Saskatchewan Clinical Reference Tool for HIV

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Objectives

- Simple and practical approaches for primary care practitioners in Saskatchewan for the most common clinical scenarios around HIV.
- Divided into three main categories: diagnosis, initial evaluation, and maintenance of therapy.
- Feedback and criticism welcomed – *alexander.wong@usask.ca*

Diagnosis of HIV Infection

- Why is it important to test for HIV?
- Who do I test for HIV infection?
- How do I counsel patients prior to testing for HIV?
- What tests do I order for a patient that I want to test for HIV infection?
- What constitutes a positive result for HIV, and what do I tell a patient who has a positive result for HIV?
- What do I do when the test returns “indeterminate”?
- What do I do next when a patient is newly diagnosed with HIV?

Diagnosis of HIV Infection

- **Why is it important to test for HIV?**
  - There are individual-level benefits for the patient and societal benefits when an individual who is positive for HIV is identified.
  - Early identification allows for prompt initiation of antiretroviral therapy (ART), which improves life expectancies for HIV-positive individuals to that of the general population.
  - Successful treatment with ART reduces an individual's HIV viral load, which in turns reduces their risk of transmission significantly.
  - Knowledge of one's HIV status modifies risk behaviours.
- **What are the consequences of not testing for HIV?**
  - Many individuals remain unaware that they are HIV-positive. In the United States and Canada, it is estimated that ~20% of individuals who are HIV-positive are unaware of their status.
  - In Canada, 75,500 individuals are living with HIV, and an estimated 16,020 are unaware of their diagnosis.
  - Many patients who are HIV-positive have numerous encounters with the health care system but are not tested.

Diagnosis of HIV Infection

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- **Who do I test for HIV infection?**
  - Voluntary confidential HIV testing and counseling should be considered **at least once every five years in all adults**, and can be considered more frequently based on risk factors.
  - Target groups include:
    - **All patients between ages of 13 and 70 unaware of their HIV status.**
    - All persons sexually active with multiple / successive partners who have not had HIV testing in the last year.
    - All patients who request HIV testing.
    - All pregnant women.
    - All patients assessed for a sexually-transmitted infection, hepatitis B, or hepatitis C.
    - All persons with a current or previous history of illicit drug use.
    - All persons from endemic countries.
    - All patients with active or latent tuberculosis.
    - All patients with signs/symptoms consistent with HIV-related disease.
      - **Acute HIV:** fever, lymphadenopathy, sore throat, rash, myalgias/arthralgias, headache, mucocutaneous ulcerations (mouth, anus, penis, esophagus)
      - **Chronic HIV:** thrush, unexplained weight loss or fevers, generalized lymphadenopathy, aseptic meningitis, herpes zoster (especially if involving more than one dermatose), any opportunistic infection, Kaposi's sarcoma.

Diagnosis of HIV Infection

- **How do I counsel patients prior to testing for HIV?**
  - HIV testing requires the **documented consent** of the individual being offered testing. Consent must be voluntary and informed. Even if a patient declines testing, it is important to document this.
  - **Verbal informed consent** is all that is required for HIV testing, as opposed to written / signed consent.
  - When you obtain verbal informed consent, document this clearly on the patient record. (e.g. V*erbal consent obtained for HIV testing.*)
  - It is important to **normalize testing** for HIV and other blood-borne infections and to adopt an inclusive testing strategy rather than one focused on identification of risk.
    - Normalizing testing helps to eliminate stigma and discriminatory attitudes towards HIV and helps providers overcome their own perceived barriers to testing.

