

**Beth Israel Deaconess Medical Center
Healthcare Associates
Primary Care HIV Manual**

September 2020

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The recommendations contained in this monograph are based upon published guidelines for HIV-infected adults. Because the field of HIV disease is constantly advancing and standards of practice continue to evolve, practitioners should be familiar with the current medical literature and request advice as necessary from clinicians experienced in the field.

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Overview

The care of HIV-infected patients has undergone dramatic changes over the past two decades with the use of combination antiretroviral therapy and viral load and resistance testing in clinical practice. Patients are hospitalized less frequently with opportunistic infections and are living longer. However, with this encouraging news have come important challenges. For patients, they include long-term adherence to a medical regimen and dealing with its potential toxicities. For health care practitioners, they include keeping up with a changing but incomplete knowledge base and addressing the needs of an aging population, some of whom may develop other chronic medical issues, as well as addressing HIV prevention effectively in primary care practice.

The management of HIV disease lends itself to a primary care approach. Most successful models are multidisciplinary, integrating case management, behavioral health, and pharmacists within the care team. In addition to history and physical examination, the initial evaluation of HIV-infected patients should include assessment of their knowledge of the disease and emotional state. Baseline laboratory studies are performed to screen for occult disease and guide drug usage, to determine HIV disease status, and to look for evidence of concurrent infections. The CD4 cell count and viral load are essential for guiding therapeutic decisions.

Antiretroviral therapy is recommended in all HIV-infected patients regardless of their clinical status or CD4 cell count. There are both individual (decreased morbidity and mortality) and public health (decreased transmission) benefits of treatment. The recommended initial regimen is a nucleoside reverse transcriptase inhibitor (NRTI) x 2 *plus* an integrase inhibitor. Drug combinations over the past decade have consisted of a decreased number of pills that are dosed less frequently and associated with fewer side effects and long-term toxicities. Factors that may have a negative impact on adherence should be reviewed and addressed prior to initiation of therapy. Most patients will achieve viral suppression with their initial regimen, and the majority of these will continue to have undetectable virus on a long-term basis with good medication adherence. The success rate often decreases with subsequent regimens. All HIV-infected patients, regardless of whether they are receiving antiretroviral therapy, should be monitored with CD4 cell count and viral load tests. HIV resistance testing is indicated when the viral load is not maximally suppressed on antiretroviral therapy.

Complications have been associated with the long-term treatment of HIV infection. These include: 1) coronary artery disease; 2) premature bone loss; 3) lipodystrophy syndrome (body fat maldistribution, hyperlipidemia, glucose intolerance), mostly from exposure to older NRTIs; 4) avascular necrosis of hips; 5) lactic acidemia/acidosis; and 6) peripheral neuropathy.

Opportunistic infection (OI) prophylaxis for PCP is indicated if the CD4 cell count is less than 200/mm³; TMP-SMX is the drug of choice. Prophylaxis for toxoplasmosis is indicated in patients with positive toxoplasmosis serology if the CD4 cell count is less than 100/mm³. Prophylaxis for MAC infection is indicated in patients with chronic HIV infection and CD4 cell count less than 50/mm³ if they are not virally suppressed. OI prophylaxis for these infections can often be safely discontinued following immune reconstitution with antiretroviral therapy.

Routine health care maintenance issues in HIV-infected patients include immunizations (e.g., pneumococcal, hepatitis B, hepatitis A, influenza vaccines), periodic screening for concurrent infections (e.g., viral hepatitis, syphilis, other sexually transmitted diseases, tuberculosis), regular Pap smears in women and anal Pap smears in at-risk populations, and other appropriate age- and sex-related screening interventions.

COVID-19 and HIV Infection

Limited available data do not indicate that the disease course of COVID-19 (SARS-CoV-2) in persons with HIV infection differs from that of seronegative individuals. However, it is important to remember that patients may have other risk factors for increased morbidity and mortality, including age >60 years, hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, and obesity.

Chapter 1. HIV Testing and Counseling

Background

Health care personnel in Massachusetts are required by statute to obtain verbal informed consent from the patient or his/her health care proxy prior to HIV antibody testing. An HIV antibody test can be ordered by a treating physician or authorized HIV counselor. Pretest and post-test counseling, while often useful, should not be barriers to testing. All newly diagnosed cases of HIV infection are reportable to the Massachusetts Department of Public Health.

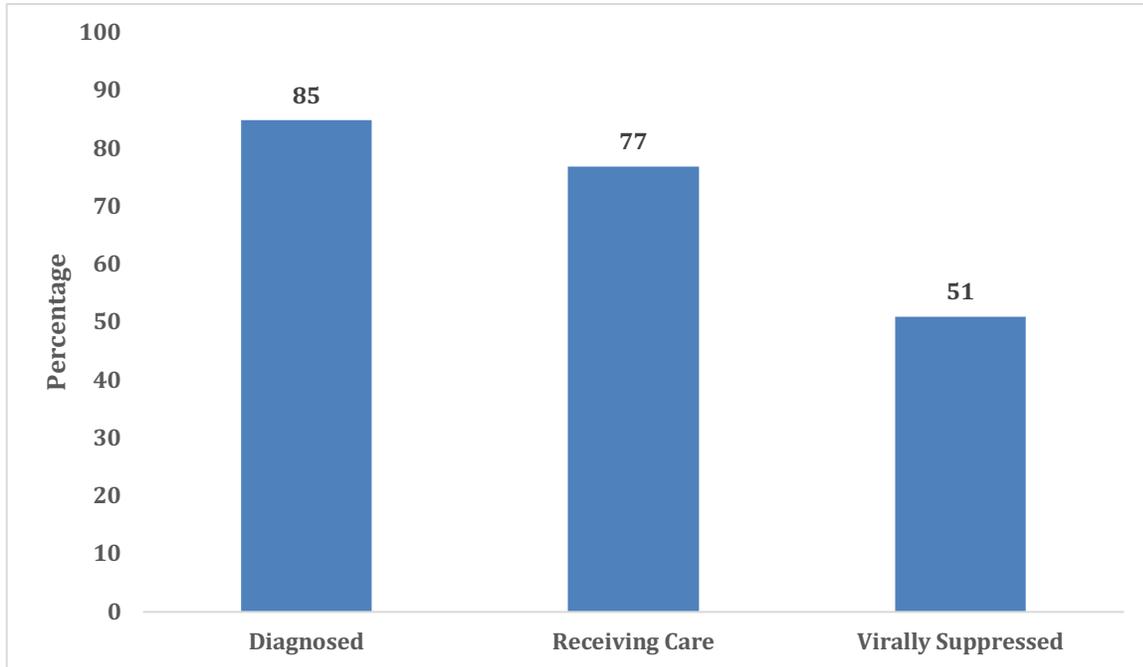
Epidemiology of HIV/AIDS and Risk of HIV Transmission

Despite advances in treatment, HIV infection remains a leading cause of morbidity and mortality. There are an estimated 1.1 million HIV-infected persons in the United States, and there were 37,832 new diagnoses in 2018. From 2010 to 2017, the number of new diagnoses decreased by 11%; however in certain demographic groups, the numbers have increased. Gay and bisexual men are the most affected by HIV, accounting for 69% of all new diagnoses and 86% of diagnoses in men.

Despite significant advances in HIV testing and medical treatment, only 63% of Americans achieve viral suppression. Figure 1-1 from the Centers for Disease Control and Prevention (CDC) of the HIV care continuum depicts that a significant number of people living with HIV drop off at each stage.

In response to these sobering statistics, the CDC has launched the Ending the HIV Epidemic campaign with a goal to reduce new HIV infections by 90% by 2030. This campaign is focused on three pillars: 1) ensuring patients are tested to know whether or not they are infected; 2) providing treatment for those who are infected to ensure their health and to reduce transmission; and 3) providing pre-exposure prophylaxis (PrEP) for those who have an ongoing risk of acquiring HIV.

Figure 1-1. HIV Infection in the United States: The Care Cascade



<https://www.cdc.gov/nchstp/newsroom/2019/hiv-vital-signs.html>

Estimated HIV Transmission Rate per Event by Exposure Route

Parenteral

- Transfusion of contaminated blood 92.5%
- Needle-sharing injection-drug use 0.63%
- Occupational needle-stick exposure 0.23%

Sexual

- Unprotected receptive anal intercourse 1.38%
- Unprotected insertive anal intercourse 0.11%
- Unprotected receptive vaginal intercourse 0.08%
- Unprotected insertive vaginal intercourse 0.04%
- Unprotected receptive oral intercourse low
- Unprotected insertive oral intercourse low

<https://www.cdc.gov/hiv/risk/estimates/riskbehaviors.html>

These estimates are provided by the CDC. It is important to note that these figures are approximate and may vary depending on the viral load of the source, the presence of other sexually transmitted diseases in both persons, male circumcision (for insertive vaginal intercourse), and other factors. Biting, spitting, and sharing sex toys are of negligible risk.

Guidelines

The CDC recommends inclusion of HIV antibody testing as part of the routine health care of adults and adolescents. The key points of these guidelines follow:

- All healthy adolescent and adult patients should be screened at least once during their lives after notification that an HIV test will be performed unless they decline (“opt-out” testing)
- Specific informed consent is unnecessary
- Persons at high risk for HIV infection should be screened at least annually
- Prevention counseling should not be required as part of routine HIV testing, but it is encouraged for persons at high risk

HIV antibody testing should never be construed by patients as coercive. As these federal recommendations are implemented over time, the hope is that a higher percentage of HIV-infected persons will become aware of their serostatus and that decreased HIV transmission will result through a reduction in risk behaviors and the institution of antiretroviral therapy.

Traditional Indications for Testing

Historical

- Men who have sex with men
- Persons with multiple sexual partners
- Current or past injection-drug users (IDUs)
- Recipients of blood products between 1978 and 1985
- Persons with current or past sexually transmitted diseases
- Commercial sex workers and their sexual contacts
- Persons who have been sexually assaulted
- Persons who have had occupational exposures
- Pregnant women and women of childbearing age
- Children born to HIV-infected mothers
- Sexual partners of those at risk for HIV infection
- Persons who consider themselves at risk or request testing
- Persons infected with hepatitis B considering treatment
- Persons considering pre-exposure prophylaxis (PrEP)

Clinical

- Tuberculosis
- Syphilis
- Recurrent or disseminated shingles
- Unexplained chronic constitutional symptoms
- Unexplained generalized adenopathy
- Unexplained chronic diarrhea or wasting
- Unexplained encephalopathy
- Unexplained thrombocytopenia
- Thrush or chronic/recurrent vaginal candidiasis
- HIV-associated opportunistic diseases (e.g., Pneumocystis pneumonia, Kaposi's sarcoma)
- Suspected primary HIV syndrome

Primary HIV infection is a nonspecific viral illness that occurs on average two weeks after exposure and is characterized by fever, adenopathy, pharyngitis, rash, and myalgia/arthralgia. It should be considered in the patient with a prolonged or atypical viral illness or with an EBV (monospot)-negative mononucleosis syndrome. In the patient with suspected primary HIV infection or recently acquired HIV infection, the fourth-generation HIV test (see below) should be adequate in most instances, but a concurrent HIV viral load is recommended if the test is negative and there is a high clinical index of suspicion for the diagnosis. The viral load is often very high (e.g., millions of copies/ml) in this setting. It is important to note that low titer false-positive HIV viral load assays have been reported in persons with acute non-HIV-related illness.

Contraindications to HIV Testing

- Inability of patient to understand implications of test result
- Acute psychosis, major depression, or suicidality
- Lack of adequate personal support system

Potential Benefits and Risks of HIV Testing

- Individual health benefits include antiretroviral therapy, prophylaxis for opportunistic infections, screening and prophylaxis for tuberculosis, screening for and treatment of syphilis and other sexually transmitted diseases, administration of appropriate vaccinations, and institution of other health care maintenance measures.
- Public health benefits include decrease in HIV transmission through identification of primary HIV infection, reduction of high-risk behaviors and lowering of viral loads, and monitoring of HIV infection epidemiology.
- Risks include false-positive test result, false-negative test result, adverse psychological reactions, breach of confidentiality, and social discrimination.

Pretest Counseling

Pretest counseling often includes the following:

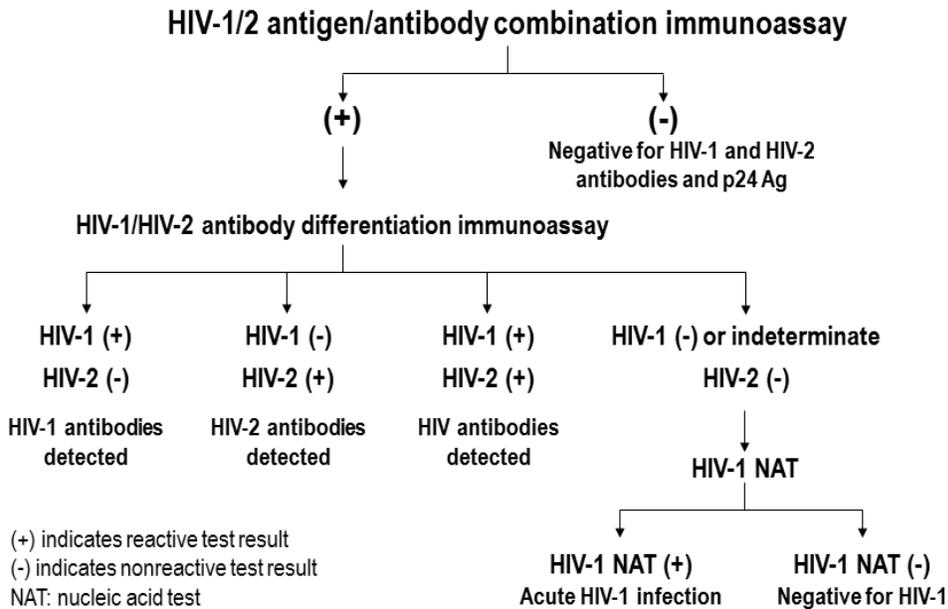
- Distinguishing between anonymous and confidential testing and discussing the availability of home-testing kit
- Reviewing natural history of HIV infection
- Reviewing reasons for testing and expectations
- Reviewing individual risk behaviors and risk-reduction measures
- Discussing meaning of positive and negative results
- Assessing personal and social supports

HIV Diagnostic Testing

Earlier HIV testing consisted of antibody testing using an enzyme-linked immunosorbent assay (ELISA) followed by a confirmatory Western blot (WB) test. A fourth-generation assay, which detects both the HIV p24 antigen and HIV 1 and 2 antibodies, is now recommended by the CDC (Figure 1-2). The inclusion of the p24 antigen narrows the “window period” where HIV antibody may not yet be detected and increases the likelihood of diagnosing acute HIV infection.

Rapid immunoassay tests that detect HIV antibody (e.g. OraQuick) in blood or oral fluid within 20 minutes have been developed. A positive rapid HIV antibody test should still be confirmed with the more specific WB. A newer rapid immunoassay (Alere Determine) detects HIV p24 antigen and HIV 1 and 2 antibodies within 20 minutes. These enable clinicians to provide definitive negative and preliminary positive results immediately.

Figure 1-2. HIV Testing Algorithm with 4th Generation Immunoassay



Centers for Disease Control and Prevention. Detection of acute HIV infection in two evaluations of a new HIV diagnostic testing algorithm - United States, 2011-2013. *MMWR* 2013; 62:489.

Risk Reduction Counseling

Risk reduction counseling is an important component of both pretest and post-test counseling. It should include the following advice:

- Reduce or limit the number of sexual partners
- Use latex condoms with water-based lubricant for all sexual activity
- Consider initiation of PrEP if at ongoing high risk (see Chapter 12)
- Detoxification or methadone maintenance program for IDUs
- Use sterile needles; however, if equipment is shared, make sure it is cleaned with bleach as recommended
- Do not share personal items such as razors and toothbrushes

Chapter 2. Initial Evaluation of Patients

History

In addition to reviewing the past medical and family medical histories, medications (prescription, OTC, and complementary drugs), and allergies of the patient with newly diagnosed HIV infection, the following issues should be addressed:

- HIV risk behaviors (sexual and drug use)
- Knowledge of HIV infection
- Emotional response to diagnosis
- Family and social situation
- Employment and insurance status
- Travel history
- Exposure to tuberculosis, syphilis, other sexually transmitted diseases, and viral hepatitis (A, B, and C)
- Status of immunizations

In the patient with established HIV infection followed previously by another practitioner, knowledge of prior opportunistic diseases, CD4 cell counts (nadir and recent), HIV viral load results (highest and recent), and antiretroviral therapy chronology, including drugs used and reasons for their discontinuation, are also important. Prior HIV genotypes should also be obtained to determine the full spectrum of resistance mutations.

Review of Systems and Physical Examination

Attention should focus on the following organ system symptoms and signs and on screening for HIV-related conditions:

- Constitutional symptoms: fever, chills, night sweats, weight loss
- Integument: seborrhea, psoriasis, onychomycosis, herpes simplex virus, varicella-zoster virus, Kaposi's sarcoma, generalized adenopathy
- HEENT: altered vision, dysphagia, cytomegalovirus (CMV) retinitis, thrush, oral hairy leukoplakia, periodontal disease
- Pulmonary: cough, dyspnea, evidence of pneumonia
- Gastrointestinal: odynophagia, diarrhea, organomegaly, anal condyloma/dysplasia/carcinoma
- Genitourinary: vaginitis, pelvic inflammatory disease, genital warts, cervical dysplasia/carcinoma
- Neurological: headache, problems with memory, change in behavior or personality, focal abnormalities

Laboratory Studies

Baseline laboratory evaluation is performed to assess for organ system dysfunction, to stage and monitor HIV disease, and to screen for other important disorders. Recommended studies include the following:

- Complete blood and differential counts
- Glucose, BUN/creatinine, liver function tests
- HgbA1c and fasting lipid profile
- Urinalysis
- CD4 cell count (see below)
- HIV viral load (see below)
- HIV genotype test
- Syphilis serology (treponemal or nontreponemal test)
- Anti-HAV
- Hepatitis B serologies
- Anti-HCV
- Toxoplasmosis (IgG) serology
- PPD or gamma-interferon release assay
- Cervical Pap smear in women (see Chapter 8)
- Anal Pap smear in persons at risk (see Chapter 8)
- *Chlamydia* and GC assays in persons at risk in exposed body locations (urethra, vagina, cervix, rectum, throat)

HLA-B*5701 testing should be performed prior to initiating abacavir therapy as patients who test positive have a high risk of hypersensitivity reaction to this drug. A G6PD qualitative screening test (if *Pneumocystis jirovecii* (*carinii*) pneumonia [PCP] prophylaxis with dapsona is contemplated) and CMV IgG antibody test (if blood transfusions are anticipated) are also appropriate. It may be reasonable to perform a chest x-ray in some clinical circumstances (e.g., history of injection-drug use).

