PRE-EXPOSURE AND POST-EXPOSURE PROPHYLAXIS

Chapter 4

PROPHYLAXIS OF BACTERIAL INFECTIONS

PREVENTION OF NEONATAL GROUP B STREPTOCOCCAL DISEASE

Maternal colonisation is the single most important risk factor for early onset group B streptococcal (GBS) infection.

Prevention of early onset group B streptococcal infection in neonates requires:

- Routine maternal screening for colonisation between 35 and 37 weeks of gestation.

Intrapartum antibiotic prophylaxis according to the indications.

MATERNAL SCREENING FOR GROUP B STREPTOCOCCAL COLONISATION

- Both anorectal and vaginal cultures are collected because the rectum is the natural reservoir for GBS. The yield of vaginal cultures for GBS is only 60% of the yield of vaginal and rectal cultures combined.
- Use of a speculum is not required. Sample the lower vagina. Sampling the cervix or vaginal fornices results in a significantly lower yield and is not recommended.
- Cost-effective swabbing with a single-swab method is recommended. The lower one third of the vagina is swabbed circumferentially with a cotton swab that is then inserted through the anal sphincter 2 cm into the rectum and rotated 360 degrees. The swab is then placed directly into transport media and sent for culture. If preferred, a two-swab technique can be used.
- The sensitivity of combined rectal and vaginal cultures at 36 weeks of gestation is about 90%. In contrast, the sensitivity of cultures taken six or more weeks before delivery for predicting colonisation status at delivery is only about 40%. Therefore, cultures obtained more than five weeks before delivery may not accurately predict colonisation at delivery.

INDICATIONS FOR INTRAPARTUM ANTIBIOTIC PROPHYLAXIS

- Positive maternal GBS screening cultures at 35–37 weeks of gestation
- Maternal antenatal GBS bacteriuria in any concentration in the current pregnancy
- Previous delivery of an infant with GBS disease
- Rupture of membranes for $>$ 12 hours
- Delivery at $<$ 37 weeks gestation
- Intrapartum temperature $\geq$ 38°C
- Intra-amniotic infection

INTRAPARTUM ANTIBIOTIC PROPHYLAXIS IS NOT INDICATED IF:

- An elective caesarean section is planned
- A caesarean section is performed before onset of labour with intact membranes
- Vaginal and rectal cultures at 35–37 weeks of gestation are negative

PROPHYLACTIC ANTIBIOTIC REGIMENS

Intrapartum antibiotic prophylaxis is most effective if administered at least four hours before delivery. Since the time of delivery cannot be predicted, prophylaxis should begin at hospital admission and continued until delivery.

Rx	PREFERRED ANTIBIOTIC REGIMEN	ALTERNATIVE ANTIBIOTIC REGIMEN	REGIMEN IF PENICILLIN ALLERGIC
	Penicillin G 5 million units IV (loading dose) followed by 2.5 million units every four hours until delivery	Ampicillin 2 g IV (loading dose) followed by 1 g 4 hourly until delivery	Low risk of anaphylaxis: Cefazolin 2 g IV loading dose then 1 g 8 hourly until delivery High risk of anaphylaxis: If susceptible, give clindamycin 900 mg IV 8 hourly until delivery. If resistant to clindamycin, then give vancomycin 1 g IV 12 hourly until delivery

NEWBORN ANTIBIOTIC REGIMENS

- Empiric, universal antibiotic administration to neonates, regardless of maternal colonisation status, is not recommended.
- Selective neonatal prophylaxis is recommended when maternal GBS carriage has been documented but less than four hours of antibiotic prophylaxis has been given before delivery, chorio-amnionitis is suspected, or signs of neonatal sepsis are present.
- Neonates who appear to be septic, and those who are born to mothers with chorio-amnionitis, should have a septic work-up performed, including blood cultures and a lumbar puncture before administration of empiric antibiotics.

PROPHYLAXIS FOLLOWING EXPOSURE TO MENINGOCOCCAL, HAEMOPHILUS INFLUENZAE TYPE B AND BORDETELLA PERTUSSIS INFECTION

Post-exposure antibiotic prophylaxis (PEP) is recommended for contacts of patients with invasive meningococcal (*Neisseria meningitidis*), *H. influenzae* type b illness including meningitis, and *Bordetella pertussis* infection.

PROPHYLAXIS FOLLOWING EXPOSURE TO INVASIVE MENINGOCOCCAL INFECTION

Antibiotic prophylaxis should be used to prevent the transmission of *Neisseria meningitidis* from infected individuals to close contacts. The risk of contracting secondary disease is greatest immediately after the onset of symptoms in the index case; therefore chemoprophylaxis should ideally be given within 24 hours of identifying the index case. It is of no value if administered after 10 days of identification of the index case. The index case also requires antibiotic treatment, prior to discharge from hospital to eradicate nasopharyngeal carriage (unless treated with ceftriaxone or cefotaxime).

Meningococcal antibiotic prophylaxis is recommended only for close or primary contacts, namely:

- Individuals who have had prolonged close contact (more than eight hours) with the index case. These include household members, roommates, young adults in dormitories, children at a crèche.
- Individuals who have been directly exposed to the patient's oral secretions from one week before the onset of the patient's symptoms up until 24 hours after initiation of antibiotics in the patient. These include those involved in mouth-to-mouth resuscitation, endotracheal intubation, endotracheal tube management, nasopharyngeal suctioning or intimate kissing.

Prophylaxis is not recommended if exposure to the index patient is brief – this includes virtually all healthcare workers unless there is direct exposure to respiratory secretions (e.g. suctioning or intubation).

Rx	NEISSERIA MENINGITIDIS PROPHYLAXIS: ADULTS
	Ciprofloxacin 500 mg PO as a single dose OR Ceftriaxone 250 mg IM as a single dose (drug of choice in pregnancy) OR Rifampicin 600 mg PO 12 hourly for two days (4 doses)
	NEISSERIA MENINGITIDIS PROPHYLAXIS: CHILDREN
	Ceftriaxone 125 mg IM as a single dose (age < 12 years), OR Rifampicin Age < 1 month: 5 mg/kg PO 12 hourly for 2 days (4 doses) Age > 1 month: 10 mg/kg PO 12 hourly for 2 days (4 doses)

PROPHYLAXIS FOLLOWING EXPOSURE TO INVASIVE HAEMOPHILUS INFLUENZAE TYPE B INFECTION

Secondary cases of *Haemophilus influenzae* type b (Hib) may occur following contact with a patient with invasive Hib disease, including meningitis. A secondary case is defined as an illness occurring within 60 days of contact with an index case.

Rifampicin is recommended for chemoprophylaxis because it achieves high concentrations in respiratory secretions and eradicates nasopharyngeal carriage in more than 95% of carriers. Post-exposure prophylaxis is indicated for all household or day-care contacts who are younger than 10 years of age, pregnant and breastfeeding women, immunocompromised and asplenic persons. Hib vaccine must also be given to children if not already vaccinated and other vaccinations should be updated as needed.