Diagnosis of HIV Infection

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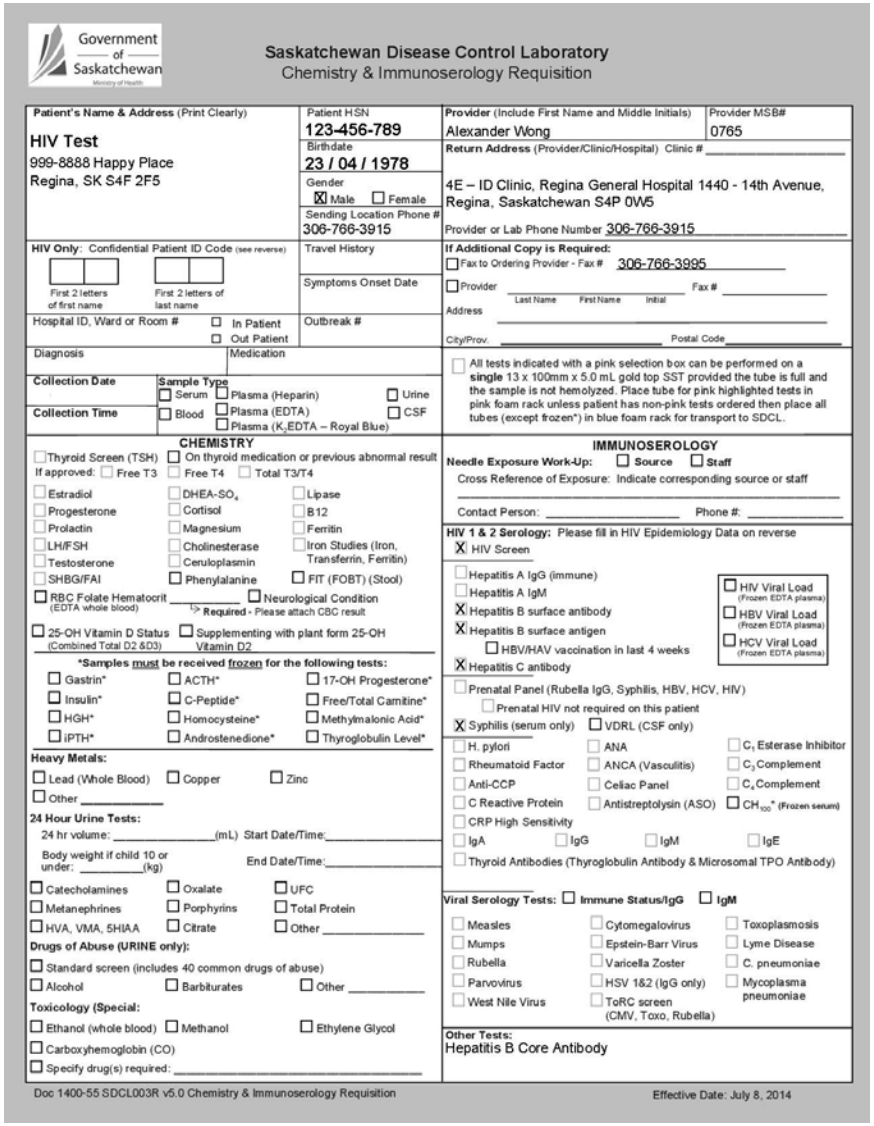
- **What tests do I order for a patient that I want to test for HIV infection?**
  - Order an ***HIV Screen*** on the SDCL Immunoserology requisition.
  - Consider screening for other blood-borne infections and sexually transmitted infections, including but not limited to:
    - Urine NAT for chlamydia / gonorrhea
    - Syphilis serology.
    - Hepatitis C antibody.
    - Hepatitis B surface antibody, surface antigen, and core antibody.
  - **SDCL Immunoserology Requisition:** HIV screen, hepatitis C antibody, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody (written), syphilis (serum only).
  - **SDCL Microbiology Requisition:** Chlamydia & Gonorrhoea Screen (Urine)
  - If there has been recent risk exposure, consider **serial testing** (e.g. 6 weeks and 4 months later) as 4th generation testing takes median of 15-20 days to become positive after exposure.

SDCL Immunoserology



Government of Saskatchewan

Saskatchewan Disease Control Laboratory
Chemistry & Immunoserology Requisition

Patient's Name & Address (Print Clearly)
HIV Test
999-8888 Happy Place
Regina, SK S4F 2F5

Patient HSN: 123-456-789
Birthdate: 23 / 04 / 1978
Gender: ☒ Male ☐ Female
Sending Location Phone #: 306-766-3915

Provider (Include First Name and Middle Initials): Alexander Wong
Provider MSB#: 0765
Return Address (Provider/Clinic/Hospital) Clinic #:
4E – ID Clinic, Regina General Hospital 1440 - 14th Avenue, Regina, Saskatchewan S4P 0W5
Provider or Lab Phone Number: 306-766-3915

HIV Only: Confidential Patient ID Code (see reverse)
First 2 letters of first name | First 2 letters of last name
Travel History
Symptoms Onset Date
Hospital ID, Ward or Room # ☐ In Patient ☐ Out Patient
Outbreak #
Diagnosis
Medication

If Additional Copy is Required:
☐ Fax to Ordering Provider - Fax # 306-766-3995
☐ Provider (Last Name, First Name, Initial) Fax #
Address
City/Prov. Postal Code

Collection Date
Collection Time
Sample Type
☐ Serum ☐ Plasma (Heparin) ☐ Urine
☐ Blood ☐ Plasma (EDTA) ☐ CSF
☐ Plasma (K_2EDTA – Royal Blue)

☐ All tests indicated with a pink selection box can be performed on a **single** 13 x 100mm x 5.0 mL gold top SST provided the tube is full and the sample is not hemolyzed. Place tube for pink highlighted tests in pink foam rack unless patient has non-pink tests ordered then place all tubes (except frozen*) in blue foam rack for transport to SDCL.

CHEMISTRY
☐ Thyroid Screen (TSH) ☐ On thyroid medication or previous abnormal result
If approved: ☐ Free T3 ☐ Free T4 ☐ Total T3/T4
☐ Estradiol ☐ DHEA-SO_4 ☐ Lipase
☐ Progesterone ☐ Cortisol ☐ B12
☐ Prolactin ☐ Magnesium ☐ Ferritin
☐ LH/FSH ☐ Cholinesterase ☐ Iron Studies (Iron, Transferrin, Ferritin)
☐ Testosterone ☐ Ceruloplasmin
☐ SHBG/FAI ☐ Phenylalanine ☐ FIT (FOBT) (Stool)
☐ RBC Folate Hematocrit _____ (EDTA whole blood) ☐ Neurological Condition
↳ **Required** - Please attach CBC result
☐ 25-OH Vitamin D Status (Combined Total D2 &D3) ☐ Supplementing with plant form 25-OH Vitamin D2

