

Alberta Guidelines for Post-Exposure Management and Prophylaxis:

HIV, Hepatitis B, Hepatitis C and Sexually Transmitted Infections

Alberta Guidelines for Post-Exposure Management and Prophylaxis: HIV, Hepatitis B, Hepatitis C and Sexually Transmitted Infections

Ministry of Health, Government of Alberta

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Table of Contents

ACRONYM LIST	5
QUICK REFERENCE GUIDE	7
INTRODUCTION	18
Goal	19
Target Audience	19
Roles and Responsibilities	19
Occupational Health and Safety Act	19
Mandatory Testing and Disclosure Act	20
GENERAL CONSIDERATIONS FOR HIV PEP	21
Rationale for HIV PEP	21
Evidence for the Use of PEP	21
Animal Studies	21
Human Studies	21
<i>Vertical Transmission</i>	21
<i>Occupational Exposure</i>	22
<i>Sexual Exposure</i>	22
Factors Reducing the Efficacy of PEP	22
Considerations for Providing PEP	23
Safety	23
Cost	24
Behavior	24
Anxiety	24
Consideration of other HIV Prevention Interventions	25
Social and Ethical Considerations	25
Risk of HIV Transmission and Factors Influencing Risk	25
Suppressed Viral Load	26
Consensual Exposure to HIV	27
Infrequent Consensual Exposure	27
Related Consensual Exposure	27
Pre-Exposure Prophylaxis	28
MANAGEMENT OF HIV PEP	29
Management of the Exposed Site	29
Recommendations for Prescribing PEP	29
Assessment of the Exposed	29
Assessment of the Source	30
Needlestick Injury in the Community Setting	31

Human Bites.....	31
Timing of PEP	31
Duration of PEP	32
Choice and Number of Antiretroviral Drugs used for PEP	32
Nucleoside Reverse Transcriptase Inhibitors (NRTI)	33
Integrase Strand Transfer Inhibitors (INSTI)	33
Children	34
Pregnancy	35
Breastfeeding	36
Dispensing of HIV PEP	37
Education	37
Follow up of Patients Prescribed HIV PEP	37
 HEPATITIS B VIRUS (HBV)	 38
HEPATITIS C VIRUS (HCV)	40
SEXUALLY TRANSMITTED INFECTIONS (STIs)	41
REFERENCES	42
APPENDIX	50
Table 1. Risk of HIV transmission per exposure from a known HIV-positive individual.....	50
Table 2. HIV/AIDS Diagnosis Data.....	51
Table 3. Risk Assessment	52
 ACKNOWLEDGEMENTS	 53

Acronym List

AIDS	Acquired Immunodeficiency Syndrome
Anti-HBs	Hepatitis B surface antibody
ART	Antiretroviral therapy
ARV	Antiretroviral
BBFE	Blood and Body Fluid Exposure
BBP	Blood-borne Pathogen
CADTH	Canadian Agency for Drugs and Technology in Health Care
CDC	US Centres for Disease Control and Prevention
CDN	Canadian
CT	Chlamydia
DNA	Deoxyribonucleic acid
DRV/r	Ritonavir-boosted Darunavir
DTG	Dolutegravir
EFV	Efavirenz
EIA	Syphilis Enzyme immunoassay
FDA	US Food and Drug Administration
FTC	Emtricitabine
GC	Gonorrhea
HBeAg	Hepatitis B “e” antigen
HBIG	Hepatitis B Immune Globulin
HBsAg	Hepatitis B surface antigen
HHS	US Department of Health and Human Services
Anti-HBs	Antibody to hepatitis B surface antigen
Anti-HBc	Antibody to hepatitis B core antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIVQUAL	Human Immunodeficiency Virus- qualitative viral load test
HIVQUANT	Human Immunodeficiency Virus- quantitative viral load test
HCV-RNA	Hepatitis C Virus-Ribonucleic acid
HIV	Human Immunodeficiency Virus
IU/L	International unit/Litre
IDU	Injection drug use
ICER	Incremental cost effectiveness ratio
INSTI	Integrase Strand Transfer Inhibitor
kg	kilogram
3TC	Lamivudine
LMP	Last Menstrual Period
LPV/r	Ritonavir-boosted Lopinavir
mg	milligram
ml/mL	milliliter
MDR	Multi-drug resistance
MMWR	Morbidity and Mortality Weekly
MSM	Men Who Have Sex With Men
MTDA	Mandatory Testing and Disclosure Act
NAAT	Nucleic Acid Amplification Test
NTD	Neural Tube Defects
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor

OHS	Occupational Health and Safety
PEP	Post-Exposure Prophylaxis
PHAC	Public Health Agency of Canada
PI	Protease inhibitor
POCT	Point-of-Care Test
PrEP	Pre-Exposure Prophylaxis
PWID	People Who Inject Drugs
QALY	Quality Adjusted Life Year
RAL	Raltegravir
RCTs	Randomized Control Trials
RNA	Ribonucleic acid
RPR	Rapid Plasma Reagin
SIV	Simian Immunodeficiency Virus
STI	Sexually Transmitted Infection
TDF	Tenofovir Disoproxil Fumarate
US/USA	United States/United States of America
VL	Viral Load
WHO	World Health Organization
ZDV	Zidovudine

Quick Reference Guide: Tables and Figures

Figure 1. Algorithm: Detailed HIV Risk Assessment for Post-Exposure following BBFE	8
Table 1. Factors that Increase the Risk of HIV Transmission.....	9
Table 2. Testing Recommendations-All.....	10
Table 3A. HIV Post-Exposure Prophylaxis Recommendations for Sexual Exposures.....	11
Table 3B. HIV Post-Exposure Prophylaxis Recommendations for Other Exposures.....	12
Table 4. HIV PEP Drug Regimen – Adult and Adolescent Regimen.....	13
Table 5. HIV PEP Drug Regimen – Pediatric Regimen.....	14
Table 6. HIV PEP - Pregnancy Regimen.....	15
Table 7. HBV PEP - High Risk Source.....	16
Table 8. HBV PEP - Low Risk Source.....	17

Quick Reference Guide:

Figure 1- DETAILED HIV RISK ASSESSMENT for Post-Exposure Following BBFE

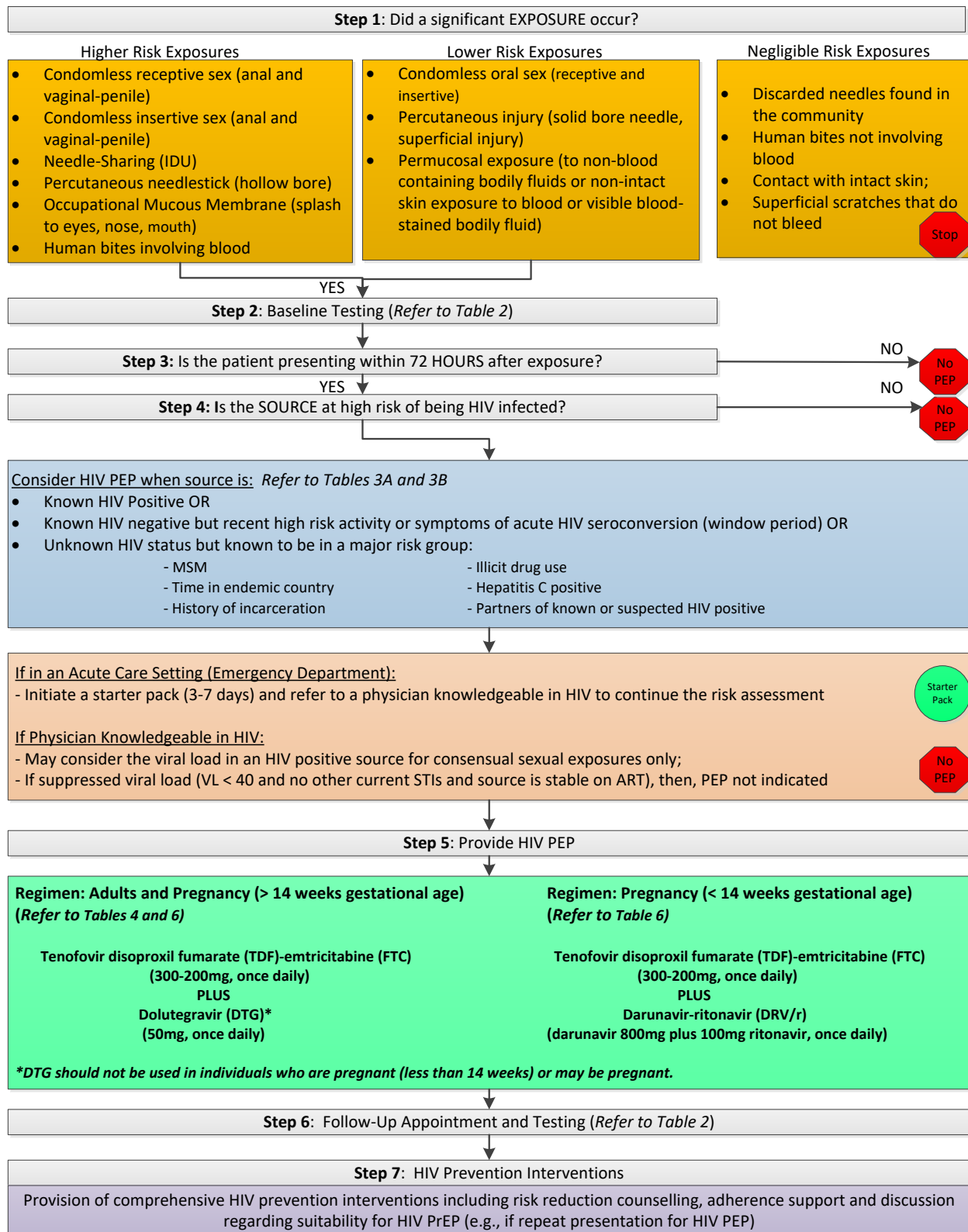


Table 1. Factors that increase the risk of HIV transmission

Factors that increase the risk of HIV transmission from a sexual exposure (Adapted from New York State Department of Health AIDS Institute, 2018)
<ul style="list-style-type: none"> • A high plasma viral load (VL) in the source is the strongest predictor of HIV sexual transmission (PHAC, 2013). The risk of HIV transmission is directly related to the HIV VL of the source (PHAC, 2013; Hughes <i>et al.</i>, 2012; Attia <i>et al.</i>, 2009; Gray <i>et al.</i>, 2001; New York State Department of Health AIDS Institute, 2018) especially during acute HIV infection when the rate of transmission has been shown to be almost 12 fold higher than exposures occurring after the viral set point (Wawer <i>et al.</i>, 2005). • The presence of a sexually transmitted infection (especially genital ulcer disease) (BC's PEP Guidelines, 2018; PHAC, 2013; New York State Department of Health AIDS Institute, 2018; CDC, 2015; Gray <i>et al.</i>, 2001). STIs increase HIV transmissibility 2 to 3 times (PHAC, 2013). Jarzebowski <i>et al.</i>, 2012 demonstrated that early syphilis can increase HIV transmission risk. The large study demonstrates that early syphilis is associated with a significant rise in VL, even among patients on effective ART. • Trauma at the site of the exposure (mucosal or skin break) (New York State Department of Health AIDS Institute, 2018) (Draughon JE, 2012; BC's PEP Guidelines, 2018) • Lack of barrier protection (male or female condoms) – Condoms provide important protection against HIV when used correctly and consistently (PHAC, 2013; PHAC, 2013; New York State Department of Health AIDS Institute, 2018; BC's PEP Guidelines, 2018). • Blood exposure – Exposure especially to fresh blood as noted by the exposed person (New York State Department of Health AIDS Institute, 2018). • Ejaculation- In MSM, the risk of HIV acquisition per episode of unprotected anal intercourse was higher with ejaculation (1.43%) relative to no ejaculation (0.65%) (Jin <i>et al.</i>, 2010). • Lack of male circumcision (Moses <i>et al.</i>, 1994; New York State Department of Health AIDS Institute, 2018; BC's PEP Guidelines, 2018)- Increases the risk of female-to-male sexual transmission of HIV by 50% to 60% (PHAC, 2013). • Oral mucosa is not intact (oral lesions, wounds, ulcers)- for oral sex exposure (New York State Department of Health AIDS Institute, 2018)
Factors that increase the risk of HIV transmission from a needle-sharing or needlestick injury (Adapted from New York State Department of Health AIDS Institute, 2018; BC's PEP Guidelines, 2018)
<ul style="list-style-type: none"> • A high VL in the source and source is not receiving ART or is on ART with a non-suppressed VL (See section on Suppressed Viral Load); • Hollow-bore needle and gauge size; • Deep skin penetration; and • Presence of blood on the needle- especially fresh blood.