Rx	HAEMOPHILUS INFLUENZAE TYPE B PROPHYLAXIS: ADULTS
	Rifampicin 600 mg PO daily for 4 days
	HAEMOPHILUS INFLUENZAE TYPE B PROPHYLAXIS: CHILDREN
	Age > 3 months: Rifampicin 20 mg/kg PO (not to exceed 600 mg) once daily for 4 days Age < 3 months: Rifampicin 10 mg/kg PO once daily for 4 days

NOTE

If any antibiotic other than ceftriaxone or cefotaxime was used to treat the index case, rifampicin must be prescribed as well to eradicate nasopharyngeal carriage.

PROPHYLAXIS FOLLOWING EXPOSURE TO BORDETELLA PERTUSSIS

Post-exposure prophylaxis for contacts of a pertussis case is indicated for the following contacts (if within 21 days of cough onset in the index case):

- All household or institutional contacts of a pertussis case, regardless of their age or vaccination status.
- All persons exposed to pertussis that are at high risk of severe illness, or persons at risk of transmitting the infection to another vulnerable person at risk of severe infection, should receive post-exposure prophylaxis. These include:
  - Neonates born to symptomatic mothers
  - Infants less than one year of age
  - Women in their third trimester of pregnancy (to protect their newborn baby)
  - All persons with pre-existing health conditions such as cardiac or pulmonary disease that may be exacerbated by a pertussis infection
  - Immunocompromised persons
  - Contacts that will have close contact with infants under 12 months, pregnant women or persons with chronic health conditions
  - Contacts in high-risk settings that include infants aged < 12 months or women in the third trimester of pregnancy e.g. childcare settings, maternity wards, neonatal ICUs

BORDETELLA PERTUSSIS PROPHYLAXIS

The following are options – choice is based on availability, age of the patient and any contraindications

AZITHROMYCIN

- Age < 6 months: 10 mg/kg PO once daily for 5 days
- Age ≥ 6 months and children: 10 mg/kg PO on day 1 then 5 mg/kg PO once daily (maximum 500 mg) on days 2–5
- Adults: 500 mg PO on day 1 then 250 mg PO once daily on days 2–5

CLARITHROMYCIN

Age < 1 month: Not recommended

Age 1–5 months: 15 mg/kg PO per day in two divided doses for 7 days

Age ≥ 6 months and children: 15 mg/kg PO per day in two divided doses for 7 days

Adults: 500 mg PO 12 hourly for 7 days

ERYTHROMYCIN

Age < 1 month: Not recommended

Age 1–5 months: 40 mg/kg PO per day in 4 divided doses for 14 days

Age ≥ 6 months: 40 mg/kg PO per day in 4 divided doses for 14 days

Adults: 500 mg PO 6 hourly for 14 days

COTRIMOXAZOLE

Age < 2 months: Contraindicated

Age ≥ 2–5 months: TMP/SMX (8/40 mg/kg/day) PO in 2 divided doses for 7 days

Age ≥ 6 months and children: TMP/SMX (8/40 mg/kg/day) PO in 2 divided doses for 7 days

Adults: TMP/SMX (320/1600 mg/day) PO in 2 divided doses for 7 days

PROPHYLAXIS AFTER RAPE OR HIGH-RISK SEXUAL EXPOSURE

- Obtain expert advice regarding forensic examination and specimens, pregnancy, physical trauma and counselling.
- Collect specimens from the site of contact (vagina, rectum, pharynx) for detection of STDs (PCR, microscopy and culture).
- Collect blood for baseline syphilis, hepatitis B, hepatitis C, HIV serology and a pregnancy test.
- Drug testing if the victim has amnesia for any time surrounding the event – submit urine for a benzodiazepine screen and EDTA blood for flunitrazepam (Rohypnol® – the 'date rape drug'). Ideally samples should be submitted to a forensic laboratory – it is important to maintain a chain of custody.
- Provide post-exposure prophylaxis for HIV, hepatitis B and other sexually transmitted infections.
- Provide emergency post-coital contraception.

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POST-EXPOSURE PROPHYLAXIS FOR GONORRHOEA, CHLAMYDIA AND INCUBATING SYPHILIS

Ceftriaxone 250 mg IM as a single dose

AND

Metronidazole 2 g PO as a single dose

AND

Azithromycin 1 g PO as a single dose OR doxycycline 100 mg PO 12 hourly for 7 days

POST-EXPOSURE PROPHYLAXIS FOR HIV

Refer to the section on HIV post-exposure prophylaxis in this chapter

POST-EXPOSURE PROPHYLAXIS FOR HEPATITIS B

Refer to the section on HBV post-exposure prophylaxis in this chapter

POST-COITAL CONTRACEPTION

Post-coital emergency contraception: mifepristone 600 mg PO as a single dose OR levonorgesterel 1.5 mg PO as a single dose (Norlevo® or Escapelle®)

FOLLOW-UP TESTS

- Perform a follow up clinical examination for STDs after 2 weeks. Test by means of a multiplex STD PCR if symptomatic
- Perform follow up serology for syphilis and HIV at 6 weeks and 3 months post-exposure
- If HBV post-exposure prophylaxis was given then test for HBsAg and anti-HBs 4–8 weeks after the last dose of HBV vaccine

PROPHYLAXIS OF VIRAL INFECTIONS

PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION

The RSV season in South Africa is usually from February to June (KZN from December). Palivizumab (Synagis®) is a humanised RSV monoclonal antibody which is used to protect children at risk of severe RSV infection. The dose of palivizumab is 15 mg/kg given monthly by means of an intramuscular injection for five months usually starting January, with the last dose in May. High-risk premature infants should start prophylaxis while still in hospital.

INDICATIONS FOR PALIVIZUMAB

- Premature infants born < 36 weeks gestation and < 6 months of age at the start of the RSV season. Prophylaxis is continued until the end of the RSV season (last dose in May).
- Children of any gestation and < 24 months of age with:
  - Chronic lung disease of prematurity
  - Chronic lung disease
  - Primary immunodeficiency
  - Haemodynamically significant congenital heart disease
  - Premature neonates with ongoing respiratory or cardiac compromise (diuretic, oxygen or corticosteroid dependent

PROPHYLAXIS MAY BE CONSIDERED FOR CHILDREN:

- Who are profoundly immunocompromised
- With pulmonary neuromuscular disease

THE VALUE OF PALIVIZUMAB PROPHYLAXIS IS UNCLEAR IN CHILDREN WITH:

- Down's syndrome
- Cystic fibrosis
- Recurrent wheezing
- Nosocomial outbreaks of RSV infection

HIV PRE-EXPOSURE PROPHYLAXIS (PREP)

PrEP is defined by the World Health Organisation as the use of antiretroviral drugs by HIV-uninfected people, before potential exposure, to prevent HIV infection. In South Africa, Truvada® [tenofovir (TDF)/emtricitabine (FTC)] has been approved for PrEP use by the Medicine Control Council. Studies have indicated that with high levels of adherence, PrEP is highly effective in preventing HIV transmission.