***Samples must be received frozen for the following tests:**
☐ Gastrin* ☐ ACTH* ☐ 17-OH Progesterone*
☐ Insulin* ☐ C-Peptide* ☐ Free/Total Carnitine*
☐ HGH* ☐ Homocysteine* ☐ Methylmalonic Acid*
☐ iPTH* ☐ Androstenedione* ☐ Thyroglobulin Level*

Heavy Metals:
☐ Lead (Whole Blood) ☐ Copper ☐ Zinc
☐ Other _____

24 Hour Urine Tests:
24 hr volume: _____(mL) Start Date/Time:_____
Body weight if child 10 or under: _____(kg) End Date/Time:_____
☐ Catecholamines ☐ Oxalate ☐ UFC
☐ Metanephrines ☐ Porphyrins ☐ Total Protein
☐ HVA, VMA, 5HIAA ☐ Citrate ☐ Other _____

Drugs of Abuse (URINE only):
☐ Standard screen (includes 40 common drugs of abuse)
☐ Alcohol ☐ Barbiturates ☐ Other _____

Toxicology (Special:
☐ Ethanol (whole blood) ☐ Methanol ☐ Ethylene Glycol
☐ Carboxyhemoglobin (CO)
☐ Specify drug(s) required: _____

IMMUNOSEROLOGY
Needle Exposure Work-Up: ☐ **Source** ☐ **Staff**
Cross Reference of Exposure: Indicate corresponding source or staff
Contact Person: _____ Phone #: _____

HIV 1 & 2 Serology: Please fill in HIV Epidemiology Data on reverse
☒ HIV Screen
☐ Hepatitis A IgG (immune)
☐ Hepatitis A IgM
☒ Hepatitis B surface antibody
☒ Hepatitis B surface antigen
☐ HBV/HAV vaccination in last 4 weeks
☒ Hepatitis C antibody
☐ HIV Viral Load (Frozen EDTA plasma)
☐ HBV Viral Load (Frozen EDTA plasma)
☐ HCV Viral Load (Frozen EDTA plasma)
☐ Prenatal Panel (Rubella IgG, Syphilis, HBV, HCV, HIV)
☐ Prenatal HIV not required on this patient
☒ Syphilis (serum only) ☐ VDRL (CSF only)

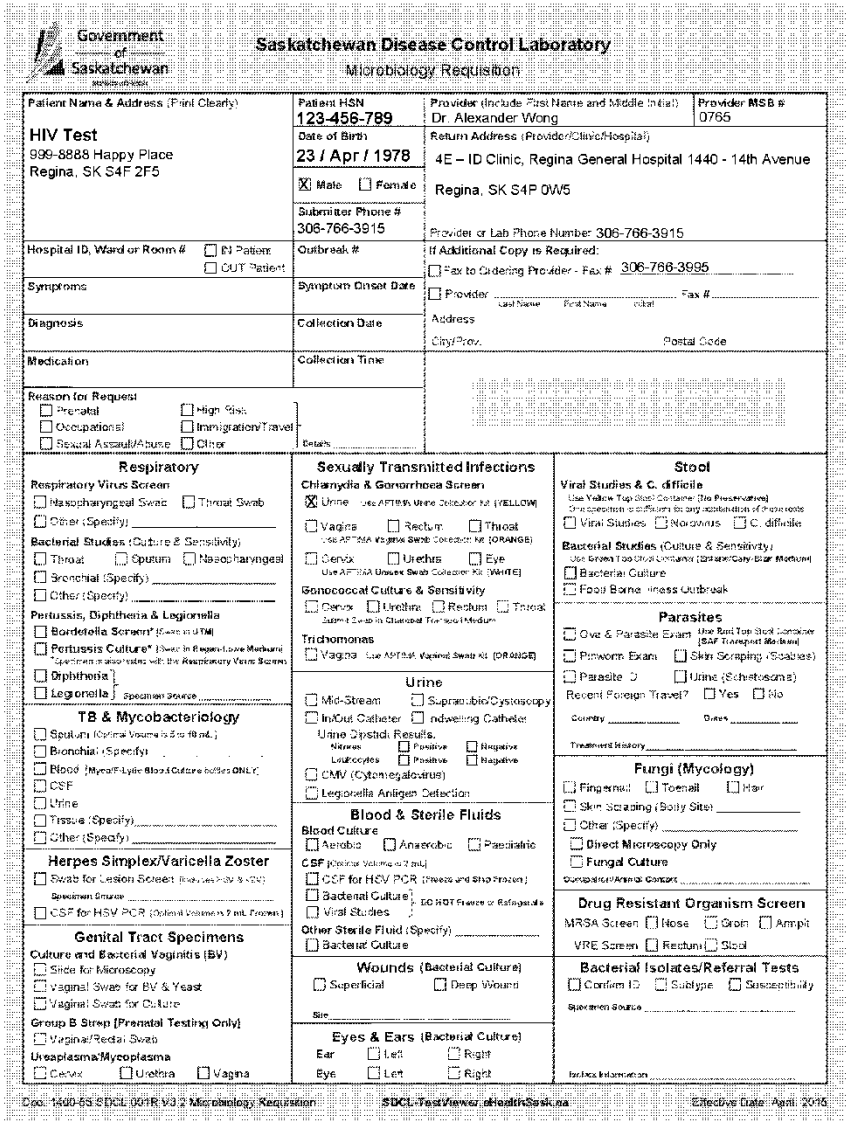
☐ H. pylori ☐ ANA ☐ C_1 Esterase Inhibitor
☐ Rheumatoid Factor ☐ ANCA (Vasculitis) ☐ C_3 Complement
☐ Anti-CCP ☐ Celiac Panel ☐ C_4 Complement
☐ C Reactive Protein ☐ Antistreptolysin (ASO) ☐ CH_{100}* (Frozen serum)
☐ CRP High Sensitivity
☐ IgA ☐ IgG ☐ IgM ☐ IgE
☐ Thyroid Antibodies (Thyroglobulin Antibody & Microsomal TPO Antibody)

