MANAGEMENT OF HEALTHCARE WORKERS WITH OCCUPATIONAL EXPOSURE TO HIV, HEPATITIS B AND C

MINISTRY OF HEALTH
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CONTENTS

Tables

Appendices

References

SUMMARY

This document provides guidelines for the management of health care workers (HCW) occupational exposure to blood and body fluids that may contain the hepatitis viruses (HBV and HCV) and human immunodeficiency virus (HIV), and recommendations for post-exposure prophylaxis (PEP).

Recommendations for PEP are related to the risk of infection from selected exposures and the serological status of the exposure source. Recommendations for HBV post-exposure management include initiation of the hepatitis B vaccine series to any susceptible, unvaccinated person who sustains an occupational blood or body fluid exposure. Post-exposure prophylaxis (PEP) with hepatitis B immune globulin (HBIG) and/or hepatitis B vaccine series should be considered for occupational exposures after evaluation of the hepatitis B surface antigen status of the source and the vaccination and vaccine-response status of the exposed person.

Immune globulin and antiviral agents (e.g., interferon with or without ribavirin) are not recommended for PEP of hepatitis C. For HCV post-exposure management, the HCV status of the source and the exposed person should be determined, and for HCW exposed to an HCV positive source, follow-up HCV testing should be performed to determine if infection develops. In the case of HIV, for high-risk exposures a four-week course of expanded regimen is recommended.

The focus of these guidelines is occupational exposure to blood and blood products. Saliva, tears, sweat, urine and breastmilk are not associated with the risk of HIV transmission in an occupational setting. Advances in the prevention and treatment of these blood-borne viruses, especially HIV and AIDS are progressing at a rapid rate and recommended clinical practice may change over time.

HCW must report occupational exposures immediately after they occur, particularly because HBIG, hepatitis B vaccine, and HIV PEP are most likely to be effective if administered as soon after the exposure as possible. HCW who are at risk for occupational exposure to blood-borne pathogens should familiarized themselves with the principles of post-exposure management as part of job orientation and ongoing job training.

These guidelines complement related guidelines issued by the Occupational Health Division of the Department of Health Services, Ministry of Health, namely:

i) Guidelines on Health and Safety at Workplace for Healthcare Personnel, and,
ii) Guidance and Recommendations on Healthcare Workers Infected With HIV, Hepatitis B or Hepatitis C

1. INTRODUCTION

1.1 Exposure Settings

Avoiding occupational blood exposures is the primary way to prevent transmission of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in health-care settings. However, hepatitis B immunization and post-exposure management are integral components of a complete program to prevent infection following blood-borne pathogen exposure and are important elements of workplace safety.

Health-care workers (HCW) are defined as persons (e.g., employees, students, contractors, attending clinicians, public-safety workers, or volunteers) whose activities involve contact with patients or with blood or other body fluids from patients in a health-care, laboratory, or public-safety setting.

HCWs, especially those whose work involves:
1) blood collection or the use of sharp instruments such as needles and scalpels;
2) the insertion of intravenous catheters; or,
3) minor and major surgery,
are at increased risk. There is also a potential risk to workers handling soiled linen, clinical wastes and those involved in handling corpses and performing post mortem examinations.

An exposure that might place a HCW at risk for HBV, HCV, or HIV infection is defined as a percutaneous injury (e.g., a needlestick or cut with a sharp object) or contact of mucous membrane or non-intact skin (e.g., exposed skin that is chapped, abraded, or afflicted with dermatitis) with blood, tissue, or other body fluids that are potentially infectious. ‘Body fluids’ include semen, vaginal secretions or other fluids contaminated with visible blood.

In addition to blood and body fluids containing visible blood, semen and vaginal secretions also are considered potentially infectious. Although semen and vaginal secretions have been implicated in the sexual transmission of HBV, HCV, and HIV, they have not been implicated in occupational transmission from patients to HCW. The following fluids also are considered potentially infectious: cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid. The risk for transmission of HBV, HCV, and HIV infection from these fluids is unknown; the potential risk to HCP from occupational exposures has not been assessed by epidemiologic studies in health-care settings. Faeces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered potentially infectious unless they contain blood. The risk for transmission of HBV, HCV, and HIV infection from these fluids and materials is extremely low.

For human bites, the clinical evaluation must include the possibility that both the person bitten and the person who inflicted the bite were exposed to blood-borne pathogens. Transmission of HBV or HIV infection only rarely has been reported by this route.

Transmission of blood borne viruses is minimised by strict adherence to standard universal precautions and by adoption of procedures to sterilise or disinfect equipment in contact with blood or blood products. Universal precautions require that HCWs treat the blood and body fluids of *all* persons as potential sources of infection, independent of perceived risk or diagnosis.

HCWs must ensure that they know about infection risks and that they comply with infection control procedures. This includes:
1) the use of protective equipment (e.g. gloves, goggles and aprons);
2) covering skin lesions, cuts or abrasions with occlusive dressings; and,
3) that equipment in contact with blood and body fluids is appropriately disinfected and sterilised.

