INDIAN HEALTH SERVICE

HIV Primary Care Treatment Guidelines for Adults and Adolescents

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BACKGROUND

Clinical care of the patient with HIV infection is a rapidly evolving field. Recent advances in the treatment of HIV make management of this infection possible in the primary care setting at any Indian Health Service (IHS) facility. This document describes standards of care for adults and adolescents living with HIV/AIDS who receive care at IHS facilities. Children living with HIV are not addressed in this document and should be seen by pediatric HIV specialists. The IHS updates these standards periodically.

THE PRIMARY CARE VISIT

The initial primary care visit after a new diagnosis of HIV infection is perhaps the most important visit of all. The patient has just received intimidating and frightening news and is at a vulnerable point in life. The duty of the primary care provider is to listen carefully to the patient's concerns, establish rapport, and offer reassurance that care will be provided in a compassionate, non-judgmental, and culturally appropriate manner. It is essential to treat the patient as a person and not a diagnosis. Additionally, rapid initiation of HIV treatment is key to achieving virologic suppression, prevent transmission, and improve uptake of HIV therapy. Whenever possible, antiretroviral therapy (ART) should be initiated at the initial visit or as soon as possible thereafter, while establishing rapport and providing deserved reassurance.

HISTORY[i]

During the course of taking a medical history, it is essential to establish when the patient first received their HIV diagnosis. Other helpful pieces of information include a history of prior opportunistic infections, malignancies, and the initial CD4 count and HIV viral load. Obtaining the previous HIV antiretroviral therapy history, and reasons for any regimen changes, e.g. intolerance or virologic resistance, is vital if the patient can provide it. A psychiatric history is essential, including past diagnoses such as depression, anxiety, post-traumatic stress disorder, and substance misuse. Obtain the patient's social history, including substance use (tobacco, alcohol, drugs) and sexual practices (including sex of partners, exposure sites, number of partners, partners' HIV status, disclosure of HIV diagnosis to partners, condom use, and partners' use of HIV pre-exposure prophylaxis). It is helpful to ask about social supports,

employment, housing, and income at one of the early clinic visits. Completing a standard review of symptoms is imperative.

PHYSICAL EXAM[ii]

A standard HIV physical exam should include the following individual elements:

- Vital signs;
- Eyes: assess sclerae for icterus suggesting liver disease; uveitis, photophobia or irregular pupils may suggest ocular syphilis, and retina for cotton wool spots (commonly seen with HIV) and for retinitis;
- Oropharynx: assess the mucosa for thrush secondary to candida, the tongue for hairy leukoplakia (vertical striations on the lateral surface suggesting advanced stage 3 HIV disease), mucous patches and chancres indicating syphilis, and the gingiva for signs of gingivitis;
- Lymph nodes: assess all lymph node groups, including cervical, axillary, epitrochlear, and inguinal;
- Lungs: evaluate for signs of pneumonia and effusion;
- Abdomen: assess for tenderness and hepatosplenomegaly;
- Genital: evaluate genitalia for warts, ulcers, discharge, or other signs of infection.
- Anal: evaluate for ulceration, mass, and discharge; and
- Neurologic: evaluate for signs of dementia, peripheral neuropathy, and focal deficits suggesting a mass lesion or stroke.

LABORATORY EVALUATION[iii]

Patients treated in IHS facilities for HIV will have the following tests performed at their baseline evaluation and during their follow up visits as noted.

Test	Frequency	Comments
CD4 Count	At diagnosis, then every 12 weeks after starting ART until virological suppression is achieved. Monitor CD4 count every 3-6 months when CD4 < 300. If 300< CD4 <500, then every year. If CD4 > 500, then monitoring is optional. CD4 monitoring is indicated at any time there is loss of virological control.	Use one laboratory and methodology.
HIV Viral Load	At diagnosis, then at 4 weeks and 12 weeks after starting ART. After that, obtain an HIV viral load every 3 months for the first 2 years. Viral load testing can safely be done every 6 months after 2 years of viral suppression (HIV viral load < 200 copies/mlmL).	Use one laboratory and methodology.
Genotypic antiretroviral Resistance Test (GART)	At diagnosis on all patients, at the time of initiation of ART (if delayed) and subsequently only with the failure of virologic control or change in ART regimen.	Test all patients before starting antiretroviral therapy.
Rapid Plasma Reagin (RPR) test and titer	At diagnosis and at least yearly. Syphilis staging is important if RPR is positive at any time. Routine monitoring may be as	Syphilis staging guides therapy duration. Lumbar Puncture (LP) if positive only if exam

Test	Frequency	Comments
	frequent as Q 3 months in people with ongoing risk for acquisition.	suggests ocular, otic or neurosyphilis. A positive RPR must be confirmed with a direct treponemal test such as TPPA.
GC/Chlamydia	At diagnosis and at least yearly. Consider 3-6 month monitoring in people with ongoing STI risk.	Based on sites of exposure, order urine, rectal and pharyngeal testing, regardless of reported condom use.
Quantiferon or T-SPOT.TB assay or Purified Protein Derivative (PPD)	At diagnosis and yearly (if in a high.	See treatment recommendation below for positive test response.
HBsAg, HBsAb, HBcAb, HCV Ab, Hep A total Ab	Once for all patients. Test men who have sex with men (MSM), transgender women, and people who inject drugs (PWID). Hepatitis C repeated annually.	Vaccinate for hepatitis A if serology is negative. HepB vaccination is indicated if no evidence of prior infection or if prior HepB vaccination series was not completed. Positive HCV Ab tests should be reflexed to quantitative RNA for confirmation.
Toxoplasma Antibody (Ab)	Once	Prophylaxis if CD4 count <100
CMV Ab	Once only if at low risk (non-MSM, non-PWID).	Repeat CMV testing only necessary for those who are negative initially.
Varicella Ab	Once if no history of chickenpox or shingles.	Consider vaccination if negative and CD4 count > 200.
Chest X-Ray (CXR)	CXR is adequate for positive TB test evaluation if no symptoms of active	Sputum culture is the gold standard of active TB infection and should be

