

8 Prevention of Hepatitis A, B and C and Other Hepatotoxic Factors in People Living with HIV

Clinical Protocol for the WHO European Region

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I. Prevention strategies

The strategies for limiting the spread of hepatitis include:

- vaccination against hepatitis B and A;
- prevention of mother-to-child transmission of hepatitis B virus (HBV) and hepatitis C virus (HCV);
- reducing risk of infection through safer sexual behaviour and reducing harm related to injecting drug use;
- counselling to reduce liver-related harm;
- prevention through transfusion of blood and blood products; and
- prevention in health care settings.

1. Vaccination against hepatitis B and A

1.1. Hepatitis B

All HIV patients not coinfecting with HBV should be vaccinated against it. (See also Protocol 12, *Immunization of people living with HIV and people at risk for HIV infection.*)

The schedule for HBV vaccine in HIV-infected adult patients (1, 2) is as follows.

- HBV vaccination should start with the conventional dose (20 µg at months 0, 1 and a third time between months 6 and 12) for patients with a CD4 count >500 cells/mm³.
- In individuals with CD4 cell counts between 200 cells/mm³ and 500 cells/mm³, an intensive vaccination schedule is recommended (20 µg at months 0, 1, 2 and 12). Patients who do not respond to this first cycle, measured by level of hepatitis B surface antibody (HBsAb) (<10 IU/litre) should receive booster doses or start a new vaccination cycle with 40 µg at months 0, 1, 2 and 6–12 (3).
- It is generally accepted that an adequate response to hepatitis B vaccine is the production of serum HBsAb at levels >100 IU/litre (or at least 10 IU/litre). Studies on vaccination in HIV patients have used either the 0/1/6-month or the 0/1/2/12-month hepatitis B schedule (3, 4).
- Patients with CD4 counts <200 cells/mm³ should receive antiretroviral treatment (ART) first. Vaccination should be deferred until a clinically significant immune reconstitution has been achieved, preferably after the CD4 count has increased to >200 cells/mm³.
- Compared to HIV-negative patients, those who are HIV-positive:
 - are less likely to respond to HBV vaccine;
 - have lower mean antibody titres (by a factor of about 30); and
 - lose “protective” antibody levels more quickly (40% loss in one year versus 5% loss in those who are HIV-negative).
- Routine or direct administration of booster doses is not recommended. Humoral response to HBV vaccine may decline progressively over time, and may put the patient at risk of acute infection in case of exposure. Yearly monitoring of HBsAb is recommended, and booster doses should be given when HBsAb <10 IU/litre. For further information on hepatitis B vaccine, please refer to Protocol 12, *Immunization of people living with HIV and people at risk for HIV infection.*

Hepatitis B vaccine response correlates with CD4 count, as shown in Table 1.

| TABLE 1. | | HEPATITIS B VACCINE RESPONSE AT DIFFERING CD4 COUNTS (3,5) | |
|--|--|---|--|
| CD4 count (cells/μl) | | % of patients achieving HBsAb >10 IU/litre | |
| >500 | | 87 | |
| >350 with standard dose | | 39 | |
| >350 with doubled dose | | 64 | |
| <350 | | 26 ^a | |

^a Physicians should weigh the risk of HBV infection against the benefit of vaccination in severely immunocompromised patients.

Other adult populations at risk for HBV who should be vaccinated include:

- sexual partners of HBV carriers
- men who have sex with men (MSM)
- sex workers (SWs)
- other people with multiple sexual partners
- patients with STIs
- IDUs
- prisoners, both male and female¹
- patients on haemodialysis
- health care workers exposed to blood or blood products.

For HBV vaccination of children and use of hepatitis B immunoglobulin (HBIG), please refer to Protocol 12, *Immunization of people living with HIV and people at risk for HIV infection*.