Table 2. Testing Recommendations- ALL

General guidelines:

- If source tests negative for HIV, HBV or HCV, no further testing beyond baseline is required in the source or exposed, except, if source is considered to be 'high-risk' and in the "window period", follow exposed guidelines below.
- If source or exposed tests positive for HIV, HBV or HCV at baseline, follow exposed guidelines below.

Test	Source	Exposed			
	Baseline	Baseline	4-6 weeks after exposure	12 weeks after exposure	6 months after exposure
HIV antibody^{a1}	✓ ^{a2}	✓	✓ ^{a3,a4}	✓	✓ ^{a5}
HIV QUANT (viral load)	✓ ^{a6}				
Hepatitis B^b: Hepatitis B surface antigen Hepatitis B surface antibody	✓	✓ ✓	1-6 months (as indicated in HBV PEP Tables 7 and 8)		✓
Hepatitis C antibody	✓ ^c	✓			
HCV RNA			✓ (6 weeks)		
		Sexual Exposure			
Syphilis serology	✓	✓ ^d	✓ (4 weeks)	✓	
Gonorrhea (GC) NAAT	✓	✓		✓ ^e	
Chlamydia (CT) NAAT	✓	✓		✓ ^e	
Pregnancy		✓			
		Follow-Up HIV PEP			
Complete Blood Count with Differential		✓ (and 2 weeks only with ZDV)	✓ (only with ZDV)		
Creatinine		✓ (and 2 weeks)	✓		
Adherence Support		✓ (and 2 weeks)	✓		

^{a1} Any positive POCT result must be followed up with a confirmatory 4th generation HIV test.

^{a2} Rapid point-of-care testing should be considered for a source aged > 12 years when available.

^{a3} HIV testing should occur after completion of the 28-day antiretroviral (ARV) regimen. To ease the burden of testing, HIV antibody may be delayed until week 6 to coincide with the HCV-RNA test.

^{a4} If a exposed develops illness consistent with acute seroconversion to HIV (e.g., fever, headache, rash, lymphadenopathy) within 4 to 6 weeks of exposure, a HIVQUAL (quantitative viral load) test may be performed when a prompt diagnosis is required.

^{a5} Should be considered when: (1) PEP has been extended significantly past 28 days; (2) exposed patient is HCV infected/co-infected;(3) there is a strong indication of potential exposure to HIV-2.

^{a6} HIVQUANT is a quantitative viral load test to be ordered under the guidance of an Infectious Disease Specialist or a PEP prescriber following Alberta Health guidelines, or in direct consultation with the virologist on call.

^b If exposed known to be immune to HBV (anti-HBs ≥ 10 IU/L) or HBsAg positive, source and exposed testing is unnecessary.

^c If source or exposed tests HCV-antibody positive at baseline, a follow-up HCV-RNA test should be performed to confirm infection. HCV-RNA testing is recommended as it can identify acute infection within 2 weeks of exposure where the HCV serological window period is 5-10 weeks.

^d A screening test for syphilis should be performed (e.g., EIA or rapid plasma reagin).

^e For exposed diagnosed with a CT or GC infection, re-screening should occur 3-6 months after treatment. Test of cure (if desired or indicated) for GC should be done at 3-4 weeks after completion of STI treatment.

Table 3A. HIV Post-Exposure Prophylaxis Recommendations for Sexual Exposures*

Type of Exposure (condomless)	Source Status			
	HIV Positive		Unknown HIV Status	
	HIV VL unknown/ detectable (> 40 copies/mL)	HIV VL confirmed undetectable (See section on suppressed viral load) (< 40 copies/mL)**	From major risk group	Not known to be in a major risk group OR Unknown risk factors for HIV OR Unknown
High-risk				
Receptive anal sex CONSENSUAL	Recommended	Not recommended	Recommended	Not recommended
NON-CONSENSUAL	Recommended	Recommended	Recommended	Not recommended
Insertive anal sex CONSENSUAL	Recommended	Not recommended	Case-by-Case	Not recommended
Receptive vaginal-penile sex CONSENSUAL	Recommended	Not recommended	Case-by-Case	Not recommended
NON-CONSENSUAL	Recommended	Recommended	Case-by-Case	Not recommended
Moderate Risk				
Insertive vaginal-penile sex CONSENSUAL	Recommended	Not recommended	Case-by-Case	Not recommended

* Recommended: Risk about 1/1000 (0.1%) or greater;

Case-by-Case: Risk between 1/1000 and 1/10,000 (0.01%) if there are other factors present that may increase the risk of transmission (Table 1, page 9);

Not recommended: Risk less than 1/10,000 (0.001%) or below

** Viral load in an HIV positive source will be considered only in the context of a consensual sexual exposure and not for non-consensual sexual exposures based on the evidence at the present time.

Table 3B. HIV Post-Exposure Prophylaxis Recommendations for Other Exposures *

Type of Exposure	Source Status		
	HIV Positive**	Unknown HIV Status	
		From major risk group	Not known to be in a major risk group OR Unknown risk factors for HIV OR Unknown
High-risk			
Needle sharing, IDU	Recommended	Recommended	Not Applicable
Percutaneous, hollow bore needlestick	Recommended	Case-by-Case	Not recommended
Occupational mucous membrane (splashes to eyes, nose and mouth; risk may be lower with non-intact skin)	Recommended	Case-by-Case	Not recommended
Human bites involving blood	Recommended	Case-by-Case	Not recommended
Low Risk			
Receptive oral sex (condomless)	Case-by-Case	Not recommended	Not recommended
Insertive oral sex (condomless)	Case-by-Case	Not recommended	Not recommended
Percutaneous injury (solid bore needle, superficial injury), Permucosal exposure to non-blood containing bodily fluids or non-intact skin exposure to blood or visible blood-stained bodily fluid	Not recommended	Not recommended	Not recommended
Negligible Risk			
Discarded needles found in the community; Human bites not involving blood; Contact with intact skin; Superficial scratches that do not bleed	Not recommended	Not recommended	Not recommended

* Recommended: Risk about 1/1000 (0.1%) or greater;

Case-by-Case: Risk between 1/1000 and 1/10,000 (0.01%) if there are other factors that may increase the risk of transmission (Table 1, page 9);

Not recommended: Risk less than 1/10,000 (0.001%) or below

** Viral load in an HIV positive source should not be considered in the context of an occupational exposure due to a lack of direct evidence at this time.

HIV PEP Drug Regimens

Table 4. Adult and Adolescent (≥ 12 years of age) Regimen

Three-drug regimens (Additional information on drug dosages and side effects is available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf)
tenofovir disoproxil fumarate (TDF) – emtricitabine (FTC) † (300 – 200 mg, once daily) Plus dolutegravir (DTG) § (50 mg, once daily)

Adverse effects and drug interactions

† *TDF*: The most serious side effect is harm to the kidneys but this is typically associated only with long-term use (Product Monograph, Gilead, May, 2017). Expert consultation should be sought when using TDF/FTC in patients with impaired creatinine clearance: dose should be reduced to one tablet every 48 hours in patients with a creatinine clearance of 30 to 49 ml per minute; one tablet every 72 hours in patients with a creatinine clearance of 15-29 mL per minute; and, one tablet every 96 hours in patients with a creatinine clearance of less than 15 or on hemodialysis (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2018).

TDF may cause reduced bone density in humans with long-term use only (Product Monograph, Gilead, May, 2017).

§ *DTG*: Antacid medications, calcium supplements and iron supplements can interfere with the absorption of this medication and make it less effective. Do not take antacids or calcium/iron supplements during the six hours before this medication or at least two hours after it is ingested (Product Monograph, ViiV, February, 2017).

Special Considerations

† *Hepatitis B Infection*: In patients co-infected with HBV, ‘flare-ups’ of Hepatitis B Virus Infection may occur when this drug is discontinued (Product Monograph, Gilead, May, 2017). Patients with chronic hepatitis B virus infection who require PEP may still receive a regimen containing TDF/FTC, but close clinical and laboratory monitoring for hepatitis flares, in consultation with a hepatitis B specialist, should be considered upon completion of PEP.

§ *Children/Pregnancy*: DTG is not indicated in children weighing less than 30 kg (Product Monograph, ViiV, February, 2017). DTG is not recommended in pregnant women during the first trimester or women who may be pregnant, see Table 6 (Panel on Antiretroviral Guidelines for Adults and Adolescents, December 7, 2018).

HIV PEP Drug Regimens

Table 5. Pediatric Regimens

Three-drug regimen (Additional information on for drug dosages and side effects is available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/PediatricGuidelines.pdf)	
Children >14 days - <2 years of age <i>or</i> For those who cannot chew or swallow pills	zidovudine (ZDV) syrup – lamivudine (3TC) § oral solution Plus lopinavir ^{§§} - ritonavir [†] (LPV/r) oral solution
Children 2 years - <12 years of age	zidovudine (ZDV) – lamivudine (3TC) [§] Plus raltegravir (RAL) [†]

[†] The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.

[§] Do not use fixed dose combination products (e.g., zidovudine-lamivudine) in patients with a creatinine clearance of less than 50 ml per minute, on dialysis, or who have impaired hepatic function (Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, 2018).

^{§§} Caution should be used when administering lopinavir to patients with hepatic impairment (Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, 2018).

[†] Raltegravir is FDA-approved for infants and children weighing ≥ 2kg and can be started at birth (Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, 2018). It is available in film-coated tablets, chewable tablets and single packets of granules for oral suspension. No dosage adjustment is necessary for patients with mild to moderate hepatic insufficiency or in patients with renal impairment (Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, 2018).

HIV PEP Drug Regimens

Table 6. Pregnancy Regimen

Three-drug regimen (Additional information on drug dosages and side effects is available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf)	
Pregnant > 14 weeks gestational age by last menstrual period	<p>tenofovir disoproxil fumarate (TDF) – emtricitabine (FTC) § (300 – 200 mg, once daily)</p> <p>Plus</p> <p>dolutegravir (DTG) † (50 mg, once daily)</p>
Pregnant ≤ 14 weeks gestational age by last menstrual period	<p>tenofovir disoproxil fumarate (TDF) – emtricitabine (FTC) § (300 – 200 mg, once daily)</p> <p>Plus</p> <p>darunavir^{††}-ritonavir^{††} (DRV/r) (darunavir 800 mg plus ritonavir 100 mg, once daily)</p>

In women who are more than 14 weeks since their last menstrual period (LMP), the preferred regimen is DTG and TDF/FTC. However, all patients who are offered this medication should be counselled on the benefits and risks of using DTG, including the possible risk of neural tube defects (NTDs). DTG should not be initiated in any HIV-exposed individual who is pregnant less than or equal to 14 weeks from LMP or those who are not using effective birth control (Panel on Antiretroviral Guidelines for Adults and Adolescents, December 7, 2018). The preferred HIV PEP regimen in the first trimester of pregnancy is DRV/r and consultation with an HIV expert is recommended. In instances of sexual assault (or otherwise), where measures are being taken to prevent pregnancy, DTG may be used following a conversation with the client about potential risks.