1.2 Treatment of an Exposure Site

Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water; mucous membranes should be flushed with water. No evidence exists that using antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk of blood-borne pathogen transmission; however, the use of antiseptics is not contraindicated. The application of caustic agents (e.g., bleach) or the injection of antiseptics or disinfectants into the wound is not recommended.

1.3 Evaluation of the Exposure

The exposure should be evaluated for the potential to transmit HBV, HCV, and HIV based on the type of body substance involved and the route and severity of the exposure. Blood, fluid containing visible blood, or other potentially infectious fluid (including semen; vaginal secretions; and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids) or tissue can be infectious for blood-borne viruses. Exposures to these fluids or tissue through a percutaneous injury (i.e., needlestick or other penetrating sharps-related event) or through contact with a mucous membrane are situations that pose a risk for blood-borne virus transmission and require further evaluation. For HCV and HIV, exposure to a blood-filled hollow needle or visibly bloody device suggests a higher risk exposure than exposure to a needle that was most likely used for giving an injection.

For skin exposure, follow-up is indicated only if it involves exposure to a body fluid and evidence exists of compromised skin integrity (e.g., dermatitis, abrasion, or open wound). In the clinical evaluation for human bites, possible exposure of both the person bitten and the person who inflicted the bite must be considered. If a bite results in blood exposure to either person involved, post-exposure follow-up should be provided.

1.4 Evaluation of the Exposure Source

The person whose blood or body fluid is the source of an occupational exposure should be evaluated for HBV, HCV, and HIV infection. Information available in the medical record at the time of exposure (e.g., laboratory test results, admitting diagnosis, or previous medical history) or from the source person, might confirm or exclude blood-borne virus infection.

If the HBV, HCV, and/or HIV infection status of the source is unknown, the source person should be informed of the incident and tested for serologic evidence of blood-borne virus infection. Any persons determined to be infected with HBV, HCV, or HIV should be referred for appropriate counseling and treatment. Confidentiality of the source person should be maintained at all times.

If the exposure source is unknown or cannot be tested, information about where and under what circumstances the exposure occurred should be assessed for the likelihood of transmission of HBV, HCV, or HIV. Certain situations as well as the type of exposure might suggest an increased or decreased risk; an important consideration is the prevalence of HBV, HCV, or HIV in the population group (i.e., institution or community) from which the contaminated source material is derived. For example, an exposure that occurs in a geographic area where injection-drug use is prevalent or involves a needle discarded in a drug-treatment facility would be considered to have a higher risk for transmission than an exposure that occurs in a nursing home for the elderly.

Testing of needles or other sharp instruments implicated in an exposure, regardless of whether the source is known or unknown, is not recommended. The reliability and interpretation of findings in such circumstances are unknown, and testing might be hazardous to persons handling the sharp instrument.

1.5 Exposure Incident Report

If an occupational exposure occurs at any time (during working or outside office hours), **immediately** inform the infection control team. An “Accident at Work Reporting Form” (see **Appendix 1**) must also be filled recording the circumstances and any post-exposure management and submitted to the Occupational Health Division at Bandar Seri Begawan Health Center (Tel: 2230043 and Fax: 2230044) as soon as possible for further management.

1.6 Compensation

The Department of Labor is the appropriate authority to address compensation issues for employees who acquire an illness or injury in the course of their work. For current information about workers compensation matters, employees are advised to contact the above department.

2. HEPATITIS B

2.1 Occupational Transmission of HBV

2.1.1 Risk for Occupational Transmission of HBV

HBV infection is a well recognized occupational risk for HCW. The risk of HBV infection is primarily related to the degree of contact with blood in the work place and also to the hepatitis B e antigen (HBeAg) status of the source person. In studies of HCW who sustained injuries from needles contaminated with blood containing HBV, the risk of developing clinical hepatitis if the blood was both hepatitis B surface antigen (HBsAg)- and HBeAg-positive was much higher (22%--31%) compared to the risk of developing clinical hepatitis from a needle contaminated with HBsAg-positive, HBeAg-negative blood (1%--6%).

Although percutaneous injuries are among the most efficient modes of HBV transmission, these exposures probably account for only a minority of HBV infections among HCW. HBV has been demonstrated to survive in dried blood at room temperature on environmental surfaces for at least 1 week. Thus, HBV infections that occur in HCW with no history of non-occupational exposure or occupational percutaneous injury might have resulted from direct or indirect blood or body fluid exposures that inoculated HBV into cutaneous scratches, abrasions, burns, other lesions, or on mucosal surfaces.

Blood contains the highest HBV titers of all body fluids and is the most important vehicle of transmission in the health-care setting. HBsAg is also found in several other body fluids, including breast milk, bile, cerebrospinal fluid, feces, nasopharyngeal washings, saliva, semen, sweat, and synovial fluid. However, the concentration of HBsAg in body fluids can be 100—1000 fold higher than the concentration of infectious HBV particles. Therefore, most body fluids are not efficient vehicles of transmission because they contain low quantities of infectious HBV, despite the presence of HBsAg.

Because of the high risk of HBV infection among HCW, routine pre-exposure vaccination of HCW against hepatitis B and the use of standard precautions to prevent exposure to blood and other potentially infectious body fluids have been recommended.