Test	Frequency	Comments
	TB and no cough of any duration.	obtained if any symptoms accompany a positive TB test.
CMP/CBC	Q 3-4 months or when conducting CD4 count and HIV viral load.	
Urinalysis	Obtain at baseline, annually and at ART initiation, if delayed.	
Pregnancy	Obtain at baseline and before ART initiation if delayed.	
Cervical Papanicolaou test (abbreviated as Pap test, also known as Pap smear, cervical smear, cervical screening or smear test)	Testing at baseline followed by annual Pap. Co-testing for human papillomavirus (HPV) is indicated only for those 30 years or older.	After three negative annual Pap tests, patients can be tested every 3 years ("Co-testing" for women over 30 years old)
Trichomonas vaginalis	Women should be screened on entry into care and annually. If positive, retesting 3 months after treatment is recommended.	Extragenital trichomonas testing is not recommended.
Anal Pap smear	Anal cytology can be considered but guidelines are not established and risk vs benefit is unclear.	Prior to initiating anal cytology providers must have a referral source for High Resolution Anoscopy and treatment of abnormalities.
Lipids	Baseline and annually.	
Basic chemistry	Baseline, with ART initiation or modification and 2-8 weeks later, then every 6 months.	
Hgb A1c and fasting glucose	Baseline and annually.	
G-6-PD level	Once	

Test	Frequency	Comments
HLA B*5701 assay	Once if considering ART that includes abacavir.	Used to detect risk for abacavir hypersensitivity syndrome.

ANTIRETROVIRAL THERAPY[iv]

Antiretroviral therapy for HIV is now available on the IHS Core Formulary. The standard indication for antiretroviral therapy is now quite simple:

Treat All HIV positive people regardless of CD4 count

Treatment not only preserves the health of people living with HIV but it also is an important prevention tool. Viral suppression prevents transmission. It is for both of these reasons that rapid initiation of antiviral therapy is the goal for all people newly diagnosed with HIV. The DHHS Antiretroviral Guidelines (https://aidsinfo.nih.gov/guidelines) along with the IHS Core Formulary, provide the basis for the recommended medications for use by IHS providers in non-pregnant people living with HIV. The preferred single-tablet regimen for most patients is Tenofovir Alafenamide/Emtricitabine/Bictegravir (Biktarvy™) one tablet by mouth (p.o.) daily if there are no resistance mutations to the three components noted on the initial genotypic antiretroviral resistance test (GART). Avoid prescribing this drug to persons with a creatinine clearance less than 30 mL/min.

A second acceptable regimen on the IHS Core Formulary for patients intolerant of the first regimen is Abacavir/Lamivudine/Dolutegravir (Triumeq™) one tablet daily. This single pill regimen requires pre-screening to make sure the patient is HLA B*5701 negative to avoid a potentially fatal hypersensitivity reaction to abacavir. Some studies have linked the abacavir component in this pill to cardiovascular complications, so this is not the first choice regimen for patients with established heart disease or high risk for heart disease. The integrase inhibitors in these two tablets, dolutegravir and bictegravir, interact with antacids, rifamycins, anti-epileptics,

and metformin. It is wise to use a drug interaction app before starting these antivirals or adding new medications. Medication adherence is considered the most important aspect of medication management to achieve viral suppression. A lack of, or loss of, viral suppression is usually due to adherence problems. Pharmacists, case managers and peer counselors are all resources, in addition to medical providers, for patient support in the case of adherence problems. ART refill history will frequently confirm adherence problems.

Medication management of HIV during pregnancy is also addressed in the DHHS Antiretroviral Guidelines (https://aidsinfo.nih.gov/guidelines). Pregnant women during the first trimester and non-pregnant women with HIV considering becoming pregnant can be offered tenofovir disproxil fumarate/emtricitabine (Truvada™) plus raltegravir or dolutegravir. Dolutegravir has a slightly increased risk for neural tube defects over raltegravir (3/1000 vs 1/100). Doloutegravir is once daily while raltegravir is twice daily, thus improving adherence. Dolutegravir is considered preferred during pregnancy and with those wishing to conceive due to its adherence advantage. The increased risk for neural tube defects must be discussed with patients when initiating treatment with dolutegravir. Raltegravir is considered the alternate but is twice daily. Avoid tenofovir alafenamide (Vemlidyor Descovy™), the boosting agent cobicistat, and bictegravir in pregnancy as their safety in pregnancy is unknown.

Please consult an HIV specialist if:

1) The viral load fails to become suppressed below 200 copies at 4-6 months;
2) The viral load initially falls below 20 copies but later rebounds to greater than 200;
3) The patient is a pregnant woman; or
4) The patient is co-infected with hepatitis B or C.

The following web page provides more information about antiretroviral therapy. Search for **DHHS Antiretroviral Guidelines:**

https://aidsinfo.nih.gov/guidelines

The **National HIV Curriculum,** developed by the AIDS Education Training Center and University of Washington, is another reliable resource:

https://www.hiv.uw.edu

The **UCSF HIV Warm-Line** is for consultation on complex antiretroviral therapy and related HIV management questions: **1-800-933-3413.**

Finally, the **Indian Country HIV ECHO Teleconference** is a unique monthly teaching and clinical management advice resource. The ECHO is held the second Wednesday of every month at noon Mountain Time. This teleconference, co-sponsored by IHS and the University of New Mexico, provides technical assistance, education and training for those providing care to people living with HIV. Please contact IHSECHO@unm.salud.edu to connect with this service.