RISK FACTORS FOR HIV INFECTION INCLUDE

- Having an HIV-infected partner who is not virologically suppressed
- Having a sexual partner with an unknown HIV status
- Serodiscordant couples trying to conceive
- Having multiple sexual partners
- Being a commercial sex worker
- Having a history of inconsistent condom use
- Recurrent post-exposure prophylaxis users
- Recent sexually transmitted infections
- Having a history of sex whilst under the influence of alcohol or drugs

PREP SHOULD BE CONSIDERED FOR HIV-UNINFECTED PERSONS WITH A SIGNIFICANT RISK OF ACQUIRING HIV INFECTION (AS ABOVE), IN PARTICULAR:

- Any sexually active HIV-uninfected persons who requests PrEP, especially if risk factors are present
- IV drug users
- Adolescents and sex workers especially young MSM (men who have sex with men) and adolescent girls

ELIGIBILITY FOR HIV PREP USE

HIV-uninfected persons that are willing and able to adhere to PrEP in the absence of any contraindications to PrEP use.

CONTRAINDICATIONS FOR PREP USE

- Pre-existing HIV infection or evidence of possible acute HIV infection
- Creatinine clearance of less than 60 mL/min
- Adolescents < 35 kg or < 15 years of age who are not Tanner stage three (sexual maturity rating) or greater
- Unwilling/unable to adhere to daily PrEP
- Unwilling/unable to return for three monthly follow up visits

PREGNANCY AND BREASTFEEDING

The risk of HIV infection is increased during pregnancy, as well as the risk of HIV transmission to an infant born to a mother who becomes infected during pregnancy or breastfeeding. Therefore, an HIV-uninfected woman, who has risk factors for HIV infection as listed above, may benefit from PrEP use throughout her pregnancy and breastfeeding to protect herself and her infant.

In PrEP clinical trials women were taken off medication as soon as pregnancy was detected. During these trials, no adverse effects were associated with PrEP use by women in early pregnancy or for their infants. In addition, no adverse effects have been found among infants exposed to TDF/FTC when taken as part of an antiretroviral therapy regimen by HIV-infected women during pregnancy or breastfeeding. These drugs are generally regarded as safe and well tolerated for both mothers and foetuses, however, there are ongoing clinical trials that aim to shed further light on the safety of PrEP during pregnancy.

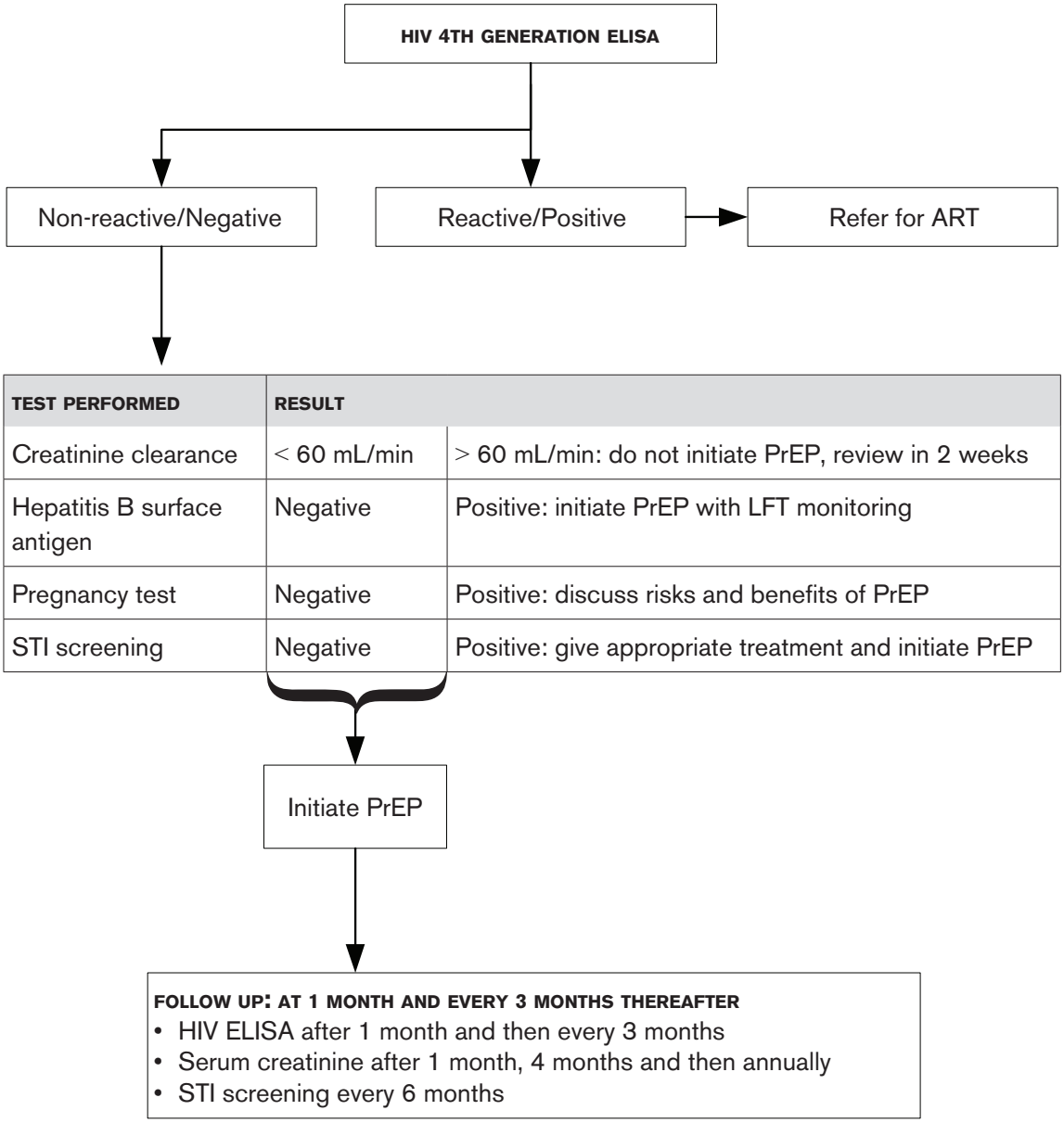
BASELINE LABORATORY TESTING PRIOR TO GIVING PREP

- 4th generation HIV ELISA
- Hepatitis B screening: HBsAg and HBsAb
  - If HBsAg is positive, PrEP can still be given but adequate monitoring of liver function must be performed. Both TDF and FTC have hepatitis B antiviral activity
  - If both HBsAg and HBsAb is negative, the patient must be vaccinated against hepatitis B
- Serum creatinine
  - If the creatinine clearance < 60 mL/min then do not give PrEP and re-evaluate in two weeks
- Pregnancy test
  - Discuss the risks and benefits of PrEP use if the patient is pregnant
- STI screen
  - Syphilis serology
  - STI PCR panel on first void urine or swab specimen if resources allow

FOLLOW-UP TESTING

- HIV ELISA at one month and every three months thereafter
- Serum creatinine at one month, four months and annually thereafter
- STI testing every six months

HIV PREP FLOW DIAGRAM



TEST PERFORMED	RESULT	
Creatinine clearance	< 60 mL/min	> 60 mL/min: do not initiate PrEP, review in 2 weeks
Hepatitis B surface antigen	Negative	Positive: initiate PrEP with LFT monitoring
Pregnancy test	Negative	Positive: discuss risks and benefits of PrEP
STI screening	Negative	Positive: give appropriate treatment and initiate PrEP

