

**B. Screening should be repeated every 3–6 months once on HD depending on the prevalence of HBV infection in the unit.**

*(Evidence level: C)*

### **Commentary on Guideline VI.6.1**

Serological tests for the detection of viral markers include HBs Ag, HBe Ag, anti-HBe, anti-HBc, and anti-HBs. They are mandatory to detect HBV infection and to determine which patients should be vaccinated.

### **Guideline VI.6.2**

**A. Screening for HCV antibodies should be performed in all patients starting HD or transferring from another unit.**

*(Evidence level: A)*

**B. Screening should be repeated at least every 6 months once on HD.**

*(Evidence level: C)*

**C. HCV screening should include an ELISA assay and a confirmatory testing with a more specific assay (RIBA).**

*(Evidence level: B)*

### **Commentary on Guideline VI.6.2**

The tests recommended in the first place are second and third generation ELISA assays. Positive tests should be confirmed by analytic tests such as RIBA (Recombinant ImmunoBlot Assay) [155]. However, if plasma ALT is persistently elevated in patients who are anti-HCV negative, in the absence of another aetiology, testing for HCV RNA should be considered [156]. The detection of HCV RNA by reverse transcriptase–polymerase chain reaction (RT–PCR) has been used as the gold standard to identify HCV infection [157] but there are difficulties in interpreting this test. HCV RNA has been detected in only 52–93% of dialysis patients with anti-HCV [157]. Several possibilities could account for the presence of anti-HCV antibodies in the absence of HCV RNA. Viraemia could be intermittent and the number of copies of HCV RNA may be less than the limit of detection. Antibody to HCV may persist even after the viral RNA has disappeared. On the other hand, only 83% of HCV RNA-positive dialysis patients are positive for anti-HCV antibodies and 2.5–12% of anti-HCV-negative dialysis patients test positive for HCV-RNA [157]. The patient may be in the ‘window’ period between infection and seroconversion. After anti-HCV antibody has persisted for a certain period of time it can disappear despite the persistence of HCV RNA [158].

Routine serological testing for HCV is a useful tool for monitoring the incidence and the prevalence of the infection in a dialysis unit, for monitoring

## **VI.6 Prevention and management of HBV, HCV and HIV in HD patients**

### **Guideline VI.6.1**

**A. Screening for HBV markers should be performed in all patients starting HD or transferring from another unit whether they received anti HBV vaccination or not.**

*(Evidence level: A)*

nosocomial HCV transmission and optimizing patient care [159].

### Guideline VI.6.3

**A. Screening for HIV infection should be done in all patients starting HD or transferring from another unit after getting informed consent. Once on routine HD, screening is not recommended.**

*(Evidence level: C)*

#### Commentary on Guideline VI.6.3

Identification of HIV carriers with end-stage renal disease should be encouraged because of several reasons: appropriate counselling to prevent transmission, to advise on the contraindication for transplantation, anti-retroviral therapy, and prophylaxis against opportunistic infections.

However, if universal precautions are adequately respected the risk of transmission from patient to patient is very low and according with the CDC recommendations, routine screening of HD patients for HIV infection is not necessary [43,160].

### Guideline VI.6.4

**A. Universal precautions for prevention of transmission of blood-borne pathogens in the health care setting should be rigorously respected in all HD units. These include:**

- cleaning and disinfection of instruments, machines and environmental surfaces after each treatment;
- avoidance of sharing articles among patients;
- frequent hand washing and use of disposable gloves;
- use of protective eye wear and face mask.

*(Evidence level: C)*

**B. Dialyzed HBs Ag-positive patients should be treated in separate rooms with dedicated machines.**

*(Evidence level: C)*

**C. In addition to universal precautions, which are the most efficacious preventive measures, treatment of anti-HCV patients in separate areas with dedicated staff is recommended in units with a high prevalence of HCV infection.**

*(Evidence level: C)*

#### Commentary on Guideline VI.6.4

Probably blood transfusions were initially the main source of introduction of the HBV and HCV into dialysis unit. The use of HBs Ag-free blood since 1970 and more recently the systematic screening of blood donors for HCV has led to disappearance or a dramatic decrease in the incidence of post-transfusion hepatitis.

Before the availability of passive and active immunization against HBV, general prophylactic measures were the only means of preventing and controlling HBV infection in dialysis units. They are still the only means of protection against the spread of HCV and HIV [161].

Several observations argue that nosocomial transmission is the principal mode of HCV infection in HD units. Some HD patients with HCV have never received a blood transfusion. The prevalence of HCV-positive patients on HD is greater in patients treated in centres than in patients maintained on home HD and those on peritoneal dialysis [162,163]. Molecular evidence for nosocomial spread of HCV has been offered by virological studies [164,165–170].