PREVENTION OF OPPORTUNISTIC INFECTIONS[v]

Prophylactic therapy for HIV associated opportunistic infections has made a significant impact on HIV morbidity and mortality. Department of Health and Human Services (DHHS) guidelines indicate the subsequent preventive treatments for the following infections:

Organism	CDC count cutoff	Drug regimens (in order of preference
Pneumocystis	≤ 200 cells/mm^3	1)TMP/SMZ DS or SS 1 p.o. daily 2) TMP/SMZ DS 1 p.o. 3x per week 3) Dapsone 100 mg p.o. daily (check G-6-PD level before starting) 4) Atovaquone 1500 mg p.o. daily 5) Aerosolized pentamidine 300 mg per month
Toxoplasmosis	≤100 cells/mm^3 & (+) serology	1) TMP /SMZ DS 1 p.o. daily 2) Dapsone 50 mg p.o. daily *plus* Pyrimethamine 50 mg p.o. weekly *plus* leukovorin 25 mg p.o. weekly. (check G-6-PD level before starting dapsone)
Mycobacterium avium complex	≤ 50 cells/mm^3 and not starting ART	1) Azithromycin 1200 mg p.o. weekly (check AFB blood culture before Rx) 2) Clarithromycin 500mg p.o bid

Providers should base institution of prophylactic therapy on the most recent CD4 count. For patients receiving preventive therapy for the following organisms, you may stop once there is immune reconstitution:

Criteria for stopping primary prophylaxis

Pathogen	Criteria	Comment
Pneumocystis	CD4 count >200 for 3 months	Restart when CD4 count < 100 or CD4 count 100-200 and HIV RNA is detectable
M. avium	Effective ART initiated	Restart when CD4 count < 50 only if not on fully suppressive ART
Toxoplasmosis	CD4 count is >200 for 3 months	Restart when CD4 count < 100 or CD4 count 100-200 and HIV RNA is detectable

HEALTH MAINTENANCE[vi]

Partner Notification

Referrals should be made routinely to the local tribal or other local government HIV partner notification program for contact investigation. Testing of contacts and referral of HIV-positive contacts for evaluation and treatment is urgent, yet voluntary. Refer partners of people newly diagnosed with HIV for assessment and inform them of their eligibility for Pre-Exposure Prophylaxis (PrEP) for HIV.

Case Management/Home Care

Optimal HIV care should involve immediate enrollment in a local case management program. Case management could include a designated HIV nurse case manager and HIV home care technician(s). Another option is to work with pre-existing resources, such as local IHS public health nursing programs, IHS pharmacists, social workers and tribal community health representative programs. Many states and localities have a local HIV case management program that can conduct outreach to assist people living with HIV with support services and adherence assistance. Teaching resources for use in the clinic and field are available on the IHS HIV webpage at https://www.ihs.gov/hivaids/resources/.

Eye Care

HIV-positive patients need an annual eye clinic check-up to evaluate for the presence of HIV-related eye disease, and to refer for appropriate care when present.

Dental Care

HIV-positive patients need an annual dental clinic check-up to evaluate for the presence of HIV-related oral disease, and to refer for appropriate care when present.

Gynecological Care

Women living with HIV need routine gynecologic care including cervical pre-cancer/cancer screening. Routine mammography is indicated as per USPTF guidelines.

Women aged <30 years

- The Pap test is the primary mode for cervical cancer screening for women <30 years.
- Commence screening within 1 year of the onset of sexual activity regardless of mode of HIV transmission (e.g., sexual activity, perinatal exposure) but no later than 21 years old.
- Conduct Pap test at the time of initial diagnosis with HIV for women with HIV who are 21 to 29 years old.
    - If the initial Pap test is normal, the next Pap test should be in 12 months.
    - If the results of the 3 consecutive Pap tests are normal, follow-up Pap tests should be every 3 years.

Women aged ≥30 years

- Either Pap testing only or Pap testing and HPV co-testing is acceptable for screening women living with HIV >30 years of age.
- *Pap test only:*
    - Perform a Pap test at the time of HIV diagnosis (baseline), then every 12 months.
    - If the results of the 3 consecutive Pap tests are normal, follow-up Pap tests should be every 3 years.
    - Continue cervical cancer screening throughout the woman's lifetime (and do not, as in the general population, end at 65 years of age).
- *Pap and HPV co-testing*:
    - Perform co-testing with Pap and HPV at the time of diagnosis or age 30.
    - Co-test *negative* women (i.e., a normal Pap and negative HPV test) can have their next cervical cancer screening in 3 years.
    - Pap test normal but *positive for HPV,* repeat co-testing in one year (unless genotype testing for 16 or 16/18 is positive). If either of the co-tests at one year is abnormal (i.e., abnormal cytology or positive HPV), refer to colposcopy.
    - If the initial HPV results identify HPV16 or HPV16/18, then refer to colposcopy. If the HPV testing is positive, but the genotype specific testing for HPV16 or

HPV 16/18 is negative, then repeat co-testing in one year is recommended. If either of the co-tests at one year is abnormal (i.e., abnormal cytology or positive HPV), refer to colposcopy.

Colorectal/Anal Cancer Screening

Anal cancer screening with anal PAP testing is offered in some locations. Because its effectiveness in prevention of squamous cell carcinoma of the anus is unknown, its routine use is not recommended until further information is available. For those providers considering anal PAP testing it is important to have a proper referral source available for follow up testing and treatment for any person with an abnormal result. Colon cancer screening follows established guidelines for the general population. USPTF recommends beginning screening at age 50 for those with normal risk.

Sexually Transmitted Infection (STI) Screening Including Anal and Pharyngeal Testing

Annual screening for all patients for gonorrhea/chlamydia and syphilis is recommended. More frequent testing is frequently necessary and is recommended for all patients who are sexually active with more than one partner (consider q 3-6 months). Appropriate sites for gonorrhea/chlamydia testing must be determined through sexual history taking. Anal and oral swabs are indicated when patients engage in receptive anal or oral intercourse. Frequency of syphilis screening should match gonorrhea/chlamydia screening as risk factors for acquisition are identical. Note: CDC does not recommend oral chlamydia screening, however oral swabs are routinely done with a system that does both gonorrhea and chlamydia at the same time.

Lipid Screening

HIV-positive patients need annual lipid screening, plus screening after a change in antiretroviral therapy. Atorvastatin or Rosuvastatin, are preferred agents for treating hyperlipidemia in HIV positive persons. The American Heart Association (AHA) recognizes HIV as a risk enhancer for atherosclerotic coronary vascular disease. Consider moderate-dose statin therapy for HIV-positive persons with an ASCVD 10-year risk score of 5 percent or more per current AHA treatment guidelines.

Bone Health

DEXA scans are indicated for post-menopausal women, and for men age 50 or higher with HIV, especially those on Tenofovir. Vitamin D level testing is recommended once around the time of entrance to care. Vitamin D replacement is provided if 25 hydroxyvitamin D levels are below 20 ng/ml. Follow up testing is routinely done for those on replacement.