2.1.2 Hepatitis B Vaccination

Any person who performs tasks involving contact with blood, blood-contaminated body fluids, other body fluids, or sharps should be vaccinated against hepatitis B.

Hepatitis B vaccine can be administered at the same time as other vaccines with no interference with antibody response to the other vaccines. If the vaccination series is interrupted after the first dose, the second dose should be administered as soon as possible. The second and third doses should be separated by an interval of at least 2 months. If only the third dose is delayed, it should be administered when convenient.

HCW who have contact with patients or blood and are at ongoing risk for percutaneous injuries should be tested 1-2 months after completion of the 3 dose vaccination series for anti-HBs. Persons who do not respond to the primary vaccine series (i.e., anti-HBs <10 mIU/mL) should complete a second 3-dose vaccine series or be re-evaluated to determine if they are HBsAg-positive. Revaccinated persons should be retested at the completion of the second vaccine series. Persons who do not respond to an initial 3-dose vaccine series have a 30%-50% chance of responding to a second 3-dose series. Non-responders to vaccination who are HBsAg-negative should be considered susceptible to HBV infection and should be counseled regarding precautions to prevent HBV infection and the need to obtain HBIG prophylaxis for any known or probable parenteral exposure to HBsAg-positive blood.

Booster doses of hepatitis B vaccine are not necessary (unless indicated i.e. immunocompromised), and periodic serologic testing to monitor antibody concentrations after completion of the vaccine series and there is evidence of immunologic response, is not recommended. Any blood or body fluid exposure sustained by an unvaccinated, susceptible person should lead to the initiation of the hepatitis B vaccine series.

Please see **Appendix 2** on FAQ's on Hepatitis B vaccination. Current hepatitis B vaccine used by the Ministry of Health is Engerix^{TM}-B

2.1.3 PEP for HBV

2.1.3.1 Efficacy of PEP for HBV

In the occupational setting, in an unvaccinated HCW or a known-non responder, single or multiple doses of HBIG initiated within 1 week following percutaneous exposure to HBsAg-positive blood or blood of unknown source provides an estimated 75% protection from HBV infection. In addition, because persons requiring PEP in the occupational setting are generally at continued risk for HBV exposure, they should receive the hepatitis B vaccine series.

2.1.3.2 Safety of PEP for HBV

The most common side effects from hepatitis B vaccination are pain at the injection site and mild to moderate fever. Other less commonly reported side effects includes alopecia (mostly temporary) and anaphylaxis.

HBIG is prepared from human plasma known to contain a high titer of antibody to HBsAg (anti-HBs). The plasma from which HBIG is prepared is screened for HBsAg and antibodies to HIV and HCV. Serious adverse effects from HBIG when administered as recommended have been rare. Local pain and tenderness at the injection site, urticaria and angioedema might occur; anaphylactic reactions, although rare, have been reported following the injection of human immune globulin (IG) preparations. Persons with a history of anaphylactic reaction to IG should not receive HBIG.

2.1.3.3 PEP for HBV During Pregnancy.

No apparent risk exists for adverse effects to developing fetuses when hepatitis B vaccine is administered to pregnant women. The vaccine contains noninfectious HBsAg particles and should pose no risk to the fetus. HBV infection during pregnancy might result in severe disease for the mother and chronic infection for the newborn. Therefore, neither pregnancy nor lactation should be considered a contraindication to vaccination of women. HBIG is not contraindicated for pregnant or lactating women.

2.2 Management of Exposures to HBV

For percutaneous or mucosal exposures to blood, several factors must be considered when making a decision to provide prophylaxis, including the HBsAg status of the source and the hepatitis B vaccination and vaccine-response status of the exposed person. Such exposures usually involve persons for whom hepatitis B vaccination is recommended. Any blood or body fluid exposure to an unvaccinated person should lead to initiation of the hepatitis B vaccine series. Persons who have been previously infected with HBV are immune to reinfection and **do not** require PEP.

When HBIG is indicated, it should be administered (under medical supervision) as soon as possible after exposure (preferably within 24 hours). The effectiveness of HBIG when administered >7 days after exposure is unknown. When hepatitis B vaccine is indicated, it should also be administered as soon as possible (preferably within 24 hours) and can be administered simultaneously with HBIG at a separate site (vaccine should always be administered in the deltoid muscle).

For exposed persons who are in the process of being vaccinated but have not completed the vaccination series, vaccination should be completed as scheduled. Persons exposed to HBsAg-positive blood or body fluids who are known not to have responded to a primary vaccine series should receive a single dose of HBIG and reinitiate the hepatitis B vaccine series with the first dose of the hepatitis B vaccine as soon as possible after exposure. Alternatively, they should receive two doses of HBIG, one dose as soon as possible after exposure, and the second dose 1 month later. The option of administering one dose of HBIG and reinitiating the vaccine series is preferred for nonresponders who did not complete a second 3-dose vaccine series. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.

A summary of prophylaxis recommendations for percutaneous or mucosal exposure to blood according to the HBsAg status of the exposure source and the vaccination and vaccine-response status of the exposed person is shown in **Table 1** (page 10) below.