Initiate PrEP

FOLLOW UP: AT 1 MONTH AND EVERY 3 MONTHS THEREAFTER

- HIV ELISA after 1 month and then every 3 months
- Serum creatinine after 1 month, 4 months and then annually
- STI screening every 6 months

PRESCRIPTION INTERVALS

- At initiation: provide only one month's supply
- At one month: repeat HIV ELISA and serum creatinine. Provide three months' supply
- Every three months: repeat HIV ELISA and provide three months' supply

HIV PRE-EXPOSURE PROPHYLAXIS

Truvada® (300 mg tenofovir/200 mg emtricitabine) 1 tablet PO once daily

PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV

All patients, including pregnant women, diagnosed with HIV infection should be advised that lifelong antiretroviral therapy (ART) is indicated regardless of their clinical stage or CD4 count (TEMPRANO and START clinical trials). Thus all pregnant women must be given ART for both their own health and to prevent HIV transmission to their infant. The aim is to ensure that pregnant women have an undetectable HIV viral load during their pregnancy and in particular during labour and delivery. Refer to the section on pregnant women in the chapter 'Management of HIV infection in adults' for details on treatment and monitoring during pregnancy.

In addition, antiretroviral post-exposure prophylaxis must be given at birth to all HIV-exposed infants to prevent mother-to-child transmission (PMTCT) regardless of whether maternal ART was given or not as detailed below.

BASIC PRINCIPLES OF INFANT POST-EXPOSURE PROPHYLAXIS

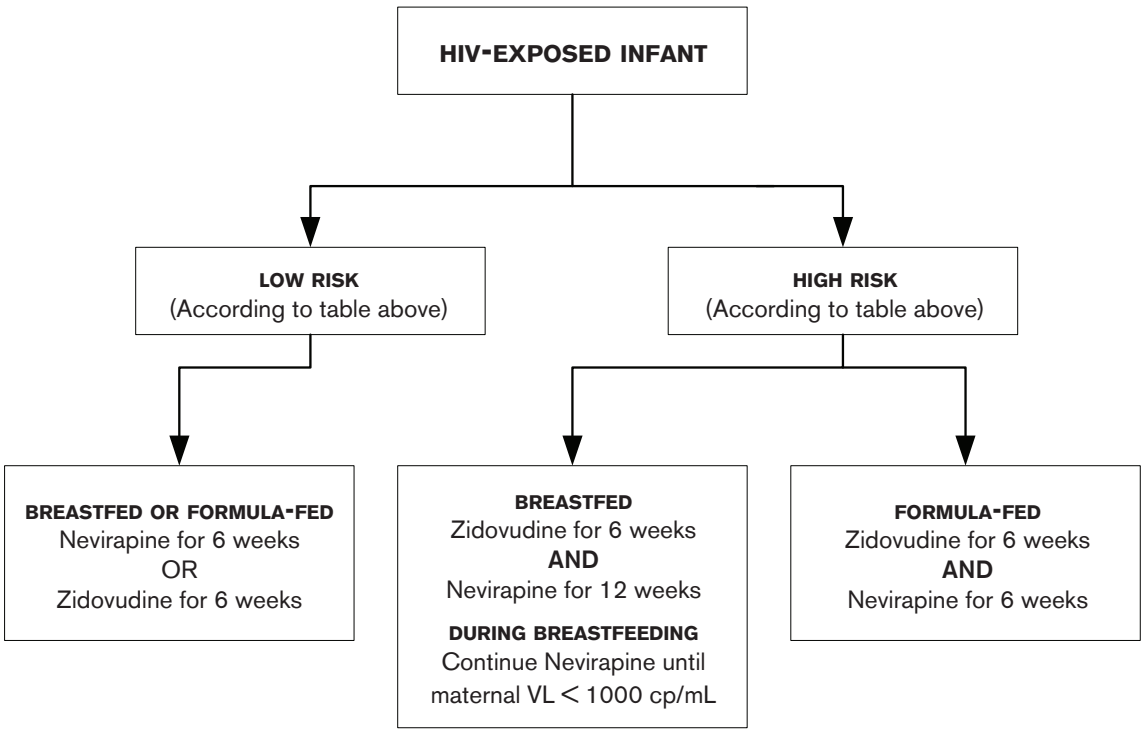
- The first dose of antiretroviral medication to the newborn must be given as soon as possible after birth (preferably within one hour).
- We recommend the following as per international guidelines:
  - Infants born to an HIV-infected mother with a detectable HIV viral load at 36 weeks gestation: triple post-exposure prophylaxis, and no breastfeeding.
  - Infants born to an HIV-infected mother with an undetectable HIV viral load at 36 weeks gestation: nevirapine OR zidovudine for six weeks, and no breastfeeding.
- Neonates who are nil per mouth (NPO) should receive intravenous zidovudine until oral medication can be given.
- Zidovudine prophylaxis:
  - A four-week zidovudine prophylaxis regimen can be given for full-term infants if the mother has received standard ART throughout pregnancy with a sustained undetectable HIV viral load and there are no concerns related to maternal adherence.
  - In all other cases, the infant should receive a six week course of zidovudine as part of a combination infant prophylaxis regimen.

INFANT ANTIRETROVIRAL POST-EXPOSURE PROPHYLAXIS: PUBLIC HEALTH APPROACH (DOH GUIDELINE/WESTERN CAPE GUIDELINES)

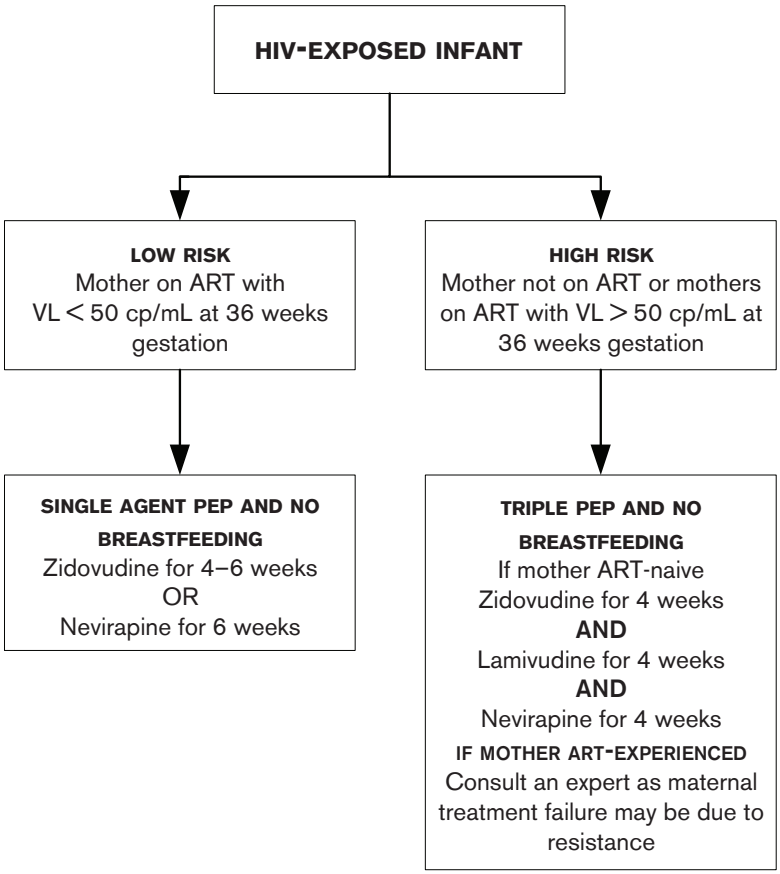
The PMTCT regimen that is given depends on the risk of HIV transmission from mother to infant.