Tuberculosis (TB) Screening And Management of Latent Tuberculosis Infection (LTBI)

TB screening is done at diagnosis, and then annually thereafter. DHHS guidelines do not necessarily recommend annual TB screening for the general population. However AI/AN people are frequently cited as being at elevated risk for TB infection. Annual screening is recommended. Perform a TB skin test (PPD) with a cut-off of 5 mm for a positive test or Interferon Gamma Release Assay (IGRA) such as the Quantiferon test. Quantiferon testing offers the advantage of a single visit, saving time and money for the patient and clinic outreach staff. A symptom review and CXR are mandatory to show there is no active tuberculosis before making the diagnosis of LTBI. Differentiation of LTBI from active TB is important because active TB treated only with INH or INH/RIF can result in drug resistant TB. Negative skin test results or negative IGRA testing does not rule out active TB. Induce sputum for AFB smear and culture if patient has any symptoms suggesting active TB even if chest films are normal. Delay LTBI treatment until sputum results are available. Consider immediate treatment for active TB

if patient is acutely ill. IHS recommends consultation with an HIV/TB specialist for all patients with HIV and active TB co-infection.

Diagnosis of LTBI depends on PPD > 5mm or positive IGRA test with a completely negative history and system review. Isoniazid plus rifapentine for 12 weeks is the preferred LTBI regimen if ART drug interactions allow. Raltegravir based ART with tenofovir disproxidil fumarate/emtricitabine (Truvada) regimen is preferred while rifapentine is being administered. If rifapentine is not advisable due to drug interaction, 9 months of daily INH is a suitable alternative for LTBI treatment. Pyridoxine 50 mg PO daily is recommended when administering INH to prevent peripheral neuropathy.

Nutritionist Consultation

HIV-positive patients should see a nutritionist yearly at a minimum. Guidelines indicate more frequent monitoring if the patient is malnourished or has diabetes.

Hepatitis Testing

Guidelines indicate baseline testing for hepatitis A (HAV Ab), hepatitis B (HB sAg, HB cAb, HB S Ab) and hepatitis C (HCV Ab). If Hep A or Hep B non-immune, then vaccinate. Unless already immune or infected, offer annual testing for hepatitis B and C to patients with high-risk behavior (MSM or PWID). Treatment of Hepatitis C with a direct acting agent combination of drugs such as sofosbuvir/velpatasvir (Harvoni) or glecaprevir/pibrentasvir (Mavyret), or others, is highly recommended for all people with HIV. Consult an HCV treatment expert either in direct consultation or utilize IHS HCV ECHO for guidance. People with HIV/HCV co-infection are known to progress to liver cirrhosis faster than average. Screening for reinfection of HCV after HCV is treated must be done with HCV RNA testing as HCV Ab testing usually remains positive life long, even after HCV is successfully treated.

Vaccines

Immunize all patients with hepatitis B, influenza, TdAP, meningococcal, and pneumococcal vaccines. Patients should receive both the conventional PPSV-23 (Pneumovax™) and the PCV-13 (Prevnar™) vaccines. First, give PCV 13 followed 2 months later by PPSV-23 vaccine. Give a second dose of PPSV-23 5 years later. All patients require a hepatitis B surface antibody test after immunization to document immunity. If they do not respond with (+) HB sAb (> 10mIU/mL), then a double dose hepatitis B vaccine can be given at 0, 1, 2, and 6 months to HIV-positive patients who have not responded to primary immunization, as an alternative to repeating the initial standard vaccine series of three injections. Another alternative is to consider use of Heplisav, an adjuvanted HepB immunization. Document hepatitis A immunity, and if non-immune give the hepatitis A vaccine series. If serologic testing is not available, then immunization should be done if not previously documented. Availability of serologic testing should not be a barrier to immunization. According to the Advisory Committee on Immunization Practices (ACIP), provide the HPV vaccine to males and females through age 26. However, the U.S. Food and Drug Administration (FDA) allows for HPV vaccination through age 45. Given the high incidence of HPV and HPV-related cancers in people who are HIV-positive, HPV immunization is recommended for all patients through age 45. Also note that the 3 dose series is indicated for all those receiving HPV immunization over the age of 15. Consider the varicella primary vaccination for adults who are varicella seronegative and have a CD4 count greater than 200. Shingrix is recommended for HIV-positive people 50 years of age and older regardless of CD4 count. Recommendations call for MenACWY vaccines (Menactra® and Menveo®) for all HIV-positive adults with repeat vaccine at 2 months then every 5 years afterward.

Mental Health

Screen all patients for depression, anxiety, suicidal ideation, and substance use disorder at every visit. Refer any patient with an abnormal mental health or substance use screen result to a mental health provider or substance use disorder counselor. At every visit, provide a domestic violence screening for all patients with appropriate referrals for a positive screening.

Spiritual Health

Ask patients about their spiritual health during clinic visits and refer to a traditional healer, chaplain, or another provider for spiritual health.

HIV PREVENTION IN PRIMARY CARE

The CDC now encourages providers to teach people living with HIV the concept of "U=U" or "Undetectable equals Un-transmittable[vii]." As long as the person who is HIV-positive has an HIV viral load consistently less than 200 copies/ml, there is essentially no risk of transmission to their HIV uninfected partner. Condom usage should still be promoted to prevent transmission of sexually transmitted infections between partners. PrEP is recommended for any person with an HIV positive partner where the partner is not on ART or is not consistently with a suppressed HIV viral load (less than 200 copies/mL). PrEP is also recommended when the HIV negative partner has additional partners or engages in injection equipment sharing.

GUIDELINES FOR THE PRIMARY AND GENDER-AFFIRMING CARE OF TRANSGENDER AND GENDER NONBINARY PEOPLE

UCSF Transgender Care at the University of California - San Francisco produced Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People.