The following tests are important for the staging and monitoring of HIV disease:

CD4 Cell Count

- Main surrogate marker for HIV disease progression
- Normal range is 350 to 1100/mm³; there is average decline of 75-100/mm³ per year without treatment but variability between patients and in a given patient over time
- Intercurrent illnesses may transiently affect value
- There is some inter-laboratory variability, so use caution in interpreting widely disparate values

- Clinical uses are to determine need for antimicrobial prophylaxis and to assess prognosis

HIV Viral Load

- Measurement of viral RNA in plasma by polymerase chain reaction (PCR)
- Lower limit of detection of ultrasensitive PCR assay is < 20 copies/ml
- Note that some viral load results may be reported as log₁₀ copies/ml (20 copies/ml = 1.3 log₁₀ copies/ml)
- High level correlates with CD4 cell count decline and clinical disease progression
- Normal variability of 0.3 log (three- to five-fold)
- Intercurrent illnesses and immunizations may transiently affect value
- Clinical uses are to monitor antiretroviral therapy

Spectrum of HIV Disease

Patients are at risk for complications at the following CD4 cell count thresholds:

CD4 Cell Count > 500/mm³

- Most patients asymptomatic
- Bacterial infections (e.g., pneumococcal), pulmonary tuberculosis, shingles, other dermatologic conditions

CD4 Cell Count 500-200/mm³

- Many patients asymptomatic
- Generalized adenopathy, thrush, Kaposi's sarcoma

CD4 Cell Count < 200/mm³

- PCP, toxoplasmosis, cryptococcosis

CD4 Cell Count < 50/mm³

- CMV and *Mycobacterium avium* complex infections
- Increased risk of lymphoma
- Most deaths occur in this range

It is important to note that the risk for a specific opportunistic disease increases the longer the CD4 cell count is below threshold and the more it drops below that level. For instance, the risk of a patient developing PCP is far greater if the CD4 cell count is 200/mm³ for three months than it is if the CD4 cell count is 200/mm³ for one week.

The CD4 percentage (CD4 count/total lymphocyte count) may be useful adjunctively in clinical settings in which the CD4 cell count may not accurately reflect the patient's immune status (e.g., anatomic or functional asplenism).

Chapter 3. Stratified Management

Specific management considerations in HIV-infected patients include initiation and continuation of antiretroviral therapy, antimicrobial prophylaxis against opportunistic infection, and health care maintenance issues.

All patients with newly diagnosed HIV infection regardless of CD4 count should be started on antiretroviral therapy (see Chapter 4).

If the CD4 count is $< 200/\text{mm}^3$, pneumocystis prophylaxis should also be initiated (see Chapter 5). Trimethoprim-sulfamethoxazole (TMP-SMX) is the drug of choice. Dapsone, atovaquone, and aerosol pentamidine are alternatives. TMP-SMX is also effective for toxoplasmosis prophylaxis, which is initiated in the patient with CD4 cell count $< 100/\text{mm}^3$ and a positive toxoplasmosis serology. Alternative toxoplasmosis prophylaxis in TMP-SMX allergic patients is dapsone with pyrimethamine plus folinic acid.

MAC prophylaxis is no longer recommended in patients with a new diagnosis of HIV infection who immediately start antiretroviral therapy (see Chapter 6). However, it is still advised in patients with chronic HIV infection who are not virally suppressed.

Primary prophylaxis against coccidioidomycosis and histoplasmosis may be indicated in patients with a low CD4 cell count who live in endemic areas. See published guidelines for more information.

Follow-up Visits

Medical visits should be scheduled with appropriate frequency to monitor for disease progression and complications and to monitor drug therapies. In general, patients with advanced HIV disease require more frequent visits than those with earlier stages.

Initial evaluation is generally accomplished in two visits over a short interval. At the first, a history and physical examination are performed, and baseline laboratory studies are obtained. At the second, results of evaluation are reviewed, and a management plan is discussed. Issues to be addressed should include any active medical problems, opportunistic infection prophylaxis, antiretroviral therapy, health care maintenance, and patient education.

After antiretroviral therapy is initiated, a follow-up visit is arranged in four weeks to assess tolerability of medication regimen and to repeat laboratory parameters used to determine its effectiveness. Once a patient is on a stable treatment regimen, follow-up visits every three to six months are recommended unless intercurrent problems require more frequent appointments.

Laboratory Testing

Once patients are on a stable antiretroviral regimen, laboratory evaluation at follow-up visits should include the following:

Test	Interval
Complete blood and differential counts	Every 3-6 months
BUN/creatinine, liver function tests	Every 3-6 months
HgbA1c and fasting lipid profile	Once per year if normal
CD4 cell count	Every 3-12 months
HIV viral load	Every 3-6 months
Sexually transmitted diseases	At least annually (evaluate risk at each visit)
Hepatitis C infection	At least annually
Cervical and anal cancer screening	See Chapter 8

Regarding CD4 count...

- CD4 count response to antiretroviral therapy varies widely, but a poor response is rarely an indication for modifying regimen
- In patients with suppressed viral loads who are immune reconstituted, the CD4 count provides limited information
- CD4 count testing is recommended at baseline and every 3 to 6 months thereafter
- It may be extended to every 12 months in patients who are clinically stable with a suppressed viral load for ≥ 2 years and is optional for those with CD4 count $> 500/\text{mm}^3$ in this setting

Regarding HIV viral load...

- For most individuals who are adherent to their antiretroviral regimens and who do not harbor resistance mutations to the prescribed drugs, viral suppression is generally achieved in 12 to 24 weeks
- Viral load testing is recommended at baseline, 2 to 4 weeks after ART initiation, every 4 to 8 weeks until the viral load is suppressed, and every 3 to 4 months thereafter
- It may be extended to every 6 months in patients with a suppressed viral load for ≥ 2 years

Chapter 4. Antiretroviral Therapy

Background

The past two decades have shown great advances in the management of HIV disease with almost all patients benefiting from antiretroviral therapy. The following recommendations are based on our current understanding of the pathophysiology of HIV disease and the results of clinical trials. They reflect the guidelines of US Department of Health and Human Services. *Because of the changing nature of clinical practice in this area, expert consultation should be sought when initiating or changing drug regimens.*

Pathophysiology of HIV Infection

Viral replication occurs throughout the course of HIV infection at very high rates. It is estimated that 10^{10} viral particles are produced each day. The patient's immune system keeps pace with this activity during the clinical latency period. However, in the absence of effective antiretroviral treatment, the immune system ultimately reaches a "point of exhaustion," at which viral replication exceeds its ability to produce CD4 cells. This leads to a decline in immunologic function and the development of clinical manifestations including opportunistic infections and neoplasms.

The rate of viral replication is thought to stabilize after primary infection at a particular level or "set point." This level may be maintained within a ten-fold range over months and possibly years. The viral load is highly correlated with the rate of disease progression and mortality.

General Guidelines

The primary goal of antiretroviral therapy is to keep the viral load as low as possible for as long as possible. Maximal suppression of the virus makes it more difficult for resistance to develop. Partial suppression results in the emergence of resistant mutant strains in the viral population. These are present because of the rapid turnover of HIV and the many random errors made during replication. They predominate in the context of ineffective treatment because of a competitive advantage over pansensitive ("wild type") virus.

Three-quarters of patients or more will achieve maximal viral suppression with their initial regimen, and the majority of these will continue to have undetectable virus on a long-term basis with good medication adherence. The success rate often decreases with subsequent regimens. Current antiretroviral regimens are not curative probably because of persistence of HIV in quiescent CD4 lymphocytes and because of "sanctuary sites," which are regions of the body, such as the central nervous system and gonads, in which some drugs do not penetrate well.

Combination antiretroviral therapy is the standard of care for HIV infection. Monotherapy and less potent combination regimens lead to the development of viral resistance within weeks to months. Antiretroviral drugs are classified by their mode of action against the virus as follows: 1) nucleoside reverse transcriptase inhibitors (NRTIs); 2) non-nucleoside reverse transcriptase inhibitors (NNRTIs); 3) protease inhibitors (PIs); 4) entry inhibitors (EIs); 5) integrase inhibitors (IIs); and 6) post-attachment inhibitors. In addition, there are two medications (cobicistat and ritonavir) which serve as pharmacologic boosters but do not have direct activity against the virus. Commonly used drug preparations based on recommended and alternative regimens are listed below.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
abacavir	ABC	Ziagen
emtricitabine	FTC	Emtriva
lamivudine	3TC	Epivir
tenofovir disoproxil fumarate	TDF	Viread
zidovudine	ZDV	Retrovir
abacavir/lamivudine	ABC/3TC	Epzicom
tenofovir alafenamide/emtricitabine	TAF/FTC	Descovy
tenofovir disoproxil fumarate/emtricitabine	TDF/FTC	Truvada
zidovudine/lamivudine	ZDV/3TC	Combivir
tenofovir disoproxil fumarate/lamivudine	TDF/3TC	Cimduo

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
efavirenz	EFV	Sustiva
etravirine	ETR	Intelence
rilpivirine	RPV	Edurant
doravirine	DOR	Pifeltro

Protease Inhibitors (PIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
atazanavir	ATV	Reyataz
darunavir	DRV	Prezista
atazanavir/cobicistat	ATV/c	Evotaz
darunavir/cobicistat	DRV/c	Prezcobix
lopinavir/ritonavir	LPV/r	Kaletra

Integrase Inhibitors (IIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
bictegravir	BIC	(not available alone)
dolutegravir	DTG	Tivicay
elvitegravir	EVG	(not available alone)
raltegravir	RAL	Isentress

Entry Inhibitors (EIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
enfuvirtide (fusion inhibitor)	T-20	Fuzeon
maraviroc (CCR5 antagonist)	MVC	Selzentry

Attachment Inhibitors (AIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
fostemsavir	FTR	Rukobia

Post-attachment Inhibitors (PAIs)

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
ibalizumab-uiyk	IBA	Trogarzo

Pharmacologic Boosters

<u>Generic Name</u>	<u>Abbreviation</u>	<u>Brand Name</u>
cobicistat	c, COBI	Tyboost
ritonavir	r, RTV	Norvir

Multiclass Combination Preparations

TDF/FTC/EFV (Atripla)
TDF/3TC/EFV (Symfi and Symfi Lo)
TDF/FTC/RPV (Complera)
TDF/FTC/EVG/c (Stribild)
TDF/3TC/DOR (Delstrigo)
TAF/FTC/EVG/c (Genvoya)
TAF/FTC/RPV (Odefsey)
TAF/FTC/BIC (Biktarvy)
TAF/FTC/DRV/c (Symtuza)
ABC/3TC/DTG (Triumeq)
DTG/RPV (Juluca)
DTG/3TC (Dovato)

A complete listing of FDA approved drugs, along with dosing, toxicity, and other information for individual agents are described in the drug glossary (see Chapter 14). Antiretroviral agents vary considerably in their dosing and frequency, how they should be administered (with food or fasting), their side effect profiles, and their potential interactions with other drugs.

Specific Guidelines

When should antiretroviral therapy be initiated?

Antiretroviral therapy is recommended in all HIV-infected patients regardless of their clinical status or CD4 cell count. There are individual (decreased morbidity and mortality) and public health (decreased transmission) benefits of treatment. These are strong recommendations based mostly upon the results of randomized controlled trials. Patients starting antiretroviral therapy should understand its potential benefits and risks and the importance of medication adherence, and they should be willing to commit to taking it on a long-term basis. There is some evidence supporting the immediate initiation of treatment. However, this approach should not be considered in patients at risk for immune reconstitution inflammatory syndrome or in those not ready to commit to treatment. Baseline laboratory testing, including CD4 cell count and viral load measurement, should still be obtained before initiating therapy (see Chapter 2).

What agents should be used?

Combination therapy using three drugs is recommended as initial therapy in the absence of virologic resistance.

There are two major guidelines serving to inform the use of antiretroviral therapy: the Department of Health and Human Services (DHHS) Antiretroviral Guideline Panel (available as a living document at www.aidsinfo.nih.gov and the International AIDS Society-USA (IAS-USA) panel. We present the DHHS guideline here.

Recommended initial regimens include BIC/TAF/FTC, DTG/ABC/3TC for patients who are HLA-B*5701 negative, DTG plus (TAF or TDF) plus (FTC or 3TC), DTG/3TC, and RAL plus (TAF or TDF) plus (FTC or 3TC) (Table 4-1). DTG/3TC can be used as an initial regimen in patients with HIV RNA $\leq 500,000$ copies/mL who do not have concurrent HBV infection.

Table 4-2 shows other recommended initial regimens to be considered in certain clinical situations. These are effective and tolerable but have some disadvantages when compared with the regimens listed in Table 4-1 or have fewer supporting data.

Pre-treatment HIV viral load, CD4 cell count, HLA-B*5701 status, and medical

comorbidities (e.g., coronary artery disease, chronic renal disease, osteoporosis, neuropsychiatric condition) may affect the selection of a specific drug combination. In addition, the regimen's genetic barrier to resistance, side effect profile, pregnancy safety, drug interactions, and convenience of administration should also be taken into account.

Patient adherence to medical therapy is essential. Frequently missed doses will render a drug regimen ineffective and lead to the development of resistance. Every effort should be made to address factors, such as active substance abuse or significant psychological problems, in advance which may interfere with adherence.

Factors having a negative impacted on medication adherence include:

- Lack of education about HIV disease
- Denial, anxiety, or depression
- Alcohol or drug use
- Poor social situation
- Inadequate health insurance
- Number of medications/pills
- Frequency of dosing
- Stringent dosing requirements
- Presence of side effects

Useful interventions to promote medication adherence include:

- Take time to educate and explain goals of therapy and need for adherence
- Develop concrete plan for specific regimen
- Minimize dosing frequency and number of pills
- Simplify food requirements
- Inform patient about potential side effects, and anticipate and treat them
- Avoid adverse drug interactions
- Provide written schedule, pictures of medications, pill boxes, and mechanical aids
- Recruit family and friends to support treatment plan

NNRTIs, PIs, and cobicistat have many potential drug interactions. Some agents are contraindicated for co-administration, and others may require dosage adjustment. More detailed information is available in the guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov.

How should antiretroviral therapy be monitored?

Patients started on antiretroviral therapy should return in four weeks to assess toxicity of the regimen and to repeat safety studies (CBC, glucose, renal and hepatic function tests, and lipid profile), CD4 cell count, and viral load. The viral load should decrease at least three-fold over this period of time. The CD4 count and viral load should be repeated

monthly until virologic suppression is achieved. Once this task has been accomplished, follow-up laboratory studies should be performed every three to six months.

Except for short-term interruption because of toxicity or an acute illness that precludes oral therapy, antiretroviral drugs should be continued indefinitely. The safety and effectiveness of treatment interruption strategies have not been demonstrated. Patients interested in this type of management should be encouraged to join a clinical trial.

When should an antiretroviral drug regimen be modified?

Indications for modification of a drug regimen include inadequate viral load suppression, a rising viral load after suppression has been achieved, the inability to tolerate medication(s) or pill burden. Inadequate viral load suppression or a rising viral load is the first evidence of resistance. This finding should prompt inquiry into the patient's medication adherence. If it has been compromised, every effort should be made to address the factors involved, and the viral load should be repeated one month later before considering modification of the regimen.

If a modified regimen is necessary, how should new drugs be selected?

If the regimen is being changed because of development of viral resistance, an entirely new combination that does not share cross-resistance with current drugs is recommended. A careful prior antiretroviral drug history and HIV resistance testing (see below) are important in selecting new agents. *Interpretation of resistance testing is a complicated and evolving field, and expert consultation is strongly recommended for practitioners with limited clinical experience.*

HIV Resistance Testing

The HIV genotype test provides a genetic “blueprint” of the predominant viral strain. It determines the presence of specific mutations in the HIV genome that correlate with clinical resistance to individual antiretroviral drugs. Results are generally interpreted using rules-based algorithms. The phenotype test provides a drug-sensitivity profile. It measures the inhibitory concentration (50% or 90%) of drugs and compares them to values seen with a pansensitive (“wild type”) strain. Changes of greater than 2.5- to 4-fold are reliably detected. Results are generally categorized as sensitive, resistant, or intermediate. Resistance testing for IIs is available but generally not included in conventional genotypes.

HIV genotype testing is more readily available and less costly than phenotype testing but provides an indirect measure of susceptibility. Phenotype testing is generally preferred when multiple complex resistance mutations are anticipated. Both tests examine only the predominant virus isolated and may miss resistant background strains. Because of this characteristic, they are better at identifying drugs to which the virus is resistant than in predicting which ones will be effective. The [Stanford HIV Drug Database](#) is a useful tool

for determining the effect of active and archived resistance mutations. It enables practitioners to input all prior genotypes to determine which antiviral drugs are likely to be most effective in an individual patient.

Special Considerations in Pregnant Women

Antiretroviral therapy is recommended in HIV-infected pregnant women and is highly effective at reducing perinatal transmission. Detailed guidelines for the use of these drugs during pregnancy, at the time of delivery, and post-partum in the infant are available in [Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States](#) (available as a living document).