§ TDF/FTC- Has a high placental transfer to fetus and no evidence of human teratogenicity (can rule out 1.5-fold increase in overall birth defects) (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2018). Human studies demonstrate no consistent link to low birth weight, but data are conflicting about potential effects on growth outcomes later in pregnancy. If HBV co-infected, a HBV flare may occur if TDF is stopped. Renal function should be monitored because of potential for renal toxicity.

† DTG: Antacid medications, calcium supplements and iron supplements can interfere with the absorption of this medication and make it less effective. Do not take antacids or calcium/iron supplements during the six hours before this medication or at least two hours after it is ingested (Product Monograph, ViiV, February, 2017). High placental transfer to fetus. Preliminary data suggest no increased risk of teratogenicity in humans (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2018).

†† DRV: Low placental transfer to fetus. No evidence of human teratogenicity. Must be boosted with low dose ritonavir (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2018).

Table 7. HBV PEP - High Risk Source

Source is Known HBsAg Positive (infected) <u>OR</u> Source Status Unknown but Known to be High-risk <u>OR</u> Source Status Unknown or Not Available for Testing (Adapted from: Canadian Immunization Guide, 2018; Alberta Immunization Policy)					
RECIPIENT	RECIPIENT's MANAGEMENT				
	Results	Next steps			
Unvaccinated Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune for this exposure. Offer hepatitis B vaccine series for long-term protection.			
	• anti-HBs negative (<10 IU/L) • HBsAg negative	HBIG and first dose of 3 dose vaccine series	Complete vaccine series. Test anti-HBs and HBsAg. Ensure testing is at least 1 month after the last dose of vaccine and at least 6 months after HBIG.	• anti-HBs positive	Consider immune
				• anti-HBs negative • HBsAg negative	Second series of vaccine. Test 1 month after vaccine series.
				• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines.
• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.				
Vaccinated: Documented and valid 3 dose series (age appropriate and spaced appropriate) Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune No further follow-up required.			
	• anti-HBs negative • HBsAg negative	HBIG and one dose of vaccine.	Test anti-HBs and HBsAg. Ensure testing is at least 1 month after the last dose of vaccine and at least 6 months after HBIG.	• anti-HBs positive	Consider immune
				• anti-HBs negative • HBsAg negative	Complete second series of vaccine. Test 1 month after vaccine series.
				• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines.
• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.				
Vaccinated: Documented and valid two complete series of vaccine Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune No further follow-up required.			
	• anti-HBs negative • HBsAg negative	Non-responder. No further vaccine indicated.		HBIG x 2. Give the 2 nd dose of HBIG one month after 1 st dose.	Test 6 months after HBIG for HBsAg.
		• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.		
Vaccinated: One or two doses of 3 dose series Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune for this exposure. Complete hepatitis B vaccine series for long-term protection.			
	• anti-HBs negative • HBsAg negative	HBIG and complete vaccine series. Test anti-HBs and HBsAg. Ensure testing is at least 1 month after the last dose of vaccine and at least 6 months after HBIG.	• anti-HBs positive • HBsAg negative	Consider immune	
			• anti-HBs negative • HBsAg negative	Second series of vaccine. Test 1 month after vaccine series.	
			• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.	
• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.				

Notes

- If recipient is known to be anti-HBs positive (≥ 10 IU/L) following a documented and valid series (*age appropriate and spaced appropriate*) or if known to be HBsAg positive, hepatitis B testing does not need to be repeated.
- Offer HBIG if antibody testing for recipient is not available within 48 hours and the source is known HBsAg positive.
- **High-risk source:** individuals with multiple sexual partners, MSM, sexual partner infected with HBV, close family contact with HBV infected individual, history of injection drug use, immigration from a HBV endemic country (prevalence $\geq 8\%$), and history of blood transfusions prior to 1970.
- **Immunocompromised people,** protection may wane, subsequent HBV exposure in these individuals can result in acute disease or carrier state. Therefore, these individuals should be tested and offered a booster as needed.
- **HBIG** dose is 0.06 mL/kg I.M. Dose should be administered as soon as possible after exposure ideally within 24 hours. For percutaneous or mucosal exposures, HBIG may be given up to 7 days following the exposure. For sexual exposures HBIG may be given up to 14 days following the exposure.

Table 8. HBV PEP - Low Risk Source

Source is Known HBsAg negative (uninfected) <u>OR</u> Source Status Unknown but Known to be Low Risk (Adapted from: Canadian Immunization Guide, 2018; Alberta Immunization Policy)					
RECIPIENT	RECIPIENT's MANAGEMENT				
	Results	Next steps			
<i>Unvaccinated</i> Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune for this exposure. Offer hepatitis B vaccine series for long-term protection.			
	• anti-HBs negative (<10 IU/L) • HBsAg negative	First dose of 3 dose vaccine series	Complete vaccine series. Test anti-HBs and HBsAg 1-6 months after vaccine series	• anti-HBs positive	Consider immune
				• anti-HBs negative • HBsAg negative	Second series of vaccine. Test 1 month after vaccine series.
				• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines.
• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.				
<i>Vaccinated: Documented and valid 3 dose series (age appropriate and spaced appropriate)</i> Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune No further follow-up required.			
	• anti-HBs negative • HBsAg negative	One dose of vaccine.	Test anti-HBs and HBsAg 1-6 months after vaccine series	• anti-HBs positive	Consider immune
				• anti-HBs negative • HBsAg negative	Complete second series of vaccine. Test 1 month after vaccine series.
				• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines.
• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.				
<i>Vaccinated: Documented and valid two complete series of vaccine</i> Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune No further follow-up required.			
	• anti-HBs negative • HBsAg negative	Non-responder. No further vaccine indicated.		No further follow-up.	
	• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.			
<i>Vaccinated: One or two doses of 3 dose series</i> Test for: • anti-HBs • HBsAg	• anti-HBs positive • HBsAg negative	Consider immune for this exposure Complete vaccine series for long-term protection.			
	• anti-HBs negative • HBsAg negative	Complete vaccine series. Test anti-HBs and HBsAg at least 1-6 months after vaccine series	• anti-HBs positive • HBsAg negative	Consider immune	
			• anti-HBs negative • HBsAg negative	Second series of vaccine. Test 1 month after vaccine series.	
			• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.	
• anti-HBs negative • HBsAg positive	Refer to Public Health Hepatitis B disease management guidelines for follow-up.				

Notes:

- If recipient is known to be anti-HBs positive (≥ 10 IU/L) following a documented and valid series (*age appropriate and spaced appropriate*) or known to be HBsAg positive, hepatitis B testing does not need to be repeated.
- **Low risk source** - individuals who do NOT have the following risk factors: multiple sexual partners, MSM, sexual partner infected with HBV, close family contact with HBV infected individual, history of injection drug use, immigration from a HBV endemic country (prevalence $\geq 8\%$), and history of blood transfusions prior to 1970.
- **Immunocompromised people**, protection may wane, subsequent HBV exposure in these individuals can result in acute disease or carrier state. Therefore, these individuals should be tested and offered a booster as needed.

Alberta Guidelines for Post-Exposure Management and Prophylaxis: HIV, Hepatitis B, Hepatitis C and Sexually Transmitted Infections

Introduction

This document provides guidance for the most appropriate use of post-exposure prophylaxis (PEP) to reduce the risk of transmitting Human Immunodeficiency Virus (HIV), Hepatitis B (HBV), Hepatitis C (HCV), and other sexually transmitted infections (STI) following a blood or bodily fluid exposure (BBFE). The scope of this document includes two settings:

- non-occupational (community) exposures (including those through sexual assault); and
- occupational exposures.

The *Mandatory Testing and Disclosure Act* (MTDA) was established to provide an additional mechanism to gain information to guide PEP decisions in certain well-defined situations. While the clinical management recommendations do not differ significantly in these three situations, the responsibilities for implementation and funding for prophylaxis of BBFE vary considerably. This guidance includes a brief description of roles and responsibilities for each of these three settings. The guidance in this document does not indicate an exclusive course of treatment or serve as an absolute standard of medical care. Variations, taking into account individual circumstances, may be appropriate and clinical discretion remains paramount. In addition, this document does not address PEP for perinatal exposures.

The '*Alberta Guidelines for Post-Exposure Management and Prophylaxis*' has been updated based on new evidence and approaches to the provision of PEP both nationally and internationally. This guidance applies to all residents of Alberta including those living in First Nations communities. It will be reviewed and revised by Alberta Health on an ongoing basis.

Goal

The goal of these guidelines is to reduce the risk of transmission of blood-borne pathogens (BBP) to individuals exposed to HIV, HBV and HCV through exposures as employees, community exposures, or sexual assault/abuse. This is accomplished by:

- pre-exposure preventive measures;
- standardized BBFE assessment;
- assessment of transmission risk in exposed individuals;
- laboratory testing of the exposed individuals and the source individual if possible;
- provision of post-exposure prophylaxis for exposed individuals where indicated;
- provision of risk reduction counselling; and
- appropriate management and follow-up.

Target Audience

This guidance is intended for health care workers, clinicians and policy-makers who are involved in the management, care and treatment of individuals who have had a significant exposure to blood and/or bodily fluids in the work place or community.

Roles and Responsibilities

The role of public health professionals is predominantly to follow-up on significant exposures that occur in **community** settings. Most often these are exposures in non-occupational settings. Public health professionals provide the initial assessment, evaluation and follow-up for the PEP protocol in these situations.

Significant exposures that occur in any **occupational** settings are not generally considered the responsibility of public health. However, in certain situations (such as private physician or dentist offices) where the employer does not have the expertise or capacity to provide post-exposure management, the provision of initial assessment and management of individuals exposed in occupational settings may be facilitated by public health professionals on a case-by-case basis and where no other expertise exists to provide this service.

In case of an exposure in the work place, the employer is responsible to make sure that first aid is made available to the affected worker(s), and that workers are made aware of the requirement to report and seek medical attention for such exposures. An employer is responsible for providing and paying for first aid and medical services (through insurance in most cases) as they are not funded through the publicly funded health system.

Occupational Health and Safety Act

In Alberta, Occupational Health and Safety (OHS) legislation places an onus on employers to ensure that worker exposure to BBP or other biohazardous material is avoided or minimized as much as possible. Biohazardous material means “a pathogenic organism, including a blood-borne pathogen, that,

because of its known or reasonably believed ability to cause disease in humans, would be classified as Risk Group 2, 3, or 4 as defined by the Public Health Agency of Canada (PHAC), or any material contaminated with such an organism” (as per the definition listed in the OHS Code, Part 1, Definitions). Employers are to ensure that, where an exposure to biohazardous material may occur in the workplace, the biohazardous material is treated as potentially infectious, protective work practices are established, and workers are informed of the health hazards associated with exposure to biohazardous material and trained in such practices.

The Alberta OHS Code, Part 35, Health Care and Industries with Biological Hazards, also includes the **requirement** for an employer to establish policies and procedures for the post-exposure management of workers with potential exposures to blood-borne pathogens.

“An employer must establish policies and procedures for the post-exposure management of workers exposed to biohazardous material.” -OHS Code, Part 35, Section 530

As required by section 8 of the OHS Regulation, all policies and procedures **must** be in writing and available to workers.

Mandatory Testing and Disclosure Act

The *Mandatory Testing and Disclosure Act* (MTDA) provides a mechanism for certain individuals exposed to the risk of communicable disease infection through contact with another individual (the source) to compel them to provide a bodily substance for testing. An order for testing may be issued if the Court is satisfied that the information that may be obtained under the proposed testing order cannot reasonably be obtained in any other manner.