Viral Serology Tests: ☐ **Immune Status/IgG** ☐ **IgM**
☐ Measles ☐ Cytomegalovirus ☐ Toxoplasmosis
☐ Mumps ☐ Epstein-Barr Virus ☐ Lyme Disease
☐ Rubella ☐ Varicella Zoster ☐ C. pneumoniae
☐ Parvovirus ☐ HSV 1&2 (IgG only) ☐ Mycoplasma pneumoniae
☐ West Nile Virus ☐ ToRC screen (CMV, Toxo, Rubella)

Other Tests:
Hepatitis B Core Antibody

Doc 1400-55 SDCL003R v5.0 Chemistry & Immunoserology Requisition
Effective Date: July 8, 2014

SDCL Microbiology



Government of Saskatchewan

Saskatchewan Disease Control Laboratory

Microbiology Requisition

Patient Name & Address (Print Clearly)

HIV Test
999-8888 Happy Place
Regina, SK S4F 2F5

Patient HSN: 123-456-789

Date of Birth: 23 / Apr / 1978

☒ Male ☐ Female

Submitter Phone #: 306-766-3915

Provider (Include First Name and Middle Initial): Dr. Alexander Wong

Provider MSB #: 0765

Return Address (Provider/Clinic/Hospital): 4E – ID Clinic, Regina General Hospital 1440 - 14th Avenue, Regina, SK S4P 0W5

Provider or Lab Phone Number: 306-766-3915

If Additional Copy is Required:
☐ Fax to Ordering Provider - Fax # 306-766-3995
☐ Provider ____ Fax # ____
Address
City/Prov. Postal Code

Hospital ID, Ward or Room # ☐ IN Patient ☐ OUT Patient

Outbreak #

Symptoms

Symptom Onset Date

Diagnosis

Collection Date

Medication

Collection Time

Reason for Request
☐ Prenatal ☐ High Risk
☐ Occupational ☐ Immigration/Travel
☐ Sexual Assault/Abuse ☐ Other
Details

Respiratory

Respiratory Virus Screen
☐ Nasopharyngeal Swab ☐ Throat Swab
☐ Other (Specify)

Bacterial Studies (Culture & Sensitivity)
☐ Throat ☐ Sputum ☐ Nasopharyngeal
☐ Bronchial (Specify)
☐ Other (Specify)

Pertussis, Diphtheria & Legionella
☐ Bordetella Screen*
☐ Pertussis Culture*
*Specimen is also tested with the Respiratory Virus Screen
☐ Diphtheria
☐ Legionella Specimen Source

TB & Mycobacteriology
☐ Sputum
☐ Bronchial (Specify)
☐ Blood (Myco/F-Lytic Blood Culture bottles ONLY)
☐ CSF
☐ Urine
☐ Tissue (Specify)
☐ Other (Specify)

Herpes Simplex/Varicella Zoster
☐ Swab for Lesion Screen
Specimen Source
☐ CSF for HSV PCR (Optimal Volume is 2 mL Frozen)

Genital Tract Specimens

Culture and Bacterial Vaginitis (BV)
☐ Slide for Microscopy
☐ Vaginal Swab for BV & Yeast
☐ Vaginal Swab for Culture

Group B Strep (Prenatal Testing Only)
☐ Vaginal/Rectal Swab

Ureaplasma/Mycoplasma
☐ Cervix ☐ Urethra ☐ Vagina

Sexually Transmitted Infections

Chlamydia & Gonorrhoea Screen
☒ Urine Use APTIMA Urine Collection Kit (YELLOW)
☐ Vagina ☐ Rectum ☐ Throat
Use APTIMA Vaginal Swab Collection Kit (ORANGE)
☐ Cervix ☐ Urethra ☐ Eye
Use APTIMA Unisex Swab Collection Kit (WHITE)

Gonococcal Culture & Sensitivity
☐ Cervix ☐ Urethra ☐ Rectum ☐ Throat
Submit Swab in Charcoal Transport Medium

Trichomonas
☐ Vaginal Use APTIMA Vaginal Swab Kit (ORANGE)

Urine
☐ Mid-Stream ☐ Suprapubic/Cystoscopy
☐ In/Out Catheter ☐ Indwelling Catheter
Urine Dipstick Results
Nitrites ☐ Positive ☐ Negative
Leukocytes ☐ Positive ☐ Negative
☐ CMV (Cytomegalovirus)
☐ Legionella Antigen Detection

Blood & Sterile Fluids

Blood Culture
☐ Aerobic ☐ Anaerobic ☐ Paediatric

CSF (Optimal Volume is 2 mL)
☐ CSF for HSV PCR (Freeze and Ship Frozen)
☐ Bacterial Culture
☐ Viral Studies
DO NOT Freeze or Refrigerate