Transgender people have a gender identity that differs from the sex which they were assigned at birth and are estimated to represent 0.5% of the U.S. population.1 Numerous needs assessments have demonstrated that transgender people often encounter a range of barriers to accessing primary health care. A 2015 survey of 27,715 transgender people in the U.S. found that negative experiences with doctors and other health care providers varied by race and ethnicity. Of the 302 American Indian and Alaska Native respondents, 50 percent reported the highest level of

[1] Conron KJ, Scott G, Stowell GS, Landers SJ. Transgender Health in Massachusetts: Results From a Household Probability Sample of Adults. Am J Public Health. 2012 Jan;102(1):118–22.

negative experiences.2 Additionally, more than one-third (37 percent) of American Indian and Alaska Native respondents reported that at some point in the past year they needed health care but did not seek it due to fear of being disrespected or mistreated as a transgender person.

Two-Spirit *and LGBTQ (2S/LGBTQ*) Health

2S/LGBTQ is an inclusive abbreviation for Two-Spirit, Lesbian, Gay, Bisexual, Transgender, and Queer/Questioning.

Historically, American Indian and Alaska Native individuals have supported and celebrated expansive definitions of gender and sexual orientation. Sexual orientation, gender identity, and gender roles were often blurred, and there was general acceptance for all gender expressions and lack of need for restrictive definitions. This gender mindfulness demonstrates the expanse of terminology that exists, describing multiple genders and sexual identities in Native communities (Jacobs, Thomas, & Lang, 1997) (Pruden, 2014).

While variety in terminology remains, the unifying term 'Two-Spirit' describes an individual who has both a male and female essence. The assignment of male or female sex at birth does not matter. The term also expresses traditional Indigenous understanding of a non-female, non-male gender.

The creation of a safe, inclusive, and welcoming space is critically important in providing gender-affirming care. It is also important to recognize that no matter how safe the space we create may be, it may not always be safe for 2S/LGBTQ individuals to be out to their families and communities. Providers can remain supportive and allow 2S/LGBTQ individuals to trust us in a space of support and respect, while respecting and maintaining confidentiality as appropriate.

[2] James, S. E., Herman, J. L., Rankin, S., Keisling, M., Mottet, L., & Anafi, M. (2016). The Report of the 2015 U.S. Transgender Survey. Washington, DC: National Center for Transgender Equality https://www.transequality.org/sites/default/files/docs/USTS-Full-Report-FINAL.PDF

The National LGBTQ Health Education Center has developed a series of case studies focused on helping health providers address implicit bias related to LGBTQ patients.

https://www.lgbthealtheducation.org/publication/learning-to-address-implicit-bias-towards-lgbtq-patients-case-scenarios/

How to use pronouns: There is no "right answer" to a perfect encounter with your 2S/LGBTQ patient. However, developing a trusting relationship with them and understanding them as a whole person are some benchmarks for which to aim. Asking questions about the patient's pronouns is a great place to start. Because gender identity is typically formed between the ages of 2-4 years old, health care providers can begin asking questions about gender from an early age (Martin & Ruble, 2010).

Pronouns are important to a person's identity. Pronouns allow people to be genuinely seen and heard in all settings (home, school, work, sporting events, a doctor's office). You cannot always assume pronouns based on how someone looks, so it is best to ask them which pronouns they use. Asking about someone's pronoun is also a sign of respect. Using the wrong pronoun or forgetting to ask for someone's pronouns might cause people to feel ignored or alienated.

It is okay to feel uncomfortable asking about pronouns at first. It may take some time to make this part of your routine, but pronouns will help to make others feel comfortable. They can also help you form more trusting relationships.

Ways to ask about which pronouns someone uses

- Keep it simple
- Introduce yourself using your chosen name and pronouns.
    - "What name do you go by?" and "What would you like to be called?"
    - "What pronouns do you use?"
- Be respectful and non-judgmental.
- This may feel uncomfortable or awkward at first, but it can help you create an inclusive and affirming environment.

When you realize you have made a mistake about someone's name or pronouns, the best thing to do is apologize and ask questions so you can learn for next time. You can ask clarifying questions right away or later on. The important thing is that you learn from your mistake and show that you are acting with respect.

The importance of a chosen name: Use the patient's preferred name to show that you respect and understand their identity. For individuals who are socially transitioning, using a new name can be a powerful step. Using a chosen name has a remarkable impact on health. In one research study, youth who were able to use their chosen names in more than one place (school, home, work, and with friends) had lower rates of depression and suicidal thoughts (Russell, Pollitt, Li, & Grossman, 2018). There was also a 56 percent decrease in suicidal behavior.

The American Academy of Pediatrics (AAP) released a policy statement in 2018 entitled, "*Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents.*" It promotes a gender-affirming model that focuses on family resiliency and freedom for each child to develop and experience life as their desired gender.

https://pediatrics.aappublications.org/content/142/4/e20182162

Your clinic can also uphold 2S/LGBTQ cultural competency by developing paths for feedback and understanding community opinions. Feedback from patients and their families can help inform future changes and make the clinic increasingly welcoming.

By following suggestions provided in the toolkit entitled, "*Celebrating Our Magic: Resources for American Indian/Alaska Native transgender and Two-Spirit youth, their relatives and families, and their healthcare providers*," you can learn how to become a supportive figure for your American Indian and Alaska Native 2S/LGBTQ patients, even if you do not identify as 2S/LGBTQ yourself.

http://www.npaihb.org/download/Toolkit_v6_24.pdf

Other considerations include:

- Listening to your patients and their families.
- Asking about gender pronouns, gender identity, and chosen name.
- Respecting confidentiality.
- Understanding that not all patients you interact with will be out to their friends, families, and communities.
- Considering patient safety when developing care plans.
- Avoiding judgmental comments by thinking before you respond.
- Asking how you can be helpful and provide support.
- Showing respect, even if you do not agree with a decision.
- Recognizing your limits as an ally.