The MTDA in no way affects the initial routine clinical management of a patient exposed to a bodily substance of another individual (source). Management of an individual with a BBFE that meets the criteria under the MTDA should be managed in accordance with these guidelines. Assessment and initiation (offering) of PEP should be completed in accordance with these guidelines, recognizing that early initiation of PEP greatly enhances effectiveness, and information gained from a MTDA submission should only serve to inform withdrawal of PEP as required. A decision to provide PEP should not be delayed until information is obtained from a MTDA submission.

The MTDA and the assessment and reporting processes only apply when the exposed has come into contact with the bodily fluid of a source person in specific emergency situations as outlined below:

- While providing emergency assistance to a source individual who is ill, injured or unconscious as a result of an accident or other emergency, or
- While performing duties as a firefighter, paramedic or peace officer.

It is important that the exposed be treated and the Physician Report completed by a physician knowledgeable in assessing and managing BBFE. The assessment and reporting processes as outlined in this document are important for all applications under the MTDA. More information and guidance to physicians regarding assessment and management of a patient who wishes to make an application under the MTDA is available at <https://www.alberta.ca/mandatory-testing-and-disclosure.aspx>.

General Considerations for HIV PEP

Rationale for HIV PEP

Pathogenesis studies conducted in health care workers occupationally exposed and animal models demonstrate that HIV PEP provides an opportunity to interrupt the HIV viral life cycle following an exposure. Evidence suggests it may take up to 48-72 hours for HIV to be detected in the lymph nodes and up to five days to be detected in the blood (Spira et al., 1996; Pinto et al., 1997) following infection. Initiation of short-term antiretroviral (ART) treatment was shown to be more effective in reducing viral dissemination and replication in almost all tissues when initiated earlier after infection in animal models (Bourry et al., 2010).

Evidence for the Use of PEP

There is a lack of definitive evidence on the efficacy of PEP. Randomized controlled trials (RCTs) have not been performed to determine the efficacy of PEP for exposures due to ethical considerations. There are also many case reports of PEP failures from both occupational and non-occupational exposure events. These guidelines are based on the current practice, both nationally and internationally, as well as evidence extrapolated from studies involving animals, vertical transmission and occupational exposure that have been published in the literature.

Animal Studies

Further evidence of the protective effect of PEP in preventing HIV acquisition was shown in a systematic review and meta-analysis of PEP studies in nonhuman primate models of HIV (Irvine *et al.*, 2015). Twenty-five studies (408 primates) were included in the review. The risk of seroconversion was 89% lower among animals exposed to PEP compared with those that did not receive PEP (odds ratio, 0.11 with a 95% confidence interval of 0.05-0.23). Inoculation was mainly subcutaneous and prophylaxis was given orally in some studies. However, the overall quality of the studies was relatively low. There was low heterogeneity ($I^2 = 0.0\%$) in the studies included.

Human Studies

Vertical Transmission

In AIDS Clinical Trials Group 076 study, there was a protective effect when neonates were given a six-week regimen of zidovudine (ZDV) within 48 hours of delivery compared to those who did not receive ZDV immediately after delivery (Wade *et al.*, 1998). Recent evidence in pregnant women who had not received ART suggests that two-drug or three-drug ART regimens are more effective than one-drug in preventing mother-to-child transmission (Nielson-Saines K *et al.*, 2012). The limitations of these studies is that with a different mode of exposure, results from vertical transmission studies may have little relevance for occupational and non-occupational exposures.

Occupational Exposure

A case-controlled retrospective study of health care workers that were occupationally exposed percutaneously to HIV demonstrated that a 28-day regimen of ZDV had a protective effect (Cardo *et al.*, 1997). The study demonstrated that after controlling for different factors associated with the risk of HIV transmission, the odds of HIV infection among health care workers who took ZDV PEP was reduced by approximately 81% (odds ratio, 0.19 with a 95% confidence interval of 0.06-0.52). The study also demonstrated that significant risk factors for HIV transmission were: a deep injury, injury with a device visibly contaminated with blood, exposure to a source who died of immunodeficiency syndrome and a procedure involving a needle placed directly in the source's artery or vein. Limitations of the study was the small number of cases (n=33) and cases and controls were from different countries.

Sexual Exposure

There are no RCTs that determine the efficacy of PEP following sexual exposure. An observational study from Brazil conducted in men who have sex with men (MSM) treated with PEP after a high-risk exposure resulted in less seroconversions in individuals receiving PEP relative to those who did not receive therapy (Schechter *et al.*, 2004). They found that PEP was effective but the HIV incidence remained the same because this cohort did not access PEP after subsequent high-risk HIV exposures. More recently, in a prospective study of 3,547 non-occupational exposures in a large Canadian MSM cohort, efficacy of a three-drug regimen was estimated at approximately 99% (Thomas *et al.*, 2015). The authors found only one case of seroconversion attributable to PEP failure (failure rate is 0.04%) concluding that HIV PEP is a successful method to prevent HIV infection after sexual exposure (condomless anal sex) in MSM. In a systematic review and meta-analysis of fifteen studies (1830 PEP initiations), the authors reported that PEP failure as measured by seroconversion was rare and could not be compared across regimens because of the paucity of events and different protocols for longer-term monitoring after PEP (Ford *et al.*, 2015). Phase III trials of HIV pre-exposure prophylaxis (PrEP) have shown high rates of efficacy (up to 99%) using daily tenofovir disoproxil fumarate (TDF) alone or TDF in combination with emtricitabine (FTC) in high-risk heterosexuals and MSM populations (Baeten *et al.*, 2012; Baeten *et al.*, 2016; Choopanya *et al.*, 2013; CADTH, 2016). In some guidelines, the evidence for PrEP has implications for the utilization of PEP.

Factors Reducing the Efficacy of PEP

HIV PEP is not 100% effective in preventing all potential exposures from becoming infections. Factors that may reduce efficacy and/or pose risks include:

- Delayed initiation;
- Undiagnosed baseline HIV infection;
- Transmission of resistant virus;
- Poor adherence and regimen completion due to side effects; and
- Continued high-risk behaviors.

Evidence supporting the early initiation of PEP as a key factor in efficacy is derived from both animal studies (Tsai *et al.*, 1998; Bourry *et al.*, 2010; Whitney *et al.*, 2014; Irvine *et al.*, 2015) and human studies involving occupationally exposed health care workers (Cardo *et al.*, 1997; Pinto *et al.*, 1997). A recent (2017) retrospective study of 1744 cases of PEP following sexual exposure found that seroconverters

were more likely than non-seroconverters to report later initiation of PEP within the 72-hour window, incomplete medication adherence and methamphetamine use (Beymer *et al.*, 2017). Haidari *et al.*, 2015 conducted a multicenter retrospective case review of PEP failures following sexual exposure that found out of the 19 PEP failures, 18 (95%) were HIV-positive at baseline (point-of-care test negative that were found to be positive for HIV following confirmatory testing).

With respect to drug resistance in Canada, 13.9% of specimens from people newly diagnosed were resistant to at least one drug class and 2.3% were resistant to multiple drug classes according to a 2017 report (Canadian HIV Strain and Resistance Surveillance Program 2012-2013). When examined by exposure category, MSM and injection drug use (IDU) were the exposure categories with the highest drug resistance (16.0% and 18.3%, respectively). Over three-quarters (83.7%) of the specimens with drug resistance were resistant only to one class of medications. The majority of drug resistant specimens (45.0%) were resistant to non-nucleoside reverse transcriptase inhibitors (NNRTI) while 27.1% were resistant to nucleoside reverse transcriptase inhibitors (NRTI) and 11.6% to a protease inhibitor (PI) only. In specimens that were multi-drug resistant (MDR) (e.g., resistant to two or more drug classes), resistance to both NNRTI and NRTI was the most common (12.0% of all specimens with drug resistance). Transmitted resistance to integrase strand transfer inhibitors (INSTIs) was shown to be rare in 2008-2011 (Doyle *et al.*, 2015).

Poor adherence was attributed to 3 of the 7 PEP failures (43%) in a study of 702 subjects who had been exposed to HIV through sexual or injection drug use (Roland *et al.*, 2005). Overall adherence to PEP was determined to be 70% (1902 of 2731 treated patients) based on a recent Canadian prospective cohort study by Thomas *et al.*, 2015. In this study, side effects were responsible for regimen switching in 90% of cases and discontinuation of treatment in 70% of cases.

Among 788 MSM non-occupational PEP users in a recent United States (US) study, subsequent HIV incidence was 2.2 cases per 100 person-years. Incident HIV infection was associated with younger age, being Latino and/or being African American (Jain *et al.*, 2015). Repeated non-occupational PEP use was not associated with incident HIV infection.

In summary, the only quantitative estimate of the risk reduction from HIV PEP in the occupational setting was 81% with ZDV monotherapy (Cardo *et al.*, 1997). Given the newer three-drug regimens currently available, the efficacy of HIV PEP will be considerably higher. However, the quality of evidence for HIV PEP efficacy is low, based on observational studies only, and limited by the ethical considerations of conducting higher quality studies in humans (Canadian Guidelines, 2017).

Considerations for Providing PEP

Safety

The side effects and toxicity profiles of antiretroviral medications must be balanced with the benefits of PEP therapy. Safety data and the real-world experience of clinicians has to be considered in the development of the risk thresholds for PEP.

Cost

Cost effectiveness estimates for HIV PEP programs depend primarily on the exposure route and the prevalence of HIV infection among source persons. While the cost of a 28-day regimen of PEP is approximately \$1500-\$1700 (2017 Canadian or CDN dollars) (based on the cost of brand name drugs) and is publicly funded in most jurisdictions, estimates of the lifetime direct and indirect costs for an HIV-positive individual are approximately \$1.3 million (2009 CDN dollars) according to Kingston-Riechers in 2011. With the availability of generic TDF/FTC in Canada, the cost of a full course of HIV PEP is anticipated to decline to approximately \$500-\$700 (2018 CDN dollars). A retrospective cost analysis from the San Francisco PEP program determined that it was cost effective (defined as less than \$60,000 per quality-adjusted-life year or QALY) with a cost utility ratio of \$12,567 per QALY saved (2000 US dollars) (Pinkerton *et al.*, 2004a). PEP programs were the most cost effective for high-risk exposures such as MSM (\$4,907/QALY) (2000 US dollars). The majority of the HIV infections prevented by PEP were among men and women who reported receptive anal intercourse exposure. In a further San Francisco study, the overall cost utility ratio for the PEP program was \$14,449/QALY (2000 US dollars) and for men seeking PEP after male-male receptive anal intercourse, it was cost-saving (Pinkerton *et al.*, 2004b). Modelling studies in Australia and France indicate cost-savings if PEP is targeted to high-risk exposures (Guinot *et al.*, 2009; Herida *et al.*, 2006). Recently, the use of dolutegravir (DTG) plus backbone was shown to be cost effective in treatment-naïve and treatment-experienced patients compared to raltegravir (RAL) plus backbone and in treatment-naïve patients compared with darunavir/ritonavir (DRV/r) plus backbone and efavirenz (EFV) plus TDF/FTC (Restelli *et al.*, 2017). A cost effective program was defined as having an incremental cost effectiveness ratio or ICER of less than €40,000 per QALY (2014 EU currency) which equates to approximately \$55,000 in Canadian dollars (2014).

Behavior

There is inconsistent evidence that the provision of PEP has led to an increase in risk-taking behaviors. Older literature suggests that awareness, availability and use of PEP was associated with no change or decreased at risk behavior in some populations. However, more recent studies indicate that high-risk behavior continues after PEP and there is a small population level impact of PEP as in Australia (Poynten, 2007). These results showed that an estimated 1-9 HIV infections had been prevented with the provision of PEP compared with 1138 newly acquired infections following high-risk sexual exposures in the same geographical area. Heuket *et al.*, 2012 has demonstrated that MSM recently prescribed PEP had a higher incidence of HIV relative to controls indicating ongoing risk behavior. MSM who use crystal methamphetamine were significantly more likely to seroconvert compared with MSM who did not use crystal methamphetamine (Oldenburg *et al.*, 2015). This group returned more frequently for repeat PEP and was more likely to have unprotected anal intercourse with knowledge of their partner's HIV positive status. Recently, individuals who reported methamphetamine use in the past year were more likely to seroconvert (33%) especially if they also reported they were not adherent to medication (Beymer *et al.*, 2017). Studies demonstrating ongoing high-risk behavior after PEP emphasize the importance of harm reduction referral and risk reduction counselling where appropriate.