RISK FOR HIV TRANSMISSION	RECOMMENDED PMTCT
LOW RISK	
Mother on ART with documented VL < 1000 c/mL less than 12 weeks before delivery	Nevirapine daily for 6 weeks (regardless of feeding choice) OR Zidovudine twice daily for 6 weeks* *Infants who do not tolerate NVP or develop NVP toxicity

HIGH RISK	
MATERNAL RISK FACTORS Mother's most recent HIV VL ≥ 1000 c/mL e.g. • Mother recently started on ART • Mother newly diagnosed • Treatment failure Increased risk of HIV transmission during delivery irrespective of maternal VL: • Clinical chorioamnionitis • Spontaneous preterm labour at < 37 weeks gestation • Prolonged rupture of membranes > 18 hours **INFANT RISK FACTORS** • Abandoned newborns and orphans with HIV exposure confirmed by HIV ELISA testing • Born before 37 weeks gestational age • Birth weight < 2500 g regardless of gestation • Any sick HIV-exposed newborn	If breastfeeding: Zidovudine twice daily for 6 weeks **AND** Nevirapine daily for at least 12 weeks** **Only stop NVP once maternal VL < 1000 copies/mL If formula feeding: Zidovudine twice daily for 6 weeks **AND** Nevirapine daily for 6 weeks



INFANT ANTIRETROVIRAL POST-EXPOSURE PROPHYLAXIS: INTERNATIONAL GUIDELINES



ZIDOVUDINE (ORAL) FOR PEP IN HIV-EXPOSED INFANTS: BIRTH TO 6 WEEKS

GESTATIONAL AGE/BIRTH WEIGHT	AGE	DAILY DOSE
< 35 weeks	Birth to 6 weeks	2 mg/kg/dose 12 hourly
< 2 kg and > 35 weeks	Birth to 6 weeks	4 mg/kg/dose 12 hourly
> 2 kg and > 35 weeks	Birth to 6 weeks	12 mg 12 hourly

NEVIRAPINE (ORAL) FOR PEP IN HIV-EXPOSED INFANTS: BIRTH TO > 9 MONTHS OF AGE

AGE	WEIGHT	AGE/DAILY DOSE
Birth – 6 weeks	< 2.0 kg	Birth to 2 weeks: 2 mg/kg 2–6 weeks: 4 mg/kg
	2.0–2.5 kg	Birth to 6 weeks: 10 mg
	> 2.5 kg	Birth to 6 weeks: 15 mg
	Any weight	6–12 weeks: 20 mg
6 weeks – 6 months	All	20 mg/day

6 month – 9 months	All	30 mg/day
> 9 months	All	40 mg/day

LAMIVUDINE (3TC) FOR PEP IN HIV-EXPOSED INFANTS

AGE	GESTATION	DOSE
Birth to 4 weeks	≥ 32 weeks	2 mg/kg PO twice daily
4–6 weeks	≥ 32 weeks	4 mg/kg PO twice daily

ZIDOVUDINE (IV) FOR PEP IN HIV-EXPOSED INFANTS

≥ 35 weeks gestation	1.5 mg/kg/dose 6 hourly
< 35 weeks gestation	1.5 mg/kg/dose 12 hourly

Once full enteral feeds are tolerated, resume oral NVP; at discharge, provide NVP.

HIV POST-EXPOSURE PROPHYLAXIS: OCCUPATIONAL AND NON-CCUPATIONAL EXPOSURE IN ADULTS

INTRODUCTION

The approach to occupational, sexual and other forms of HIV-exposure (bites, assault, trauma, injecting drug use, etc.) is similar. HIV post-exposure prophylaxis (PEP) is highly effective if taken early and for the full duration prescribed as suggested by animal data, case control studies and PMTCT data. There have been few documented PEP failures, mainly associated with poor adherence, suboptimal dosing or delayed administration.

APPROXIMATE RISK OF HIV-ACQUISITION PER EXPOSURE EVENT (HIV-INFECTED SOURCE)

OCCUPATIONAL	NON-OCCUPATIONAL
Sharps injury – 0.3% Mucosal splash injury – 0.09% Non-intact skin exposure < 0.09% The risk increases when a sharps injury is deep, involves a hollow needle used in a vein or artery or when the source patient is more infectious (terminal HIV infection, seroconversion illness or known to have a high HIV viral load).	Needle sharing – 0.5% Unprotected receptive anal intercourse – 1.1%* Insertive vaginal or anal intercourse – 0.1%*

*Overt or occult traumatic lesions may increase the risk in survivors of sexual assault.

BASIC PRINCIPLES OF HIV POST-EXPOSURE PROPHYLAXIS

- All forms of exposure to HIV-infected or sources with unknown status require the use of three antiretroviral (ARV) medications for post-exposure prophylaxis:
  - Triple ARV regimens in treatment settings have been proven superior to mono or dual therapy regimens
  - If triple ARV regimens cannot be tolerated a two and even one drug regimen can be considered
- HIV PEP is given for a period of 28 days. Less than two weeks is associated with minimal efficacy and more than 28 days confers no added benefit.

- HIV PEP should be started as soon as possible, ideally within 24 hours of the exposure event. It must not be withheld pending testing of the source patient.
- HIV PEP is usually not given if more than 72 hours have lapsed after the exposure. However, PEP can be considered up to one week post a high-risk exposure. Beyond seven days post-exposure, prophylaxis is not given.
- HIV PEP should not be given to persons who are already HIV-infected. These patients should be referred for antiretroviral therapy (ART).
- HIV PEP is not routinely recommended after sexual exposure with an HIV-infected source on ART with a confirmed and sustained (> six months) undetectable HIV viral load. However, if there are any doubts about the HIV viral load history or the source's adherence to ART then PEP should be given.
- Other blood-borne viruses e.g. hepatitis B and hepatitis C also requires investigation and management to prevent infection from infected sources.

POTENTIALLY INFECTIOUS BODY FLUIDS

Blood, tissue, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid, penile pre-ejaculate and semen, vaginal secretions, breast milk.

NON-INFECTIOUS BODY FLUIDS

Stool, nasal secretions, saliva, sweat, tears, urine and vomit unless visibly contaminated with blood.