HIV PRIMARY CARE SCREENING CHECKLIST

Baseline Evaluation:

- CD4 Count
- HIV Viral Load
- HIV Genotypic Antiretroviral Resistance Test
- RPR
- GC/CT for all sites of potential exposure
- Hepatitis A total Ab, HBsAg, HBsAb, HBcAb, HCV Ab with PCR reflex when positive
- Quantiferon or Tuberculosis skin test (CXR if positive)
- Toxoplasma Antibody
- HLA B*5701Varicella Antibody if no documented history of chickenpox/shingles
- CBC
- CMP
- Lipid panel
- G6PD test
- Hemoglobin A1c and/or fasting glucose
- UA
- Urine Pregnancy, if female
- Cervical Pap smear

Quarterly evaluation:

- CD4 Count
- HIV Viral Load
- CMP
- CBC
- STD screening to be considered including GC/CT and RPR (syphilis)

Annual Evaluation:

- RPR
- GC/CT (urine test for all, pharyngeal/rectal if there is exposure)
- HCV Ab with reflex PCR if positive
- Quantiferon or Tuberculosis skin test (CXR if positive)
- UA
- Eye Exam
- Dental Exam
- Cervical PAP smear (for at least 3 consecutive years per above noted guideline)

Other Periodic Screening:

- DEXA scan (per above recommendation)
- Colorectal Cancer Screening (per USPTF recommendation)
- Mammography
- Low dose chest CT for lung cancer screening for current/former smokers with 30 + pack year smoking exposure (USPTF recommendation)
- Abdominal aortic aneurysm screening for men age 65-75 with smoking history (USPTF recommendation)

ABBREVIATIONS

Abbreviation	Meaning
3HP	3HP is one of the regimens recommended by the CDC for treatment of latent tuberculosis infection. The term 3HP comes from the regimen duration (once weekly doses for 3 months) and the abbreviations of each of the two drugs Isoniazid (INH) and Rifapentine (RPT) in the regimen.
AAHIVS	American Academy of HIV Medicine Specialist
ACIP	Advisory Committee on Immunization Practices
AFB	An acid-fast bacteria (AFB) culture is done to find out if a person has tuberculosis (TB) or another mycobacterial infection. Besides TB, the other main mycobacterial infections are leprosy and a TB-like disease that affects people with HIV/AIDS. To do an AFB culture, providers take a sample of phlegm or sputum or a tiny bit of tissue. They "culture" it by putting it in a special container with food the bacteria needs to grow. They then check it over a few weeks to see whether the bacteria grow. If they do, a mycobacterial infection is present.
ART	Antiretroviral Therapy. ART are medications that treat HIV. The drugs do not kill or cure the virus. However, when taken in combination, they can prevent the growth of the virus. When the virus is slowed down, so is HIV disease. Antiretroviral drugs are referred to as ARV. Combination ARV therapy (cART) refers to highly active ART (HAART).
AHA	American Heart Association
AIDS	Acquired immunodeficiency syndrome (AIDS) is the most advanced stage of HIV infection. To be diagnosed with AIDS, a person with HIV must have an AIDS-defining condition or have a CD4 count less than 200 cells/mm3 (regardless of whether the person has an AIDS-defining condition). By damaging the immune system, HIV interferes with the body's ability to fight the organisms that cause infections. HIV is a sexually transmitted infection (STI) or it may be transmitted by exposure to HIV-infected blood.
CBC	Complete Blood Count. A complete blood count (CBC) is a blood test used to evaluate one's overall health and detect a wide range of disorders, including anemia, infection, and leukemia. A CBC test measures several components and features of one's blood, including red blood cells, which carry oxygen.
CD4	In molecular biology, CD4 (cluster of differentiation 4) is a glycoprotein found on the surface of immune cells such as T helper cells, monocytes, macrophages, and dendritic cells.
CDC	Unites States (U.S.) Centers for Disease Control and Prevention

Abbreviation	Meaning
CMP	The comprehensive metabolic panel, or chemical screen, (CMP; CPT code 80053) is a panel comprised of 14 blood tests that serve as an initial broad medical screening tool.
CMV Ab	Cytomegalovirus (CMV) is a common virus that usually causes no symptoms or only mild illness. CMV testing detects antibodies (Ab) in the blood that the body produces in response to the infection with CMV.
CT	CT scans are also referred to as computerized axial tomography. CT, or CAT scans. CT scans are special X-ray tests that produce cross-sectional images of the body using X-rays and a computer.
CXR	Chest radiography, lung radiography.
DEXA	Dual Energy Absorptiometry (DEXA), an imaging technique that uses two low-dose X-Rays with different levels of energy to produce a detailed image of body components; used primarily to measure bone mineral density.
DS	Double Strength
ECHO	Extension for Community Healthcare Outcomes is a tele-consulting and tele-mentoring partnership between specialists and providers in rural and underserved communities. Provides HIV, HCV, and numerous other teleconsultative services.
FACP	Fellow of the American College of Physicians
FDA	United States (U.S.) Food and Drug Administration
G-6-PD	Glucose-6-phosphate dehydrogenase deficiency is a genetic disorder that occurs almost exclusively in males. This condition mainly affects red blood cells, which carry oxygen from the lungs to tissues throughout the body. In affected individuals, a defect in an enzyme called glucose-6-phosphate dehydrogenase causes red blood cells to break down prematurely. This destruction of red blood cells is called hemolysis.
GC	Abbreviation for the guanine and cytosine base pair in polynucleic acids; gonococcus; gonorrhea.
HBsAb	Abbreviation for hepatitis B Surface Antibody test, which looks for antibodies that one's immune system makes in response to the surface protein of the hepatitis B virus. The hepatitis B surface antibody is also referred to as anti-HBs and should not be confused with HBsAg, which stands for hepatitis B surface antigen.
HBsAg	Hepatitis B surface antigen - A "positive" or "reactive" HBsAg test result means that the person is infected with hepatitis B. This test can detect the actual presence of the hepatitis B virus (called the "surface antigen") in a person's blood. If a person tests "positive," then further testing is needed to determine if this is a new "acute" infection or a "chronic" hepatitis B infection. A positive HBsAg test result denotes an