Other Sterile Fluid (Specify)
☐ Bacterial Culture

Wounds (Bacterial Culture)
☐ Superficial ☐ Deep Wound
Site

Eyes & Ears (Bacterial Culture)
Ear ☐ Left ☐ Right
Eye ☐ Left ☐ Right

Stool

Viral Studies & C. difficile
Use Yellow Top Stool Container (No Preservative)
Only specimens submitted for any combination of these tests
☐ Viral Studies ☐ Norovirus ☐ C. difficile

Bacterial Studies (Culture & Sensitivity)
Use Green Top Stool Container (Cary-Blair Medium)
☐ Bacterial Culture
☐ Food Borne Illness Outbreak

Parasites
☐ Ova & Parasite Exam Use Red Top Stool Container (SAF Transport Medium)
☐ Pinworm Exam ☐ Skin Scraping (Scabies)
☐ Parasite ID ☐ Urine (Schistosoma)
Recent Foreign Travel? ☐ Yes ☐ No
Country Dates
Treatment History

Fungi (Mycology)
☐ Fingernail ☐ Toenail ☐ Hair
☐ Skin Scraping (Body Site)
☐ Other (Specify)
☐ Direct Microscopy Only
☐ Fungal Culture
Occupation/Animal Contact

Drug Resistant Organism Screen
MRSA Screen ☐ Nose ☐ Groin ☐ Armpit
VRE Screen ☐ Rectum ☐ Stool

Bacterial Isolates/Referral Tests
☐ Confirm ID ☐ Subtype ☐ Susceptibility
Specimen Source
Isolate Information

Doc. 1400-65 SDCL 001R V3.2 Microbiology Requisition | SDCL-TestViewer.eHealthSask.ca | Effective Date: April, 2015

Diagnosis of HIV Infection

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- **What constitutes a positive result for HIV, and what do I tell a patient who has a positive result for HIV?**
  - SDCL currently uses a 4th-generation combined HIV antigen / antibody test, whose sensitivity in chronic HIV infection is near 100%, although sensitivity in acute HIV infection is variable.
  - Confirmatory Western Blot testing is performed on all positive HIV screens to ensure that the result is not a false positive. **Only** when Western Blot is positive is result reported to ordering provider and medical health officer for health region.
  - It is **crucial** to deliver positive result in person, not over phone or electronic medium such as email or text message.
  - Public Health can assist providers who cannot reach individuals who are diagnosed HIV positive, including providing home visits if required by the provider.
  - *"Unfortunately, your testing for HIV was positive. We need to order some more tests, and have you see a specialist who provides HIV care. HIV is not a death sentence, and with medication the lifespan of someone with HIV is nearly identical to that of someone who does not have HIV."*

Diagnosis of HIV Infection

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- **What do I do when the test returns "indeterminate"?**
  - The main concern is whether an "indeterminate" result represents a true positive result or not.
  - False negatives are the primary concern with any screening assay. Reasons for false negatives may include acute infection (most common), unusual HIV subtypes, and loss of antibody production in advanced disease.
  - If there is concern for a false negative test, then depending on the scenario there may be a role to either repeat the test after several weeks (e.g. acute infection), or consider performing HIV RNA testing.
  - False positive serologic tests are rare, but may be caused by receiving an HIV vaccine or rarely other vaccines. Repeating HIV serologic testing and an HIV viral load may help confirm the false positive initial result.
  - Indeterminate results occur when the screening test is indeterminate or positive and confirmatory testing is negative. Indeterminate results may be due to HIV infection (e.g. partial seroconversion, infection with HIV-2) or non HIV-related factors including cross-reacting antibodies from pregnancy or influenza vaccination.
  - Patients with an indeterminate result should have an HIV RNA checked, as well as testing for HIV-2 if risk factors exist.
  - **Call an ID specialist for support as needed.**

Diagnosis of HIV Infection

- **What do I do next when a patient is newly diagnosed with HIV?**
  - Counsel the patient regarding the diagnosis.
    - *"HIV is not a death sentence, and with excellent medication the lifespan of someone with HIV is nearly equivalent to someone without HIV."*
    - Public Health will be contacting for purposes of contact tracing.
    - A referral will be made immediately to a multidisciplinary care team for further assessment.
  - Refer the patient immediately to the appropriate care facility.
  - **Saskatoon – Westside Clinic:** 1528-20th Street W, phone 306-664-4310, fax 306-934-2506
  - **Saskatoon – Positive Living Program / Royal University Hospital:** 103 Hospital Drive, phone 306-655-1783, fax 306-655-0614
  - **Regina Infectious Diseases Clinic:** 4E – Regina General Hospital, phone 306-766-3915, fax 306-766-3995.
  - **Prince Albert / Access Place: 1**01 15th Street East, phone 306-765-6541.