Anxiety

Anxiety following an exposure is common and referral to counselling and mental health services is appropriate for psychological support. Anxiety should not impact PEP assessment and should not influence the decision to provide PEP.

Consideration of other HIV Prevention Interventions

PEP should be considered within the context of other HIV prevention interventions. PHAC's evidence synthesis (2017) on the risks of HIV transmission concluded that condoms provide important protection against HIV and other sexually transmitted infections when used correctly and consistently. It has been demonstrated that ART-based viral suppression reduces HIV transmission by more than 96% at the individual and population level (Cohen *et al.*, 2011). More recently, several large randomized controlled trials provide strong evidence for PrEP, the use of certain antiretroviral medications by HIV-uninfected persons at high and ongoing risk of HIV acquisition starting before and continuing after potential HIV exposure events (Baeten *et al.*, 2012; Choopanya *et al.*, 2013; CADTH, 2016; Canadian Guidelines, 2017). Based on the strong evidence supporting these other HIV prevention interventions, HIV PEP should be considered as one of a combination of measures to reduce HIV transmission.

Social and Ethical Considerations for the Provision of PEP

There are a number of social and ethical considerations for the provision of PEP as a standard of care in Alberta. Considerations are based on both factual information and evaluative judgments where factual information was unavailable. Some of the considerations in the development of this document include:

- PEP can preserve life and health;
- Timely PEP is currently the most effective way of reducing the risk of acquiring HIV infection in an individual who has been exposed to the virus;
- Alberta's guidelines are founded on the principle of equity;
- Alberta's guidelines are based on clinical considerations of risk while recognizing considerations for the psychological impact of PEP;
- Alberta's guidelines reduce financial or administrative barriers to PEP;
- Alberta's guidelines are built on the principles of informed choice;
- PEP has been established as a standard of care in Alberta and there is no evidence to support a change to this standard of care. Withdrawing this standard of care is not appropriate; and
- Alberta supports provision of PEP, when indicated, to people who have had accidental and consensual exposures.

Risk of HIV Transmission and Factors Influencing Risk

The HIV transmission risk for a single-exposure event is determined by:

$$\text{RISK OF HIV TRANSMISSION} = \text{RISK PER EXPOSURE} \times \text{RISK THAT THE SOURCE IS HIV POSITIVE}$$

The estimated risk of HIV transmission by exposure type from a known HIV positive source with a detectable viral load is shown in the Appendix, Table 1, page 50.

When the HIV status of the source is unknown, the HIV risk of exposure may be inferred from the estimated probability of being HIV positive when the source is known to be in a major risk group or not known to be in a major risk group, based on British Columbia's published data, as given in the Appendix,

Table 2, page 51. PHAC has estimated the prevalence of HIV in Alberta to the end of 2016 to be 5,479 individuals (range: 4,800-6,160). In 2017, Alberta's HIV diagnostic rate was 6.5 per 100,000 population (source: IHDA) which is comparable to the national rate in 2016 (6.4 per 100,000 population) (Bourgeois *et al.*, 2017). HIV risk assessment was estimated using British Columbia's published community prevalence estimates for the highest risk group (e.g., MSM) which will provide an acceptable proxy for assessing the risk of HIV acquisition in Alberta (Appendix, Table 3, page 52).

In addition, there are other factors that may increase the risk of HIV transmission that should be accounted for in the HIV risk assessment (Table 1, page 9).

Suppressed Viral Load

The HPTN 052 study, a RCT in heterosexual serodiscordant couples, demonstrated a 93% lower risk of linked HIV transmission with suppressive ART after five years of follow-up (Cohen *et al.*, 2016; Safran *et al.*, 2015; Cohen *et al.*, 2011). All transmission events occurred before viral suppression was reached or after virologic failure. The PARTNER study demonstrated no transmissions when the HIV-positive partner maintained a suppressed viral load (< 200 copies/mL) with ART in spite of a large number of condomless sex acts with serodiscordant partners (22,000 acts in MSM; 36,000 acts in heterosexuals) (Roger *et al.*, 2016; Roger *et al.*, 2014). The OPPOSITES ATTRACT study also showed no transmissions in MSM couples having condomless sex (5905 acts) when the HIV-positive partner maintained a suppressed (< 200 copies/mL) viral load on ART (Grulich *et al.*, 2015).

Based on this evidence, the source viral load should only be considered in the risk assessment process for consensual sexual exposures and should be done in consultation with a clinician knowledgeable about HIV. In order for a source to be considered to have a 'suppressed viral load' for the purposes of the risk assessment, the source needs:

- 1- Most recent serum viral load must be < 40 copies/mL (< 1.84 log₁₀) and tested within the last six months; AND
- 2- No current other STIs at the time of exposure; AND
- 3- Stable on ART (as determined by a clinician knowledgeable in HIV) with no indication of issues impacting, or potentially impacting, medication adherence.

When in doubt about the viral load of the source, its interpretation, or application to the risk assessment process- the remaining criteria should be used in the risk assessment process.

This updated guideline does not recommend PEP for individuals who have had a consensual sexual exposure from a source who is known to be HIV-positive but has a suppressed viral load.

These guidelines have adopted the use of viral load < 40 copies/mL threshold to define undetectable viral load. This is consistent with the Canadian Guidelines, 2017 that have been clarified on this issue (Clarification, Canadian Guidelines, June 25, 2018). The basis for the definition of undetectable viral load < 40 copies/mL is that it is the most commonly used definition in clinical care in Canada. However, it is acknowledged that numerous studies on viral load used different thresholds most often < 200 copies/mL.

Clinical discretion is advised where there are interim fluctuations in the viral load and consultation with an HIV specialist should be sought if there is uncertainty regarding interpretation or implications of viral load test results.

For situations other than consensual sexual exposures, it is possible that the same principles of viral load suppression and risk of HIV transmission also apply. However, there is currently no data to support applying this principle to other blood and bodily fluid exposures (e.g., needlestick injuries or traumatic sexual assault) at this time.

Consensual Exposure to HIV

Infrequent Consensual Exposure

HIV post-exposure prophylaxis should be provided (where indicated within this guideline) to persons exposed to HIV as part of their personal lives (e.g., consensual adult sex or sharing drug injection equipment). PEP is recommended in situations where there is a significant exposure from a known HIV-positive source or from a high-risk but unknown HIV status source. Examples of situations that may prompt a request for PEP include: condom slippage, breakage or condomless sex, unsafe needle sharing, and accidental exposure in serodiscordant partners.

Repeated Consensual Exposure

The use of HIV PEP for repeated consensual risk-taking behaviour (e.g., occupational sex trade workers, MSM with several partners engaging in unprotected sexual exposures and injection drug use with significant needle-sharing activities) must be considered within the context of other primary prevention strategies. Evidence from three retrospective cohort studies indicates that discrete high-risk groups prescribed PEP at no cost were more likely to continue sexual risk behavior and subsequently acquire HIV relative to the same high-risk groups not prescribed PEP (Mitchell *et al.*, 2017, Heuker *et al.*, 2012, Zablotska *et al.* 2011). Studies by Beymer *et al.*, 2017 and Oldenburg *et al.*, 2015 demonstrate that patients who report methamphetamine use are more likely to seroconvert after PEP following a sexual exposure compared to those who had not used methamphetamine.

In circumstances of ongoing consensual exposure to HIV or repeat presentation for PEP, Alberta's recommendation is to consult with a physician knowledgeable in HIV prevention. These individuals should be referred to Alberta's STI clinics and/or infectious disease physicians for comprehensive HIV prevention interventions including risk reduction counselling and discussion regarding suitability for PrEP.

Persons who engage in frequent and ongoing high-risk behaviors that require PEP more than once, may be considered for PrEP at the end of the 28-day course of PEP in consultation with a physician knowledgeable in HIV prevention. PrEP can be started immediately after completion of PEP where appropriate.

Pre-Exposure Prophylaxis (PrEP)

Eligibility criteria for PrEP varies significantly between jurisdictions (CADTH, 2017). It is acknowledged that consideration for PrEP in individuals taking PEP is a new policy area and will require further analysis. Individuals who are currently on PrEP and who present with a BBFE, should be referred to their prescribing physician for a risk assessment following a potential high-risk exposure to HIV.

The clinical guidelines on the use of PrEP is available at:

<https://www.albertahealthservices.ca/assets/info/hp/srh/if-hp-srh-hiv-prep-guidelines.pdf>.

Information on the Alberta HIV PrEP Program commencing October 1, 2018 may be found at:

<https://www.albertahealthservices.ca/info/Page16048.aspx> .

Management of HIV PEP

Management of the Exposed Site

Body sites, wound and skin exposed to potentially infectious fluid should be cleansed immediately with soap and water. Alcohol, hydrogen peroxide, bleach or other chemical cleansers/antiseptics/disinfectants should be avoided. No attempt to “milk” the wound should be made. Squeezing the wound may promote hyperemia and inflammation at the wound site, potentially increasing exposure if HIV is present in the contaminating fluid. Allow injury/wound site to bleed freely, and then cover lightly. Exposed mucous membranes (including the eyes) should be flushed with water or normal saline.

Recommendations for Prescribing PEP

A risk-benefit analysis should be conducted for every individual after a significant blood or bodily fluid exposure to inform the decision to provide PEP. A decision to initiate PEP should consider the risk of transmission following an exposure event, the risk of the source being HIV-positive or from a major risk group and other factors such as high viral load in the source. See the **ALGORITHM** (Figure 1, page 8) for management of HIV post-exposure prophylaxis following a blood or bodily fluid exposure which includes a starter pack initiation in an acute care setting and/or a detailed HIV risk assessment by a physician knowledgeable in HIV in a non-acute care setting.

These guidelines use the following transmission risks to determine if PEP is indicated:

- If risk is about 1/1000 (0.1%) or greater, PEP is generally recommended;
- If risk is between 1/1000 and 1/10,000 (0.01%), PEP is considered on a case-by-case basis if there are other factors that may increase the risk of transmission (Table 1, page 9); and
- If risk is 1/10,000 and below, PEP is not generally recommended.

The recommendations are summarized in Tables 3A and 3B, **PEP RECOMMENDATIONS** (page 11-12) for HIV.

Assessment of the Exposed

Initiate a PEP starter pack immediately for the exposed if PEP is recommended in the risk assessment in an acute care setting followed by a rapid referral to a physician knowledgeable in HIV for a detailed risk assessment (Figure 1, page 8). A physician knowledgeable in HIV conducts the detailed risk assessment to initiate or continue PEP in a non-acute care setting.

It is recommended that baseline HIV serology be completed for all individuals not previously known to be HIV positive. If the exposed is known to be HIV positive, PEP is not indicated. HIV-positive individuals should be managed in accordance with Alberta Health’s Public Health Disease Management Guidelines available here [human-immunodeficiency-virus](#). The use of ART for patient management in known HIV-positive individuals should be done in conjunction with a physician knowledgeable in HIV.

If the exposed person develops illness consistent with acute HIV seroconversion (e.g., fever, headache, rash and lymphadenopathy) within 4 to 6 weeks of the exposure, a HIVQUAL (qualitative viral load test) may be considered.

A lack of HIV test results for the exposed should **not** prohibit the timely initiation of PEP therapy where a high-risk transmission event has occurred.