Abbreviation	Meaning
	infection that can spread the hepatitis B virus to others through a person's blood.
HBcAb	Hepatitis b core antibody. Hepatitis b core antibody is an antibody created when the body responds to hepatitis B infection. When positive, it signifies prior exposure and infection. Positive HBcAb and positive HBsAb signifies clearing of hepatitis B infection. Positive HBcAb and negative HBsAb suggests ongoing hepatitis B infection. People with hepatitis B core antibody and surface antibody are potentially at risk to reactivate hepatitis B infection if they become immune suppressed.
HCV Ab	Hepatitis C antibody. This is the first test for determining whether a person has been infected with hepatitis C. The results will come back as either positive or negative. If this test result is positive, it means one's body was exposed to the hepatitis C virus and made antibodies. However, it does not tell a person whether they are still infected with hepatitis C. If the antibody test result is positive, one should be tested for hepatitis C RNA (see "Hepatitis C RNA"), which determines whether the person is chronically infected. The lab will perform this RNA test automatically if one's hepatitis C antibody test is positive. If the antibody test result is negative, it means the person has not been infected with the hepatitis C virus, and further testing for hepatitis C usually is not needed with an uncommon exception that people who are significantly immune suppressed may have active HCV infection with no antibody response. This uncommon situation will only become evident if HCV RNA testing is ordered.
Hep A total Ab	Hepatitis A total antibody. This test is used to help diagnose a liver infection due to the hepatitis A virus (HAV). The total HAV antibody test detects both IgM and IgG antibodies and thus may be used to identify both current and past infections.
HHS	U.S. Department of Health and Human Services
HIV	HIV stands for human immunodeficiency virus. It weakens a person's immune system by destroying important cells that fight disease and infection. No cure exists for HIV. But with proper medical care, HIV can be controlled.
HLA B	HLA-B (major histocompatibility complex, class I, B) is a human gene that provides instructions for making a protein that plays a critical role in the immune system. HLA-B is part of a family of genes called the human leukocyte antigen (HLA) complex.
HLA B*5701	A specific HLA marker which, when positive, signifies risk for abacavir hypersensitivity. Abacavir hypersensitivity is a dangerous condition that can be fatal if a person who is HIV-positive is given

Abbreviation	Meaning
	abacavir. A negative HLA B*5701 test should always precede administration of an abacavir-containing HIV regimen.
HPV	Human papillomaviruses are a group of related viruses. They can cause warts on different parts of one's body. There are more than 200 types. About 40 of those types affect the genitals. They are spread through sexual contact with an infected partner. Some strains can put a person at risk for cancer.
IGRA	Interferon-Gamma Release Assays are whole-blood tests that can aid in diagnosing Mycobacterium tuberculosis infection. They do not help differentiate latent tuberculosis infection (LTBI) from tuberculosis disease.
IHS	Indian Health Service
INH	Isoniazid, a medication used to treat latent TB infection.
LP	A lumbar puncture (spinal tap) is performed in a person's lower back, in the lumbar region. During a lumbar puncture, a needle is inserted between two lumbar bones (vertebrae) to remove a sample of cerebrospinal fluid. This is the fluid that surrounds one's brain and spinal cord to protect them from injury.
MSM	Abbreviation for men who have sex with men
Pap	The Papanicolaou test (abbreviated as Pap test, also known as Pap smear, cervical smear, cervical screening or smear test) is a method of cervical screening used to detect potentially precancerous and cancerous processes in the cervix (opening of the uterus or womb).
PCV-13	Pneumococcal conjugate vaccine (called PCV13) protects against 13 types of pneumococcal bacteria. PCV13 is routinely given to children at 2, 4, 6, and 12–15 months of age. It is also recommended for children and adults 2 to 64 years of age with certain health conditions, and for all adults 65 years of age and older.
PPD	A purified protein derivative skin test is a test that is used to diagnose latent tuberculosis infection.
PPSV-23	Pneumococcal polysaccharide vaccine protects against 23 types of neumococcal bacteria. This vaccine helps prevent invasive infections like meningitis and bacteremia.
PrEP	Pre-exposure prophylaxis (or PrEP) is when people at high risk for HIV take daily medicine to prevent HIV. PrEP can prevent establishment of HIV infection if a person is exposed to HIV. When taken daily, PrEP is highly effective for preventing HIV from sex or injection drug use. PrEP is much less effective when it is not taken consistently. Studies have shown that PrEP reduces the risk of getting HIV from sex by about 90 percent when taken daily. Among people who inject drugs,

Abbreviation	Meaning
	PrEP reduces the risk of getting HIV by at least 74 percent when taken daily.
PWID	Abbreviation for person(s) who inject drugs.
QFT	QuantiFERON, also known as QFT, is the registered trademark of the test for tuberculosis infection or latent tuberculosis. QIAGEN manufactures QFT, which is an interferon-γ release assay (IGRA) used in tuberculosis diagnosis.
RPR	A rapid plasma reagin (RPR) test is a blood test used to screen a person for syphilis. It works by detecting the nonspecific antibodies that the body produces while fighting the infection. Syphilis is a sexually transmitted infection (STI) caused by the spirochete bacterium Treponema pallidum. RPR titers are used to monitor the effectiveness of syphilis treatment.
RPT	Rifapentine, a medication used to treat latent TB infection.
SMZ-TMP	This medication is a combination of two antibiotics: sulfamethoxazole and trimethoprim. It is used to treat a wide variety of bacterial infections (such as middle ear, urine, respiratory, and intestinal infections). It is also used to prevent and treat a specific type of pneumonia (pneumocystis-type).
STD/STI	Sexually Transmitted Disease/Sexually Transmitted Infection
TB	Tuberculosis
TdAP	TdAP is a combination vaccine that protects against three potentially life-threatening bacterial diseases: tetanus, diphtheria, and pertussis (whooping cough). Td is a booster vaccine for tetanus and diphtheria. It does not protect against pertussis. Tetanus enters the body through a wound or cut.
UA	Abbreviation for urinalysis.
UCSF	The University of California, San Francisco (UCSF) is a public research university in San Francisco, California. It is part of the University of California system, and it is dedicated entirely to health science. It is a major center of medical and biological research and teaching.