Table 1: Recommended Postexposure Prophylaxis For Occupational Exposure To Hepatitis B Virus

Vaccination and antibody response status of exposed workers	Treatment		
	Source HBsAg positive	**Source HBsAg negative**	**Source unknown**
Unvaccinated	HBIG* X 1 and initiate Hep B vaccine series	Initiate Hep B vaccine series	Initiate Hep B vaccine series
Previously vaccinated • Known responder (documented evidence of adequate levels of anti HBs > or equal to 10 mIU/mL)	No treatment	No treatment	No treatment
• Known non responder (no or inadequate response to vaccination i.e. anti HBs level of < 10mIU/mL)	HBIG X 1 and initiate revaccination (if HCW have not receive the second 3-dose series) **or** HBIG X 2 (for HCW who have received the second 3 dose-series and failed to respond)	No treatment	If known high risk source, treat as if source were HBsAg positive
• Antibody response unknown	Test exposed HCW for anti HBs: 1. If adequate (i.e. anti HBs > or equal to 10 mIU/mL), no treatment is necessary **or** 2. If inadequate (anti HBs <10 mIU/mL), administer HBIG X 1 and vaccine booster	No treatment	Test exposed HCW for anti HBs: 1. If adequate(i.e. anti HBs > or equal to 10 mIU/mL), no treatment is necessary **or** 2. If inadequate(anti HBs <10 mIU/mL), administer vaccine booster and recheck titer in 1-2 months

***HBIG** Hepatitis B immunoglobulin; dose is 0.06 mL/kg intramuscularly

2.3 Counseling for HCW Exposed to Viral Hepatitis B

HCW exposed to HBV-infected blood do not need to take any special precautions to prevent secondary transmission during the follow-up period; however, they should refrain from donating blood, plasma, organs, tissue, or semen. The exposed person does not need to modify sexual practices or refrain from becoming pregnant. If an exposed woman is breast feeding, she does not need to discontinue.

No modifications to an exposed person's patient-care responsibilities are necessary to prevent transmission to patients based solely on exposure to HBV-positive blood. As recommended for all HCW, those who are chronically infected with HBV should follow all recommended infection-control practices, including standard precautions and appropriate use of hand washing, protective barriers, and care in the use and disposal of needles and other sharp instruments.

Infected HCW will be counseled and contact tracing activities carried out by the Epidemiologist of the Disease Control Division at the Health Screening Center in Berakas.

3. HEPATITIS C

3.1 Occupational Transmission of HCV

HCV is not transmitted efficiently through occupational exposures to blood. The average incidence of anti-HCV seroconversion after accidental percutaneous exposure from an HCV-positive source is 1.8% (range: 0%--7%). Transmission rarely occurs from mucous membrane exposures to blood, and no transmission in HCW has been documented from intact or nonintact skin exposures to blood. The risk for transmission from exposure to fluids or tissues other than HCV-infected blood also has not been quantified but is expected to be low.

3.2 Management of Exposures to HCV

The following are recommendations for follow-up of occupational HCV exposures:

- For the source, perform testing for anti-HCV.
- For the person exposed to an HCV-positive source
    - perform baseline testing for anti-HCV and ALT activity; and
    - perform follow-up testing (e.g., at 3-6 months) for anti-HCV and ALT activity (if earlier diagnosis of HCV infection is desired, testing for HCV RNA may be performed at 6-12 weeks).
- Confirm all anti-HCV results reported positive by enzyme immunoassay using supplemental anti-HCV testing (e.g. recombinant immunoblot assay [RIBA™]).

IG and antiviral agents are not recommended for PEP after exposure to HCV-positive blood. In addition, no guidelines exist for administration of therapy during the acute phase of HCV infection. However, limited data indicate that antiviral therapy might be beneficial when started early in the course of HCV infection.

Please see next page (page 13) on summary of recommendations following occupational exposure to HCV.

3.3 Counseling for HCW Exposed to Viral Hepatitis C

Counseling for HCW exposed to HCV-infected blood is similar to that of exposure to HBV-infected blood. Additionally, no recommendations exist regarding restricting the professional activities of HCW with HCV infection. As recommended for all HCW, those who are chronically infected with HCV should follow all recommended infection-control practices, including standard precautions and appropriate use of hand washing, protective barriers, and care in the use and disposal of needles and other sharp instruments.

SUMMARY OF RECOMMENDED MANGAMENT FOR OCCUPATIONAL EXPOSURE TO HEPATITIS C VIRUS

Known hepatitis C infected source

- Perform HCV RNA testing and ALT activity from HCW
- Perform HCV RNA testing at 6 and 12 weeks
- Obtain serum for anti-HCV testing and ALT activity at 12 and 24 weeks

Source known not to be infected with hepatitis C

- Obtain baseline serum for storage from HCW
- Perform HCV RNA testing, anti HCV and ALT activity as above if symptoms or signs of liver disease develop

Hepatitis C status of source unknown or unavailable

- Obtain baseline serum for storage from HCW

High risk

- Manage as known infected source

Low risk

- Obtain serum for anti-HCV testing and ALT activity at 24 weeks

Note:

There is currently no post-exposure prophylaxis for hepatitis C.