Initial Evaluation

- How do I evaluate a patient who is newly diagnosed with HIV infection?
  - **An excellent and practical resource is "Initial evaluation of the HIV-infected adult" in UpToDate – these slides are summarized from this document.**
  - **Two main clinical guideline documents for reference:**
    - Primary care of HIV-infected individuals, published by the HIV Medicine Association of the Infectious Diseases Society of America (link).
    - European AIDS Clinical Society guidelines (link).
  - In Saskatchewan, the crucial step with an individual newly-diagnosed for HIV is prompt and efficient referral to an appropriate multidisciplinary clinic. Ideally, referral takes place through direct communication with the care team so that specialist care can be facilitated as quickly as possible.
  - Obtain all contact information for patient including addresses, phone numbers, and contact information for friends and family.
  - Major goals of initial evaluation are to determine the stage of HIV disease, risk for other infections, identify co-morbidities associated with HIV, and evaluate for selection and initiation of antiretroviral therapy.

Initial Evaluation – History

- **Assess stage of HIV disease.**
  - Risk behaviours for HIV, approximate time of onset.
  - Any symptoms / signs of seroconversion illness.
  - Any history of opportunistic infections.
  - Most recent and historical CD4 counts and HIV viral loads.
  - For patients previously diagnosed, a detailed medication history including reasons for discontinuation of previous medications, CD4 and HIV viral load responses to therapy, and significant side effects and toxicities associated with therapy.
- **Past medical history.**
  - **Focus on common co-morbidities, especially those which affect choice of antiretroviral therapy and/or response.**
  - Cardiovascular risk factors including diabetes mellitus, hypertension, and dyslipidemia.
  - Tuberculosis, including previous diagnosis, exposure, and/or testing results.
  - Viral hepatitis, as co-infection with either hepatitis B or hepatitis C is common due to similar routes of transmission.
  - All sexually-transmitted infection history, including previous diagnosis and treatment, as well as results of gynecological and anal cytology testing.
  - Psychiatric history should also be determined, especially depression and the presence of depressive symptoms.

Medications & Adherence

- **A complete antiretroviral drug history should be obtained.**
  - For those who are antiretroviral experienced, a complete drug history, ideally with start and stop dates, should be obtained. It is usually necessary to review past records from other clinics and care settings.
  - Adherence to medications should be assessed, and any history of drug allergies or drug hypersensitivities should be elicited.
  - Ideally, drug histories should be correlated with CD4 counts and HIV viral load results to ensure accuracy of adherence reporting.
- **All other medications, including complementary and over-the-counter medications, should be described.**
  - Drug-drug interactions are relevant with many antiretroviral regimens and all prescribed, alternative, complementary, and over-the-counter medications should be documented clearly.

Immunizations & Vaccines

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- **All immunizations received and sero-statuses should be documented accurately.**
  - Although clinical guidelines have been in place since 1999 regarding the importance of vaccination with a variety of agents (pneumococcal, tetanus toxoid, hepatitis A, hepatitis B), studies of outpatient HIV clinics continue to document low rates of screening and immunization.
  - Serostatuses, when appropriate, should be documented at baseline screening.

- **Vaccination Recommendations**
  - There are three primary categories of vaccines that HIV-infected individuals should receive:
    - **Inactivated vaccines as per the general adult population:** seasonal influenza vaccine, tetanus toxoid and reduced diphtheria +/ acellular pertussis (Td or TdaP), HPV vaccine (up to age 26).
    - **Vaccines for which HIV itself is indication:** pneumococcal vaccine (PCV-13 followed by PPV-23), hepatitis B vaccine (if not already immune).
    - **Other vaccines with indication:** hepatitis A vaccine, meningococcal vaccine, Hib vaccine, MMR (if not already immune and CD4 > 200), varicella vaccine (if not already immune and CD4 > 200-350).
  - Zoster vaccine appears safe and immunogenic in HIV-infected adults with CD4 > 200, but optimal timing is unclear. Zoster vaccine can be considered in patients over age 60, and is contraindicated in patients with CD4 < 200.

Social & Family Histories

- **The social history should elicit ongoing risk for HIV transmission, and identify potential barriers to medication adherence.**
  - Employment, housing, and insurance status of the patient.
  - Past and current substance use.
  - Tobacco / cigarette history.
  - Sexual history which should include condom and contraceptive use.
- **Family histories should focus on cardiovascular events and malignancy.**
  - A family history of coronary artery disease (specifically in first-degree relatives before age 55 for male relatives and age 65 for female relatives), diabetes mellitus, dyslipidemia, and malignancy should be determined.

Review of Systems

- **A thorough review of systems should focus on the presence of constitutional symptoms, and for those with advanced immunosuppression, the presence of signs and symptoms suggestive of the presence of opportunistic infections.**
  - Constitutional symptoms such as fevers, night sweats, and weight loss.
  - **CMV retinitis:** new visual floaters, changes in vision.
  - **Candidiasis:** thrush, dysphagia/odynophagia.
  - **Tuberculosis:** cough, shortness of breath, hemoptysis.
  - **Disseminated MAC:** abdominal pain, diarrhea.
  - **Toxoplasmosis:** headache, focal neurological symptoms.
  - **HIV Associated Neurocognitive Disorders (HAND):** forgetfulness, inability to concentrate, behavioral/mood changes (apathy, lack of motivation).
  - **HIV Associated Neuropathy:** tingling and numbness in the toes and lower extremities (rare in upper extremities), neuropathic pain.

