vaccination Immunity

HBV vaccine produces protective antibody (anti-HBs) in more than 90% of healthy persons (1-2). Revaccination of those persons who did not respond to the primary series has produced antibody in only one-third. Thus, there seems little need to test for immunity following vaccination except for dialysis patients, whose subsequent management depends on knowing their immune status.

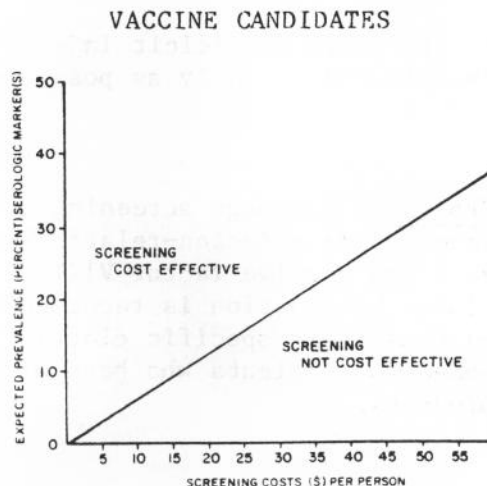
### Pre-Exposure Vaccination

Persons at substantial risk of HBV infection who are demonstrated or judged likely to be susceptible should be vaccinated. They include:

**Health-Care Workers-** Health-care workers (medical, dental, laboratory, and support groups) have varied risks of exposure to HBV depending on their jobs. Those workers for whom vaccine is recommended should be vaccinated as soon as possible after beginning work in a high-risk environment, ideally during their period of training.

**Hospital Staff-** Hospital staff are at increased risk of HBV infection because of contact with blood and blood products. The risk for hospital personnel can vary both among hospitals and within hospitals. In developing specific immunization strategies, hospitals should use available published data about the risk of infection (8-10) and, in addition, may wish to evaluate their own clinical and institutional experience with hepatitis B.

FIGURE 1. COST EFFECTIVENESS OF PRE-VACCINATION SCREENING OF HEPATITIS B VIRUS



Studies in urban centers have indicated that occupational groups with frequent exposure to blood and/or needles have a substantial risk of acquiring HBV infection. The highest risk is for individuals with frequent blood exposure, including the following groups: medical technologists, operating room staff, phlebotomists and intravenous therapy nurses, surgeons and pathologists, and oncology and dialysis unit staff. Other groups that have been shown to be at increased risk in some hospitals include: emergency room staff, nursing personnel, and physicians. To quantitate HBV risks among workers, groups can be ranked according to their frequency of blood/needle exposure. Additional information can be obtained from employee health records, serologic prevalence surveys, and estimates of HBsAg prevalence among patients.

Other Health-Care Workers- Other health workers, based outside of hospitals, who have frequent contact with blood or blood products are at increased risk of acquiring HBV infection. These include dental professionals (dentists, oral surgeons, dental hygienists), laboratory and blood bank technicians, dialysis center staff, morticians, and similar professionals.

Clients and Staff of Institutions for the Mentally Retarded- Susceptible clients and selected staff of institutions for the mentally retarded should be vaccinated. Risks for staff are comparable to those for health-care personnel in other high-risk environments. However, the risk in institutional environments is associated not only with blood exposure, but is also consequent to bites and contact with skin lesions, saliva, and other infective secretions.

Hemodialysis Patients- Numerous studies have established the high risk of HBV virus transmission in hemodialysis units. While recent data have shown a decrease in the rate of HBV infection in hemodialysis units following introduction of environmental control measures, vaccination is recommended for susceptible patients.

Homosexually Active Males- Susceptible homosexually active males should be vaccinated regardless of their age or duration of their homosexual practices. It is important to vaccinate persons as soon as possible after their homosexual activity begins. Homosexually active females do not appear to be at increased risk of sexually transmitted HBV infection.

Illicit Injectable Drug Users- All users of illicit injectable drugs who are susceptible to HBV should be vaccinated as early as possible after their drug use begins.

Recipients of Certain Blood Products- Although screening of all blood donors for HBsAg has decreased the incidence of transfusion-related HBV infection, patients with clotting disorders who receive factor VIII or IX concentrates have an elevated risk of HBV infection. Vaccination is recommended for these persons, and should be initiated at the time their specific clotting disorder is identified. Screening is recommended for patients who have already received multiple infusions of these products.

Household and Sexual Contacts of HBV Carriers- Household contacts of HBV carriers are at high risk of HBV infection. Sexual contacts appear to be at greatest risk. Vaccination of susceptible household contacts of carriers is recommended. At present, most carriers are identified through routine screening of donated blood, diagnostic testing in hospitals, or through other screening programs among high-risk groups. As part of expanded HBV control programs, additional screening to identify HBV carriers may be warranted.

Other Contacts of HBV Carriers- Persons in contact with carriers at schools, offices, etc., are at minimal risk of contracting HBV, and vaccine is not routinely recommended for them. However, classroom contacts of deinstitutionalized mentally retarded HBV carriers who behave aggressively or have special medical problems that increase the risk of exposure to their blood or serous secretions may be at risk. In such situations, vaccine may be offered to classroom contacts.

Special High-Risk Populations- Some American populations, such as Alaskan Eskimos, and immigrants and refugees from areas with highly endemic disease (particularly eastern Asia and sub-Saharan Africa) have high HBV infection rates and deserve special attention. Depending on specific epidemiologic and public health considerations, more extensive vaccination programs may be warranted.

Inmates of Long-Term Correctional Facilities- The prison environment may provide a favorable setting for the transmission of HBV because of the frequent use of illicit injectable drugs and homosexual practices. In such institutions, prison officials may elect to undertake screening and vaccination programs.