HCW found to have acquired hepatitis C infection following occupational exposure should be referred as soon as possible for specialist assessment.

4. HIV

4.1 Occupational Transmission of HIV

The possibility of occupationally acquired HIV infection and the current lack of a definitive cure or vaccine have caused concern for HCWs.

The average risk of HIV infection from all types of reported percutaneous exposure to HIV infected blood is 0.3%. Approximately 1 in every 300-330 exposures will result in an established HIV infection in the health care worker.

The risk of HIV infection following exposure increases if:
1) the injury is deep;
2) there is visible blood on the device causing the injury;
3) the device was previously placed in the source patient's vein or artery; or,
4) the source patient has advanced HIV disease (AIDS).

The risk is considered to be higher than 0.3% if the exposure involves a large volume of blood or if the source patient has very high HIV titres in their blood. Injuries with solid needles, such as a suturing needle, carry a lower risk than a hollow bored needle.

The risk of HIV transmission after mucous membrane or skin exposure to HIV infected blood depends on the volume of blood and the titre of HIV in the blood, and is reported to be in the order of 0.1% and less than 0.1% respectively.

The risk from skin exposure to HIV infected blood is low but increases if:
1) the contact is prolonged;
2) the contact involves an extensive area of skin;
3) the skin is visibly compromised (ie. has open wounds, diseased, or is inflamed); or,
4) there is a high titre of HIV in the source patient's blood

A high HIV titre, or viral load, in the source patient's blood is often associated with advanced immune deficiency and a low CD4 cell count, the AIDS phase of HIV disease, or early HIV infection. HIV viral titres may also rise during intercurrent infections such as active tuberculosis.

4.2 Management of Exposures to HIV

4.2.1 Clinical Evaluation and Baseline Testing of Exposed HCW

HCW exposed to HIV should be evaluated within hours (rather than days) after their exposure and should be tested for HIV at baseline (i.e., to establish infection status at the time of exposure).

If the source person is HIV seronegative and has no clinical evidence of AIDS or symptoms of HIV infection and is of low risk (e.g. non-IV drug user), no further testing of the person for HIV infection is indicated. The likelihood of the source person being in the "window period" of HIV infection in the absence of symptoms of acute retroviral syndrome is extremely small.

4.2.2 PEP for HIV

Antiretroviral agents from three classes of drugs are available for the treatment of HIV infection. These agents include the nucleoside reverse transcriptase inhibitors (NRTIs), nonnucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs).

Table 2 (page 17) shows recommended PEP regimens for percutaneous occupational exposure whilst **Table 3** (page 18) shows recommended PEP regimens for mucous membrane and non-intact skin occupational exposures. These recommendations should be implemented by specialist(s) who have expertise in antiretroviral therapy and HIV transmission. Other information such as medications the exposed person might be taking and any medical conditions or circumstances (i.e., pregnancy, breast feeding, or renal or hepatic disease) that might influence drug selection must be sought.

For HIV infection to occur from percutaneous exposure or sexual transmission, the virus attaches to CD4 receptors on immune cells at the site of injury. Once attached to the surface of these cells, infection may take place. This process takes from several hours to several days to occur and provides a window of opportunity for anti-viral PEP. The sooner that PEP is started, the better the chance of reducing viral replication and enabling the body to eliminate viable virus. Reverse transcriptase inhibitors (eg. ZVD, 3TC and ddI) interfere with the ability of the virus to infect the target cell. Protease inhibitors (eg. IDV) can suppress viral replication if the cell is already infected.

Retrospective studies of HCWs who have received ZVD following an occupational exposure to HIV have shown a reduced risk of sero-conversion. There are no data currently available to directly support the addition of other antiretroviral drugs to ZVD to enhance the effectiveness of the PEP regimen. However, in HIV infected patients, combination regimens have proved superior to monotherapy in reducing viral load. Adding a protease inhibitor (eg. IDV) provides an even greater increase in antiretroviral activity. There is a possibility of drug resistance in source patients who have already been exposed for long periods to ZDV and 3TC. In such cases the addition of a protease inhibitor may add further efficacy to the PEP regimen.

Protection with PEP is not absolute and there have been reports of treatment failure. Treatment failure may be related to HIV viral strains that are resistant to drugs used in the source patient. Such resistant strains are more likely in patients who have been on 6-12 months of antiretroviral therapy and patients who also have low CD4 cell counts. Failure of PEP may also be due to high HIV viral loads in the source patient or if the PEP was initiated too late or for insufficient duration.

4.2.2.1 Recommendations for the Selection of Drugs for HIV PEP

Because PEP is potentially toxic (see **Appendix 3**), its use is not justified for exposures that pose a negligible risk for transmission. Therefore, two regimens for PEP are provided: a "basic" two-drug regimen that should be appropriate for most HIV exposures and an "expanded" three-drug regimen that should be used for exposures that pose an increased risk for transmission. Duration of treatment is for four (4) weeks.