Physical Examination

- A comprehensive initial examination, including weight/height, should be performed a part of the initial evaluation.
  - **Skin:** seborrheic dermatitis, psoriasis, Kaposi's sarcoma.
  - **Body Morphology:** fat redistribution (fat atrophy in malar region, buttocks, extremities); fat deposition (cervicodorsal fat pad a.k.a. "buffalo hump", visceral adiposity).
  - **Eyes:** consider fundoscopy in patients with advanced immunosuppression.
  - **Oral Mucosa:** candidiasis, oral hairy leukoplakia, aphthous ulcerations, HSV infection.
  - **Lymph Nodes:** ensure no bulky, asymmetric, rapidly-enlarging lymphadenopathy worrisome for disseminated infection or lymphoma.
  - **Anogenital:** evidence of STIs.
  - **Neurological:** peripheral neuropathy, asymptomatic muscle weakness, cognitive function.

Initial Laboratory Studies

- **HIV-Related Testing**
  - Confirmatory HIV serology and Western Blot (if not already done or not previously done in Saskatchewan), CD4 cell count & percentage, HIV viral load, HIV resistance testing / genotyping (reverse transcriptase gene +/- integrase gene), HLA-B5701 testing (abacavir hypersensitivity), tropism testing if CCR5 antagonist being considered.
- **Baseline Organ Function**
  - Complete blood count with differential, renal function (serum creatinine), hepatic function, glucose and lipid profile.
- **Co-Infection Testing**
  - Hepatitis A IgG Antibody, Hepatitis B surface antigen, Hepatitis B surface antibody, antibody to hepatitis B total core antigen, Hepatitis C antibody, PPD / Mantoux testing or TB interferon-gamma testing (chest x-ray only if screening positive), syphilis serology, urine NAT for chlamydia & gonorrhea, vaginal swab NAT for *Trichomonas*, CMV IgG, VZV IgG, toxoplasma IgG.

Initial Laboratory Studies

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- **Screening for HPV-Associated Neoplasia**
  - Pap testing should be performed as part of the initial evaluation in all HIV-infected women.
  - HIV-infected individuals should be screened for anal intraepithelial neoplasia through anal cytology (anal Pap testing) when there is local expertise in cytologic result interpretation and availability of a referral structure for high-resolution anoscopy with biopsy in addition to ablative treatments & follow-up.
  - Anal cancer rates are low in HIV-infected individuals less than 30, so screening can be delayed in these individuals till after age 30.
- **Selective Testing on Case-by-Case Basis**
  - Testing for G6PD deficiency can be considered if certain drugs used in the setting of HIV infection (e.g. dapsone, primaquine) are considered.
  - Baseline bone mineral densitometry screening for osteoporosis is recommended for all post-menopausal women and men over age 50 with HIV infection, although supportive evidence is limited.

Evaluation for ART

- An exhaustive description of the initiation, management, and monitoring of ART is beyond the scope of this reference tool.
- The goal of antiretroviral therapy (ART) is to prolong life and improve its quality, restore and preserve immunologic function, and maximally and durably suppress the HIV viral load.
- Based on recent published data, ART is now recommended for **ALL** HIV-infected individuals.
- Many findings on history and initial laboratory laboratory testing contribute to decisions on the initiation and selection of an ART regimen.
- The initial evaluation is also an important time to educate the patient regarding ART as well as evaluating readiness for initiation of ART and any potential concerns with medication adherence.

OI Prophylaxis

- Opportunistic infections are defined as those which are more frequent or severe because of immune suppression. The use of prophylactic agents can reduce the risk of opportunistic infections significantly.
- **CD4 ≤ 200:** TMP-SMX for prophylaxis against *Pneumocystis carinii* pneumonia. Alternatives include dapsone or atovaquone suspension.
- **CD4 ≤ 100:** TMP-SMX for prophylaxis against Toxoplasma for those with positive serology.
- **CD4 ≤ 50:** Macrolide (clarithromycin or azithromycin) for prophylaxis against MAC; blood cultures for MAC isolation should be obtained before prophylaxis is initiated if there is any suspicion of clinical disease.
- No specific prophylaxis or work-up is indicated for coccidiodomycosis, histoplasmosis, or cryptococcus in Saskatchewan.

Monitoring During ART

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- No specific prophylaxis or work-up is indicated for coccidiodomycosis, histoplasmosis, or cryptococcus in Saskatchewan.

Monitoring During ART

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- **Overview**
  - Appropriate patient monitoring to assess therapeutic response and to identify adverse events related to chronic administration of ART is crucial.
  - Failure to respond to a recommended ART regimen is almost always a result of suboptimal adherence or viral resistance, less commonly issues around drug interactions and absorption may play a role.
- **Monitoring Adherence**
  - Strict adherence is crucial when patients are initiating or changing an ART regimen.
  - To promote adherence, patients should understand the direct link between adherence and drug resistance.
  - Potential barriers to adherence may include medication-specific issues such as the frequency and timing of doses, sizes of pills, food restrictions, and side effects. Patient-specific factors such as depression and substance abuse may also play a role.
  - Adherence is difficult to assess, and patients often exaggerate adherence to their care providers.