EXPOSURE WITH POTENTIALLY INFECTIOUS BODY FLUIDS VIA THE FOLLOWING ROUTES REQUIRES PEP

- Percutaneous injury, e.g. needlestick or cut with a sharp object e.g. scalpel blade, lancet, aspiration needle on laboratory equipment, suture needle, broken glass
- Contact with a mucous membrane, e.g. eyes, mouth or nose
- Contact with non-intact skin, e.g. exposed skin that is chapped, abraded, or afflicted with dermatitis (eczema)
- Unprotected sexual activity including, but not limited to, penetrative intercourse and survivors of sexual assault
- Human bites and punching that resulted in opening of the skin

THE FOLLOWING EXPOSURES DO NOT REQUIRE HIV PEP

- The exposed individual is already HIV-infected
- The source is confirmed HIV-negative by a laboratory ELISA test and a window period infection has been excluded.
- An exposure to non-infectious body fluids

IMMEDIATE ACTION AFTER EXPOSURE

NEEDLESTICK INJURY OR CUTS

- Encourage bleeding and gently wash the area with soap and water for at least 30 seconds
- Do not scrub the wound whilst washing
- Do not suck the wound
- Cover with a plaster or dressing if needed

MUCOUS MEMBRANES: NOSE, MOUTH AND EYES

Flush with water or sterile saline solution for at least 30 seconds

LABORATORY TESTING

SOURCE PATIENT	INJURED/EXPOSED PATIENT
HIV 4th generation ELISA (antibody and p24 antigen)	HIV 4th generation ELISA (antibody & p24 antigen)
Hepatitis B surface antigen (HBsAg)	Hepatitis B surface antibody (HBsAb)
Hepatitis C ELISA, and if positive request HCV PCR	Hepatitis C ELISA if source patient is HCV-infected (PCR positive)

HIV POST-EXPOSURE DRUG REGIMENS

Three antiretroviral drugs must be given consisting of two NRTIs and either an integrase inhibitor or protease inhibitor as a third drug

NRTI OPTIONS	THIRD DRUG OPTIONS
PREFERRED Tenofovir (TDF) **AND** Lamivudine (3TC) or emtricitabine (FTC) **ALTERNATIVE** Zidovudine (AZT) **AND** Lamivudine (3TC) or emtricitabine (FTC)	**PREFERRED** **Integrase inhibitors** Raltegravir (RAL) OR Dolutegravir (DTG) **ALTERNATIVE** **Protease inhibitors** Lopinavir/ritonavir (LPV/r) OR Atazanavir /ritonavir (ATV/r) OR Darunavir/ritonavir (DRV/r)

AVOID

- Efavirenz or efavirenz containing combinations (e.g. Atripla®) due to high risk of central nervous system side effects
- Nevirapine: should never be used for PEP due to potential severe side effects, e.g. hepatotoxicity and Stevens-Johnson syndrome

HIV POST-EXPOSURE REGIMENS

FIRST-LINE ARV PEP REGIMEN

Truvada® (tenofovir 300 mg/emtricitabine 200 mg) 1 tablet PO given once daily

AND

Isentress® (raltegravir 400 mg) 1 tablet PO 12 hourly

SECOND-LINE ARV PEP REGIMEN

Combivir® (zidovudine 300 mg/lamivudine 150 mg) 1 tablet PO 12 hourly

AND

Aluvia® (lopinavir/ritonavir 400/100 mg) 2 tablets PO 12 hourly

- If tenofovir/emtricitabine cannot be given, substitute with zidovudine/lamivudine
- If raltegravir cannot be given, substitute with lopinavir/ritonavir

SUMMARY OF ARV DRUGS USED FOR PEP

- Tenofovir (TDF) 300 mg PO once daily
- Lamivudine (3TC) 150 mg PO 12 hourly or 300 mg PO once daily
- Emtricitabine (FTC) 200 mg PO once daily
- Lopinavir/ritonavir (LPV/r) 400 mg/100 mg PO 12 hourly or 800 mg/200 mg once daily
- Atazanavir/ritonavir (ATV/r) 300 mg/100 mg PO once daily
- Raltegravir (RAL) 400 mg PO 12 hourly
- Dolutegravir (DTG) 50 mg PO once daily
- Darunavir AND ritonavir (DRV/r) 800 mg AND 100 mg PO once daily or 600 mg AND 100 mg PO 12 hourly

LABORATORY INVESTIGATIONS AND POSSIBLE ARV SIDE EFFECTS

ANTIRETROVIRAL	RECOMMENDED LABORATORY TESTS	SIDE EFFECTS/COMPLICATIONS
Tenofovir	Serum creatinine at baseline	Contraindicated in kidney disease
Zidovudine	Full blood count at baseline, 2 weeks and 4 weeks	Anaemia Neutropenia
Lamivudine	None	Well tolerated
Emtricitabine	None	Well tolerated
Raltegravir	None	Well tolerated
Lopinavir/ritonavir	None	GIT upset, potential for drug interactions
Atazanavir /ritonavir	None	Unconjugated hyperbilirubinaema
Darunavir/ritonavir	None	GIT upset, contains a sulph-onamide moiety (use with caution in patients with sulpha allergy)

PREGNANCY AND BREASTFEEDING

PEP is indicated at any time during pregnancy when a significant exposure has occurred, despite possible risk to the woman and the foetus. The recommended PEP regimen is the same for pregnant women as for non-pregnant adults. Pregnant women presenting for PEP as a result of risky sexual behaviour should be considered for PrEP after completion of the 28 day PEP regimen. Breastfeeding should be avoided until the three month post-exposure follow-up HIV ELISA test is negative.

FOLLOW-UP TESTING

- Repeat HIV ELISA testing should be done at six weeks and three months post-exposure for the healthcare worker/exposed patient, if the source patient is HIV-infected. A negative HIV ELISA test at six weeks following exposure, in the absence of re-exposure, rules out the possibility of HIV infection in the majority of cases. Three month follow-up HIV ELISA testing is performed to detect the very unusual occurrence of delayed seroconversion should HIV infection have occurred following exposure.
- HIV PCR or viral load testing is not recommended following exposure to determine possible early HIV infection. This is because the time points following exposure when HIV PCR and viral loads become positive, should infection occur, are not known. In addition, PEP can delay infection post-exposure, and a negative PCR or viral load performed early after exposure does not exclude the possibility of HIV infection.
- If HIV seroconversion is detected in an exposed patient then they must be referred for ART.

HIV POST-EXPOSURE PROPHYLAXIS FOR CHILDREN

The principles of HIV PEP in children are the same as in adults. However, the lack of availability of age-appropriate antiretroviral formulations for children limits regimen choice and the alignment of post-exposure prophylaxis regimens with those of adults.