Assessment of the Source

Every effort should be made as early as possible to determine the HIV status of the source (ideally with a rapid point of care test) wherever it is available. For example, nearly all occupational exposures involve known sources. Information regarding risk factors may be obtained with permission along with HIV baseline testing, whenever possible. If the source's baseline HIV test is negative, prophylaxis is not needed.

In situations with a known HIV positive source and a consensual sexual high-risk exposure, a quantitative HIV viral load test (e.g., HIVQUANT) should be requested at the time of the exposure or consent sought to check Netcare records. Where the source is known and available, the health care provider should obtain consent (if not already obtained) to access medical records related specifically to the assessment of risk of transmission to the exposed including:

- HIV viral load test results, if source is known to be HIV-positive;
- Antiretroviral use;
- Drug resistance test results;
- Serology for hepatitis B and hepatitis C test results; and
- STI testing where applicable.

Viral load is factored into the detailed risk assessment by the physician knowledgeable in HIV. The risk of transmission from an HIV positive source who is receiving ART is reduced depending on the viral load of the source in the appropriate context. **The issue of viral load in an HIV positive source should be considered in the context of a consensual sexual situation and not in the context of non-consensual sexual situations or occupational exposures due to a lack of direct evidence.** When a person with HIV is on ART, takes their medications consistently as prescribed and maintains a confirmed suppressed viral load, there is effectively no HIV transmission risk to their sexual partners (Tam T. and Morrison H. Statement on behalf of the Council of the Chief Medical Officers of Health, November 30, 2017; LeMussurier *et al.*, 2018). When the viral load is less than 40 copies (detection limit of current assays), then, PEP should generally be discontinued (or not provided) for consensual sexual exposures. Viral load is generally not taken into account in situations of non-consensual sexual or occupational exposures as the evidence is lacking and PEP should be continued, if warranted, for 28 days. Although the risk of transmission from an occupational exposure from a source with an undetectable plasma viral load is recognized to be very low, recent guidance recommends that PEP should still be offered (Kuhar *et al.*, 2018). Plasma viral load reflects cell-free virus in peripheral blood; there can be persistence of HIV in latently infected cells, even though the patient is taking ART as prescribed.

If the source's HIV status is known to be HIV negative, but had recent high-risk activity or symptoms suggestive of acute HIV seroconversion (e.g., window period), then, **PEP should be initiated immediately and continued for 28 days.**

When the source's HIV status is unknown but known to be from a major risk group, PEP may be indicated for high-risk exposures or provided on a case-by-case basis depending on the relative level of risk. In these circumstances, the risk of exposure can be estimated from local prevalence data within a high-risk group and the type of exposure (Appendix, Table 3, page 52).

These guidelines define individuals at high-risk for being HIV-positive as:

- Injection drug use;
- MSM;
- Time in endemic country;
- Hepatitis C positive;
- History of incarceration; and/or
- Partners of known or suspected HIV-positive individuals.

The physician knowledgeable in HIV should provide the exposed with comprehensive HIV prevention interventions that may include risk reduction counselling and evaluation for PrEP (e.g., if PEP was prescribed more than once).

Needlestick Injury in the Community Setting

The risk of HIV transmission from discarded needles in the community, particularly to exposure to dried blood on syringes, is extremely low (Zamora *et al.*, 1998). PEP is rarely indicated for cold needlesticks in the community.

Human Bites

The risk of HIV transmission through human bites is generally considered to be very low if saliva is not contaminated with blood; blood-stained saliva represents a potentially greater risk (CDC, 2016). For bites with visible blood in the saliva, HIV PEP is indicated for the individual exposed to blood, either the bitten individual, the biter, or both, when the source is known HIV positive or on a case-by-case basis when the source is from a major risk group.

Timing of PEP

PEP should be started **AS SOON AS POSSIBLE**. Ideally PEP should be started within 1 to 4 hours of the exposure, and no longer than 72 hours, as efficacy declines with time. The evidence base is from animal studies. A recent (2015) meta-analysis of 25 nonhuman primate studies found a significant association between the timing of PEP and seroconversion providing further evidence supporting the importance of initiating PEP as early as possible following exposure (Irvine *et al.*, 2015). In a pathogenesis study, initiation of combination ART treatment was shown to be more effective in reducing viral dissemination and replication in all tissues when initiated early after infection (Bourry *et al.*, 2010). These studies are consistent with earlier studies that demonstrated greater efficacy the sooner PEP is

administered (Tsai *et al.*, 1998; Otten *et al.*, 2000). However, it is unlikely to be of benefit if administered more than 72 hours post exposure (Otten *et al.*, 2000).

The first study to demonstrate that a delay in PEP initiation for sexual exposures is associated with seroconversion was published by Beymer *et al.*, 2017. This study determined a 3-fold increased odds of seroconversion for individuals who initiated PEP 48 hours or more after exposure compared with individuals who initiated PEP within the first 48 hours after exposure. These findings corroborate that timing of PEP is an important predictor of seroconversion. The authors noted that best practice in New York State guidelines was to administer the first dose of medication at the beginning of the visit to decrease the exposure to dose interval.

The majority of national and international guidelines recommend an upper limit of 72 hours for PEP initiation. In a 2014 study, ART was initiated on day 3 following an intrarectal inoculum of simian immunodeficiency virus (SIV) in rhesus monkeys. This blocked emergence of viral RNA and proviral DNA in peripheral blood, lymph nodes and gastrointestinal tract but on discontinuation of ART after 24 weeks, all animals exhibited viral rebound. The study shows that the viral reservoir is seeded very early following mucosal SIV infection of rhesus monkeys and prior to viremia. This evidence supports the 72-hour maximum window for PEP administration as well as efforts to administer PEP as soon as possible after infection.

Alberta recognizes the 72-hour limit for PEP consistent with the majority of guidelines but recommends administering the first dose as early as possible after exposure since this may lower the likelihood for seroconversion.

Duration of PEP

The recommended duration of PEP based on animal data (Tsai, 1998) and efficacy in occupational studies (Cardo, 1997) is **28 days** (Canadian Guidelines, 2017). All of the guidelines reviewed support the 28-day course of PEP including Alberta's guidelines.

In situations where ≥ 72 consecutive hours of HIV PEP medications have been missed, stopping PEP should be considered (Canadian Guidelines, 2017).

Choice and Number of Antiretroviral Drugs used for PEP

The 2014 World Health Organization (WHO) guidelines for post-exposure prophylaxis developed recommendations that recognize the need to simplify risk assessment and prescribing practices across all exposures (Ford and Mayer, 2015). Based on strong evidence of improved tolerability and adherence rates of newer three-drug regimens, almost all of the guidelines currently advise a triple therapy regimen. However, there is no evidence to support the greater efficacy of three drugs over two drugs for HIV PEP. The Canadian guidelines (2017) recommend three antiretroviral agents as the standard PEP regimen to be used whenever PEP is indicated. Estimates of HIV transmission risk per act vary in the literature and are difficult to interpret due to other risk factors. Data on provincial practice over the last three years indicates that practitioners are already prescribing a three-drug regimen containing Truvada® (tenofovir disoproxil fumarate/emtricitabine) combined with an INSTI in most individuals who present for HIV PEP. Given the evidence on tolerability and safety profiles of new drugs and other considerations, the expert committee supports a universal three-drug PEP regimen for all age classes and special populations to

make the guidelines easier to interpret and use for health care providers especially in emergency situations and in remote communities.

Nucleoside Reverse Transcriptase Inhibitors (NRTI)

A fixed dose generic combination tablet of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) is recommended as the NRTI backbone for the treatment of HIV in adults and in pregnancy based on virologic efficacy, tolerability, safety, adherence and convenience (once daily dosing).

Evidence from a RCT evaluating a three-drug regimen consisting of TDF/FTC and raltegravir (RAL) demonstrated that side effects were significantly less common than those reported by historical controls, who used a three-drug regimen with ZDV, lamivudine (3TC), and a boosted PI. A systematic review of drugs used in PEP in adults demonstrated the safety, tolerability and efficacy of newer backbone drugs for PEP including TDF, FTC and 3TC (Ford *et al.*, 2015). A prospective cohort study demonstrated that patients taking three-drug TDF/FTC based regimens were significantly more adherent (72% adherent) as compared with ZDV/3TC based regimens (59% adherent). This was attributed to better tolerability of TDF/FTC based regimens relative to ZDV/3TC based regimens. Tenofovir and emtricitabine also demonstrate good genital tract penetration in animal models (Le Grand *et al.*, 2000) and in human studies (Taylor *et al.*, 2010). High efficacy rates for TDF/FTC have been shown in PrEP studies in high-risk heterosexuals (Baeten *et al.*, 2012, Thigpen *et al.*, 2012), MSM (Grant *et al.*, 2010) and in injection drug users (Choopanya *et al.*, 2013).

These studies form the basis of the recommendation that TDF/FTC (coformulated in generic form) be the preferred backbone for HIV PEP consistent with the Canadian Guidelines (2017) and most jurisdictional guidelines. However, TDF has been associated with declines in kidney function and reductions in bone mineral density with long-term use; this is unlikely to be clinically significant with short-term use for PEP (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2018).

Integrase Strand Transfer Inhibitors (INSTI)

An INSTI and two NRTIs is the recommended initial regimen for treatment for most people with HIV that takes into consideration virologic efficacy, favorable tolerability and toxicity profiles, drug-drug interactions and ease of use (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2018). Generally, an INSTI-based regimen is considered highly effective, has few adverse effects and has no significant cytochrome p450 associated drug interactions (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2018). When INSTIs are compared head-to-head with boosted PIs, the INSTI is typically better tolerated with fewer treatment discontinuations (Molina *et al.*, 2015). The mode of action for INSTI drugs is that they act before viral integration with cellular DNA to prevent the establishment of HIV infection. For these reasons, an INSTI was selected as the recommended third drug class for the first-line PEP regimen.

In 2007, RAL was the first INSTI licensed by Health Canada and the US Food and Drug Administration (FDA) for the treatment of HIV. The advantages of RAL include potent antiviral activity, limited drug-drug interactions, good tolerability and the most extensive post-marketing experience. RAL has been shown to have a longer post-infection efficacy window supporting its use in HIV PEP regimens (Marsden *et al.*, 2012). Recently, the efficacy of once-daily RAL 1200 mg (formulated as two 600-mg tablets) was

compared to RAL 400 mg twice daily, each with TDF/FTC, and showed similar responses in nonpregnant adults.

Dolutegravir (DTG) is a second-generation integrase strand transfer inhibitor with a plasma half-life of 14 hours, which supports once-daily dosing. There is no relevant induction of cytochrome P450 or food effect and low potential for drug-drug interactions. It is on the list of preferred agents for HIV PEP medications in combination with TDF and FTC in the majority of guidelines. It has a higher genetic barrier to resistance than other INSTIs and has proven efficacy based on multiple clinical trials.

Overall, clinical trials using DTG for treatment of HIV indicate that DTG is well tolerated. The most common side effects associated with DTG were nausea, headache and diarrhea with $\leq 1\%$ of patients developed serious adverse events that were treatment related and $\leq 3\%$ of patients discontinued treatment related to adverse events. Adverse reactions associated with treatment discontinuation were either similar or lower than comparators, supporting its efficacy.

The adherence and safety of DTG (50 mg daily) with TDF/FTC has been studied as three-drug HIV PEP in 100 gay and bisexual men in Australia (McAllister *et al.*, 2017) at three sexual health clinics and two emergency departments. PEP completion rate was 90% (95% confidence interval from 84% to 96%). Adherence to PEP was 98%. Although the sample size is small, DTG as daily PEP was well tolerated, safe and demonstrated high completion rates and levels of adherence to medication.

There is sufficient practical real-world experience with DTG in Alberta in support of the decision to recommend DTG as the preferred third drug in combination with generic TDF/FTC in adults and adolescents (aged 12 years and older). In remote communities, where DTG may not be available, RAL may be used. Alberta's recommended regimen for PEP in **ADULTS and ADOLESCENTS** is outlined in Table 4, page 13.