Recent data suggest that the risk of neural tube defects (NTDs) in infants born to women receiving DTG at the time of conception is lower than previously reported (0.3% rather than previously reported 0.9%), but higher than in those on non-DTG containing regimens (0.1%). As a result, the following should be considered before initiating dolutegravir and other IIs as initial therapy:

- The *preferred* options in women of childbearing potential and during pregnancy are:
 - TDF/(FTC or 3TC) plus DRV/r
 - TDF/(FTC or 3TC) plus ATV/r
 - TDF/(FTC or 3TC) plus RAL
 - ABC/3TC plus (RAL or DRV/r or ATVr)
- Providers should discuss the benefits of using DTG and the risk of NTDs with the person of childbearing potential, for shared decision making
- DTG may be used as an *alternative* ARV for women of childbearing potential and trying to conceive, or in those not on a form of contraception.
- For those using effective contraception, DTG may be used as a recommended option
- It is not yet known whether there is a class effect across all integrase inhibitors.
- There are insufficient data to know whether use of BIC around conception and during pregnancy is safe.
- EVG/c should not be used in pregnancy because of low concentrations in the second and third trimesters.

Table 4-1. Recommended Initial Regimens for Most Patients with HIV^a

- BIC/TAF/FTC [Biktarvy]
- DTG/ABC^b/3TC [Triumeq] (only for patients who are HLA-B*5701 negative) or DTG plus tenofovir^c/FTC^d
- DTG plus tenofovir^c/FTC^d
- RAL^e plus tenofovir^c/FTC^d
- DTG/3TC [Dovato] (only for patients with HIV RNA \leq 500,000 copies/mL and no concurrent HBV infection)

Table 4-2. Recommended Initial Regimens in Certain Clinical Situations

II-Based Regimens:

- Elvitegravir/c/TAF/FTC [Genvoya] or Elvitegravir/c/TDF/FTC [Stribild]

PI-Based Regimens:

- DRV/c/TAF/FTC [Symtuza] or DRV/r plus TAF/FTC^d
- (DRV/c or DRV/r) plus TDF/FTC^d
- (ATV/c or ATV/r) plus tenofovir^c/FTC^d

NNRTI-Based Regimens:

- DOR/TDF/3TC [Delstrigo] or DOR plus TAF/FTC
- EFV/TDF/FTC [Atripla] or EFV plus TAF plus FTC^d
- RPV/TAF/FTC [Odefsey] or RPV/TDF/FTC [Complera] (only for patients with HIV RNA < 100,000 copies/mL and CD4 count > 200 cells/mm³)

Regimens to Consider When ABC, TAF, and TDF Cannot Be Used or Are Not Optimal:

- DTG plus 3TC (only for patients with HIV RNA \leq 500,000 copies/mL and no concurrent HBV infection)
- DRV/r plus RAL BID (only for patients with HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm³)
- DRV/r once daily plus 3TC

^a There is concern for possible NTDs associated with IIs. See alternative options for women of childbearing potential.

^b In patients with or at high risk of cardiovascular disease, consider a tenofovir-containing regimen over abacavir-containing regimen.

^c TAF and TDF are two forms of tenofovir approved by the FDA. TAF has fewer bone and kidney toxicities, while TDF is associated with lower lipid levels.

^d Lamivudine (3TC) may be substituted for emtricitabine (FTC) or vice versa

^e RAL can be given as RAL 400mg BID or RAL 1200 mg (two 600-mg tablets) once daily

Adapted from and available as a living document from <https://aidsinfo.nih.gov/guidelines>.

Chapter 5. Pneumocystis Pneumonia Prophylaxis

Background

Despite advances in the management of HIV disease, *Pneumocystis jirovecii* (previously known as *carinii*) pneumonia (PCP) remains an important complication and cause of morbidity. PCP antimicrobial prophylaxis is very effective and has been demonstrated to prolong life. The risk of developing PCP becomes significant when the patient's CD4 cell count falls to less than 200/mm³ or the CD4 percentage falls to less than 14%, and it increases progressively as these further decline.

PCP presents subacutely with fever, malaise, dyspnea on exertion, and a nonproductive cough. Physical examination may be normal or show scattered rales on auscultation of the lungs. The chest x-ray typically reveals diffuse bilateral “ground glass” interstitial infiltrates but may be normal in early infection. Oximetry often shows decreased oxygen saturation following exertion. Diagnosis is generally made by induced sputum with identification of the organism on direct fluorescent antibody test; bronchoscopy with lavage may be necessary in a minority of cases. 1,3 β-D-glucan is a component of the cell wall of pneumocystis cysts and is often increased in patients with PCP. This test has a high sensitivity for PCP pneumonia but a low specificity, as many other fungal diseases and medications can falsely elevate β-glucan levels. Treatment of PCP consists of trimethoprim-sulfamethoxazole (TMP-SMX) or an alternative drug for three weeks. Adjunctive corticosteroid therapy is used in patients with significant respiratory dysfunction.

Guidelines

An algorithmic approach to PCP prophylaxis is presented in Figure 5-1. Effective agents for PCP prevention include TMP-SMX, dapsone, aerosol pentamidine (AP), and atovaquone (Table 5-1). Dapsone with pyrimethamine and leucovorin is also effective.

- All HIV-infected patients whose CD4 cell count is less than 200/mm³ or CD4 percentage is less than 14, who have thrush, or who have a history of PCP and have not been immune reconstituted on antiretroviral therapy (see below) should receive prophylaxis.
- Primary prophylaxis can be safely discontinued in patients whose CD4 cell count rises above 200/mm³ for 3 months on combination antiretroviral therapy with a suppressed viral load. Secondary prophylaxis (maintenance therapy) in patients with a history of PCP can also be stopped in this context.
- TMP-SMX is the drug of choice for PCP prophylaxis. The recommended dose is one double-strength (DS) tablet once a day. It can also be given as one single strength tablet once a day or one DS tablet three times per week.

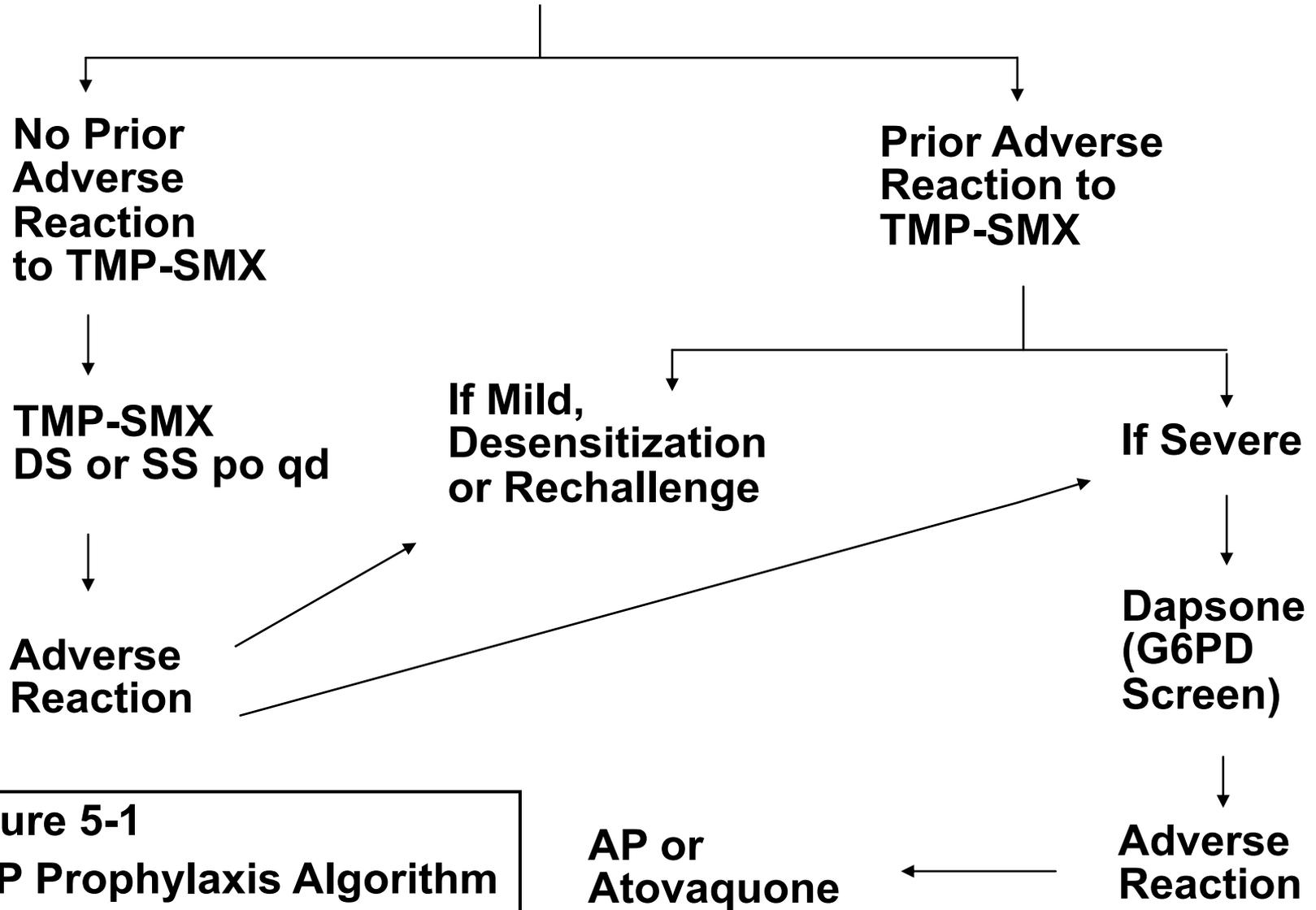
- TMP-SMX DS daily also confers protection against toxoplasmosis.
- TMP-SMX is preferred to dapsone because of increased efficacy and protection against conventional bacterial infections. It is preferred to AP because of increased efficacy, lower cost, protection against toxoplasmosis and conventional bacterial infections, and lower risk of extrapulmonary pneumocystosis. It is preferred to atovaquone because of much lower cost.
- Many patients with HIV infection develop toxicity to TMP-SMX. The most common side effects include fever, rash, and leukopenia. Strategies for managing mild reactions include discontinuation of the drug and resuming it at same or lower dose or use of a desensitization protocol (gradually increasing doses administered over several days). Many patients can be treated through mild drug reactions using acetaminophen and/or antihistamine for symptom management.
- Dapsone 100 mg po qd is recommended as the alternative agent in patients who cannot tolerate TMP-SMX. Side effects include fever, rash, and hemolytic anemia. G6PD qualitative assay should be performed before starting dapsone therapy; the drug is contraindicated in patients with G6PD deficiency. For dapsone to be effective as toxoplasmosis prophylaxis, which is indicated in context of CD4 cell count < 100/mm³ and positive IgG serology, it should be administered in conjunction with pyrimethamine 50 mg po and folinic acid 25 mg po, both given weekly. Pyrimethamine is not currently available in retail pharmacies but can be obtained through a [special pharmacy program](#).
- For patients who cannot tolerate dapsone, AP or atovaquone is recommended.
- AP 300 mg per month is given by Respirgard II jet nebulizer using 6 ml sterile water delivered at 6 L/min from a 50-psi compressed air source until the reservoir is dry, usually over 45 minutes. Active tuberculosis (TB) should be ruled out with PPD, chest x-ray, and other studies if necessary before initiating AP. Appropriate measures should be in place to prevent TB transmission in persons receiving AP. These include use of individual rooms or booths with negative pressure ventilation, air exhaust to the outside, scheduling to permit air exchange prior to use by another patient, use of particulate respirators by workers administering the drug, and restriction of patients from returning to waiting areas until their coughing subsides.
- Atovaquone is dosed as 1500 mg of suspension po qd with food. Side effects include gastrointestinal intolerance, rash, headache, and fever.

Table 5-1. Comparison of PCP Prophylaxis Regimens

Issue	TMP-SMX	Dapsone	AP	Atovaquone
Efficacy	High	Moderate	Moderate	Moderate
Toxicity	Moderate	Low-Moderate	Low	Low
Cost	Low	Low	High	High
Toxoplasmosis Protection	Yes	Yes *	No	Probably *
Bacterial Infection protection	Yes	?	No	No
Risk of Extrapulmonary Pneumocystosis	No	No	Yes	No

* In conjunction with weekly pyrimethamine and folic acid

**CD4 Count < 200, CD4 Percentage < 14,
Thrush, or Prior PCP**



**Figure 5-1
PCP Prophylaxis Algorithm**

Chapter 6. MAC Infection Prophylaxis

Background

Mycobacterium avium complex (MAC) is a slow-growing bacterium that is an important cause of disseminated infection in patients with advanced HIV disease. The risk of developing MAC infection becomes significant when the patient's CD4 cell count falls to about 50/mm³ and increases progressively as it further declines. Prophylactic antimicrobial therapy has been shown to be effective in preventing MAC infection, with the risk reduced by one-half in most studies.

MAC infection presents subacutely with nonspecific symptoms, including fever, fatigue, weight loss, and diarrhea. Physical examination may show few, if any, abnormalities. Diagnosis is generally made by isolator blood culture, although the organism can also be cultured from body tissues (e.g., bone marrow, liver). Treatment of MAC infection requires a combination of antimycobacterial drugs given for a prolonged period of time.

Guidelines

Antimicrobial prophylaxis is no longer recommended in patients with a new diagnosis of HIV infection and a CD4 cell count less than 50/mm³ who immediately start antiretroviral therapy. However, it is still advised in patients with chronic HIV infection and a CD4 cell count less than 50/mm³ who are not virally suppressed. Effective drugs include the macrolides azithromycin (1200 mg po weekly or 600 mg po twice per week) and clarithromycin (500 mg po bid); and rifabutin (300 mg po qd).

Azithromycin and clarithromycin are preferred to rifabutin because they are more effective. In addition, rifabutin requires dosage adjustment or is contraindicated for use with some protease inhibitors and non-nucleoside reverse transcriptase inhibitors. Both macrolides have the advantage of conferring protection against infection with bacterial respiratory pathogens such as pneumococcus. Clarithromycin is costlier than azithromycin, and their toxicities, which are primarily gastrointestinal, appear comparable. While the combination of a macrolide with rifabutin provides additional protection against MAC infection than either agent alone, there is also a greater risk of drug toxicity.

Before MAC prophylaxis is started, clinical assessment to rule out disseminated infection is recommended. If warranted, an isolator blood culture should be obtained.

Primary prophylaxis can be safely discontinued in patients whose CD4 cell count rises above 100/mm³ or who achieve a suppressed viral load for 3 months on combination antiretroviral therapy. Secondary prophylaxis in patients with established MAC infection can be discontinued if the CD4 cell count rises above 100/mm³ for 6 months and they are asymptomatic and have completed 12 months of antimicrobial therapy.

Chapter 7. Immunizations

Background

Patients with HIV disease are at increased risk for a variety of infections that can potentially be prevented by using available vaccine preparations.

Immunizations should be given as early in the course of HIV disease as possible for optimal effect. Patients with relatively preserved immune function are more likely to have a favorable response to vaccine challenge than those who are significantly immunocompromised. Booster doses may be necessary in some patients. Initiation of combination antiretroviral therapy in patients with advanced HIV disease may improve the immunologic response to vaccine preparations.

Killed or inactivated vaccines are considered safe in this population. Live pathogen vaccines, such as measles, mumps, rubella (MMR), varicella, should be avoided in HIV-infected adults with a CD4 cell count $< 200/\text{mm}^3$. MMR and varicella vaccines can be used in patients with a higher count. The new recombinant zoster vaccine (Shingrix) is being studied in HIV-infected patients, but it appears to be safe and immunogenic. Influenza and other vaccine preparations have been shown to transiently stimulate HIV replication and increase the viral load. However, this phenomenon does not appear to have an impact on overall disease progression.

Guidelines

Specific immunization recommendations for HIV-infected patients are presented in Table 5-1. Pneumococcal vaccine should be administered to all HIV-infected patients. There are two types available: a 23-valent polysaccharide vaccine (PPSV23) and a 13-valent conjugate vaccine (PCV13). Meningococcal conjugate vaccine should also be administered to all HIV-infected patients. There are two available products: MenACWY-D or MenACWY-CRM. Either may be used, but the same vaccine preparation should be given for all doses in an individual patient.

The HBV immunization series should be given to patients who have a negative screening serologic test for this infection. HAV vaccine should be administered to men who have sex with men and to patients with chronic hepatitis C virus (HCV) infection. HAV vaccine should also be considered in injection-drug users, another population in which outbreaks have been described. Influenza vaccine is especially important in persons with historical risk factors for exposure to the virus and the presence of conditions associated with increased morbidity from influenza. Routine use of hemophilus B (Hib) vaccine is not recommended in adults, but asplenic patients and those with a history of recurrent *Haemophilus influenzae* infection should be immunized. The indications for HPV vaccine in HIV-infected patients are the same as in the general population.

Table 5-1. Immunizations in HIV-infected Adults			
Vaccine	Status	Dose/Regimen	Comments
<i>Haemophilus influenzae</i> , type B, virus vaccine	Recommended in selected settings	0.5 mL IM	Administer to asplenic patients and patients with a history of recurrent <i>Haemophilus spp.</i> infections.
Hepatitis A virus vaccine	Recommended in selected settings	1 mL IM at 0 and 6-12 months; also available in combination with recombinant hepatitis B virus vaccine (GSK)	Administer to men who have sex with men, injection-drug users, and persons with chronic liver disease. Vaccinated patients should be tested for an antibody response 1 month after vaccination; those who do not respond should be revaccinated.
Hepatitis B virus vaccine	Recommended in selected settings	20 µg IM recombinant hepatitis B virus vaccine (CpG-adjuvanted) (Dynavax), given at 0 and 1 month; or 20 µg IM recombinant hepatitis B virus vaccine (GSK) or 10 µg IM recombinant hepatitis B vaccine (Merck & Co.) given at 0, 1, and 6 months;	Administer to patients without serologic evidence of past or present hepatitis B virus infection. Vaccinated patients should be tested for HBsAb response 1 month after the final dose; repeating the vaccine series at the same or higher dose may be considered for those who do not respond. Patients who do not respond to two series are considered non-responders and should not receive additional series. In patients with CD4 count < 200 at time of initial vaccination and lack of serologic response, revaccination should occur once the CD4 cell count is > 350.
Human papillomavirus vaccine	Recommended in all adults at least through age 26	0.5 mL IM at 0, 1-2, and 6 months (HPV 9-valent recombinant) (Merck)	For patients who have previously completed series with recombinant bivalent or quadrivalent, consider additional full series of 9-valent recombinant vaccine. Recommended in all adults through age 26; shared decision-making for adults age 27 to 45. Not recommended during pregnancy.
Influenza virus vaccine	Recommended	0.5 mL IM annually prior to influenza season; high dose may be considered in patients ≥ 65 years	Especially important in patients at high risk for exposure to or morbidity from influenza. There is evidence that the vaccine may transiently promote HIV replication which does not appear to be clinically significant.
Meningococcal conjugate vaccine	Recommended	0.5 mL IM at 0 and 8-12 weeks Meningococcal Polysaccharide Diphtheria Toxoid Conjugate	Administer booster dose every 5 years. Administer each at least 4 weeks after completion of all pneumococcal conjugate vaccines.