CHILDREN AND ADOLESCENTS ARE POTENTIALLY AT RISK OF ACQUIRING HIV FROM A VARIETY OF EXPOSURES:

- Needlestick injury
- Sexual abuse
- Sexual activity in adolescence
- Pre-mastication of food
- Breast milk e.g. wet nurses
- Biting: if there is blood in the mouth of the biting individual (e.g. bleeding gums), or if the skin of the bitten child is breached

HIV POST-EXPOSURE REGIMENS

CHILDREN 4 WEEKS TO < 2 YEARS OF AGE

Preferred: Combivir® (zidovudine /lamivudine) AND Aluvia® (lopinavir/ritonavir 400/100 mg)

CHILDREN 2–5 YEARS OF AGE

Preferred: Combivir® (zidovudine /lamivudine) AND Aluvia® (lopinavir/ritonavir 400/100 mg)

Alternative: Combivir® (zidovudine /lamivudine) AND Isentress® (raltegravir)

CHILDREN 6–10 YEARS OF AGE

Preferred: Combivir® (zidovudine /lamivudine) AND Isentress® (raltegravir)

Alternative: Combivir® (zidovudine /lamivudine) AND Aluvia® (lopinavir/ritonavir 400/100 mg)

CHILDREN > 10 YEARS OF AGE AND OVER 35 KG (ABLE TO SWALLOW TABLETS)

Preferred: Truvada® (tenofovir/emtricitabine) AND Isentress® (raltegravir)

Alternative: Combivir® (zidovudine/lamivudine) AND Aluvia® (lopinavir/ritonavir)

ANTIRETROVIRAL DRUGS

NAME	FORMULATIONS	DOSAGE IN CHILDREN	NOTES
Raltegravir (Isentress®)	**Tablets** 400 mg **Chewable tablets** 25 mg 100 mg	**Tablets** > 25 kg: 400 mg BD **Chewable tablets ± 6mg/kg/dose** 7–9 kg: 50 mg BD 10–13 kg: 75 mg BD 14–19 kg: 100 mg BD 20–27 kg: 150 mg BD 28–39 kg: 200 mg BD > 40 kg: 300 mg BD	Can be given to children older than 2 years of age Note: chewable tablet formulation is not bioequivalent to tablet formulation hence different dosing
Tenofovir (TDF)	**Tablets (unscored)** 300 mg		In South Africa, tenofovir is approved for use in children older than 12 years of age. In the US, where reduced tablet formulations and powered formulations are available, it is used in children > 2 years of age at a daily dose of 8 mg/kg

Refer to the chapter 'Management of HIV infection in children' for other ARV drug dosages.

HEPATITIS A VIRUS POST-EXPOSURE PROPHYLAXIS

POST-EXPOSURE PROPHYLAXIS SHOULD BE CONSIDERED FOR THE FOLLOWING NON-IMMUNE CONTACTS

- Household contacts
- Sexual contacts
- Children and staff in day-care/crèche facilities
- Contacts in situations in which hygiene is likely to be suboptimal, e.g. homes for the mentally and physically disabled, or where faecal incontinence is encountered
- Other contacts, e.g. healthcare workers who were exposed to faecal material without the use of the necessary precautions/infection control measures

	DAYS SINCE EXPOSURE		
AGE	**≤ 14 DAYS**	**15–27 DAYS**	**≥ 28 DAYS**
Healthy, < 1 year of age	HNIG*	HNIG for high risk, immunocompromised and chronic liver disease contacts may be considered.	No prophylaxis is recommended
Healthy, 1–40 years of age	Vaccine		
Healthy, > 40 years of age	Vaccine and HNIG		
Immunocompromised	Vaccine and HNIG		
Chronic liver disease	Vaccine and HNIG		

*HNIG may be considered, caregivers should be vaccinated

The efficacy of hepatitis A vaccine alone in persons over 40 years is not well established and human normal immune globulin (HNIG) should be given in addition to vaccine. If HNIG is given 15–27 days post-exposure, it may not prevent infection, but may reduce the severity of infection in high-risk exposed individuals.

HEPATITIS A POST-EXPOSURE PROPHYLAXIS

Vaccine (Havrix®, Avaxim®): 2 doses given IM one month apart

AND/OR

Human normal immune globulin (HNIG) (Beriglobin®, Intragam®): 0.02–0.04 mL/kg given IM.

Vaccine and immune globulin should be given at different sites (deltoid muscle in adults, anterolateral thigh in children)

WORK/SCHOOL EXCLUSION

Exclusion from work is not required except in the case of food handlers who should be excluded for one to two weeks after onset of jaundice. The period of infectiousness is highest prior to the onset of jaundice and exclusion from school is generally recommended for a period of five days for those ≤ 5 years of age.

HEPATITIS B VIRUS POST-EXPOSURE PROPHYLAXIS

DEFINITIONS

Vaccine responder: HBsAb level after receiving three to six doses of hepatitis B vaccine is ≥ 10 mIU/mL. The individual is considered immune and is protected against HBV infection.

Vaccine non-responder: HBsAb remains < 10 mIU/mL after receiving the three doses of hepatitis B vaccine on two separate occasions (i.e., a total of six doses of vaccine) and chronic hepatitis B infection has been excluded. The individual is considered a vaccine non-responder.

RISK OF HEPATITIS B INFECTION

Following a needlestick or sharps injury, and in the absence of post-exposure prophylaxis, an exposed healthcare worker has a six percent to 30% risk of becoming infected with HBV.

THE FOLLOWING ARE HIGH-RISK EXPOSURES TO HEPATITIS B WHICH MAY REQUIRE PEP

- Exposure to the blood or bodily fluids of a hepatitis B-infected (HBsAg positive) person via:
- Percutaneous route, e.g. needlestick, IV drug abuse
- Mucocutaneous route, e.g. blood splash to eyes or mouth
- Sexual exposure
- Bite with breaking of skin

RECOMMENDED POST-EXPOSURE PROPHYLAXIS FOLLOWING A HIGH RISK EXPOSURE TO A HBSAG POSITIVE OR UNKNOWN SOURCE

EXPOSED PERSON	DESCRIPTION	ACTION
Unvaccinated/ Non-immune		Hepatitis B immune globulin (HBIG) **AND** Initiate and complete HBV vaccine course

Rx	HBV vaccinated	3 doses, known responder	No further action required
		1 series of 3 doses, response unknown/never tested	Immediately test HBsAb ≥ 10 mIU/mL: No action required < 10 mIU/mL: Give HBIG and initiate and complete 2nd course of HBV vaccine
		2 series of 3 doses, non-responder	Give 1 dose of HBIG immediately and another dose of HBIG one month later
		Did not complete vaccine series	HBIG and initiate and complete HBV vaccine course
	Newborns of HBsAg-positive mothers		Give HBIG and HBV vaccine within 24 hours of birth. Infants can slot into the normal EPI regimen for HBV vaccine (6, 10 and 14 weeks) once the birth dose has been administered

Hepatitis B vaccine and/or HBIG must preferably be given within 24–48 hours of exposure but not later than seven days post-exposure.

People that are living in the same household or institution as a known hepatitis B infected person should be vaccinated.

Rx

HEPATITIS B POST EXPOSURE PROPHYLAXIS

HEPATITIS B IMMUNE GLOBULIN (200 IU/2 ML) (HEBAGAM®)

- Newborn to < 5 years of age: 200 IU by intramuscular injection
- 5–9 years of age: 300 IU by intramuscular injection
- > 10 years of age: 500 IU by intramuscular injection

HEPATITIS B VACCINE (ENGERIX-B®, HEBERBIO HBV®)

1 ampoule/dose: 3 doses at 0, 1 and 2 months by intramuscular injection (accelerated immunisation schedule)

Note: If both hepatitis B immunoglobulin and vaccine are given simultaneously, it must be given at different injection sites

FOLLOW UP

Follow-up testing for hepatitis B core Ab and HBsAg should be done six months after the exposure to assess for HBV infection of exposed persons where post-exposure prophylaxis has been administered.