Recommended PEP Drug Regimens

1) Basic:	i)	Zidovudine (AZT) 300 mg bd; and	
		Lamivudine (3TC) 150 mg bd	**OR**
	ii)	Lamivudine (3TC) 150 mg bd; and	
		Stavudine (d4T) 40 mg bd (30 mg if wt. <30kg)	**OR**
	iii)	Didanosine (ddI) 400 mg od (buffered) or	
		250 mg od (delayed-release); and	
		Stavudine (d4T) 40 mg bd	
2) Expanded:	***Add***	Indinivir (IDV) 800 mg tds	**OR**
		Nelfinavir (NFV) 750 mg tds	**OR**
		Efavirenz (EFV) 600 mg nocte	**OR**
		Abacavir (ABC) 300 mg bd	

Selection of the PEP regimen should consider the comparative risk represented by the exposure and information about the exposure source, including history of and response to antiretroviral therapy based on clinical response, CD4+ T-cell counts, viral load measurements, and current disease stage. When the source person's virus is known or suspected to be resistant to one or more of the drugs considered for the PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended; expert consultation is advised. If this information is not immediately available, initiation of PEP, if indicated, should not be delayed; changes in the PEP regimen can be made after PEP has been started, as appropriate. Reevaluation of the exposed person should be considered within 72 hours postexposure, especially as additional information about the exposure or source person becomes available.

4.2.2.2 Timing and Duration of PEP

PEP should be initiated as soon as possible. If questions exist about which antiretroviral drugs to use or whether to use a basic or expanded regimen, starting the basic regimen immediately rather than delaying PEP administration is probably better. Therefore, if appropriate for the exposure, PEP should be started even when the interval since exposure exceeds 36 hours. Initiating therapy after a longer interval (e.g., 1 week) might be considered for exposures that represent an increased risk for transmission. Because 4 weeks of ZDV appeared protective in studies, PEP probably should be administered for 4 weeks, if tolerated.

Table2. Recommended HIV PEP for Percutaneous Injuries

	Infection Status of Source				
Exposure Type	**HIV-positive, Class 1[a]**	**HIV-positive, Class 2[a]**	**Source of Unknown HIV Status[b]**	**Unknown Source[c]**	**HIV-negative**
Less severe[d]	Recommend basic 2-drug PEP	Recommend expanded ≥3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP[e] for source with HIV risk factors[f]	Generally, no PEP warranted; however, consider basic 2-drug PEP[e] in settings in which exposure to HIV-infected persons is likely	No PEP warranted
More severe[g]	Recommend expanded 3-drug PEP	Recommend expanded ≥3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP[e] for source with HIV risk factors[f]	Generally, no PEP warranted; however, consider basic 2-drug PEP[e] in settings in which exposure to HIV-infected persons is likely	No PEP warranted

[a] HIV-positive, class 1--Asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2--Symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up for all exposures.

[b] For example, deceased source person with no samples available for HIV testing

[c] For example, a needle from a sharps disposal container

[d] For example, solid needle or superficial injury

[e] The recommendation "consider PEP" indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

[f] If PEP is offered and administered and the source is later determined to HIV-negative, PEP should be discontinued.

[g] For example, large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient's artery or vein

Table 3. Recommended HIV PEP for

Mucous Membrane Exposures and Nonintact Skin[a] Exposures

	Infection Status of Source				
Exposure Type	**HIV-positive, Class 1[b]**	**HIV-positive, Class 2[b]**	**Source of Unknown HIV Status[c]**	**Unknown Source[d]**	**HIV-negative**
Small volume[e]	Consider basic 2-drug PEP[f]	Recommend basic 2-drug PEP	Generally, no PEP warranted[g]	Generally, no PEP warranted	No PEP warranted
Large volume[h]	Recommend basic 2-drug PEP	Recommend expanded ≥3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP[f] for source with HIV risk factors[g]	Generally, no PEP warranted; however, consider basic 2-drug PEP[f] in settings in which exposure to HIV-infected persons is likely	No PEP warranted

[a] For skin exposures, follow-up is indicated only if evidence exists of compromised skin integrity (e.g., dermatitis, abrasion, or open wound).

[b] HIV-positive, class 1--Asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2--Symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up for all exposures.

[c] For example, deceased source person with no samples available for HIV testing

[d] For example, a splash from inappropriately disposed blood

[e] For example, a few drops

[f] The recommendation "consider PEP" indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

[g] If PEP is offered and administered and the source is later determined to HIV-negative, PEP should be discontinued.

[h] For example, a major blood splash

4.2.2.3 PEP for Pregnant HCW

If the exposed person is pregnant, the evaluation of risk of infection and need for PEP should be approached as with any other person who has had an HIV exposure. However, the decision to use any antiretroviral drug during pregnancy should involve discussion between the woman and relevant health care professionals regarding the potential benefits and risks to her and her fetus.

Certain drugs should be avoided in pregnant women. Because teratogenic effects were observed in primate studies, EFV is not recommended during pregnancy. Reports of fatal lactic acidosis in pregnant women treated with a combination of Stavudine (d4T) and ddI have prompted warnings about these drugs during pregnancy. Because of the risk of hyperbilirubinemia in newborns, IDV should not be administered to pregnant women shortly before delivery.