		Vaccine (MenACWY-D, Menactra) (Sanofi Pasteur) Meningococcal Oligosaccharide Diphtheria Conjugate Vaccine (MenACWY-CRM, Menveo) (Novartis Vaccines and Diagnostics)	
Pneumococcal vaccine	Recommended	0.5 mL IM Pneumococcal 13-valent conjugate vaccine (PCV13) (Wyeth Pharmaceuticals, a subsidiary of Pfizer) 0.5 mL IM or SC Pneumococcal 23-valent polysaccharide vaccine (PPSV23) (Merck & Co.)	Administer to all patients. Give booster dose of PPSV23 every five years and final dose at age 65, once ≥ 5 years from last <ul style="list-style-type: none"> • Pneumococcal vaccine-naïve persons: PCV13 first followed by PPSV23 at least 8 weeks later • Previous vaccination with PPSV23: PCV13 at least 1 year after the last PPSV23 dose; for those who require additional doses of PPSV23, the first should be given no sooner than 8 weeks after PCV13 and at least 5 years after most recent PPSV23 dose.
Tetanus toxoid	Recommendations same as in seronegative patients	0.5 mL IM	Td booster is recommended every 10 years. Tdap should replace a single dose of Td for adults older than 65 years who have not previously received a dose of Tdap.
Zoster vaccine	Advised in age ≥ 50 years if CD4 count > 200 (no formal ACIP recommendation)	0.5 mL at 0 and 2 to 6 months Zoster vaccine recombinant, adjuvant (Shingrix) (GSK)	

HBsAb indicates hepatitis B virus surface antibody; IM, intramuscularly; SC, subcutaneously; Td, tetanus and diphtheria vaccine; Tdap, tetanus, diphtheria, and pertussis vaccine.

Chapter 8. Cervical and Anal Cancer Screening

Rationale and Background

HIV disease is associated with an increased risk of cervical and anal dysplasia, a precursor of cancer, in both women and men. Most patients who develop this condition have a history of human papillomavirus (HPV) infection, which is the sexually transmitted pathogen that causes genital warts. In many cases, the virus will be cleared by the body's immune system. However, in HIV-infected patients there is a much higher incidence of both cervical and anal dysplasia because of a decreased rate of viral clearance.

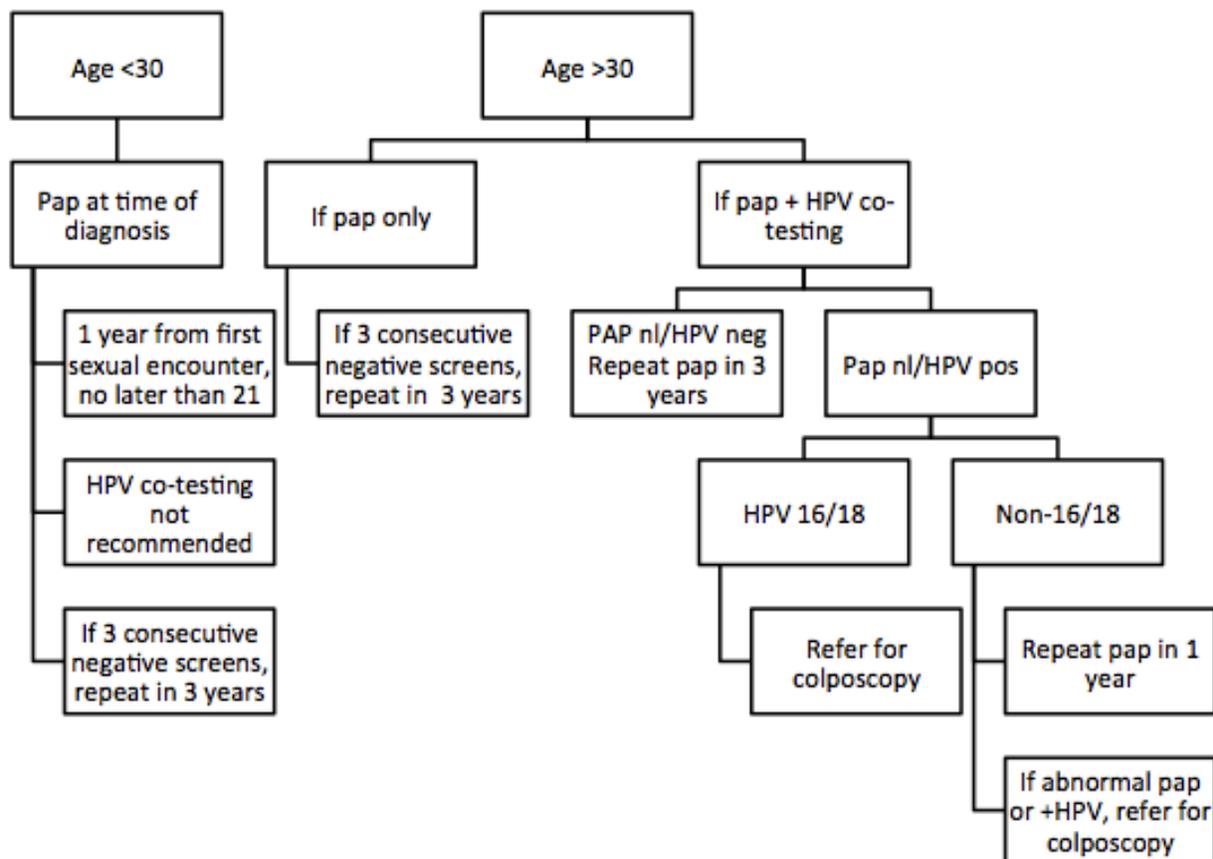
The Pap smear has been demonstrated to be a useful screening test for cervical dysplasia. Its routine use in populations at risk decreases morbidity and mortality from cervical neoplasia. Similarly, the Pap smear has been applied as a screening exam for anal dysplasia; however specific guidelines on its use are still in development.

Cervical Pap Smear

A pelvic examination and Pap smear should be performed as part of the initial evaluation of all HIV-infected women. Colposcopy is not recommended as a screening test in this population. Updated guidelines from the CDC recommend an approach to screening which mirrors the algorithm for seronegative women (Figure 8-1). However, in patients with a CD4 count $<200/\text{mm}^3$ or detectable HIV viral load, annual testing should still be performed. In addition, in women who have had an abnormal cervical or anal pap smear or who have tested positive for HPV, annual testing should be continued.

Women with abnormal Pap smear results showing cellular atypia (atypical squamous cells of undetermined significance [ASCUS]) or any degree of cervical dysplasia (low-grade or high-grade squamous intraepithelial lesion [SIL]) should be referred to a gynecologist for further diagnostic evaluation. In general, colposcopy and biopsy are performed.

Figure 8-1. Algorithm for Cervical Cancer Screening in HIV-infected Women *



* Algorithm is appropriate for women with a sustained CD4 count above 200/mm³. In women with a CD4 count < 200/mm³ and/or detectable viral load, annual Pap testing is still recommended.

Adapted from “Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents,” available as living document from www.aidsinfo.nih.gov.

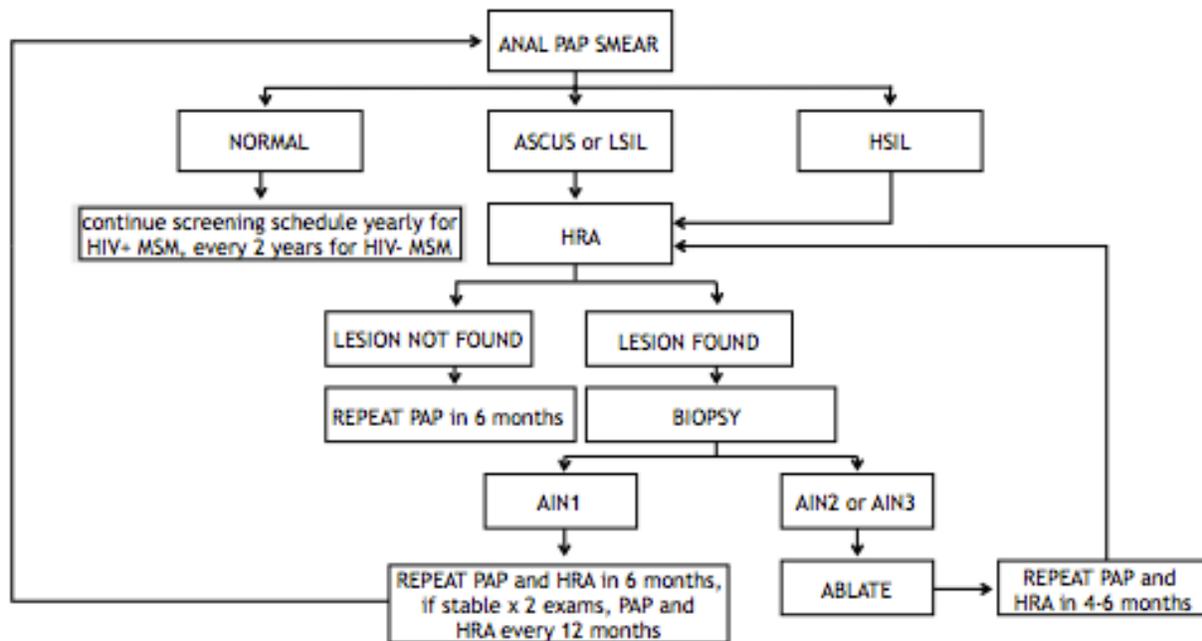
Anal Pap Smear

It is unknown whether screening for anal dysplasia with Pap smears confers a morbidity or mortality benefit, and there are no guidelines for anal Pap smear screening. However, based upon available information, an anal Pap smear should be considered annually in HIV-infected patients who have had anal receptive intercourse or with a history of anogenital warts or other HPV-related conditions. Screening for anal cancer should only be performed if there is the ability to refer for high resolution anoscopy (HRA). HIV infection is an independent risk factor for anal neoplasia. Other risk factors include cigarette smoking, multiple sexual partners, known HPV infection, and receptive anal intercourse.

The technique consists of inserting a moistened Dacron swab 2-4 cm into the anal canal above the squamocolumnar transition zone. The swab should then be moved slowly in and out without completely withdrawing, while rotating it 360 degrees. It is fixed in the same manner and interpreted using identical criteria as a cervical Pap smear. HPV co-testing is not recommended. Standardized approaches for the management of anal dysplasia have been developed and are being evaluated (Figure 8-2). Prior to an anal pap smear, patients should be advised not to douche, have an enema, or insert anything into their anus for 24 hours. An annual digital rectal examination is recommended annually but should be performed after the anal cytology is obtained.

If the anal pap smear is normal, ongoing annual screening should be recommended. If abnormal anal cytology is present, a HRA is recommended. It is performed in a similar manner to colposcopy, utilizing a microscope to better visualize the anal canal, to identify abnormal areas and obtain biopsy samples. The tissue is evaluated with both acetic acid (abnormal tissue appears white) and Lugol's iodine (abnormal tissue does not stain). Histopathology of these biopsy sites allows for grading to determine the severity of disease and further management.

Figure 8-2. Algorithm for Management of Anal Pap Smear Results



ASCUS, atypical squamous cells of uncertain significance; LSIL, low -grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AIN, anal intraepithelial neoplasia; HRA, high resolution anoscopy.

Panther LA, Schlecht HP, Dezube BJ. Spectrum of human papillomavirus-related dysplasia and carcinoma of the anus in HIV-infected patients. *AIDS Reader* 2005;15:79-91.

Chapter 9. Tuberculosis

Background

Tuberculosis (TB) is a significant cause of morbidity and mortality in HIV-infected patients. The annual risk of reactivation of latent TB (LTBI) in patients with untreated HIV is up to three times that of individuals who are HIV seronegative. Treatment of latent TB is effective in HIV-infected patients with a positive test and decreases the likelihood of active TB.

TB may present with extrapulmonary manifestations in advanced HIV disease, and cutaneous anergy (lack of reactivity to skin tests) is more common in this context. Diagnosis may be delayed because of these characteristics. Multidrug-resistant (MDR) strains, which are problematic to treat, are common in some parts of the country.

Screening

Screening for latent TB should be part of the initial assessment of HIV-infected patients and repeated annually in high-risk individuals if the test result is negative. Testing options include a tuberculin skin test (PPD) [purified protein derivative, intermediate strength, 5TU] or interferon-gamma release assay (IGRA).

The PPD is administered intracutaneously and read at 48-72 hours. The routine use of control agents, such as candida, tetanus toxoid, and mumps, is not recommended because of their lack of standardization. A positive test in an HIV-infected patient is defined as 5 mm or more of induration (measured across the forearm). A history of prior BCG administration should not affect the interpretation of PPD results.

The IGRA is an *in vitro* blood test of cell-mediated immune response to *M. tuberculosis*. It is highly specific and not affected by BCG vaccination status of the patient. CDC guidelines state that IGRA can be used in lieu of the PPD in all situations. However, it is preferred in patients with a history of BCG administration and in those in whom a repeat visit for PPD reading is difficult. Its sensitivity is decreased in patients with progressive immunodeficiency but less so than the PPD. For assistance with PPD and IGRA interpretation, [The Online TST/IGRA Interpreter](#) provides a comprehensive analysis of the positive and negative predictive values of the results based on a patient's country of origin, PPD and IGRA results, BCG status, age, and comorbidities.

Repeat PPD or IGRA testing is recommended in HIV-infected patients with a baseline CD4 cell count less than 200/mm³ and a negative result once the CD4 cell count is above this threshold on antiretroviral therapy.

Treatment of Latent TB

Antimicrobial therapy is recommended for HIV-infected patients regardless of age with any of the following:

- Positive PPD or IGRA with no evidence of active TB
- History of a positive PPD or IGRA and no documentation of treatment with no evidence of active TB
- Recent exposure to active pulmonary TB, regardless of screening test results, with no evidence of active TB

Antimicrobial therapy is generally not recommended in HIV-infected persons with anergy who have historical risk factors for TB exposure, such as injection-drug use, alcoholism, homelessness, incarceration, living in shelter or institution, and originating from a country endemic for TB.

A chest x-ray should be performed on all patients with a positive PPD or IGRA before initiating treatment to rule out active pulmonary TB. If extrapulmonary disease is suspected clinically, the appropriate additional diagnostic evaluation should also be completed.

Isoniazid (INH) 300 mg po qd given with pyridoxine 25 mg po qd is the preferred regimen (Table 9-1). Treatment is continued for nine months. Alternative regimens, which include isoniazid with rifapentine or rifampin alone, may be desirable given their shortened duration and better side effect profile, but may be associated with more drug-drug interactions.

Hepatotoxicity to INH is uncommon in patients younger than 35 years old but increases with advancing age. The drug should be discontinued if clinical stigmata of hepatitis develop or if liver transaminases increase to ≥ 5 times baseline. Other potential side effects include fever and rash.

Infectious disease consultation is recommended in the treatment of latent TB with suspected MDR strains.

Treatment of Active TB

A four-drug regimen is preferred for initial empiric treatment of TB pending culture and sensitivity results. The combination of INH, RIF or another rifamycin, ethambutol, and pyrazinamide is given for 8 weeks, after which INH and RIF alone are continued if the organism is sensitive to these drugs. The total duration of treatment is generally 6 months for pulmonary TB and 6-12 months for extrapulmonary TB. Directly observed therapy (DOT) is preferred over conventional management whenever possible. All patients with INH-resistant or RIF-resistant isolates, as well as persons with a history of nonadherence, should receive DOT.

The presence of active TB requires immediate initiation of antimicrobial treatment. All HIV-infected patients with active TB should be treated with antiretroviral therapy. In patients with a CD4 cell count $< 50/\text{mm}^3$, antiretroviral therapy should be started within 2 weeks of initiating TB treatment. In patients with higher CD4 counts, antiretroviral therapy can be delayed for up to 2-4 weeks in patients with severe clinical disease and for up to 12 weeks in patients who do not have severe clinical disease (see DHHS guidelines for more information).

Rifampin, an important component of combination therapy for TB, cannot be given with many protease inhibitors, non-nucleoside reverse transcriptase inhibitors, and cobicistat (see Chapter 3). In some instances, rifabutin can be substituted for it.

Susceptibility tests should be performed on the initial TB isolate and on any isolate obtained at three months post-treatment.

Antimicrobial drug resistance should be considered if there has been prior ineffective or intermittent treatment or if there is a history of exposure to TB strains from Central or South America, Africa, or the Far East.

Infectious disease consultation is recommended in the treatment of active TB.

Table 9-1. Treatment Regimens for Latent Tuberculosis in Patients with HIV Infection

Drug	Regimen
Isoniazid with pyridoxine	INH 300 mg po qd with pyridoxine 25 mg po qd x nine months
Isoniazid and rifapentine **	900 mg INH daily and weight-based RPT * dose x one month
Rifampin **	600 mg po qd x four months

INH=isoniazid, RPT=rifapentine, DOT=directly observed therapy, ART=antiretroviral therapy.