HEPATITIS C VIRUS POST-EXPOSURE PROPHYLAXIS

There is no effective post-exposure prophylaxis but early diagnosis and treatment is important should the exposed patient become infected. The risk of HCV infection following a needlestick or sharps injury from a known HCV-infected source is ~1.8% (range 0–10%). Baseline ALT and HCV ELISA testing should be performed on the exposed healthcare worker.

Follow-up testing at six, 12 and 24 weeks is advised and if the ALT is elevated then perform a HCV PCR to determine if infection has occurred.

INFLUENZA VIRUS POST-EXPOSURE PROPHYLAXIS

Antiviral post-exposure prophylaxis for influenza is not recommended. Many cases of viral resistance to the neuraminidase inhibitors have occurred in people who have used PEP. If PEP is absolutely necessary for high-risk (severely immunocompromised) individuals, the recommendation is that therapeutic doses of oseltamivir (Tamiflu®) are used. Refer to the chapter 'Treatment of common viral infections' for drug doses.

MEASLES VIRUS POST-EXPOSURE PROPHYLAXIS

Post-exposure prophylaxis with measles vaccine or human normal immune globulin (HNIG) should be considered for household or community contacts who are measles IgG negative (non-immune) or if their immune status is unknown.

RECOMMENDED MEASLES POST-EXPOSURE PROPHYLAXIS

MEASLES VACCINE (< 72 HOURS POST-EXPOSURE)	HUMAN NORMAL IMMUNE GLOBULIN (HNIG) ONLY
Healthy, non-pregnant individuals more than 6 months of age (live attenuated vaccine)	• < 6 months of age • Immunocompromised persons • Pregnant women

MEASLES POST-EXPOSURE PROPHYLAXIS

Human normal immune globulin: 0.2–0.25 mL/kg IM (max 15 mL) (Beriglobin®, Intragam®)
Vaccine: 1 dose IM if > 1 year of age. If < 1 year, give a repeat dose at 15 months (Rouvax®)

MUMPS VIRUS POST-EXPOSURE PROPHYLAXIS

There is no effective post-exposure prophylaxis for preventing mumps infection.

RUBELLA VIRUS POST-EXPOSURE PROPHYLAXIS

- There is no effective post-exposure prophylaxis for preventing rubella infection.
- For a non-immune (rubella IgG negative), rubella-exposed pregnant mother for whom termination is not an option, a high dose of human normal immune globulin (15–20 mL Beriglobin® or Intragam®) intramuscularly is advised. This does not prevent infection, but may attenuate the disease and reduce the risk to the foetus.

RABIES VIRUS POST-EXPOSURE PROPHYLAXIS

Dog bites are the cause of most rabies cases in South Africa. The vaccination history of the animal may be unreliable and animals that have been vaccinated before three months of age and those who have not received boosters may not be protected from rabies. Post-exposure prophylaxis is thus recommended regardless of the vaccination status of the animal.

The risk of acquiring rabies depends on the site and severity of the animal bite. PEP is most effective if given immediately after the exposure; however, do not withhold PEP should there be a delay in the patient presenting to a healthcare facility.

RISK CATEGORY	TYPE OF EXPOSURE	ACTION
1	Touching or feeding animal Licking intact skin	No action required if the history is reliable
2	Nibbling uncovered skin Superficial scratch without bleeding	• Wound treatment • Give rabies vaccine • Do not give rabies immune globulin (RIG) except if immunocompromised • Stop vaccination if animal tests negative for rabies or remains well after 10 days observation (dog or cat)
3	Bites or scratches penetrating skin and drawing blood Licking of mucous membranes or broken skin	• Wound treatment • Give rabies vaccine **AND** rabies immune globulin • Give anti-tetanus vaccine and antibiotics (e.g. amoxicillin-clavulanate) • Stop vaccination if animal tests negative for rabies or remains well after 10 days observation (dog or cat)

WOUND TREATMENT

- Flush the bite site with soap and water or water alone for at least five minutes before applying disinfectant.
- Primary suturing of the bite wound and the use of local anaesthetics should be avoided.

SPECIAL CIRCUMSTANCES

- Immunocompromised persons: all category two exposures should receive both rabies vaccine and rabies immunoglobulin.
- Pregnancy is not a contraindication for rabies vaccine or rabies immune globulin.
- Any close contact with bats should be managed as a category three exposure.

RABIES VIRUS POST-EXPOSURE PROPHYLAXIS

IF PREVIOUSLY IMMUNISED

Give rabies vaccine on days 0 and 3. Do not give rabies immune globulin

NOT PREVIOUSLY IMMUNISED

NOT IMMUNOCOMPROMISED

Give rabies vaccine on day 0, 3, 7, 14 and 28 given into the deltoid (adults) or anterolateral thigh (infants)

AND (for category 3 exposures)

Rabies immunogbulin (RIG) 20 IU/kg infiltrated into the wound, remainder into the deltoid in adults or anterolateral thigh in infants (opposite side to the one used for vaccine). RIG is supplied in 2 mL ampoules containing 300 IU

IMMUNOCOMPROMISED INDIVIDUALS

Give rabies vaccine on day 0, 3, 7, 14, and 28

AND (for category 2 and 3 exposures)

Rabies immunoglobulin (RIG) 20 IU/kg infiltrated into the wound, remainder into the deltoid in adults or anterolateral thigh in infants (opposite side to the one used for vaccine). RIG is supplied in 2 mL ampoules containing 300 IU

VARICELLA ZOSTER VIRUS POST-EXPOSURE PROPHYLAXIS

The recommended post-exposure prophylaxis following varicella-zoster virus (VZV) exposure (chickenpox or shingles) depends on the context:

EXPOSED PATIENT	RECOMMENDED POST-EXPOSURE PROPHYLAXIS
Healthy non-immune contacts	VZV vaccine < 72 hours post-exposure OR acyclovir from day 7–21 post-exposure if vaccine not available
Pregnant non-immune women	Zoster immune globulin (ZIG) at any stage of pregnancy OR acyclovir from day 7–21 post-exposure if ZIG not available
Neonates born to mothers who develop chickenpox within 7 days of delivery, and up to 28 days after delivery	Zoster immune globulin (ZIG) Acyclovir if ZIG is not available
Infants under 6 months of age who are exposed to chickenpox (as maternal immunity is usually lost by 2–3 months):	Zoster immune globulin (ZIG) Acyclovir if ZIG is not available
Immunocompromised patients	Zoster immune globulin (ZIG) Acyclovir if ZIG is not available

VARICELLA POST-EXPOSURE PROPHYLAXIS

VACCINE (VARILRIX®)

< 13 years old: 1 dose by subcutaneous injection

> 13 years old: 2 doses 4 weeks apart by subcutaneous injection

ZIG (200 IU/2 ML) (VAZIGAM®)

0–5 years: 2 mL by intramuscular injection

6–10 years: 4 mL by intramuscular injection

11–14 years: 5 mL by intramuscular injection

> 15 years: 6 mL by intramuscular injection

ACYCLOVIR

Adults: 800 mg PO given 5 x daily

Children: 40 mg/kg/day PO in 4 divided doses