#### Post-Exposure Vaccination

Infants Born to HBsAg-Positive Mothers- Pregnant women who are HBsAg positive should be informed about the risk of transmission to their infants. Infants born to these women should receive HBIG (5,11). Infants whose mothers are chronic carriers will be continuously exposed to HBV throughout their childhood; therefore these infants should receive vaccine. The optimum timing for vaccination in conjunction with HBIG administration has not been established. Pending additional information, it is recommended that vaccination begin at 3 months of age or shortly thereafter. Studies to determine the immunogenicity and efficacy of vaccine at birth, with or without HBIG, are currently under way.

Sexual and Household Contacts of Acute Hepatitis B Cases and Health Workers Who Receive Needle Sticks from HBsAg-Positive Patients- Possible alternatives for post-exposure prophylaxis include HBIG, immunoglobulin (IG), HBV vaccine, or a combination of vaccine and an immune globulin. Recommendations for immune globulin use have already been published (5). Studies are currently under way to evaluate the use of vaccine in some of these settings. No recommendations can be made at this time for post-exposure use of HBV vaccine.

June, 1982

MONTH: \_\_\_\_\_

| DISEASE                        | STATE      |            |               |        |                     | REGIONS    |    |      |    |    |
|--------------------------------|------------|------------|---------------|--------|---------------------|------------|----|------|----|----|
|                                | THIS MONTH | LAST MONTH | TOTAL TO DATE |        | MEAN 5 YEAR TO DATE | THIS MONTH |    |      |    |    |
|                                |            |            | 1982          | 1981   |                     | N.W.       | N. | S.W. | C. | E. |
| CHICKENPOX                     | 83         | 241        | 732           | 1483   | 813.8               | 16         | 21 | 13   | 13 | 20 |
| MEASLES                        | 0          | 0          | 14            | 6      | 1092.2              | 0          | 0  | 0    | 0  | 0  |
| MUMPS                          | 1          | 7          | 30            | 83     | 79.6                | 0          | 0  | 0    | 1  | 0  |
| PERTUSSIS                      | 2          | 2          | 9             | 2      | 5.4                 | 0          | 2  | 0    | 0  | 0  |
| RUBELLA                        | 3          | 0          | 11            | 3      | 201.2               | 0          | 0  | 0    | 0  | 3  |
| MENINGITIS - ASEPTIC           | 6          | 7          | 43            | 39     | 40.8                | 1          | 0  | 3    | 2  | 0  |
| BACTERIAL                      | 11         | 10         | 99            | 116    | 89.2                | 3          | 1  | 3    | 3  | 0  |
| ENCEPHALITIS - INFECTIOUS      | 4          | 1          | 14            | 17     | 11.0                | 1          | 1  | 0    | 2  | 0  |
| POST-INFECTIOUS                | 1          | 0          | 1             | 2      | 4.8                 | 0          | 0  | 1    | 0  | 0  |
| HEPATITIS A (INFECTIOUS)       | 11         | 25         | 97            | 95     | 130.2               | 1          | 6  | 2    | 1  | 1  |
| B (SERUM)                      | 37         | 47         | 221           | 245    | 199.8               | 4          | 8  | 6    | 6  | 13 |
| SALMONELLOSIS                  | 147        | 113        | 558           | 641    | 426.2               | 20         | 20 | 22   | 42 | 43 |
| SHIGELLOSIS                    | 6          | 13         | 73            | 917    | 240.2               | 1          | 1  | 1    | 2  | 1  |
| TUBERCULOSIS - PULMONARY       | 73         | 27         | 277           | 49     | -                   | 0          | 0  | 0    | 0  | 0  |
| EXTRA-PULMONARY                | 11         | 8          | 49            | 53     | -                   | 0          | 0  | 0    | 0  | 0  |
| SYPHILIS (PRIMARY & SECONDARY) | 63         | 41         | 314           | 347    | 294.6               | 3          | 8  | 1    | 7  | 44 |
| GONORRHEA                      | 1863       | 2016       | 10,029        | 10,522 | 10758.8             | 0          | 0  | 0    | 0  | 0  |
| ROCKY MOUNTAIN SPOTTED FEVER   | 12         | 7          | 19            | 38     | 28.8                | 4          | 4  | 0    | 3  | 1  |
| RABIES IN ANIMALS              | 69         | 52         | 239           | 34     | 10.0                | 6          | 63 | 0    | 0  | 0  |
| MENINGOCOCCAL INFECTIONS       | 4          | 9          | 36            | 60     | 41.6                | 1          | 0  | 1    | 1  | 1  |
| INFLUENZA                      | 31         | 96         | 299           | 4844   | 2590.8              | 0          | 0  | 11   | 0  | 20 |
| MALARIA                        | 3          | 3          | 21            | 11     | 14.6                | 1          | 2  | 0    | 0  | 0  |
| OTHER: Hepatitis Unspec.       | 6          | 13         | 57            | 86     | 85.2                | 1          | 3  | 1    | 1  | 0  |
|                                |            |            |               |        |                     |            |    |      |    |    |
|                                |            |            |               |        |                     |            |    |      |    |    |
|                                |            |            |               |        |                     |            |    |      |    |    |
|                                |            |            |               |        |                     |            |    |      |    |    |

COUNTIES REPORTING ANIMAL RABIES: Fairfax 19 rac., 1 bat, 1 ferret, 1 red fox; Loudoun 39 rac.  
1 ground hog; Fauquier 3 rac., 1 gray fox; Prince Wm. 1 rac.; Stafford 1 bat; Page 1 skunk  
 OCCUPATIONAL ILLNESSES: Occupational pneumoconiosis 8; Occupational hearing loss 6; Asbestosis 4; Byssinosis 1;  
Chemical Inhalation 2.

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