4.3 Follow-up of HCW Exposed to HIV

4.3.1 Postexposure Testing

HCW with occupational exposure to HIV should receive follow-up counseling, postexposure testing, and medical evaluation, regardless of whether they receive PEP. HIV-antibody testing should be performed for at least 6 months postexposure (e.g., at 6 weeks, 12 weeks, and 6 months). Extended HIV follow-up (e.g., for 12 months) is recommended for HCW who become infected with HCV following exposure to a source coinfected with HIV and HCV.

HIV testing should be performed on any exposed person who has an illness that is compatible with an acute retroviral syndrome, regardless of the interval since exposure. HIV-antibody testing with EIA should be used to monitor for seroconversion.

4.3.2 Monitoring and Management of PEP Toxicity

If PEP is used, HCW should be monitored for drug toxicity by testing at baseline and again 2 weeks after starting PEP. The scope of testing should be based on medical conditions in the exposed person and the toxicity of drugs included in the PEP regimen. Minimally, lab monitoring for toxicity should include a complete blood count and renal and hepatic function tests. Monitoring for evidence of hyperglycemia should be included for HCW whose regimens include any PI; if the exposed person is receiving IDV, monitoring for crystalluria, hematuria, hemolytic anemia, and hepatitis also should be included. If toxicity is noted, modification of the regimen should be considered after expert consultation; further diagnostic studies may be indicated.

Mild side effects such as headache, and nausea, are often experienced in the first few days after commencing PEP. Serious side effects usually occur after prolonged use and rarely occur within the first 4 weeks of therapy.

Exposed HCW who choose to take PEP should be advised of the importance of completing the prescribed regimen, potential drug interactions, the side effects of the drugs, measures to minimize these effects, and the methods of clinical monitoring for toxicity during the follow-up period. HCW should be advised that the evaluation of certain symptoms should not be delayed (e.g., rash, fever, back or abdominal pain, dysuria or haematuria, or symptoms of hyperglycemia [e.g.thirst,frequent urination]).

HCW who fail to complete the recommended regimen often do so because of the side effects they experience (e.g., nausea and diarrhea). These symptoms often can be managed with antimotility and antiemetic agents or other medications that target the specific symptoms without changing the regimen. In other situations, modifying the dose interval (i.e., administering a lower dose of drug more frequently throughout the day, as recommended by the manufacturer), might facilitate adherence to the regimen.

4.4 Counseling and Education

Although HIV infection following an occupational exposure occurs infrequently, the emotional effect of an exposure often is substantial HIV-exposed HCW should be advised to use the following measures to prevent secondary transmission during the follow-up period, especially the first 6-12 weeks after the exposure when most HIV-infected persons are expected to seroconvert:

- exercise sexual abstinence or use condoms to prevent sexual transmission;
- avoid pregnancy; and
- refrain from donating blood, plasma, organs, tissue, or semen.

Exposed HCW should be advised to seek medical evaluation for any acute illness that occurs during the follow-up period. Such an illness, particularly if characterized by fever, rash, myalgia, fatigue, malaise, or lymphadenopathy, might be indicative of acute HIV infection but also might be indicative of a drug reaction or another medical condition.

If an exposed woman is breast feeding, she should be counseled about the risk of HIV transmission through breast milk, and discontinuation of breast feeding should be considered, especially for high-risk exposures. Additionally, NRTIs are known to pass into breast milk, as is NVP.

The patient-care responsibilities of an exposed person do not need to be modified, based solely on an HIV exposure, to prevent transmission to patients. If HIV seroconversion is detected, the person should be evaluated as per the “Guidance and Recommendations on Health Care Workers Infected With HIV, Hepatitis B and C”.

Appendix 1

Appendix 2

FAQ's ON HEPATITIS B IMMUNISATION AND THE HEALTH CARE WORKER (HCW)

? **What category of HCW needs Hepatitis B vaccine?**

HCW who have a reasonable expectation of being exposed to blood on the job should be offered Hepatitis B vaccine.

? **What is the dosage and vaccination schedule for Hepatitis B vaccination?**

The adult dosage is 20 microgrammes given intramuscularly. Recommended schedules are at 0,1 and 6 months or at 0, 1 and 2 months (with a booster vaccination at 12 months for the latter), but if a rapid vaccination is required, it can be given at 0,7 and 21 days with a booster vaccination at 12 months [only for Engerix-B (adult)].

? **If the HCW missed the second dose of vaccine by a few weeks or months, should the HCW restart the series?**

No. The vaccine series should not be restarted when doses are delayed; rather, the series should be continued where it left off ie. the HCW must receive the second dose now and the third dose 5 months later.

? **Is it safe for pregnant HCWs to receive the vaccine?**

Yes. The vaccine does not contain any component shown to pose a risk to the fetus at any time during gestation. However, vaccination should only be offered if job modification still poses a significant risk of exposure or no suitable job reassignment is available. In all other cases, vaccination can be offered post delivery.

? **When does serologic testing post vaccination be done?**

Serologic testing should be done 1-2 months post completion of the final 3rd dose of the vaccine series. An anti-HBs serologic test result of more than or equal to 10 mIU/mL indicates immunity. No further routine doses or testing are required.