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- **Visit Frequency**
  - Patients initiated on ART should typically be seen in follow-up in 1-2 weeks to ensure that adherence to the regimen is optimal, determine the presence of any side effects, and answer any questions regarding the regimen itself.
  - Repeat HIV viral loads are performed typically at 4-6 weeks post-initiation, and at 12 weeks post-initiation to ensure appropriate virologic response.
  - After patients stabilize clinically and are tolerating their medications well with predictably excellent adherence, visit frequency can be decreased to as little as 2-3 times / year.
- **General Lab Monitoring**
  - For more information, see Table 3 of the DHHS Antiretroviral Guidelines for the Treatment of Adults and Adolescents.
  - CBC & differential, BUN, serum creatinine, and liver function tests should be performed q 3-6 months.
  - Patients receiving tenofovir should have a urinalysis performed every 6 months.

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- **Virologic Response to Therapy**
  - HIV viral load should be measured at baseline and regularly for all patients during therapy as it serves as the most reliable indicator of response to therapy.
  - The goal is viral suppression below the limit of assay detection.
  - A variety of host and viral factors can affect response to ART. Generally, an initial ART regimen should achieve a one-log decline by 1-2 weeks, a two-log decline by 4 weeks, and an undetectable viral load between 8-24 weeks.
  - **Virologic failure** is generally considered when patients do not achieve a viral load < 200 within 24 weeks of initiating ART or if they have sustained recurrence of viremia to > 200 copies/mL (i.e. two consecutive measurements) after initial suppression.
  - No evidence supports that viral loads quantified as being < 200 copies/mL (aka viral “blips”). It is reasonable to emphasize the importance of adherence and to repeat a viral load in 4 weeks in patients who blip.

Monitoring During ART

- **Immunologic Response to Therapy**
  - CD4 cell counts correlate with immune response. Suppression of the HIV viral load often correlates with an increase of > 50 cells/microL at 4-8 weeks, followed then by an increase of 50-100 cells/microL each year.
  - Some patients may increase their CD4 cell counts despite having not achieved viral suppression, while other patients do not achieve immunologic reconstitution despite having viral suppression.
  - CD4 counts can be affected by lab variability, acute illness, and diurnal variation. Significant and unexplained differences in CD5 count measurements (e.g. 30% change in absolute CD4 count or 3% change in CD4 percentage) should be confirmed with repeat testing.

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- **Frequency of CD4 / HIV Viral Load Monitoring**
  - The HIV viral load should typically be repeat between 2-4 weeks after initiating ART, and then every 4-8 weeks thereafter until the viral load is fully suppressed.
  - Once the viral load is suppressed, then monitoring of the HIV viral load can be decreased to every 3-4 months. Once the patient is stably suppressed for 2 years, the frequency of monitoring can be reduced to every 6 months.
  - If a change in ART regimen is made then the viral load should be checked between 2-8 weeks following to ensure viral suppression is achieved.
  - CD4 cell counts should be checked at 3 months post-initiation of ART, and then q 3-6 months thereafter.
  - Once patients have been on ART at least two years and their CD4 count has stabilized well above the threshold for OI risk (e.g. 300-350) with consistently suppressed HIV viral loads, the CD4 count can be checked once yearly if between 300-500, or optionally once over 500.

Role of Primary Care

- **Typically, HIV-specific issues will be handled by specialty clinic.**
  - Initiation, modification, and monitoring of ART.
  - Side effects and adverse effects of ART.
  - Vaccinations.
  - Prophylaxis for opportunistic infections.
  - Barriers to engagement / retention in care (e.g. poverty, housing, addictions, mental health concerns).
- **Ideally, the primary care provider supports many other crucial issues.**
  - **Mental Health / Addictions Issues:** counsel and treat as required, refer if appropriate for additional mental health and addictions supports, or opioid substitution therapy.
  - **Malignancy screening:** Cervical Pap testing, screening for anal HPV, breast cancer screening.
  - Counselling for contraception and preconception care.
  - Screening for and managing metabolic comorbidities.

Malignancy Screening

- **Breast Cancer**
  - Mammography should be performed annually in women > 50 years of age.
  - In women between ages 40-49, providers should perform an individualized assessment of risk for breast cancer and inform them of potential benefits and risks of screening mammography.
- **Cervical Cancer**
  - HIV-infected women should have a cervical Pap test performed upon initiation of care, and this test should be repeated at 6 months and annually thereafter if results are normal.
  - Women with atypical squamous cells, atypical glandular cells, low-grade or high-grade squamous epithelial lesions, or squamous carcinoma noted by Pap testing should undergo colposcopy and directed biopsy.\
- **Anal Human Papilloma Virus**
  - HIV-infected men and women with HPV infection are at increased risk for anal dysplasia and cancer. MSM, women with a history of receptive anal intercourse or abnormal cervical Pap test results, and all HIV-infected individuals with genital warts should have anal Pap tests.

Metabolic Comorbidities

- **Screening and Management Recommendations:**
  - Fasting blood glucose and/or hemoglobin A1c should be obtained prior to and within 1-3 months after starting ART. Patients with diabetes mellitus should have an HbA1c level monitored every 6 months with a goal of < 7%.
  - Fasting lipid levels should be obtained prior to and within 1-3 months after starting ART. Patients with abnormal lipid levels should be managed according to the 2012 Canadian Cardiovascular Society guidelines.
  - Baseline bone densitometry (DXA) screening for osteoporosis in HIV-infected individuals should be performed in post-menopausal women and men >= 50 years of age.