* RPT is only recommended for patients receiving RAL or EFV

** Concomitant use of TAF with a rifamycin is not advised

Chapter 10. Viral Hepatitis

Epidemiology

Hepatitis A, B, and C infections are common in HIV disease. Approximately 25% of people with HIV are coinfecting with hepatitis C. Because hepatitis A virus (HAV) is transmitted via the fecal-oral route, it is seen mainly in men who have sex with men (MSM) as opposed to patients in other risk groups. Hepatitis B virus (HBV), which can be spread sexually or through exposure to infected blood, occurs in MSM, heterosexuals, and injection-drug users (IDUs). Hepatitis C virus (HCV), which is transmitted primarily through exposure to infected blood, affects mostly IDUs and hemophiliacs who received unscreened blood products in the past, although sexual transmission has also been described in MSM. In fact, the prevalence of HCV in HIV infected MSM is increasing. Of note, HBV and HCV are more easily transmitted (30% and 3% risk, respectively) than HIV (0.3% risk) from needlestick exposure to infected blood. Liver disease related to HCV is the second leading cause of death in HIV-infected patients.

Hepatitis A causes acute infection but not chronic liver disease. Hepatitis B is self-limited in 96% of HIV-seronegative patients, progressing to chronic infection with a variable clinical course in the remainder of patients. Hepatitis C is a chronic infection in the majority of patients and is often associated with progressive liver disease.

Clinical Manifestations

Acute viral hepatitis classically presents with anorexia, nausea, vomiting, upper abdominal pain, and jaundice but may be a nonspecific illness in some patients; fever is common with HAV infection. Rarely, fulminant hepatitis occurs with rapidly progressive hepatic dysfunction. Physical examination may show a jaundiced patient with tender hepatomegaly. Liver function tests, particularly serum transaminases and bilirubin levels, are increased. Symptoms and signs of acute hepatitis often persist for several weeks before resolving. Patients with hepatitis B or C who develop chronic infection may be asymptomatic or have exacerbations of these same symptoms with variable frequency. Over many years, they become at risk for cirrhosis and hepatoma.

The clinical course of HAV infection does not seem to be altered in the context of HIV disease. HBV infection is more likely to become chronic in HIV-infected patients, and it may progress more rapidly. Chronic HBV infection has been noted to flare when combination antiretroviral therapy is initiated, perhaps representing an immune reconstitution syndrome. It may also do so if lamivudine (3TC), emtricitabine (FTC), tenofovir (TDF), or tenofovir alafenamide (TAF) antiretroviral drugs that also have anti-HBV activity, are interrupted or discontinued.

HCV is often more aggressive in HIV-infected patients, especially in those with significant immunodeficiency. Progression of HCV disease, which takes up to 30 years or longer in an HIV-seronegative patient, may occur in less than half that time in a coinfecting patient. HIV disease may progress more rapidly in the context of HCV infection. Increased hepatotoxicity has been reported in co-infected patients receiving antiretroviral therapy, and impaired immune reconstitution has also been described in co-infected patients.

Diagnosis

Acute viral hepatitis is suggested by the clinical presentation in association with abnormal liver function tests. Differential diagnosis includes hepatotoxicity related to alcohol and medications and biliary tract disease. Diagnosis of viral hepatitis is established by serologic tests, including IgM anti-HAV for hepatitis A, hepatitis B surface antigen (HBsAg) for hepatitis B (Table 10-1), and anti-HCV for hepatitis C. If anti-HCV is positive via enzyme-linked immunosorbent assay (ELISA), the diagnosis of active hepatitis C infection should be verified with PCR for HCV RNA. Chronic hepatitis is defined as lasting 6 months or longer. Vibration-controlled transient liver elastography (FibroScan) or serologic markers of fibrosis may be recommended to establish the extent of disease in patients with chronic hepatitis and to identify those who are candidates for drug treatment. Liver biopsy, although still the gold standard in determining degree of fibrosis, is invasive and susceptible to sampling variability. In general, liver function test abnormalities do not correlate well with histologic findings.

General Management

The management of acute hepatitis, with the possible exception of HCV infection (for which treatment may be warranted if spontaneous clearance does not occur within 12 weeks) is generally supportive. Patients should be asked to maintain adequate oral intake to prevent dehydration and to rest as needed.

Patients with chronic hepatitis should be cautioned about the use of alcohol, acetaminophen, and other potentially hepatotoxic agents. Acetaminophen use should be limited to a maximum of 2 grams in 24 hours. They should be advised against sharing razors and dental equipment, and should be educated about the importance of practicing safer sex at all times because of the potential for transmission of these viruses to other individuals. Patients should be counseled to stop using illicit drugs, and in those who continue to inject, they should be counseled to avoid reusing and sharing supplies, and to dispose safely of syringes and needles after use.

All HIV-infected patients should be tested serologically for HAV, HBV, and HCV infections. Immunization against hepatitis A and B is recommended in those without previous exposure to these pathogens, although the response to vaccines may be diminished in advanced HIV disease. Hepatitis A vaccine is particularly

important because of the risk for fulminant hepatitis in HCV-infected patients who subsequently contract HAV.

Chronic Hepatitis B Management

Prior to initiation of antiretroviral therapy, patients who test positive for HBsAg should be tested for HBV DNA using a quantitative assay to determine the level of HBV replication. Because FTC, 3TC, TAF and TDF have activity against both HIV and HBV, if HBV or HIV treatment is needed, antiretroviral therapy should be initiated with the combination of TDF or TAF+FTC or TDF or TAF+3TC as the nucleoside reverse transcriptase inhibitor backbone of a fully suppressive antiretroviral regimen. If HBV treatment is needed and TDF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive antiretroviral regimen. Other HBV treatment regimens include peg-interferon alfa monotherapy or adefovir in combination with 3TC or FTC or telbivudine in addition to a fully suppressive antiretroviral regimen. Entecavir has activity against HIV; its use for HBV treatment without antiretroviral therapy in patients with dual infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be given with a fully suppressive antiretroviral regimen in HIV/HBV-coinfected patients.

Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against self-discontinuation and carefully monitored during interruptions in treatment. If antiretroviral therapy needs to be modified because of HIV virologic failure and the patient has adequate HBV suppression, the antiretroviral drugs active against HBV should be continued for HBV treatment in combination with other suitable agents to achieve HIV suppression.

Patients with chronic HBV-related cirrhosis and other at-risk groups (Asian men over the age of 40 years, Asian women over the age of 50 years, Africans/North American blacks, and patients with a family history) should be screened for hepatocellular carcinoma with an abdominal ultrasound every 6 months.

Chronic Hepatitis C Management

All HIV-infected patients should be screened for HCV infection. Patients at high risk of HCV infection should be screened annually and whenever HCV infection is suspected. Antiretroviral therapy may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most HIV/HCV-coinfected patients, including those with cirrhosis, the benefits of antiretroviral therapy outweigh concerns regarding drug-induced liver injury. Therefore, antiretroviral therapy should be initiated in most HIV/HCV-coinfected patients, regardless of CD4 cell count.

Initial antiretroviral therapy combination regimens recommended for most HIV/HCV-coinfected patients are the same as those recommended for individuals

without HCV infection. However, when treatment for both HIV and HCV is indicated, the antiretroviral regimen should be selected with special considerations of potential drug-drug interactions and overlapping toxicities with the HCV treatment regimen. Combined treatment of HIV and HCV can be complicated by drug-drug interactions, increased pill burden, and toxicities. Although antiretroviral therapy should be initiated for most HIV/HCV-coinfected patients regardless of CD4 count, in antiretroviral therapy-naïve patients with CD4 counts >500 cells/mm³, some clinicians may choose to defer antiretroviral therapy until HCV treatment is completed. In patients with lower CD4 counts (e.g., <200 cells/mm³), antiretroviral therapy should be initiated promptly, and HCV therapy may be delayed until the patient is stable on HIV treatment.

Treatment options are largely based on genotype but are also influenced by prior treatment history and presence of cirrhosis (Table 10-2). There are now two pan-genotypic regimens which are highly effective (elpatasvir-sofosbuvir and glecaprevir-pibrentasvir). All medications have significant drug interactions, some of which may preclude co-administration of other agents; review the package insert and [Hep Drug Interactions](#) for more information. The goal of anti-HCV therapy is to achieve sustained virologic response, which is defined as an undetectable HCV DNA level at 12 weeks post-treatment.

In patients with chronic HCV, it is important to determine the degree of fibrosis, as it has a significant impact on prognosis, may affect treatment considerations, and guides surveillance monitoring. Noninvasive testing methods are preferred to liver biopsy. Options include serum biomarker testing and vibration-controlled transient liver elastography. The combination of these two methods is considered the most reliable way to assess fibrosis.

In patients with mild fibrosis (METAVIR stage F0-F2), it is appropriate to monitor for advancing fibrosis annually. In patients with advanced fibrosis (METAVIR stage F3-F4), screening abdominal ultrasound should be performed every 6 months to screen for hepatocellular carcinoma, and an upper endoscopy should be performed to screen for the presence of esophageal varices.

Expert consultation is recommended for clinicians with limited experience in the treatment of chronic hepatitis C infection, which is a rapidly evolving field.

Table 10-1. Serologic Markers of Hepatitis B Infection

HBsAg	IgM anti-HBc	Anti-HBc	Anti-HBs	Interpretation
-		-	-	Susceptible
-		+	+	Immune from prior infection
-		-	+	Immune from immunization
+	+	+	-	Acute infection
+	-	+	-	Chronic infection

Table 10-2. Treatment Options for Chronic HCV Infection *

Drug Regimen	Genotypes Covered	Avoid Concurrent Use with these ART Drugs
Velpatasvir-sofosbuvir (Epclusa)	Pan-genotypic	Efavirenz, etravirine, nevirapine, tipranavir
Ledipasvir-sofosbuvir (Harvoni)	1,4,5,6	Tipranavir
Glecaprevir-pibrentasvir (Mavyret)	Pan-genotypic	Atazanavir, efavirenz, etravirine, nevirapine, ritonavir
Daclatasvir (Daklinza) + sofosbuvir (Sovaldi)	1,2,3	Tipranavir
Sofosbuvir-velpatasvir-voxilaprevir (Vosevi)	Pan-genotypic For previously treated patients	Efavirenz, etravirine, nevirapine, ritonavir-boosted atazanavir, ritonavir-boosted lopinavir, tipranavir
Elbasvir-grazoprevir (Zepatier)	1,4	Cobicistat, efavirenz, etravirine, nevirapine, all protease inhibitors

* Choice of therapy should be made by an experienced health care practitioner who is knowledgeable about potential interactions with antiretroviral drugs. Dosing and duration are determined by treatment status, presence of cirrhosis, viral subtyping, and resistance testing. Based upon these factors, additional medications, including ribavirin or pegylated interferon, may be recommended.

Chapter 11. Sexually Transmitted Diseases

General Guidelines

Persons identified as having one sexually transmitted disease (STD) are at risk for others and should be screened as appropriate. Partners of persons with an STD should be evaluated and treated as appropriate. Emphasis should be placed on prevention as well as treatment of STDs.

Considerations in HIV-infected Patients

Genital ulcer diseases, such as syphilis and herpes simplex virus (HSV) infection, predispose individuals to transmission and acquisition of HIV infection. The presentation, serology, natural history, and treatment response of syphilis may be altered in the context of HIV disease. HSV infection is often more severe and prone to relapse. It may require a higher dose and longer duration of therapy. Lesions may be atypical in appearance in the context of advanced HIV disease. Human papillomavirus (HPV) infection is common and associated with cervical and anal dysplasia/cancer. See Chapter 7 for cervical and anal Pap smear recommendations in this population. The increasing resistance of gonorrhea has resulted in changes in antibiotic recommendations. Treatment of pelvic inflammatory disease may be problematic. Routine periodic screening for STDs is recommended in at risk HIV-infected patients.

Diagnosis and Treatment

Chancroid

Syndrome is painful genital ulcer(s) with shaggy border and exudate at base associated with tender inguinal adenopathy.

Presumptive diagnosis is made by clinical appearance of lesion and ruling out other causes of genital ulcer disease (RPR; Tzanck smear, HSV culture, or dFA [direct fluorescent antibody] test).

Treatment:

- Ceftriaxone 250 mg IM once *or*
azithromycin 1 gram po once *or*
ciprofloxacin 500 mg po bid x 3 days *or*
erythromycin 500 mg po tid x 7 days

Chlamydial Infection

Syndromes include urethritis, epididymitis, cervicitis, salpingitis, proctitis, and lymphogranuloma venereum.

Diagnosis is made presumptively by demonstration of PMNs without gram-negative diplococci on gram stain of discharge and confirmed by urinary nucleic acid amplification assay (preferably of first void urinary specimen).

Treatment:

- Doxycycline 100 mg po bid x 7 days *or* azithromycin 1 gram po once

Recent sex partners of patients with chlamydial infection should be treated presumptively.

Genital Warts

Syndrome is one or more skin-colored papular lesions at sites of sexual contact. These may occur externally on the penis, vulva, or perineal region, or internally in the vagina or rectum. Genital warts are caused by HPV, most commonly strains 6 and 11. HPV is a risk factor for cervical and anal dysplasia/cancer.

Diagnosis is made by clinical appearance.

Treatment: All of the listed modalities are about equally effective, and there is a high rate of relapse although frequency is variable.

- Podophyllin 0.5% solution or gel (available with prescription)
Apply bid x 3 days followed by 4 days of no therapy
May be repeated as necessary for total of 4 cycles
- Imiquimod 5% cream (available with prescription)
Apply qhs three times per week for up to 16 weeks;
or imiquimod 3.75% cream, applied every night for up to 16 weeks;
wash area with soap and water in morning
- Cryotherapy
- Trichloroacetic acid
- Surgical removal

Gonorrhea

Syndromes include urethritis, epididymitis in men, cervicitis and salpingitis in women, rectal, pharyngeal, and disseminated infection.

Diagnosis is made presumptively by demonstration of intracellular gram-negative diplococci and confirmed by urinary nucleic acid amplification (men only) or culture.

Treatment of uncomplicated infection:

- Ceftriaxone 250 mg IM once
plus azithromycin 1 gram po once
- If ceftriaxone is not available:
Cefixime 400mg po once
plus azithromycin 1 gram po once

Treatment of complicated infection:

- Ceftriaxone 1 gram IM or IV qd x 7-10 days
plus azithromycin 1 gram po once

Recent sex partners of patients with gonorrhea infection should be treated presumptively for gonorrhea and chlamydial infection.

Herpes Simplex Virus

Syndrome is multiple clustered vesicular lesions on erythematous base; primary infection is followed by variable frequency of recurrences.

Diagnosis is made presumptively by clinical appearance of lesions and confirmed by Tzanck smear, HSV culture, or dFA test.

Treatment:

- Primary or recurrent infection →
acyclovir 400 mg po tid x 5-10 days *or*
famciclovir 500 mg po bid x 5-10 days
valacyclovir 1 g po bid x 5-10 days *or*
- Prophylaxis for patients with frequent recurrences →
acyclovir 400-800 mg po bid-tid *or*
famciclovir 500 mg po bid *or*
valacyclovir 500 mg po qd
- Topical antiviral therapies are not very effective

Lymphogranuloma Venereum

Syndrome of proctitis has been described in HIV-infected MSM. It presents with purulent rectal discharge and tenesmus associated with tender inguinal adenopathy. A genital papule or ulceration at the site of inoculation may also be present. It is caused by the L serovars of *Chlamydia trachomatis*.

Diagnosis is suspected clinically and can be confirmed by serologic testing. Other infectious causes of proctitis should be excluded.

Treatment:

- Doxycycline 100 mg po bid x 21 days *or* erythromycin 500 mg po qid x 21 days

Molluscum Contagiosum

Syndrome is multiple clustered pearl-like papular lesions on site of physical contact, but autoinoculation may also occur. It is caused by a pox-like virus.

Diagnosis is made by clinical appearance.

Treatment:

- Anti-retroviral therapy in those not previously on HIV treatment
- Cryotherapy
- Curettage
- Trichloroacetic acid

Pubic Lice

Syndrome is genital pruritus.

Diagnosis is made by recognition of lice or nits on pubic hair.

Treatment:

- Permethrin 1% cream rinse applied to affected areas and washed off after 10 minutes *or*
- Pyrethrins with piperonyl butoxide (applied to affected area and washed off after 10 minutes) *or*

- Ivermectin 250 mcg/kg po and repeated in 2 weeks *or*
- Malathion 0.5% lotion (washed off after 8-12 hours)

Recent sex partners of patients with pubic lice should be treated presumptively.

Scabies

Syndrome is a scattered pruritic, papular eruption with characteristic "burrows" sometimes noted. An aggressive form of the infestation with atypical manifestations has been described in immunocompromised patients.

Diagnosis is made by clinical appearance of skin lesions and confirmed by scraping/oil mount demonstrating the parasite.

Treatment:

- Permethrin cream 5% applied from neck down and washed off after 8-14 hours *or*
- Ivermectin 200 mcg/kg po and repeated in two weeks *or*
- Lindane (1% lotion or 30 grams of cream applied from neck down and washed off after 8 hours)

Recent sex partners and household contacts of patients with scabies should be treated presumptively.

Syphilis

Syndromes: Primary stage manifested by chancre; secondary phase manifested by mucocutaneous disease; and tertiary phase, after prolonged latency period, manifested by neurologic disease.

Diagnosis is made by clinical presentation and positive serology with a treponemal (FTA-abs or MHA-Tp) test and confirmed with a nontreponemal (RPR or VDRL) test.

Treatment:

- Primary, secondary, and early latent (< 1 yr duration) → benzathine penicillin 2.4 mU IM once
Alternative: doxycycline 100mg po BID for 10-14 days, ceftriaxone 1g IM or IV for 10-14 days, or azithromycin 2g po x 1 dose
- Late latent (> 1 yr duration) and tertiary → benzathine penicillin 2.4 mU IM weekly x 3
Alternative: doxycycline 100mg po BID for 28 days

- Neurosyphilis (any stage) → penicillin G 18-24 mU/day IV every 4 hours or continuous infusion x 10-14 days followed by regimen for late latent syphilis

RPR or VDRL will generally convert to negativity within 1-2 years in patients who have primary, secondary, or early latent syphilis. In patients with late latent and tertiary syphilis, RPR or VDRL may remain serofast at a low positive titer.