Recommendations for the prevention of spread of any type of hepatitis within dialysis centres were given as early as 1968 by the Public Health Laboratory Service [171]. ‘Recommended precautions for patients undergoing HD who have AIDS or non A non B hepatitis’ were published in 1985 by the CDC [172] and updated in 1988 as ‘Universal precautions for prevention of transmission of blood-borne pathogens in health-care setting’ [173].

Strict adherence to the general disinfection measures seems sufficient to prevent transmission of HBV particularly when few patients are HBs Ag-positive in a dialysis unit [174]. Nevertheless, the use of separate rooms and monitors for the dialysis HBs Ag-positive patients was recommended [171,175].

Contamination of hospital environmental surfaces and secondary patient-to-patient transmission are due to poor aseptic techniques and strict enforcement of universal precautions prevents HCV transmission among HD patients [176]. Although universal precautions must be accomplished in an obligatory manner they are not always carried out by the dialysis staff [177].

Whether or not HCV-positive patients should be treated in separate rooms is still debated. Some authors suggest the need for such isolation in order to limit interindividual contamination [178]. Several arguments are not in favour of such segregation. First, a substantial part of uraemic patients with PCR demonstrating HCV-RNA viraemia has a negative serology and are not identified if systematic and repeated PCR is not performed. Secondly, strict enforcement of universal precautions and systematic disinfection of the machines after each treatment has been shown to fully prevent HCV transmission to HD patients [176]. However, in a large prospective multicentre study where the prevalence of HCV infection at baseline was 32.1%, an increased risk for HCV infection was associated with anti-HCV prevalence of 30% or greater and personnel-patient ratio less than 28.2/100 patients [179]. Therefore, in addition to universal precautions, which are the most efficacious preventive measures, treatment of anti-HCV patients in separate areas with dedicated staff is recommended in units with a high prevalence of HCV infection [166].

Isolation of patients with AIDS and asymptomatic carriers of HIV and the use of separate machines are not recommended [173]. In dialysis units that conform to the practice guidelines recommended by the CDC, the risk of patient-to-patient transmission of HIV is very low [160]. The only reported cases of patient-to-patient transmission of HIV have been reported from developing countries where universal precautions were not followed [43,180].

#### Guideline VI.6.5

**A. Passive immunization or passive-active immunization against HBV should be applied for post-exposure protection after accidental inoculation in staff as preventive treatment in both health care workers and dialysis patients when unresponsive to vaccination.**  
(Evidence level: B)

#### Commentary on Guideline VI.6.5

Trials of post-exposure passive immunization with anti-hepatitis B human immunoglobulin (HBIG) preparation showed high, although not absolute, protection after accidental inoculation or projection of HBS-Ag positive material [181–183]. The protective efficacy of combined HBIG and hepatitis B vaccine was shown to be superior to that of HBIG alone [184].

#### Guideline VI.6.6

**A. A combination of AZT, lamivudine, and a protease inhibitor should be recommended for HD staff members accidentally exposed to HIV.**  
(Evidence level: C)

#### Commentary on Guideline VI.6.6

After an accidental occupational HIV exposure, there is a window of opportunity during which anti-retroviral therapy can establish its effects. The duration of this window of opportunity is not known. However, it is presumed that the chance of killing the virus is best if treatment is started within 1 h of exposure [44].

The risk of acquiring infection following an occupational exposure is only 0.32% [185] and there are no published randomized trials of AZT for post-exposure prophylaxis to health care workers exposed to HIV. Nevertheless, the US Public Health Service Guidelines recommend a combination of AZT and lamivudine for most parenteral exposures. The addition of a protease inhibitor is suggested for high-risk exposures (those with high viral loads) [186]. Therefore, exposure due to needle prick should be treated with a triple therapy.

#### Guideline VI.6.7

**A. Active immunization against HBV should be undertaken in all HD staff members.**  
(Evidence level: A)

**B. Either a 0-, 1-, 6-month or a 0-, 1-, 2- and 12-month vaccination schedule should be used.**  
(Evidence level: B)

**C. Monitoring of acquired antibody titre is advisable in these subjects. Additional doses should be administered to staff members who do not develop protective antibody titres (threshold level 10 mIU/ml).**  
(Evidence level: C)

#### Commentary on Guideline VI.6.7

Members of the HD staff may be infected by accidental needle pricks, contamination of cuts or skin lesions, blood spraying into eyes or mouth, eating, or smoking in the dialysis ward.

Although the pool of chronic HBs Ag carriers among HD patients has decreased, thus reducing the risk of contamination, new patients, especially those arriving in emergency conditions, may introduce HBV in the HD unit with the risk of contamination of staff members.