1.2. Hepatitis A

- All HCV/HIV- and HBV/HIV-coinfected patients who are not also coinfected with the hepatitis A virus (HAV) but are at risk for it should be vaccinated (see the risk of HAV infection and further strategies in Protocol 12, *Immunization of people living with HIV and people at risk for HIV infection*).
- The response rate to vaccination is reduced and correlates to CD4 count.
- Mean HAV antibody titres in HIV-positive responders are about one tenth what they are in HIV-negative responders.
- Although the absolute lower limit of antibody level required to prevent HAV infection has not been established, a study using a HAV antibody (Ab) threshold of 33 mIU/litre showed the levels of response in Table 2.

| TABLE 2. | | | HEPATITIS A VACCINE RESPONSE AT DIFFERING CD4 COUNTS (6) | |
|--|--|----------------|---|--|
| CD4 count (cells/μl) | % of patients achieving HAV Ab >33 mIU/litre | | | |
| | Month 7 | Month 9 | | |
| \geq 500 | 73 | 67 | | |
| 200–499 | 53 | 69 | | |
| <200 | 11 | 9 ^a | | |

^a Physicians should weigh the risk of HAV infection against the benefit of vaccination in severely immunocompromised patients.

¹ Prisoners are at increased risk of HBV infection due to injecting drug use and unprotected sex.

- Though response to vaccination in immunocompromised patients is reduced, WHO policy is to administer vaccine regardless of CD4 level. Immunoglobulin should be administered concurrently for those with severe immunosuppression (CD4 cell count <200).
- Non-responders to HAV vaccine should be revaccinated once their CD4 count has risen in response to HAART, ideally ≥ 500 cells/mm³.

For HAV vaccination of children and use of hepatitis A immunoglobulin, please refer to Protocol 12, *Immunization of people living with HIV and people at risk for HIV infection*.

There are certain contraindications that need to be kept in mind even though hepatitis A vaccine is inactivated and no special precautions are needed when vaccinating immunocompromised people.

- HAV vaccine should not be administered to patients with a history of serious allergic reaction to it.
- Vaccination of patients with moderate or severe acute illnesses should be deferred until their conditions have improved.
- The safety of HAV vaccination during pregnancy has not been determined. However, because it is an inactivated vaccine, the theoretical risk to the fetus is low. The risk associated with vaccination should be weighed against the risk of HAV infection.

2. Prevention of mother-to-child transmission (PMTCT)

2.1. PMTCT of HBV

- All HIV-infected women should be screened for hepatitis B surface antigen (HBsAg) as a routine part of prenatal testing.
- In pregnant HBV/HIV-coinfected women who need or do not need ART for their own health, the antiretroviral (ARV) combination has to include 3TC, as it is effective against both viruses.
- The transmission rate of HBV is reduced by replication suppression; the doses and duration at which ARVs are administered should be the same as for HIV mono-infected women (see Protocol 10, *Prevention of HIV transmission from HIV-infected mothers to their infants*).
- In children born to chronically HBV-infected mothers, administration of vaccine within 12 hours after birth provides up to 95% protective efficacy (7). Since the added value of administering HBIG concurrently with hepatitis B vaccine is quite low, its benefits and cost should be considered.
- In cases in which the mother is HBsAg-positive, the neonate should receive the single-antigen HBV vaccine along with 0.5 ml of HBIG within 12 hours of birth. These children can then receive the HBV vaccine series on a normal schedule of three doses (at 0, 1 and 6 months). In neonates weighing less than 2000 g, the initial vaccine following delivery is associated with a lower rate of immunogenicity. Therefore, these children should receive four doses of HBV vaccine (at birth and 1, 2–3 and 6–7 months) (8).
- Children of HBsAg-positive mothers should undergo testing for HBsAg and HBsAb at 9 and 18 months. If the surface antibody level is less than 10 mIU/ml, the entire three-vaccine series should be repeated. Testing for hepatitis B core antibody (HBcAb) in these children is discouraged because passively acquired maternal antibodies may be detectable up to 24 months of age.
- When a woman's HBV status is still unknown at delivery but is later discovered to be positive, HBIG may be administered up to seven days after birth. In cases of unknown maternal hepatitis status among children weighing less than 2000 g at birth, physicians should administer both the HBV vaccine and immunoglobulin.
- Neonates born to HBV-negative mothers should receive their first HBV vaccination in the hospital. Neonates weighing less than 2000 g are a prominent exception to this rule. Because of the reduced immunogenicity of the HBV vaccine in this group, vaccination should be delayed until one month of age (9).