? **What should be done if the serological test (anti HBs) is negative 1-2 months after the last dose of vaccine ie. a non responder?**

The 3 dose series should be repeated and serologic testing done again 1-2 months after the last dose of vaccine. If the HCW is still negative or the anti HBs serologic result is less than 10 mIU/mL after the second vaccine series, the HCW is considered a non-responder to hepatitis B vaccination.

The HCW should be counseled that the HCW is susceptible to HBV infection and what steps should be taken in the future to protect the HCW health.

It is also possible that the non-responder is chronically infected with HBV and HBsAg and anti HBc testing may be done (if this was not done previously).

? **How often do HCWs who've received the vaccine should be tested serologically to make sure they are protected?**

Post vaccination testing should be done 1-2 months after completion of the series. If adequate anti HBs is present (more than or equal to 10 mIU/mL), nothing more needs to be done. Periodic testing or boosting is not needed.

If post vaccination test is less than 10 mIU/mL, a second series of vaccination should be given and post vaccination testing again done after 1-2 months of completion.

? **Should a HCW who once had a recorded positive anti HBs but had it rechecked and found it to be less than 10 mIU/mL be revaccinated?**

No. Post vaccination testing only needs to be done once ie. 1-2 months after completion of the series and the result recorded. Data showed that adequate response to the 3 dose series of hepatitis B vaccination provides long term immunologic memory that gives long term protection.

Only immunocompromised patients e.g. haemodialysis patients or HIV positive persons need to have anti-HBs testing and booster doses of vaccine to maintain their anti-HBs concentrations of at least 10mIU/mL to be protected. This should be done periodically at 6 to 12 monthly intervals.

? **A HCW claims to have received the complete 3 dose series of hepatitis B vaccination but there is no documentation to prove this.**

Serologic testing should be done and if there is inadequate concentration or negative anti HBs, a repeat second series of vaccination should be administered and post vaccination testing done.

? A HCW demonstrated a positive response after only one dose of vaccination. Should the second and third doses be not administered?

No. The three doses of the vaccination series must be administered. Although 30% of previously unvaccinated healthy individuals will have a protective antibody response after only one dose of vaccine, these individuals will not have the long term protection afforded by the three-dose series. There is evidence of seroconversion after the second dose; however, the completion of the third dose is necessary to increase percentage of responders.

? A HCW who had received the vaccine and had a positive titer a few years back but now the titer is negative. What should be done?

Nothing needs to be done. Vaccine induced anti HBs levels may decline over time; however, immune memory remains intact indefinitely following immunization.

? What are the common side effects and contraindications to the vaccination?

Side effects are commonly transient and minor, and include soreness at the injection site, low grade fever, nausea, dizziness, malaise, myalgia and arthralgia.

Contraindications to the vaccination include:

- Anaphylactic sensitivity to yeast or to any of the vaccine components
- Previous anaphylactic reaction to a hepatitis B vaccine

Appendix 3

TABLE 2. Primary side effects associated with antiretroviral agents

Antiretroviral class/agent	Primary side effects and toxicities
Nucleoside reverse transcriptase inhibitors (NRTIs)	
Zidovudine (Retrovir™; ZDV; AZT)	anemia, neutropenia, nausea, headache, insomnia, muscle pain, and weakness
Lamivudine (Epivir™; 3TC)	abdominal pain, nausea, diarrhea, rash, and pancreatitis
Stavudine (Zerit™; d4T)	peripheral neuropathy, headache, diarrhea, nausea, insomnia, anorexia, pancreatitis, increased liver function tests (LFTs), anemia, and neutropenia
Didanosine (Videx™; ddI)	pancreatitis, lactic acidosis, neuropathy, diarrhea, abdominal pain, and nausea
Abacavir (Ziagen™; ABC)	nausea, diarrhea, anorexia, abdominal pain, fatigue, headache, insomnia, and hypersensitivity reactions
Nonnucleoside reverse transcriptase inhibitors (NNRTIs)	
Nevirapine (Viramune™; NVP)	rash (including cases of Stevens-Johnson syndrome), fever, nausea, headache, hepatitis, and increased LFTs
Delavirdine (Rescriptor™; DLV)	rash (including cases of Stevens-Johnson syndrome), nausea, diarrhea, headache, fatigue, and increased LFTs
Efavirenz (Sustiva™; EFV)	rash (including cases of Stevens-Johnson syndrome), insomnia, somnolence, dizziness, trouble concentrating, and abnormal dreaming
Protease inhibitors (PIs)	
Indinavir (Crixivan™; IDV)	nausea, abdominal pain, nephrolithiasis, and indirect hyperbilirubinemia
Nelfinavir (Viracept™; NFV)	diarrhea, nausea, abdominal pain, weakness, and rash
Ritonavir (Norvir™; RTV)	weakness, diarrhea, nausea, circumoral paresthesia, taste alteration, and increased cholesterol and triglycerides
Saquinavir (Fortovase™; SQV)	diarrhea, abdominal pain, nausea, hyperglycemia, and increased LFTs
Amprenavir (Agenerase™; AMP)	nausea, diarrhea, rash, circumoral paresthesia, taste alteration, and depression
Lopinavir/Ritonavir (Kaletra™)	diarrhea, fatigue, headache, nausea, and increased cholesterol and triglycerides

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