At present, several recombinant vaccines are available and all have been proven to be immunogenic in healthy subjects with seroconversion obtained in 95% or more of recipients [187,188]. Vaccination protocols in healthy adults differ among countries. Two main schedules are proposed: a 0-, 1-, 6-month or a 0-, 1-, 2- and 12-month schedule [189]. The latter protocol induces comparable anti-HBs titres following primo vaccination but higher titres following the booster injection at 1 year and may be more advantageous in terms of long-term protection [190].

Few, but an unpredictable number of health care workers develop no or low response. Therefore, in highly exposed staff members post-vaccination testing of antibody titres should be considered in order to offer an additional course of vaccination to the low responders and to propose to the still non-responsive subjects to move to less exposed work.

Staff members having isolated anti-HBc and/or low titre anti-HBs antibodies should receive one vaccine dose and if an increase in anti-HBs titre is not observed they should complete another full vaccination course [191].

#### Guideline VI.6.8

**A. Patients with progressive chronic renal failure should be vaccinated against HBV preferably before they start on HD.**  
(Evidence level: B)

**B. HD patients who have not been previously immunized against HBV should be vaccinated.**

*(Evidence level: A)*

**C. Anti-HBs testing is recommended 1–2 months after the primary series has been completed and 6–12 months thereafter, depending on the local incidence of HBV infection. Additional doses should be administered to patients who do not develop protective antibody titres (threshold level 10 mIU/ml). Subsequent routine testing is recommended every 6 months. A booster dose is recommended if the anti-HBs titre is less than 10 mIU/ml.**

*(Evidence level: C)*

### Commentary on Guideline VI.6.8

All HB vaccines have a significant protective effect against acquiring HBV infection in chronic HD patients [192–196]. However, development of anti-HB antibodies is inhibited by the defective immune response that characterizes the uraemic patient [50,59] and approximately 50–60% of the dialysis patients develop a protective anti-HBs response when the standard protocol recommended for healthy subjects is used either with plasma-derived vaccines or DNA recombinant vaccines [193–191, 196–198].

The importance of vaccination early in the course of renal disease or before dialysis is started has been stressed because it appeared to increase the rate of response [199] but impairment of the response to HB vaccine was shown even at an early stage of chronic renal failure [200]. Nevertheless, early vaccination should give better results than a vaccination performed late in the course of chronic renal failure.

Thus, reinforced protocols were proposed to overcome the deficient response of dialysis patients [201]. Three double doses or four single doses induced a significantly greater proportion of responders and significantly greater anti-HBs titres.

The intradermal (ID) route was used to enhance the seroconversion of dialysis patients to the HB vaccine [202–207]. However, there are no data regarding long-term protection and the ID route is not currently recommended.

Because of the low response to vaccination, the shorter duration of immunity and potential loss of antibodies, regular anti-HBs testing is recommended.

### Guideline VI.6.9

**A. To inhibit HBV replication alpha interferon (IFN $\alpha$ ) and/or lamivudine should be administered to transplant candidates who have biopsy-proven HBV-chronic liver disease.**

*(Evidence level: C)*

### Commentary on Guideline VI.6.9

IFN $\alpha$  is the most effective drug to inhibit viral replication [208]. However, there are few data concerning the administration of IFN to HD patients with chronic hepatitis B [209]. IFN is poorly tolerated in these patients and pharmacokinetic studies demonstrated impaired IFN metabolism with increased bioavailability in HD patients [210,211]. On the other hand, immunodeficiency is known to be a negative predictive factor of the antiviral effect of IFN therapy [209]. The preliminary data available from a small and uncontrolled trial showed that IFN is safe and effective in inducing biochemical remission [212].

Lamivudine is a nucleoside analogue able to inhibit the DNA polymerase activity of the virus [213]. This drug is effective but has severe and frequent neuromuscular side effects. It has been recently given to six dialysis patients, candidates for kidney or combined kidney and liver transplantation and has been shown to be effective in inhibiting HBV replication [214].

Whether IFN or lamivudine might offer the potential of making renal transplantation a feasible option in HD patients with chronic HBV hepatitis remains to be elucidated.

### Guideline VI.6.10

**A. Alpha IFN should be considered for HD patients with biopsy-proven chronic hepatitis due to HCV awaiting renal transplantation.**

*(Evidence level: C)*

### Commentary on Guideline VI.6.10

Alpha IFN has been used with a fair degree of success in patients with chronic hepatitis due to HCV [157]. Among HD patients, the initial response to IFN has been encouraging [215–218]. However, as in the case of non-renal patients, relapses are common after stopping treatment and long-term outcomes are unknown. IFN is poorly tolerated in HD patients with a high drop out rate [215,216,218].

The risk of long-term development of chronic liver disease after renal transplantation has led to propose treating dialysis patients with chronic hepatitis C who are candidates for renal transplantation. The course of IFN treatment should be interrupted at transplantation, but is not a reason to postpone transplantation if a kidney becomes available.