2.2. PMTCT of HCV

- HCV mother-to-child transmission (MTCT) in HIV-infected women is high (between 5% and 20%) (10). When possible, HCV treatment should be offered before pregnancy to women of childbearing age. Although several MTCT risk factors have been identified, there are currently no interventions available to prevent vertical transmission of HCV.
- Normally, elective caesarean section is advised for women who are HIV-infected as a means of preventing transmission to the infant. However, if the viral load is <1000 copies/ml, then vaginal delivery could be considered. Based on the current evidence, these same guidelines apply for women who are HCV/HIV-coinfected (11, 12).
- Prevention of ribavirin embryopathy includes:
 - a pregnancy test before starting treatment and every month during treatment; and
 - counselling (of both the woman and her partner) to avoid pregnancy and use condoms while either partner is taking ribavirin and for at least six months afterwards.

3. Preventing and reducing risk of infection

3.1. Safer sexual behaviour

- All patients – those in the general population as well as those in vulnerable populations (SWs, IDUs, MSM, etc.) – should be counselled about safer sex and the use of condoms for any form of penetrative sex. Condoms are an effective means of preventing sexual transmission of HIV infection as well as hepatitis B and C infections.
- The sexual transmission of hepatitis A is mostly found in MSM, linked to oro-anal contact; preventive measures include using either a vertically cut condom or some plastic food wrap to cover the anal area before oral contact.

3.2. Reducing harm related to injecting drug use

- In addition to risks resulting from sexual behaviour, IDUs are vulnerable to bloodborne virus (HIV, HCV, HBV, HAV and HDV) as a result of collective use of injecting equipment. In some countries in Europe, over 70% of HIV infections are attributed to IDUs (13).
- Effective evidence-based strategies to reduce risk of HBV and HCV transmission through injecting drug practices are:
 - linking to harm-reduction programmes, particularly needle exchange and opioid substitution therapy; and
 - counselling of patients with high-risk drug and sexual practices, especially those who are seropositive, on risk reduction.

For more details, please refer to Protocol 5, *HIV/AIDS treatment and care for injecting drug users*

4. Counselling to reduce liver-related harm

All patients should be counselled on ways to reduce liver-related harm.

- Alcohol consumption should be stopped or reduced to no more than 10 g/day.
- Smoking should be stopped, as it has been associated with an increased risk of hepatitis cellular carcinoma (HCC) in some studies of patients with chronic HBV disease. The effects of smoking and alcohol may be synergistic (14).
- The active component in cannabis – endocannabinoid (found in both marijuana and hashish) – has been found to have many physiological and patho-physiological functions. It has recently been implicated in the haemodynamic alterations occurring in cirrhosis (15).
- No dietary factors have been linked specifically to HBV disease activity or severity. However, excess iron is associated with reduced responsiveness to interferon treatment and increased risk for HCC. Thus, iron supplements should be avoided unless iron deficiency is present (16).
- Vitamin A in excessive amounts can be directly hepatotoxic; it is not recommended unless there is documented deficiency (17).

- Herbal supplements should be used with caution, if at all. Many of these preparations can be severely hepatotoxic (18), for example, chaparral, comfrey, germander, jin bu huan and kava kava. Due to a lack of regulation of supplements, formulations and doses can vary widely.
- Patients who have coexisting non-alcoholic fatty liver disease should be simultaneously counselled on:
 - optimizing body weight
 - achieving and maintaining normal triglyceride levels
 - controlling diabetes mellitus.

5. Prevention of transmission through transfusion of blood and blood products

Precautions to prevent infection through blood and blood products include:

- screening of all blood products for HBsAg and HCV Ab
- screening for HBcAb, and HCV RNA quantification²
- virus inactivation of plasma-derived products.

6. Prevention in health care settings

As it is not possible to identify all people infected with bloodborne pathogens, guidance to protect health care workers against HIV and hepatitis viruses is based on the concept that all patients should be assumed to be infectious. The application of universal precautions requires that all blood and body fluids be regarded as potentially infectious and that appropriate protective action be taken.

Universal precautions include:

- infection-control practices, such as appropriate sterilization of medical and dental equipment;
- discouraging the excessive use of injections and promoting safe injection practices among health care workers; and
- strongly recommending vaccination against hepatitis B for all health care workers exposed to blood or blood products.

Prevention of hepatitis B and C transmission in health care settings is similar to prevention of HIV transmission there. For further information, please refer to Protocol 13, *Post-exposure prophylaxis for HIV infection*.

² Even when this screening is performed, there is still a minor risk of transmission.

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