Lumbar puncture should be performed in patients with neurologic symptoms or signs to assess for central nervous system involvement. Some experts recommend that it be performed in HIV-infected patients in their absence when the RPR or VDRL is positive at a high titer (>1:32) or when the CD4 count is <350 cells/mm³.

Recent sex partners of patients with primary, secondary, or early latent syphilis should be treated presumptively.

Trichomonas

Syndrome is foamy vaginal discharge sometimes in association with urethritis.

Diagnosis is made by vaginal wet mount showing flagellated single-celled organisms or by urinary nucleic acid amplification test.

Treatment:

- Metronidazole 2 grams po once or 500 mg po bid x 7 days *or* tinidazole 2 grams po once

Recent sex partners of patients with trichomonas infection should be treated presumptively.

Chapter 12. Long-Term Complications

Complications have been associated with the long-term HIV infection. Some of these complications are associated with medications, and some are associated with the virus itself. These include: 1) coronary artery disease; 2) premature bone loss; 3) lipodystrophy syndrome (body fat maldistribution, hyperlipidemia, glucose intolerance), mostly from exposure to older NRTIs; 4) avascular necrosis of hips; 5) lactic acidemia/acidosis; and 6) peripheral neuropathy. Newer antiretrovirals are less likely to cause many of these complications, however their manifestations may still be present in long-term HIV survivors who were exposed to these drugs in the past.

Coronary Artery Disease

The incidence of coronary artery disease in HIV-infected patients is higher than that in seronegative patients matched for age and gender. Studies have demonstrated an increase in subclinical atherosclerosis (e.g., carotid intima media thickness) and clinical endpoints (e.g., acute myocardial infarction). HIV infection is associated with increased soluble and cellular markers of inflammation, endothelial dysfunction, and altered coagulation, all of which have been shown to contribute to cardiovascular disease. The degree to which HIV infection itself, antiretroviral therapy, and traditional risk factors contribute to increased risk in this population is unknown. The PI class appears to be associated with higher risk of coronary artery disease. ABC and EFV have also been identified in some studies as a risk factor for myocardial infarction, although the data are inconsistent. These drugs should be used with caution or avoided in patients with known cardiovascular disease.

Premature Bone Loss

Premature bone loss (osteopenia/osteoporosis) has been reported in HIV-infected patients on long-term antiretroviral therapy, especially regimens containing TDF. Interference of vitamin D metabolism by PIs and lactic acidosis related to NRTI therapy may be responsible for bone loss in this setting, and HIV infection itself may also be a contributing factor. TAF, a new prodrug of tenofovir with less toxicity, may offer an advantage over TDF. Immobility, cigarette smoking, excessive alcohol use, chronic renal failure, thyroid disease, hyperparathyroidism, hypogonadism, and chronic steroid therapy may accentuate bone loss. Baseline bone densitometry may be considered in HIV-infected patients who are 50 years old, especially if other risk factor(s) for premature bone loss are present. Calcium and vitamin D should be prescribed in high-risk patients; regular exercise and smoking cessation should be advised in all patients.

Lipodystrophy Syndrome

Lipodystrophy syndrome has been reported in HIV-infected patients on combination antiretroviral therapy, especially regimens containing d4T and/or PIs. While few patients may continue on these regimens, prior exposure may result in longstanding effects. This syndrome consists of body morphology changes (deposition of fat in abdomen, breasts,

and neck; loss of fat in face and extremities), metabolic complications (hyperlipidemia, glucose intolerance/diabetes mellitus), or both. The pathogenesis of lipodystrophy syndrome is not fully understood, and its management is syndromic (Figure 12-1).

Avascular Necrosis of the Hips

Avascular necrosis of the hips has also been described in HIV-infected patients on long-term antiretroviral therapy. It is not associated with traditional risk factors such as alcoholism and chronic steroid therapy. The condition presents as progressive unilateral or bilateral hip pain. Plain x-rays are often normal, and diagnosis is made by MRI scan. Early disease is managed symptomatically, but it may ultimately require hip replacement.

Lactic Acidosis

Lactic acidosis with a variety of clinical manifestations (peripheral neuropathy, pancreatitis, myopathy, steatosis with liver failure) has been described in HIV-infected patients on older NRTI-based regimens. It results from the inhibition of mitochondrial DNA-polymerase. Because asymptomatic lactic acidemia has poor predictive value for decompensated lactic acidosis, screening for this condition is not recommended. However, in patients on NRTI-based regimens who have unexplained constitutional or gastrointestinal symptoms, a venous lactate level is recommended. If symptomatic lactic acidemia is confirmed, modification of the antiretroviral regimen is warranted.

Peripheral Neuropathy

Peripheral neuropathy is common in HIV-infected patients. The virus and certain older NRTI drugs (didanosine [ddI], stavudine [d4T]) are usually responsible. It manifests with sensory symptoms involving the lower extremities. The diagnosis is made clinically after excluding other common causes of peripheral neuropathy. Management consists of discontinuation of the offending drug and control of HIV infection. If necessary, analgesics and antidepressants and/or anticonvulsants can be used for chronic pain management.

HIV Infection in the Older Adult

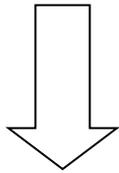
Important points to consider in caring for older HIV-infected patients (> 50 years of age) include the following:

- HIV infection, even when controlled, is associated with chronic immune activation that is superimposed upon immunologic senescence
- Older persons may be diagnosed later and have more advanced HIV infection at presentation
- There is a less robust immunologic response to antiretroviral therapy in this population
- In general, older HIV-infected patients have better medication adherence but an increased risk of drug toxicity and drug-drug interactions

- HIV-infected patients accumulate “age-related” diseases at a younger chronological age
- Incidence of coronary artery disease is higher than that in HIV-negative patients matched for age and gender
- HIV infection and its treatment and comorbidities have been associated with premature bone loss
- Increasing age may be a risk factor for HIV-associated neurocognitive dysfunction, although studies examining this issue are limited
- Lung, hepatic, and anal cancers occur at a younger age in HIV-infected adults compared to seronegative persons
- Mortality in HIV-infected persons has fallen substantially over past two decades with non-AIDS-related conditions now accounting for the majority of deaths

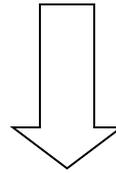
Figure 12-1 Management of Lipodystrophy Syndrome

Hyperlipidemia, insulin resistance



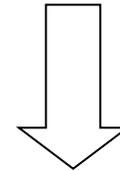
- Diet and exercise
- Switch therapy
- Insulin-sensitizing drugs (metformin)
- Statins/fibrates

Visceral fat accumulation



- Diet and exercise
- Switch therapy
- GHRH analogues (tesamorelin)
- Surgical correction

Subcutaneous fat wasting



- Switch therapy
- Insulin-sensitizing drugs
- Local injection
 - Poly-L-lactic acid
 - Calcium hydroxylapatite
 - Autologous fat transplant

Chapter 13. HIV Prevention

General approaches to HIV prevention include:

- Decreasing source of infection
 - Barrier protection
 - Sexually transmitted disease (STD) diagnosis and treatment
 - Blood product screening
 - Antiretroviral therapy of HIV-infected persons
- Decreasing host susceptibility to infection
 - Barrier protection
 - STD diagnosis and treatment
 - Pre-exposure (PrEP) and post-exposure (nPEP and PEP) prophylaxis (see below)
 - Topical microbicides
 - Circumcision
- Altering risk-taking behavior
 - Individual, couples, and community-based interventions

Sexual risk reduction counseling with patients should include discussion of:

- Importance of taking care of oneself
- Role of “safer sex” in the patient’s life
- Importance of limiting number of sexual partners
- Importance of knowing serostatus of partners
- Risk of unplanned or unprotected sexual contact when using drugs or alcohol
- Risk of HIV transmission during pregnancy
- Use of condoms during sexual activity, and identification of obstacles and strategies to overcome them

Drug use risk reduction counseling with patients should include discussion of:

- Importance of bleach to clean drug paraphernalia
- Avoidance of “shooting galleries” or trading sex for drugs
- Referral to needle exchange program if available
- Importance of drug treatment and rehabilitation
- Opportunity to discuss harm-reduction topics and/or offer referral to community-based services

Pre-Exposure Prophylaxis (PrEP)

Although the incidence of HIV infection remains stable among persons who inject drugs (PWID) and heterosexuals, it continues to increase among men who have sex with men (MSM) (12% change from 2008 to 2010). Multiple studies have shown pre-exposure prophylaxis (PrEP) with antiretroviral drugs substantially reduces the risk of HIV transmission in MSM, heterosexuals in serodiscordant relationships, and PWIDs.

PrEP may be considered in MSM or in heterosexual men or women with the following risk factors:

- HIV-seropositive sexual partner
- High number of sex partners
- History of inconsistent or no condom use
- Recent sexually transmitted infection(s)
- Commercial sex work

PrEP may be considered in PWID with the following risk factors:

- HIV-seropositive injecting partner
- History of sharing injection equipment
- Recent drug treatment

Prior to initiating PrEP, the patient must be documented as HIV-seronegative and have no symptoms or signs of acute HIV infection. Baseline laboratory evaluation should also include renal function and testing for hepatitis B virus (HBV) infection. Hepatitis B vaccination should be given to patients without serologic evidence of immunity. For patients with evidence of chronic hepatitis B infection, PrEP is not contraindicated. However, patients should be counseled that were they to stop PrEP, they are risk of hepatitis B reactivation and liver damage. These patients may need lifelong hepatitis B medication, even once they have stopped PrEP.

Truvada (fixed-dose combination of tenofovir disoproxil fumarate [TDF] 300 mg and emtricitabine [FTC] 200 mg) and Descovy (fixed-dose combination of tenofovir alafenamide fumarate [TAF] 25 mg and emtricitabine [FTC] 200 mg) are both FDA-approved for use as PrEP. In general, we advocate for continued use of Truvada as the preferred method of PrEP, except in specific scenarios where Truvada would be contraindicated (Figure 13-1). There is evidence to support the use of on-demand PrEP as an alternative to daily PrEP for MSM with infrequent sexual exposures. In this scenario, TDF/FTC is given as 2 doses 2 to 24 hours before sex, and 1 dose daily for the next 2 days (“2-1-1” dosing). With each new sexual encounter, the double dose should be given initially unless the last pre-exposure dose occurred within 7 days. Cabotegravir, an experimental long-acting injectable integrase inhibitor, also appears to be effective as prophylaxis.

Clinical follow-up and monitoring while on PrEP consists of:

- Every 3 months
 - Repeat HIV test and assess for symptoms/signs of acute infection
 - Test for sexually transmitted diseases
 - Repeat pregnancy testing in women of child-bearing age (TDF/FTC is not contraindicated in pregnancy)
 - Assess side effects, adherence, and risk behaviors
 - Provide support for medication adherence and risk-reduction
 - Respond to questions and provide any new information about PrEP

- Every 6 months
 - Monitor renal function

- Every 12 months
 - Evaluate the need to continue PrEP

Non-Occupational Post-Exposure Prophylaxis (nPEP)

While the most effective way to prevent HIV transmission is to protect against exposure, non-occupational post-exposure prophylaxis (nPEP) offers the possibility of preventing HIV transmission when exposure has already occurred.

Situations that may prompt a request for nPEP include condom slipping, breaking, or lapse in use with an HIV serodiscordant partner or with a partner whose serostatus is unknown; unsafe needle-sharing; or other mucosal or non-intact skin exposure to blood.

When determining whether to recommend initiation of nPEP, the clinician should evaluate the patient's risk based on the type of exposure (see Chapter 1). nPEP is not required after exposure through oral-to-oral contact without mucosal damage (including kissing), human bites not involving blood, exposure to solid-bore needles or sharps not in recent contact with blood, or mutual masturbation without skin breakdown/blood exposure.

For patients where nPEP is determined to be indicated, it should be given as soon as possible after the exposure and preferably within 72 hours. The currently preferred regimen includes TDF 300 mg po daily with FTC 200 mg po daily *plus* raltegravir 400 mg po twice daily *or* dolutegravir 50 mg po daily. An alternative regimen for otherwise healthy adults is TDF 300 mg po daily with FTC 200 mg po daily *plus* DRV 800 mg po daily and RTV 100 mg po daily.

Baseline evaluation of the exposed person should include HIV screening serology, pregnancy test for women, gonorrhea and chlamydia testing based on site of

exposure, and an RPR. If the source patient is available, HIV testing following consent should occur. If the HIV test is negative but there may have been exposure to HIV within 6 weeks, a plasma HIV viral load should be performed. If rapid HIV serology results are not available, nPEP should be initiated without delay. The exposed patient should continue nPEP until the source patient is determined to be negative or for 28 days. All patients receiving nPEP should be re-evaluated within 3 days after initiation to discuss the nature of the exposure, review available source data, evaluate adherence, and monitor for drug toxicities. Repeat HIV testing should occur 4 and 12 weeks after the exposure.

Occupational Post-Exposure Prophylaxis (PEP)

Post-exposure administration (PEP) of antiretroviral drugs is effective at reducing the risk of HIV transmission. Since 1999, there has been only 1 reported case of HIV seroconversion after an occupational exposure. The average risk per percutaneous exposure is estimated to be 0.23%, although it will vary depending on bore size of needle and viral load of the HIV-infected source patient.

To prevent transmission, health care workers should be educated in how to prevent needlestick injuries, and safety devices should be used at all times. Body sites exposed to potentially infectious fluid should be cleansed immediately. Soap and water should be used on skin sites, and exposed mucous membranes should be flushed. “Milking” or squeezing out needlestick injuries is not recommended as it may promote hyperemia and inflammation.

PEP should be initiated as soon as possible for exposure to blood, visibly bloody fluid, or other infectious material (semen; vaginal secretions; breast milk; and cerebrospinal, synovial, pleural, peritoneal, pericardial and amniotic fluids) from HIV-infected persons (Table 12-1). If the status of the source patient is unknown, consent should be obtained for HIV testing. If the HIV test is negative but there may have been exposure to HIV within 6 weeks, a plasma HIV viral load should be performed. Baseline HIV status of the exposed individual should also be obtained. If the source patient is HIV-positive (or until the status becomes known), PEP should be initiated as soon as possible after the exposure.

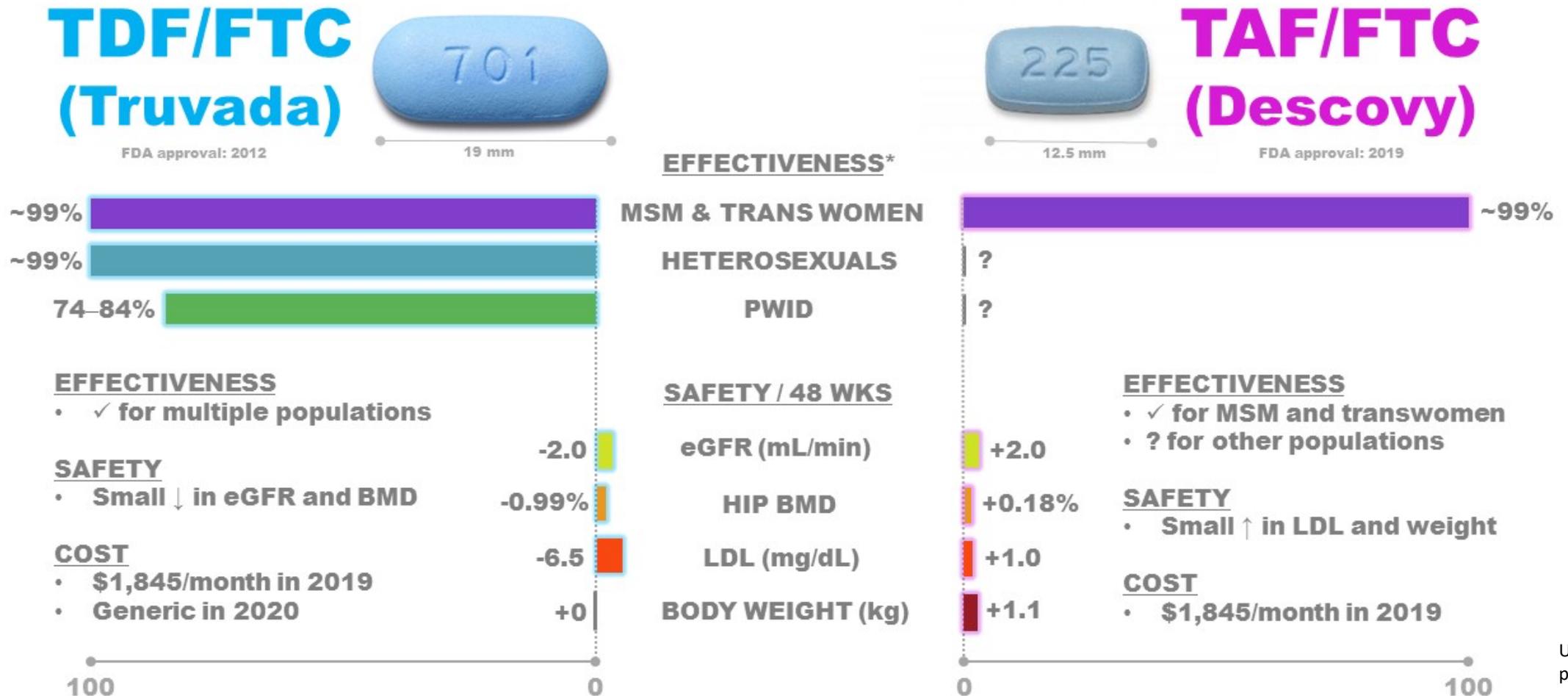
The recommended first-line regimen consists of TDF 300 mg po daily with FTC 200 mg po daily *plus* raltegravir 400 mg po twice daily or dolutegravir 50 mg po daily. Treatment is continued for 28 days. If the source patient is found to be HIV-seronegative, PEP can be discontinued. Repeat HIV testing for the health care worker should occur 4 and 12 weeks after the exposure.