GLOSSARY OF TERMS

Term	Definition
Adolescent	Adolescent is defined as any post-pubertal young person. These guidelines are intended for adults and pos-pubertal adolescents. Any prepubertal person is considered pediatric and if HIV-positive should have expert consultation as part of their management.
ASCVD 10-year risk score	Arteriosclerotic Cardiovascular Disease. The American College of Cardiology (ACC) and the American Heart Association (AHA) collaborated to create a short, 9-step calculator to estimate 10-year and lifetime risk for Arteriosclerotic Cardiovascular Disease (ASCVD). A patient's basic health information is entered into the estimator (sex, age, race, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, blood pressure-lowering medication use, diabetes status, and smoking status) and within seconds, risk rates are output and treatment recommendations are made.
Cisgender	A term used to describe a person whose gender identity aligns with those typically associated with the sex assigned to them at birth.
Cotton wool spots	An abnormal finding on a funduscopic exam of the retina of the eye. They appear as fluffy white patches on the retina. They are caused by damage to nerve fibers and are a result of accumulations of axoplasmic material within the nerve fiber layer.
DEXA scan	Dual Energy Absorptiometry (DEXA) is an imaging technique that uses two low-dose x-ray beams with different levels of energy to produce a detailed image of body components; used primarily to measure bone mineral density.
Focal deficits	A focal neurologic deficit is a problem with the nerve, spinal cord, or brain function. It affects a specific location, such as the left side of the face, right arm, or even a small area such as the tongue. Speech, vision, and hearing problems are also considered focal neurological deficits.
Genotypic antiretroviral Resistance Test (GART)	A type of resistance test that detects drug-resistant mutations in HIV genes. Resistance testing is used to guide the selection of an HIV regimen when initiating or changing antiretroviral therapy (ART).
Hepato-splenomegaly	A disorder where both the liver and spleen swell beyond their normal size, usually due to an infection such as mononucleosis or viral hepatitis. It may also be a sign of another more serious illness such as a lysosomal storage disorder.
HIV Viral Load	Measures the amount of HIV genetic material (RNA) in the blood and reports how many copies of the virus are present. Evidence shows that keeping the HIV viral load at undetectable levels decreases an infected person's risk of progressing to AIDS and significantly improves long-term health.
HLA B*5701 assay	A test that detects the presence of HLA-B*5701. HLA-B*5701 is a genetic variation that is linked to hypersensitivity to the antiretroviral (ARV) drug abacavir. A person who tests positive for HLA-B*5701 should not use abacavir or any other abacavir-containing medicine.

Term	Definition
Icterus	Yellowing of the skin and the whites of the eyes – or sclerae – caused by an accumulation of bile pigment (bilirubin) in the blood; can be a symptom of gallstones or liver infection or anemia.
M. avium	Mycobacterium avium complex (MAC) is a group of bacteria related to tuberculosis. These germs are prevalent in food, water, and soil. Almost everyone has them in their bodies. When a person has a robust immune system, they don't cause problems. But they can make people with weaker immune systems, like those with HIV, very sick.
Quantiferon assay	Also known as QFT, it is the registered trademark of the test for tuberculosis infection or latent tuberculosis. QIAGEN manufactures QFT, which is an interferon-γ release assay (IGRA) used in tuberculosis diagnosis. The QFT-GIT assay is an ELISA-based, whole-blood test that uses peptides from three TB antigens (ESAT-6, CFP-10, and TB7.7) in an in-tube format. The result is reported as quantification of IFN-gamma in international units (IU) per mL. An individual is considered positive for M. tuberculosis infection if the IFN-gamma response to TB antigens is above the test cut-off (after subtracting the background IFN-gamma response in the negative control).
Toxoplasma Ab	Toxoplasmosis is an infection caused by the parasite Toxoplasma gondii. Diagnosis can be made by serologic testing or by molecular testing. Serologic testing detects antibodies (Ab) in the blood that are produced in response to an infection and, depending on the type of antibodies present (IgG or IgM), a current or past infection can be determined. Molecular testing, such as PCR detects the genetic material (DNA) of the parasite in the blood and indicates an acute infection.
Transgender	An umbrella term for people whose gender identity and/or expression is different from cultural expectations based on the sex assigned at birth. Being transgender does not imply any specific sexual orientation. Therefore, transgender people may identify as straight, gay, lesbian, bisexual.

Term	Definition
Two-Spirit	Though Two-Spiritmay now be included in the umbrella of LGBTQ, The term "Two-Spirit" does not simply mean someone who is American Indian or Alaska Native and gay. Traditionally, Native American Two-Spiritpeople were male, female, and sometimes intersexed individuals who combined activities of both men and women with traits unique to their status as Two-Spiritpeople. In most tribes, they were considered neither men nor women; they occupied a distinct, alternative gender status. In tribes where Two-Spiritmales and females were referred to with the same term, this status amounted to a third gender. In other cases, Two-Spiritfemales were referred to with a distinct term and, therefore, constituted a fourth gender.
Varicella Ab	Varicella-zoster virus (VZV), a herpes virus, causes two distinct exanthematous (rash-associated) diseases: chickenpox (varicella) and herpes zoster (shingles). Chickenpox is a highly contagious, though typically benign disease, usually contracted during childhood. Individuals at risk for severe complications following primary VZV infection include pregnant women, in whom the virus may spread through the placenta to the fetus, causing congenital disease in the infant. Additionally, immunosuppressed patients are at risk for developing severe VZV-related complications, which include cutaneous disseminated disease and visceral organ involvement. The presence of detectable IgG-class antibodies (Ab) indicates prior exposure to the varicella-zoster virus (VZV) through infection or immunization. Individuals testing positive are considered immune to varicella-zoster.

REFERENCES/ENDNOTES

[i] National HIV Curriculum: https://www.hiv.uw.edu
[ii] National HIV Curriculum: https://www.hiv.uw.edu
[iii] Primary Care Guidelines for the Management of Persons Infected with HIV: https://www.idsociety.org/practice-guideline/primary-care-management-of-patients-infected-with-hiv/
[iv] Adult and Adolescent Antiretroviral Guidelines: http://aidsinfo.nih.gov/guidelines
[v] Adult and Adolescent Opportunistic Infection prevention and treatment guidelines: http://aidsinfo.nih.gov/guidelines
[vi] National HIV Curriculum: https://www.hiv.uw.edu
[vii] Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People: https://transcare.ucsf.edu/guidelines
United States Preventitive Task Force https://uspreventiveservicestaskforce.org
National STD Curriculum-https://www.std.uw.edu