Children

Recommendations for ART regimens for treatment in children differ from adults. The US Panel recommends an ART regimen with three drugs, including either a boosted-PI or INSTI or NNRTI plus a dual NRTI backbone (Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, 2018). Based on the extensive experience and excellent safety history, there is a recommendation for ZDV in combination with 3TC or FTC as a preferred NRTI backbone in treatment-naïve infants and children from birth to ≤ 12 years of age (Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, 2018). Pediatric drug recommendations typically include both age and weight restrictions, however, body weight is the preferred determinant when choosing a specific drug. Age should be used only as an approximate guide. Based on potency and tolerability studies in adults and children, the US Panel recommends ritonavir-boosted Lopinavir (LPV/r) for infants aged ≥ 14 days to < 2 years. Raltegravir is licensed by the FDA for the treatment of infants and children weighing ≥ 2 kg and can be started at birth. Dolutegravir has been approved in the US for use in children weighing ≥ 30 kg.

Recommended HIV PEP regimens in **CHILDREN** for both sexual or parenteral exposures are outlined in Table 5, page 14. No alternative agents are provided as allergy is not likely in this setting and it is highly unlikely that a child in this situation would have another contraindication. Additional information on adverse events and dosing may be found in references noted in Table 5.

Pregnancy

PEP is indicated at any time during pregnancy when a significant exposure has occurred. It is recommended to consult with a physician knowledgeable in HIV care or an infectious disease specialist physician when using ARVs during pregnancy.

On May 18, 2018, safety alerts were issued by the US HHS Joint Antiretroviral Guideline Panels, the FDA, the CDC and other agencies regarding potential fetal harm from exposure to DTG. The concern was from preliminary results released from an ongoing observational study in Botswana that demonstrated women who received DTG at the time of conception or early in the first trimester appear to be at higher risk of NTDs (World Health Organization, May 18, 2018). The FDA alert noted that in the Botswana study, there were no reported cases of babies born with NTD to women starting on DTG later in pregnancy. Over the next few months, data from this study and other investigations will provide further information about the safety of DTG in infants born to women taking DTG for HIV treatment.

Further to these interim statements, recommendations regarding the use of DTG in women who are pregnant or of childbearing potential were released by the US HHS Joint Antiretroviral Guideline Panels on May 30, 2018. These recommendations acknowledged the uncertainty in CDC's interim recommendation for RAL as the preferred regimen for HIV PEP in pregnant women. The May 30, 2018 recommendations state 'it is not clear if DTG is the only integrase strand inhibitor (INSTI) with the potential to cause NTDs, or if other INSTIs also carry the risk (e.g., a class effect). Although there have been no reports of NTDs associated with taking DTG or other INSTIs near the time of conception in the prospective portion of the US Antiretroviral Pregnancy Registry, the Registry is based on voluntary reporting and the number of reported INSTI exposures near the time of conception is relatively small.'

Recommendations from the Panel on Antiretroviral Guidelines for Adults and Adolescents and the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission were updated to respond to preliminary evidence on DTG and the association with neural tube defects in December 7, 2018. Based on these updated guidelines and expert opinion, Alberta's recommendation in pregnancy is:

- Following a sexual exposure, those who may be pregnant, should be tested for pregnancy. If possible, this result should be documented prior to HIV PEP initiation; however, PEP initiation should not be delayed pending the results.
- DTG should not be initiated in an HIV-exposed individual who is pregnant less than or equal to 14 weeks from LMP or those who are not using effective birth control.
- The preferred HIV PEP regimen in women less than or equal to 14 weeks from LMP is darunavir/ritonavir (DRV/r) with TDF/FTC and consultation with an HIV expert is recommended.
- In instances of sexual assault (or otherwise), where measures are being taken to prevent pregnancy, DTG may be used following a conversation with the client about potential risks.
- In women who are more than 14 weeks from LMP, DTG plus TDF/FTC is the preferred regimen but the benefits and risks of using DTG, including the possible risk of NTDs, should be discussed with the patient.

The preferred NRTI backbone for the treatment of HIV in pregnancy is TDF in combination with FTC or 3TC (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2018; British Columbia's HIV PEP Guidelines, 2018, CDC, 2016; New York State Department of Health AIDS Institute, 2018).

DTG has been classified as a preferred INSTI for the treatment of HIV in pregnant women after the first trimester based on pharmacokinetic, safety and efficacy data (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, December 7, 2018). There are no safety problems identified when DTG is initiated during pregnancy (e.g., after 14 weeks gestational age from LMP). However, preliminary data from Botswana suggest that there is an increased risk of NTDs in infants born to women who were receiving DTG at the time of conception. It is not yet known if other INSTIs pose a similar risk of NTDs (e.g., class effect). DTG is administered once daily. It is useful when drug interactions with PIs are a concern. In non-pregnant adults, it is associated with lower rates of INSTI drug resistance compared to RAL, and is suggested for women with acute infection in pregnancy. There are specific timing recommendations when taken with calcium or iron.

DRV/r is a preferred PI drug for the treatment of HIV in pregnant women based on efficacy studies in adults and experience with use in pregnancy (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2018). Pharmacokinetic data is available. There is increasing experience with use in pregnancy and it is recommended in pregnancy in the Canadian Guidelines (2017) when taken once daily. According to the PEPDar study, DRV/r is better tolerated than LPV/r for HIV PEP but has considerable potential for drug interactions (Fätkenhauer *et al.*, 2016). It has advantages if there is potential drug resistant virus in the source or if the exposed is suspected to have acute infection. It provides a PI-based regimen for patients who may have concerns with the potential class effects of INSTI-based regimens in pregnancy.

A phase IV clinical trial (PANNA) tested pharmacokinetics, safety and efficacy of RAL in HIV-1-infected pregnant women (Blonk *et al.*, 2015). In addition, data from 2001 to 2015 including 278 maternal-infant pairs who received RAL during pregnancy was reviewed (Maliakkal *et al.*, 2016). RAL is a preferred INSTI for the treatment of HIV in pregnant women based on an increasingly large base of available pharmacokinetic, safety and other data (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2018; Canadian Guidelines, 2017). However, given the uncertainties with RAL noted above, class effects problems for risk adverse patients and operational simplicity, the expert group opted for an alternative to an INSTI early in pregnancy.

The ART regimens for PEP during **PREGNANCY** are outlined in Table 6, page 15.

Breastfeeding

The recommendation to initiate PEP in the breastfeeding patient presents several concerns. Both HIV and ARV drugs may be found in breast milk and breastfeeding should be avoided for three months after the exposure to prevent HIV transmission to the infant and potential ART-related drug toxicities (Canadian Guidelines, 2017, New York State Department of Health AIDS Institute, 2018). If HIV infection can be definitely ruled out in the source person prior to three months post-exposure, then, breastfeeding can resume. Clinicians should discuss the risks and benefits with the patient and the infant's pediatrician should be informed of any potential exposure to HIV or ART medications.

Dispensing of HIV PEP

Starter kits with an adequate supply of antiretrovirals should be provided to the patient and continued until follow up with a physician knowledgeable in antiretroviral therapy is possible and a prescription can be filled. This could be anywhere from 3 to 7 day supply.

In some Alberta Health Services' zones, current practice has been to dispense the remaining 21 day supply of medication to the patient at the first follow-up visit once the physician has determined there is good tolerability and no other concerns. This is a reasonable approach given the improved tolerability and safety of current regimens compared with previous regimens (e.g., PIs). This change in dispensing practice may overcome the barrier posed by the need to return frequently for follow-up and medication dispensing in some patients. If tolerability or adherence concerns exist, a one week dispensing practice will allow for ongoing adverse event monitoring, clinical care and decreased wastage.

Based on Alberta's experience, poor adherence remains an issue in children. Current practice is to prescribe drugs for one-week-at-a-time initially since many children/parents stop the drugs after a few days thereby wasting the drugs. The remainder of the 28-day course is prescribed at their first clinical visit pending an assessment of tolerability.

A systematic review of randomized clinical trials and observational studies have demonstrated that dispensing a full course of HIV PEP versus a starter pack at the initial presentation is associated with fewer refusals and higher PEP completion rates (Ford *et al.*, 2015) although the overall quality of evidence is low. In our experience, PEP starter packs are often accessed in emergency departments and require a physician knowledgeable in HIV prevention to provide follow-up monitoring and support. Based on current practice and national guidance on dispensing, a maximum 21-day supply of HIV PEP should be dispensed at the first follow-up physician visit pending good tolerability and adherence.

Education

Patients should be counselled on the efficacy, benefits and side effects of antiretroviral therapy as well as the lack of efficacy especially if initiated later in the 72-hour maximum window. The importance of adherence to the 28-day treatment regimen in order to prevent PEP failure or drug resistance must be made clear to all patients. The need to reduce risk (e.g., by practicing safer sex, using clean needles, preventing occupational exposures, etc) and prevent transmission to others should be emphasized. Referral to harm reduction services, addiction services and mental health services, or infection prevention education and services, should be conducted as appropriate.

Follow up of Patients Prescribed HIV PEP

Ideally, a physician experienced in prescribing ART should follow patients continuing on HIV PEP. Initial PEP will most often be started in emergency departments with dispensing of starter kits to the patient until a physician knowledgeable in HIV can assess the patient and provide ongoing care.

Baseline and follow-up testing should be done in accordance with the **TESTING RECOMMENDATIONS** section, Table 2, page 10. Testing recommendations for children remain the same as for adults. Arrangements for follow-up care will vary by region.

Hepatitis B Virus (HBV)

HBV is highly infectious and estimated to be about 100 times more infectious than HIV and 10 times more infectious than HCV (MMWR, 2013). Blood from persons with an HBV infection contains the highest HBV titres of all bodily fluids and is the most important fluid capable of transmission in the health care setting (MMWR, 2013). HBV remains infectious on surfaces for at least seven days (MMWR, 2013). The estimated risk of transmission from a needlestick injury when the source is HBsAg positive and HBeAg positive is approximately 37-62% and between 23-27% when the source is HBsAg positive and HBeAg negative (Mast et al., 1993). The risk of HBV transmission from a sexual exposure is not well quantified.

Post-exposure management of percutaneous or mucosal exposures to HBV should consider several factors including the immunization and antibody status of the exposed person and the infectious status (if known) of the source person (Canadian Immunization Guide, 2018). Using these factors, a summary of **HBV PEP** is shown in Table 7, page 16 and Table 8, page 17. Recipients who demonstrate immunity will not require HBV PEP. Immunity is demonstrated by positive anti-HBs or anti-HBc total positive only (HBsAg negative).

The hepatitis B vaccine is the most important intervention for post-exposure prophylaxis and provides 90% of the protection from HBV (Canadian Immunization Guide, 2018). Passive short-term immunity with hepatitis B immune globulin (HBIG) provides some additional protection. The hepatitis B vaccine is offered at no cost to eligible individuals as part of Alberta's publicly funded immunization program. HBV PEP should be offered to susceptible individuals exposed through:

- Percutaneous or mucosal exposures to BBF capable of transmitting HBV; and
- Sexual contacts of an acute or chronic carrier of HBV.

HBV susceptibility includes individuals who are both anti-HBs negative and HBsAg negative OR both anti-HBc total negative and HBsAg negative.

Decisions about HBV PEP are made using the available information about the source, the exposed and the exposure incident.

1. Source is known and timely laboratory testing is available:

When the source is known and available for laboratory testing with results within 48 hours, serological testing for hepatitis B active infection should be done. If negative, HBIG would not be needed for the exposed. However, depending on individual situations hepatitis B vaccine should be considered for the exposed to provide future protection from hepatitis B.

Testing of the source person should be consistent with the [Public Health Disease Management Guidelines- Hepatitis B](#).