Table 12-1. Exposures for which Occupational Post-Exposure Prophylaxis is Indicated

- Break in the skin by a sharp object (hollow-bore, solid-bore, and cutting needles; or broken glassware) that is contaminated with blood or other potentially infectious material
- Bite from a patient with visible bleeding in the mouth that causes bleeding in the health care worker
- Splash of blood, visibly bloody fluid, or other potentially infectious material to a mucosal surface (mouth, nose, or eyes)
- A non-intact skin (e.g., dermatitis, chapped skin, abrasion, or open wound) exposure to blood, visibly bloody fluid, or other potentially infectious material

Figure 13-1
Drug Options for HIV Pre-exposure Prophylaxis

Which medication should I prescribe for daily PrEP?



Used with permission

Chapter 14. Drug Glossary

Antiretroviral Therapy

Nucleoside Reverse Transcriptase Inhibitors (NRTIs) *

Abacavir (ABC, Ziagen)

Indications: Treatment of HIV infection in combination with other agents.

HLA-B*5701 testing (presence associated with increased risk of hypersensitivity reaction) is recommended before using this drug in an antiretroviral regimen. If positive, patient should not be prescribed ABC.

Contraindications: Known or suspected hypersensitivity.

Dosage: 300 mg po bid. Also available as Epzicom, a fixed-dose combination of 3TC 300 mg and ABC 600 mg given once daily; Triumeq, a fixed-dose combination of ABC 600 mg, 3TC 300 mg and DTG 50 mg given once daily; and Trizivir, a fixed-dose combination of ZDV 300 mg, 3TC 150 mg, and ABC 300 mg given twice a day.

Toxicity: Four percent of patients develop a hypersensitivity reaction, usually within 6 weeks of initiating therapy. It is manifested by fever, constitutional or respiratory symptoms, gastrointestinal intolerance, and/or rash. Stopping the drug leads to rapid resolution of symptoms. *Never rechallenge a patient thought to have had a hypersensitivity reaction to abacavir as severe reactions and death have been reported.*

Other side effects include nausea, vomiting, diarrhea, headache, malaise.

Pregnancy category C.

Didanosine (ddI, Videx)

Indications: No longer recommended for treatment of HIV infection in the United States due to toxicities.

Emtricitabine (FTC, Emtriva)

Indications: Treatment of HIV infection in combination with other agents. nPEP, oPEP, and PrEP in combination with other agents. Also has activity against hepatitis B virus.

Contraindications: Known hypersensitivity.

Dosage: 200 mg po qd. Also available as Truvada, a fixed-dose combination of TDF 300 mg and FTC 200 mg given once daily; Descovy, a fixed-dose combination of TAF 25 mg and FTC 200mg given once daily; Atripla, a fixed-dose combination of TDF 300 mg, FTC 200 mg, and EFV 600 mg given once daily; Complera, a fixed-dose combination of TDF 300 mg, FTC 200 mg, and RPV 25 mg given once daily; Stribild, a fixed-dose combination of TDF 300 mg, FTC 200 mg, EVG 150 mg, and cobicistat 150 mg given once daily; Genvoya, a fixed-dose combination of TAF 10 mg, FTC 200 mg, EVG 150 mg, and cobicistat 150 mg given once daily; Odefsey, a fixed-dose combination of TAF 25 mg, FTC 200 mg, and RPV 25 mg given once daily; Biktarvy, a fixed-dose combination of TAF 25 mg, FTC 200 mg, and BIC 50 mg given once daily; and Symtuza, a fixed-dose combination of TAF 10 mg, FTC 200 mg, DRV 800 mg, and cobicistat 150 mg given once daily.

Renal dose adjustments required, based on agent used.

Toxicity: Hyperpigmentation on palms and soles.

Pregnancy category B.

Stribild, Genvoya, and Symtuza (cobicistat component) have many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Lamivudine (3TC, Epivir)

Indications: Treatment of HIV infection in combination with other agents. Also has activity against hepatitis B virus.

Contraindications: Known hypersensitivity.

Dosage: 150 mg po bid or 300 mg po qd. Also available as Combivir, a fixed-dose combination of ZDV 300 mg with 3TC 150 mg given twice a day; Cimduo, a fixed-dose combination of 3TC 300 mg and TDF 300 mg given once daily; Epzicom, a fixed-dose combination of 3TC 300 mg and ABC 600 mg given once daily; Triumeq, a fixed-dose combination of ABC 600 mg, 3TC 300 mg and DTG 50 mg given once daily; Trizivir, a fixed-dose combination of ZDV 300 mg, 3TC 150 mg, and ABC 300 mg given twice a day; Symfi, a fixed-

dose combination of 3TC 300 mg, TDF 300 mg, and EFV 600 mg given once daily; Symfi Lo, a fixed-dose combination of 3TC 300 mg, TDF 300 mg, and EFV 400 mg given once daily; Dovato, a fixed-dose combination of 3TC 300 mg and DTG 50 mg; and Delstrigo, a fixed-dose combination of 3TC 300 mg, TDF 300 mg and DOR 100 mg given once daily.

Renal dose adjustments required, based on agent used.

Toxicity: Uncommon. Headache, gastrointestinal intolerance, and insomnia have been reported.

Pregnancy category C.

Stavudine (d4T, Zerit)

Indications: No longer recommended for treatment of HIV infection in the United States due to toxicities.

Tenofovir alafenamide (TAF)

Indications: Treatment of HIV infection in combination with other agents. NPEP, oPEP and PrEP in combination with other agents. Also has activity against hepatitis B virus (Vemlidy brand name for treatment of hepatitis B).

Contraindications: Known hypersensitivity. Monitor interactions due to P-glycoprotein.

Dosage: Available as Descovy, a fixed-dose combination of TAF 25 mg and FTC 200mg given once daily; Genvoya, a fixed-dose combination of TAF 10 mg, FTC 200 mg, elvitegravir 150 mg, and cobicistat 150 mg given once daily; Odefsey, a fixed-dose combination of TAF 25 mg, FTC 200 mg, and rilpivirine 25 mg given once daily; Biktarvy, a fixed-dose combination of TAF 25 mg, FTC 200 mg, and bicitgravir 50 mg given once daily; and Symtuza, a fixed-dose combination of TAF 10 mg, FTC 200 mg, DRV 800 mg and cobicistat 150 mg given once daily.

Toxicity: Lactic acidosis, decreased bone mineral density, post treatment acute exacerbation of hepatitis B.

Currently limited data for use in pregnancy.

Genvoya and Symtuza (cobicistat component) have many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-

infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Tenofovir disoproxil fumarate (TDF, Viread)

Indications: Treatment of HIV infection in combination with other agents. NPEP, oPEP, and PrEP in combination with other agents. Also has activity against hepatitis B virus.

Contraindications: Known hypersensitivity. Monitor interactions due to P-glycoprotein.

Dosage: 300 mg po qd with food. Also available as Truvada, a fixed-dose combination of FTC 200 mg and TDF 300 mg given once daily; Cimduo, a fixed-dose combination of 3TC 300 mg and TDF 300 mg given once daily; Atripla, a fixed-dose combination of TDF 300 mg, FTC 200 mg, and efavirenz 600 mg given once daily; Complera, a fixed-dose combination of TDF 300 mg, FTC 200 mg, and rilpivirine 25 mg given once daily; Stribild, a fixed-dose combination of TDF 300 mg, FTC 200 mg, elvitegravir 150 mg, and cobicistat 150 mg given once daily; Symfi, a fixed-dose combination of 3TC 300 mg, TDF 300 mg, and EFV 600 mg given once daily; Symfi Lo, a fixed-dose combination of 3TC 300 mg, TDF 300 mg, and EFV 400 mg given once daily; and Delstrigo, a fixed-dose combination of 3TC 300 mg, TDF 300 mg, and DOR 100 mg given once daily.

Toxicity: Gastrointestinal intolerance, renal dysfunction, hypophosphatemia.

Pregnancy category B.

Stribild (cobicistat component) has many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Zidovudine (ZDV, AZT, Retrovir)

Indications: Treatment of HIV infection in combination with other agents.

In addition, ZDV may have specific benefits for patients who have HIV-related thrombocytopenia or encephalopathy.

Prevention of perinatal transmission when given prenatally and during delivery to HIV-infected mother and to infant postpartum. Combination antiretroviral therapy should be administered in this setting.

Contraindications: Known hypersensitivity.

Dosage: Treatment of HIV infection in adults: 300 mg po bid. Also available as Combivir, a fixed-dose combination of ZDV 300 mg with 3TC 150 mg given twice a day; and Trizivir, a fixed-dose combination of ZDV 300 mg, 3TC 150 mg, and ABC 300 mg given twice a day.

Toxicity: Gastrointestinal intolerance, headache, fingernail discoloration, myopathy, leukopenia, abnormal liver function tests, macrocytosis. US Black Box Warnings for hematologic toxicity, myopathy, lactic acidosis, and severe hepatomegaly.

Pregnancy category C. Recommended for pregnant women after the first trimester to prevent vertical transmission.

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Doravirine (DOR, Pifeltro)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity. Concurrent administration of strong CYP3A inducers.

Dosage: 100 mg po daily with or without food (twice daily if also taking rifabutin). Also available as Delstrigo, a fixed-dose combination of 3TC 300 mg, TDF 300 mg and DOR 100 mg given once daily

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, , or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Headache, stomach upset, fatigue.

Pharmacokinetic data are insufficient for recommendations in pregnancy.

Efavirenz (EFV, Sustiva)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity, concurrent administration with elbasvir or grazoprevi.

Dosage: 600 mg po qhs. Avoid taking with high fat meals. Also available as Atripla, a fixed-dose combination of TDF 300 mg, FTC 200 mg, and efavirenz 600 mg given once daily; Symfi, a fixed-dose combination of 3TC 300 mg, TDF 300 mg, and EFV 600 mg given once daily; and Symfi Lo, a fixed-dose combination of 3TC 300 mg, TDF 300 mg, and EFV 400 mg given once daily.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Rash is common and does not require discontinuation of the drug unless accompanied by fever, mucous membrane involvement, or other systemic manifestations. Other side effects include vivid dreams and nightmares, neurocognitive dysfunction, hyperlipidemia, abnormal liver function tests.

FDA advises women to avoid becoming pregnant while taking EFV and avoid during first trimester, although guidelines do not restrict the use of EFV.

Etravirine (ETR, Intelence)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 200 mg po bid.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Rash is common and does not require discontinuation of the drug unless accompanied by fever, mucous membrane involvement, or other systemic manifestations. Stevens-Johnson syndrome has been reported infrequently. Other side effects include nausea, diarrhea, abnormal liver function tests.

Pregnancy category B.

Nevirapine (NVP, Viramune)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity, moderate to severe hepatic disease.

Dosage: 200 mg po qd x two weeks; 200 mg po bid thereafter. Patients who develop rash during the first two weeks should not increase the dose until the rash resolves.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Rash is common (about 17% of patients, although fewer with dose escalation regimen) and does not require discontinuation of the drug unless accompanied by fever, mucous membrane involvement, or other systemic manifestations. Stevens-Johnson syndrome has been reported infrequently. Other side effects include nausea, headache, abnormal liver function tests. US Black Box Warnings: Skin reactions and hepatotoxicity.

Because of a high incidence of symptomatic hepatic events in women with CD4 cell count > 250/mm³ and in men with CD4 cell count > 400/mm³, NVP use should be avoided in these settings unless the benefit clearly outweighs the risk.

Pregnancy category B.

Rilpivirine (RPV, Edurant)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 25 mg po qd. Also available as Complera, a fixed-dose combination of TDF 300 mg, FTC 200 mg, and rilpivirine 25 mg given once daily; Odefsey, a fixed-dose combination of TAF 25 mg, FTC 200 mg, and rilpivirine 25 mg given once daily; and Juluca, a fixed-dose combination of 50 mg of dolutegravir and 25 mg of rilpivirine given once daily.

Use of Complera and Odefsey should be limited to treatment-naive patients with pre-treatment viral load <100,000 copies/mL and CD4 cell count >200 cells/mm³ because of an inferior virologic response in patients with a high baseline viral load.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Depression, insomnia, headache, rash.

Pregnancy category B.

Protease Inhibitors (PIs) **

Atazanavir (ATV, Reyataz)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 300 mg po administered with ritonavir 100 mg po as pharmacologic booster given once daily; or 400 mg po once daily in patients unable to tolerate ritonavir. Also available as Evotaz, a fixed-dose combination of ATV 300 mg and cobicistat 150 mg given once daily.

Use of ATV/r or ATV/c in combination with ABC/3TC should be limited to patients with pre-treatment HIV RNA of <100,000 copies/mL. ATV/c in combination with TDF/FTC is not recommended for patients with CrCl <70 mL/min.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Gastrointestinal intolerance, hyperbilirubinemia. Unlike other protease inhibitors, this drug does not appear to be associated with hyperlipidemia.

Pregnancy category B.

Darunavir (DRV, Prezista)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity. Sulfa allergy.

Dosage: 800 mg po qd (treatment-naïve patients) administered with ritonavir 100 mg po qd *or* 600 mg po bid (treatment-experienced patients) administered with ritonavir 100 mg po bid as pharmacologic booster. Also available as Prezcofix, a fixed-dose combination of DRV 800 mg and cobicistat 150 mg given once daily; and Symtuza, a fixed-dose combination of TAF 10 mg, FTC 200 mg, DRV 800 mg and cobicistat 150 mg given once daily.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Gastrointestinal intolerance, rash, headache, abnormal liver function tests, severe hepatotoxicity (rare).

Pregnancy category B.

Fosamprenavir (FPV, Lexiva)

Indications: Treatment of HIV infection in combination with other agents. This regimen is not recommended due to inferior potency compared to other protease inhibitors and cross resistance to darunavir.

Contraindications: Known hypersensitivity.

Dosage: 1400 mg po bid. When administered with ritonavir (100 mg po bid) as pharmacologic booster, dose is 700 mg po bid.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Gastrointestinal intolerance, rash, headache, oral paresthesias.

Pregnancy category C.

Indinavir (IDV, Crixivan)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 800 mg po q8h on an empty stomach or with a non-fat meal. When administered with ritonavir (100-200 mg po bid) as pharmacologic booster, dose is 800 mg po bid without food restrictions. Patients should drink at least 48 ounces of fluid a day.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Nephrolithiasis, gastrointestinal intolerance, hyperbilirubinemia.

Pregnancy category C.

Lopinavir/Ritonavir (LPV/RTV, LPV/r, Kaletra)

Indications: Treatment of HIV infection in combination with other agents.

Lopinavir is a protease inhibitor combined with ritonavir as pharmacologic booster.

Contraindications: Known hypersensitivity, concurrent use of ritonavir.

Dosage: Two tablets (each 200 mg lopinavir/50 mg ritonavir) po bid; four tablets po qd has been approved in treatment-naïve patients.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Gastrointestinal intolerance, weakness, headache.

Pregnancy category C.

Nelfinavir (NFV, Viracept)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 1250 mg po bid or 750 mg po tid with food. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.*

Toxicity: Diarrhea.

Pregnancy category B.

Ritonavir (RTV, r, Norvir)

Indications: Treatment of HIV infection in combination with other agents (infrequently used in this manner because of gastrointestinal toxicity and drug interactions). Often co-administered as pharmacologic booster with other protease inhibitors.

Contraindications: Known hypersensitivity.

Dosage: As therapeutic agent: 600 mg po q12h with food following two-week dose escalation regimen (day 1 and 2: 300 mg po bid; days 3-5: 400 mg po bid; days 6-13: 500 mg po bid). When administered as pharmacologic booster, dosage is reduced, based on medication combination.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Gastrointestinal intolerance, circumoral paresthesias, abnormal liver function tests.

Pregnancy category B.

Saquinavir (SQV, Invirase)

Indications: Treatment of HIV infection in combination with other agents. No longer recommended for the use in initial treatment of HIV.

Contraindications: Known hypersensitivity.

Dosage: 1000 mg po bid administered with ritonavir 100 mg po bid as pharmacologic booster. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.*

Toxicity: Gastrointestinal intolerance, abnormal liver function tests, arrhythmias.
Pregnancy category B.

Tipranavir (TPV, Aptivus)

Indications: Treatment of HIV infection in combination with other agents. No longer recommended for the use in initial treatment of HIV.

Contraindications: Known hypersensitivity.

Dosage: 500 mg po bid administered with ritonavir 200 mg po bid as pharmacologic booster. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.*

Toxicity: Gastrointestinal intolerance, abnormal liver function tests, severe hepatotoxicity (rare), intracranial hemorrhage (rare).
Pregnancy category C.

Entry Inhibitors

Enfuvirtide (T-20, Fuzeon)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 90 mg SC bid.

Toxicity: Injection site reaction.

Pregnancy category B.

Ibalizumab (Trogarzo)

Indications: Treatment of HIV infection in combination with other agents in heavily treatment experienced adults with multidrug resistance.

Contraindications: Known hypersensitivity.

Dosage: 2,000 mg IV loading dose, followed by maintenance dose of 800 mg IV every 2 weeks.

Missed dose: If a maintenance dose (800 mg) is missed by ≥ 3 days beyond the originally scheduled dosing day, a loading dose (2,000 mg) should be given as soon as possible. Resume maintenance dosing every 14 days thereafter.

Toxicity: Dizziness, rash, diarrhea, increased serum creatinine, decreased platelet count and neutrophils.

Pharmacokinetic data are insufficient for recommendations in pregnancy.

Maraviroc (MVC, Selzentry)

Indications: Treatment of HIV infection in combination with other agents.

Maraviroc is a CCR5 antagonist. HIV coreceptor tropism assay is recommended before using this drug in an antiretroviral regimen.

Contraindications: Known hypersensitivity.

Dosage: 300 mg po bid (although dosage may range from 150-600 mg po bid depending upon with what other drugs it is administered).

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of

antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Cough, arthralgia, myalgia, diarrhea, sleep disturbance, abnormal liver function tests.

Pregnancy category B.