2. Source is known but NOT available for timely laboratory testing:

The source should be assessed for the following risk factors (If risk factors are present, the source would be considered "High-risk"):

- Multiple sexual partners;
- Men-who-have-sex-with-men;
- Sexual partner infected with HBV;
- Close family contact with HBV infected individual;

- History of injection drug use;
- Immigration from a HBV endemic country (prevalence $\geq 8\%$); and
- History of blood transfusions prior to 1970.

3. **Source is unknown:**

- Source may be considered “High-risk” based on clinical discretion.

Refer to the Alberta Immunization Policy, [Biological Products](#), for further information on the HBV vaccine and for further information on HBIG.

The management of the exposed person is summarized below in both text and tables. Individuals demonstrating immunity do not require HBV PEP.

- HBV vaccine humoral immunity has been demonstrated to persist for at least 30 years among healthy vaccinated individuals who initiated hepatitis B vaccination over six months of age (Bruce *et al.*, 2016).
- **Individuals exposed to source with High-risk for HBV:** see Table 7, page 16
 - When indicated, both HBIG and the first dose of the HBV vaccine should be ideally administered to susceptible individuals **within 24 hours of exposure** (New York State Department of Health AIDS Institute, 2018) or generally within **48 hours of exposure** (Canadian Immunization Guide, 2018);
 - For sexual exposures with an acute case or chronic carrier of HBV, a single dose of HBIG and the first dose of the HBV vaccine should be given within **48 hours** of exposure, but may be given up to 14 days following the exposure (Canadian Immunization Guide, 2018);
 - For percutaneous or mucosal exposures to blood or bodily fluids potentially containing hepatitis B virus, HBIG should be given within **48 hours of exposure**, and the first dose of the HBV vaccine but may be given up to 7 days following the exposure (Canadian Immunization Guide, 2018); and
 - HBIG may be given at the same time as the HBV vaccine but at different injection sites using separate needles and syringes (Canadian Immunization Guide, 2018).
- **Individuals exposed to source with Low Risk for HBV:** see Table 8, page 17
 - Community needlestick injury exposures (when the source is unknown or has no identified risk factors) are generally low risk and may be managed with the hepatitis B vaccine only;
 - HBV transmission through bites is possible. Both the individual being bitten and the one engaging in biting are at risk of HBV exposure and should be assessed;
 - If the exposure is non-bloody saliva HBV vaccine only is indicated;
 - If there is visible blood in the saliva both HBIG and HBV vaccine are indicated for both the bitten individual and the biter; and
 - Even if the exposure is not deemed significant, HBV vaccination should still be recommended for all non-HBV-immune persons as it is expected that a majority of individuals who will present for PEP will meet the indications for provincially funded HBV immunization.

Pregnant women can safely receive both the HBV vaccination and HBIG.

There are no current antiviral agents recommended for HBV post-exposure prophylaxis.

Susceptible exposed persons should be counselled on risk reduction and measures to prevent transmission to others until the vaccine series has been completed and immunity has been confirmed.

Hepatitis C Virus (HCV)

While HCV is transmitted more efficiently by the parenteral route than HIV, it is transmitted by sexual contact much less efficiently than either HBV or HIV. The transmission probability for HCV from a needlestick exposure is approximately 1.8% (range 0-7%) (Alter, 1997).

For HCV, risk factors include:

- History of receiving multiple blood transfusions of blood or blood products prior to 1992;
- History of injection drug use including the sharing of injection drug use paraphernalia with a person known to be infected with HCV;
- Potential exposure to a person known to be infected with HCV especially with activities where blood is present such as razor/toothbrush sharing;
- Multiple sexual partners especially sex involving blood/mucosa exposures; and
- HIV co-infection.

However, individuals without detectable HCV RNA have an extremely low/negligible risk of transmitting HCV (Terreault, 2002).

Currently, there is no effective post-exposure prophylaxis for HCV but there are new and effective treatments for hepatitis C infections. In addition, some individuals infected with hepatitis C will spontaneously clear the virus on their own, usually in the first few months after infection, and without treatment.

Management of a potential HCV exposure includes:

- Baseline anti-HCV testing of the exposed individual immediately after exposure;
- If anti-HCV is not detectable at baseline, test the exposed person with HCV RNA assay at 6 weeks post-exposure. If they test HCV RNA positive, the exposed individual should be referred to an infectious disease or gastroenterology/hepatology specialist for further assessment within 1-3 months of new diagnosis.
- If anti-HCV is detectable, the HCV RNA status of the exposed individual should be confirmed and no further action regarding the exposure is required, but referral to a physician specializing in treatment for hepatitis C is indicated.

If infection persists after 3 months, then treatment should be considered.

Sexually Transmitted Infections (STIs)

Uninfected persons may or may not acquire STIs when exposed to an infected sex partner. Many factors increase the probability of transmission, including:

- the virulence of the pathogen;
- high concentration of the pathogen in semen or other genital fluids;
- presence of another STI in either the infected or susceptible person;
- type of sexual act;
- cervical ectopy;
- no condom during sexual act;
- no use of microbicides; and
- trauma associated with the sexual act.

PEP for STI prophylaxis should be considered in situations where vaginal, oral or anal penetration has occurred including consensual sexual exposures. Most sexual assault victims do not return for follow-up visits. Considerations for prophylaxis include these scenarios:

- Unsure that the patient is returning for follow-up;
- It is known that the source is infected with a specific STI;
- It is requested by the patient/guardian/parent;
- The patient has signs or symptoms of an STI;
- It should be noted that the efficacy of antibiotic prophylaxis has not been studied in sexual assault; and
- Prophylaxis should be as recommended for the treatment of specific infections as described in the Alberta Treatment Guidelines for Sexually Transmitted Infections (STIs) for Adolescents and Adults 2018.

Recommendations for the Management and Follow-Up of Sexual Abuse in Peripubertal and Prepubertal Children may be found at: [Canadian Guidelines on STIs- Sexual Abuse in Prepubertal](#). Appropriate referral and reporting of child abuse should be made in accordance with Alberta's requirements.

Recommendations for the Management and Follow-Up of Sexual Abuse in Postpubertal Adolescents and Adults may be found at: [Canadian Guidelines on STIs- Sexual Abuse in Postpubertal](#). Appropriate referral and reporting of child abuse should be made in accordance with Alberta's requirements. If pregnancy is a possible result of the sexual assault, emergency contraception pill should be considered up to 72 hours after exposure.

Follow-up after prophylaxis treatment will vary depending on the type of test performed and the type and duration of treatment given. Refer to the Canadian Guidelines on Sexually Transmitted Infections, noted above.

Refer to the Alberta Treatment Guidelines for Sexually Transmitted Infections in Adults and Adolescents, 2018, for guidance on provincial testing and treatment recommendations.

<https://open.alberta.ca/publications/treatment-guidelines-for-sti-2018>

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Appendix

Table 1. Risk of HIV transmission per exposure from a known HIV-positive individual (assuming no condoms or ART)

Type of Exposure	Estimated Risk Per Act per 10,000 exposures (95% CI) [estimated risk per act]	Reference
Parenteral		
Blood Transfusion	9250 (8900-9610) [90%]	Patel <i>et al.</i> , 2014
Needle-sharing during injection drug use	63 (41-92) [0.63%]	
Percutaneous (hollow bore needlestick)	23 (0-46) [0.23%]	
Occupational Mucous membrane exposure (splashes to eyes, nose and mouth; risk may be lower with non-intact skin)	9 (0.6-50) [0.09%]	Ippolito <i>et al.</i> , 1993
Sexual		
Receptive anal intercourse	138 (102-186) [1.38%]	Patel <i>et al.</i> , 2014
Insertive anal intercourse	11 (4-28) [0.11%]	Patel <i>et al.</i> , 2014
Receptive penile-vaginal intercourse	8 (6-11) [0.08%]	Patel <i>et al.</i> , 2014
Insertive penile-vaginal intercourse	4 (1-14) [0.04%]	Patel <i>et al.</i> , 2014
Receptive oral intercourse	Low but not zero (0-4) [0.01%]	Patel <i>et al.</i> , 2014
Insertive oral intercourse	Low but not zero (0-4) [0.01%]	Patel <i>et al.</i> , 2014
Vertical		
Mother-to-Child Transmission	2260 (1700-2900) [20%]	Patel <i>et al.</i> , 2014
Ingestion of human breast milk	0.1 to 0.4 [0.001 to 0.004%]	Havens, 2003
Other		
Biting (with saliva only)	Negligible	Pretty <i>et al.</i> , 1999
Spitting	Negligible	
Throwing Bodily Fluids (including semen and saliva)	Negligible	
Sharing Sex Toys	Negligible	

Table 2. HIV/AIDS Diagnosis Data

Total number of newly reported HIV cases and percentage of newly reported cases by exposure category over the last five years

Estimated percentage of HIV in Alberta by exposure category, 2013-2017										
(Source: Interactive Health Data Application, Alberta Health: http://www.ahw.gov.ab.ca/IHDA_Retrieval/ihdaData.do)										
Exposure Category	2017		2016		2015		2014		2013	
	No. cases	% of total	No. cases	% of total	No. cases	% of total	No. cases	% of total	No. cases	% of total
MSM	80	28%	87	31%	65	28%	75	27%	92	36%
MSM-IDU	9	3%	14	5%	8	3%	10	4%	8	3%
IDU	31	11%	27	10%	34	15%	32	11%	24	9%
Heterosexual-Partner At Risk	32	11%	29	10%	31	13%	31	11%	34	13%
Heterosexual-Endemic	16	6%	25	9%	25	11%	27	10%	25	10%
Citizenship and Immigration Canada (out of country)	80	28%	69	24%	51	22%	79	28%	58	22%
No Identified Risk Factors-heterosexual	19	7%	26	9%	16	7%	26	9%	16	6%
No Identified Risk	10	4%	7	2%	1	0%	0	0%	1	0.5%
Perinatal	1	0.5%	0	0%	0	0%	0	0%	1	0.5%
Occupational	1	0.5%	0	0%	0	0%	0	0%	0	0%
Other	4	1%	0	0%	0	0%	1	0%	0	0%
TOTAL	283	100%	284	100%	231	100%	281	100%	259	100%

Note: The exposure categories are defined based on the most representative risk factor for each individual based on the HIV algorithm hierarchy used in Alberta.

Table 3. Risk Assessment

Estimated from the likelihood of HIV transmission following a single exposure in British Columbia* with a source person in a major risk group or not known to be in a major risk group.

	Known HIV-positive	From major risk group **	Not known to be in a major risk group ***
Receptive anal sex (condomless %)	1.38%	0.3 %	0.0001%
Insertive anal sex (condomless %)	0.11%	0.025 %	0.0001%
Receptive vaginal-penile sex (condomless %)	0.08%	0.02 %	< 0.0001%
Insertive vaginal-penile sex (condomless %)	0.04%	0.01 %	< 0.0001%
Needle sharing, IDU	0.63%	0.14%	< 0.0001%
Percutaneous, hollow bore needlestick	0.23%	0.05%	< 0.0001%
Occupational mucous membrane	0.09%	0.02%	< 0.0001%
Receptive oral sex (condomless %)	0.01%	0.002%	< 0.0001%
Insertive oral sex (condomless %)	0.01%	0.002%	< 0.0001%
Percutaneous injury (solid bore needle, superficial injury), Permucosal exposure to non-blood containing bodily fluids or non-intact skin exposure to blood or visible blood-stained bodily fluid	low		
Discarded needles found in the community; Human bites not involving blood; Contact with intact skin; Superficial scratches that do not bleed	negligible		

Estimated probability of risk:

% condomless- np condom, condom breakage or unknown condom status

* Published community prevalence estimates within BC data was used. This would overestimate the figures but underestimate the risk for Alberta.

**Source is in a Major High-risk Group- 23% prevalence based on BC data (e.g., MSM major risk group as a highest risk scenario)

***Source person not known to be in a major risk group- 0.009% prevalence based on BC data

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