Integrase Inhibitors

Bictegravir (BIC)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Coadministration with dofetilide or rifampin.

Dosage: Available as Biktarvy, a fixed-dose combination of BIC 50 mg, FTC 200 mg, and TAF 25 mg given once daily.

Toxicity: Immune reconstitution syndrome, acute exacerbation of hepatitis B, worsening renal impairment, lactic acidosis.

There are insufficient data to determine safety of bictegravir-containing regimens in pregnancy.

Dolutegravir (DTG, Tivicay)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 50 mg po qd (bid when administered with efavirenz, fosamprenavir/ritonavir, tipranavir/ritonavir, or rifampin; or when there is suspected integrase inhibitor resistance). Also available as Tivicay PD: 5mg soluble tablets for oral suspension for pediatric patients, not bioequivalent dosing, dosed on weight.

Also available as Triumeq, a fixed-dose combination of ABC 600 mg, 3TC 300 mg, and DTG 50 mg given once daily; Dovato, a fixed-dose combination of 3TC 300 mg and DTG 50 mg; and Juluca, a fixed-dose combination of 50 mg of dolutegravir and 25 mg of rilpivirine given once daily.

Toxicity: Insomnia, weight gain, abnormal liver function tests, increased lipase, increased CPK level.

DTG is no longer contraindicated in pregnancy; it is a preferred therapy if continued during pregnancy for patients already suppressed on DTG or alternative regimen for women trying to conceive.

Elvitegravir (EVG)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 150 mg once daily with food.

Stribild, a fixed-dose combination of TDF 300 mg, FTC 200 mg, elvitegravir 150 mg, and cobicistat 150 mg given once daily; and Genvoya, a fixed-dose combination of TAF 10 mg, FTC 200 mg, elvitegravir 150 mg, and cobicistat 150 mg given once daily.

Stribild and Genvoya (cobicistat component) have many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference, package insert, or guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents at www.aidsinfo.nih.gov for more information.

Toxicity: Diarrhea, nausea, headache.

Pregnancy category B.

Raltegravir (RAL, Isentress)

Indications: Treatment of HIV infection in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 400 mg po bid. Also available to take 1200mg HD tablets daily. Should not be coadministered with aluminum and/or magnesium containing antacids as these products can reduce absorption of RAL.

Toxicity: Diarrhea, nausea, fatigue, myalgia, abnormal liver function tests.

Pregnancy category C.

Attachment Inhibitor

Fostemsavir (Rukobia)

Indications: Treatment of HIV infection in combination with other agents in heavily treatment-experienced adults with multidrug-resistant HIV who are failing their current regimen.

Contraindications: Known hypersensitivity.

Dosage: 600 mg po bid administered with high fat meal to improve absorption.

Toxicity: Diarrhea, nausea, headache, increase in creatinine, increase in liver function tests. Use with caution in hepatitis B and hepatitis C coinfections because of rise in transaminase levels. Use with caution in patients with preexisting cardiac disease or medications known to cause torsades as QT increases have been seen.

Pneumocystis jirovecii (carinii) Pneumonia (PCP): Treatment and Prophylaxis

Atovaquone (Mepron)

Indications: Treatment (mild to moderate infection) and prophylaxis of PCP in patients unable to tolerate TMP-SMX or dapsone.

Contraindications: Known hypersensitivity.

Dosage: 750 mg of suspension po bid with food x 3 weeks for treatment.
1500mg once daily with food for prophylaxis.

Toxicity: Gastrointestinal intolerance, rash, headache, fever.

Pregnancy category C.

Clindamycin with Primaquine

Indications: Treatment of PCP in patients unable to tolerate TMP-SMX.

Contraindications: Known hypersensitivity; glucose 6-phosphate dehydrogenase (G6PD) deficiency is contraindication to primaquine use.

Dosage: Clindamycin 600 mg IV q6-8h (or 300-450 mg po qid) and primaquine 15-30 mg base po qd x 3 weeks.

Toxicity: Clindamycin: diarrhea, nausea, rash. Primaquine: nausea, dyspepsia, hemolytic anemia (G6PD deficiency).

Pregnancy categories B (clindamycin) and C (primaquine).

Dapsone

Indications: Treatment of PCP (mild to moderate infection) in combination with trimethoprim; prophylaxis of PCP in patients unable to tolerate TMP-SMX; primary prophylaxis of toxoplasmosis in combination with pyrimethamine.

Contraindications: Known hypersensitivity, G6PD deficiency.

Dosage: PCP treatment: dapsone 100 mg qd and trimethoprim 15 mg/kg/day x 3 weeks.

PCP prophylaxis: 100 mg po qd; toxoplasmosis prophylaxis: dapsone 50 mg qd plus pyrimethamine 50 mg weekly with folic acid 25 mg.

Toxicity: Rash, fever, gastrointestinal intolerance, neutropenia, methemoglobinemia.

Pregnancy category C.

Pentamidine (Aerosol [NebuPent], Intravenous [Pentam])

Indications: Treatment and prophylaxis of PCP in patients unable to tolerate TMP-SMX or dapsone. Corticosteroids are used adjunctively in patients with PCP who have significant respiratory dysfunction (paO₂ <70 mm Hg or alveolar-arterial gradient >35 mm Hg).

Contraindications: Known hypersensitivity; severe asthma or bronchospasm, active pulmonary tuberculosis (aerosol preparation).

Dosage: Treatment: intravenous 3-4 mg/kg qd for up to three weeks.

Prophylaxis: aerosol 300 mg via Respirgard II nebulizer once a month.

Toxicity: Aerosol: bronchospasm, particularly in patients with history of asthma or chronic obstructive pulmonary disease; pharyngeal irritation; metallic taste. Intravenous: hypotension, nephrotoxicity, hypoglycemia,

hyperglycemia, leukopenia, thrombocytopenia, hypokalemia, hypocalcemia.

Pregnancy category C.

Trimethoprim-sulfamethoxazole (TMP-SMX, Bactrim, Septra)

Indications: Treatment and prophylaxis of PCP; primary prophylaxis of toxoplasmosis. Corticosteroids are used adjunctively in patients with PCP who have significant respiratory dysfunction (paO₂ <70 mm Hg or alveolar-arterial gradient >35 mm Hg).

Contraindications: Known hypersensitivity to trimethoprim or sulfonamides, megaloblastic anemia.

Dosage: Treatment of PCP: 5 mg/kg po/IV q8h of trimethoprim component (equivalent to 2 tabs po tid of DS for 65 kg patient) x 3 weeks.

Prophylaxis of PCP: one DS or SS tablet po qd. Prophylaxis of toxoplasmosis: one DS tablet po qd.

Toxicity: Side effects are common in HIV-infected patients and include gastrointestinal intolerance; rash, urticaria, photosensitivity, Stevens Johnson syndrome; fever; leukopenia, thrombocytopenia, hemolytic anemia; abnormal liver function tests; renal dysfunction, interstitial nephritis; aseptic meningitis.

Patients with history of mild to moderate drug toxicity should be given retriial of TMP-SMX or desensitized using an established protocol.

Pregnancy category C; avoid use at term because of risk of kernicterus in newborn.

Mycobacterium avium* Complex (MAC) Infection and Tuberculosis (TB): Treatment and Prophylaxis **

Amikacin (Amikin)

Indications: Treatment of MAC infection in combination with other agents.

Contraindications: Known hypersensitivity to aminoglycoside antibiotics.

Dosage: 10-15 mg/kg/day IV for first four weeks of MAC therapy.

Toxicity: Ototoxicity, especially with larger total dose and longer duration (more auditory than vestibular and usually irreversible); nephrotoxicity.

Pregnancy category D.

Azithromycin (Zithromax)

Indications: Treatment of MAC infection in combination with other agents.
MAC prophylaxis in patients with chronic HIV infection who remain viremic on ART with CD4 count < 50/mm³.

Contraindications: Known hypersensitivity to macrolide antibiotics.

Dosage: MAC treatment: 600 mg po qd; prophylaxis: 1200 mg po weekly.

Toxicity: Gastrointestinal intolerance.

Pregnancy category B.

Ciprofloxacin (Cipro)

Indications: Treatment of MAC infection in combination with other agents; treatment of TB in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 500-750 mg po bid.

Toxicity: Gastrointestinal intolerance, central nervous system dysfunction, rash.

Pregnancy category C.

Clarithromycin (Biaxin)

Indications: Treatment of MAC infection in combination with other agents.
MAC prophylaxis in patients with chronic HIV infection who remain viremic on ART with CD4 count < 50/mm³.

Contraindications: Known hypersensitivity to macrolide antibiotics.

Dosage: MAC treatment and prophylaxis: 500 mg po bid.

Toxicity: Gastrointestinal intolerance, abnormal liver function tests.

Pregnancy category C; teratogenic in animals.

Ethambutol (Myambutol)

Indications: Treatment of MAC infection in combination with other agents; treatment of TB in combination with other agents.

Contraindications: Known hypersensitivity, history of optic neuritis.

Dosage: 15-20 mg/kg po qd; adjusted dose can be administered 2-3 times per week for TB treatment (DOT).

Toxicity: Optic neuritis, rash, gastrointestinal intolerance, abnormal liver function tests.

Pregnancy category C; teratogenic in animals.

Isoniazid (INH)

Indications: Treatment of TB in combination with other agents; treatment of latent TB.

Contraindications: Known hypersensitivity, significant hepatic disease.

Dosage: Treatment of active TB: 300 mg po qd; adjusted dose can be administered 2-3 times per week for TB treatment (DOT); treatment of latent TB: 300 mg po qd or 900 mg po twice per week (DOT) for nine months. Pyridoxine 50 mg po qd should be given concurrently for prevention of peripheral neuropathy.

Toxicity: Rash, hepatotoxicity, especially in alcoholics and persons older than 50; fever; peripheral neuropathy.

Pregnancy category C.

Pyrazinamide

Indications: Treatment of TB in combination with other agents.

Contraindications: Known hypersensitivity, significant hepatic disease.

Dosage: 25 mg/kg po qd; adjusted dose can be administered 2-3 times per week for TB treatment (DOT).

Toxicity: Rash, abnormal liver function tests, hyperuricemia.

Pregnancy category C.

Rifabutin (Mycobutin)

Indications: Treatment of MAC infection in combination with other agents; treatment of TB in combination with other agents; prophylaxis of MAC infection in patients unable to tolerate clarithromycin or azithromycin.

Contraindications: Known hypersensitivity.

Dosage: Treatment and prophylaxis: 300 mg po qd; adjusted dose can be administered 2-3 times per week for TB treatment (DOT). *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Rash, orange discoloration of body secretions, gastrointestinal intolerance, abnormal liver function tests. Acute uveitis has been reported when used in association with clarithromycin.

Pregnancy category C.

Rifampin

Indications: Treatment of TB in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 600 mg po qd; adjusted dose can be administered 2-3 times per week for TB treatment (DOT). *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Rash, orange discoloration of body secretions, gastrointestinal intolerance, abnormal liver function tests.

Pregnancy category C.

Rifapentine (Priftin)

Indications: Treatment of TB in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: For latent TB, weight-based dosing given once weekly for 12 weeks in combination with isoniazid
For active TB, 600 mg twice weekly by DOT in combination with other agents.
Administer with meals.

Toxicity: Hyperuricemia, pyuria, hematuria, urinary tract infections, neutropenia, lymphocytopenia, and anemia. Known hypersensitivity.

Pregnancy category C.

Streptomycin

Indications: Treatment of TB in combination with other agents.

Contraindications: Hypersensitivity to aminoglycoside antibiotics.

Dosage: 15 mg/kg IM qd adjusted dose can be administered 2-3 times per week for TB treatment (DOT).

Toxicity: Ototoxicity, vestibular toxicity.

Pregnancy category D.

Toxoplasmosis: Treatment and Prophylaxis +

Clindamycin

Indications: Treatment of toxoplasmic encephalitis (for patients unable to tolerate sulfadiazine) in combination with pyrimethamine.

Contraindications: Known hypersensitivity.

Dosage: Initial therapy: 600 mg IV or po q6h x 6 weeks.

Maintenance therapy (secondary prophylaxis): 600 mg po q8h.

Toxicity: Diarrhea, nausea, rash.

Pregnancy category B.

Dapsone See section on PCP Treatment and Prophylaxis.

Pyrimethamine

Indications: Treatment of toxoplasmic encephalitis in combination with sulfadiazine or clindamycin.

Primary prophylaxis of toxoplasmosis in combination with dapsone.

Contraindications: Known hypersensitivity.

Dosage: Initial therapy: 100-200 mg po loading dose, followed by 50-75 mg po qd x 6 weeks in conjunction with folinic acid 10 mg po qd.

Maintenance therapy (secondary prophylaxis): 25-50 mg po with folinic acid 10 mg po qd.

Prophylaxis: 50 mg weekly with folinic acid 25 mg weekly.

Currently available only through [special pharmacy program](#).

Toxicity: Reversible bone marrow suppression, gastrointestinal intolerance.

Pregnancy category C; teratogenic in animals.

Sulfadiazine

Indications: Treatment of toxoplasmic encephalitis in combination with pyrimethamine.

Contraindications: Known hypersensitivity to sulfonamides.

Dosage: Initial therapy: 1000-1500 mg po qid x 6 weeks.

Maintenance therapy (secondary prophylaxis): 500-1000 mg po qid.

Toxicity: Fever, rash, pruritus, bone marrow suppression.

Pregnancy category C; avoid use at term because of risk of kernicterus in newborn.

Trimethoprim-Sulfamethoxazole See section on PCP Treatment and Prophylaxis.

Cytomegalovirus (CMV) Infection: Treatment and Prophylaxis

Cidofovir (Vistide)

Indications: Treatment of CMV infection, including ganciclovir-resistant strains.

Contraindications: Known hypersensitivity, significant renal dysfunction, use of other nephrotoxic medications.

Dosage: Initial therapy: 5 mg/kg IV once a week x 2.

Maintenance therapy (secondary prophylaxis): 5 mg/kg IV once every other week.

Probenecid 2 gm po 3 hr prior, and 1 gm po 2 hr prior and 8 hr after infusion should be administered to prevent nephrotoxicity; 1 liter of normal saline is also given prior to cidofovir dosing.

Toxicity: Nephrotoxicity, neutropenia. Probenecid is associated with fever, chills, headache, rash, nausea.

Pregnancy category C.

Foscarnet (Foscavir)

Indications: Treatment of CMV infection, including ganciclovir-resistant strains.

Contraindications: Known hypersensitivity, significant renal dysfunction.

Dosage: Initial therapy: 60 mg/kg IV q8h or 90 mg/kg IV q12h x 14 days.

Maintenance therapy (secondary prophylaxis): 90-120 mg/kg IV qd.

Toxicity: Nephrotoxicity, hypocalcemia, hypophosphatemia, hypokalemia, headache, fatigue, nausea, anemia, seizures.

Pregnancy category C.

Ganciclovir (Cytovene)

Indications: Treatment and prophylaxis of CMV infection.

Contraindications: Known hypersensitivity, neutropenia, thrombocytopenia.

Dosage: Initial therapy: 5 mg/kg IV q12h x 14-21 days.

Maintenance therapy (secondary prophylaxis): 5 mg/kg IV qd.

Toxicity: Neutropenia, thrombocytopenia, anemia, nausea, abdominal pain, headache, confusion.

Pregnancy category C; teratogenic in animals.

Valganciclovir (Valcyte)

Indications: Treatment and prophylaxis of CMV infection.

Contraindications: Known hypersensitivity, neutropenia, thrombocytopenia.

Dosage: Initial therapy: 900 mg po bid x 3 weeks.

Maintenance therapy (secondary prophylaxis): 900 mg po qd.

Toxicity: Neutropenia, thrombocytopenia, anemia, nausea, abdominal pain, headache, confusion.

Pregnancy category C.

Herpes Simplex Virus (HSV) and Varicella-Zoster Virus (VZV) Infections: Treatment and Prophylaxis ++

Acyclovir (Zovirax)

Indications: Treatment and prophylaxis of HSV and VZV infections.

Contraindications: Known hypersensitivity.

Dosage: HSV treatment: 400 mg po tid x 7-10 days (primary infection); 800 mg po bid x 5 days (recurrent infection); suppression: 400 mg po bid. For extensive or disseminated disease, intravenous therapy (10 mg/kg q8h) is given.

VZV treatment: 800 mg po 5x/day for 7 days. For disseminated zoster or ophthalmic involvement, intravenous therapy (10-12 mg/kg q8h) is given.

Toxicity: Nausea, renal dysfunction.

Pregnancy category C.

Famciclovir (Famvir)

Indications: Treatment and prophylaxis of HSV and VZV infections.

Contraindications: Known hypersensitivity.

Dosage: HSV treatment: 250 mg po tid x 7-10 days (primary infection); 1000 mg po bid x 1 day (recurrent infection); suppression: 250 mg po bid.

VZV treatment: 500 mg po tid x 7 days.

Toxicity: Headache, nausea.

Pregnancy category B.

Valacyclovir (Valtrex)

Indications: Treatment and prophylaxis of HSV and VZV infections.

Contraindications: Known hypersensitivity.

Dosage: HSV treatment: 1 gram po bid x 7-10 days (primary infection); 500 mg po bid x 3 days (recurrent infection); suppression: 500-1000 mg po qd.

VZV treatment: 1 gram po tid x 7 days.

Toxicity: Headache, nausea, abnormal liver function tests.

Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome has been reported in patients with advanced HIV disease.

Pregnancy category B.

Fungal Infections: Treatment and Prophylaxis

Amphotericin B

Indications: Pharmacist-prepared suspension for treatment of oral candidiasis; intravenous drug for treatment of systemic fungal infections.

Contraindications: Known hypersensitivity.

Dosage: Oral candidiasis: 1-5 ml of suspension po qid x 14 days.

Systemic fungal infections: intravenous doses range from 0.3-1.0 mg/kg/day depending on the pathogen and type of infection. Lipid complex preparations are less toxic but very expensive.

Toxicity: Oral suspension: nausea, vomiting, diarrhea, rash; intravenous drug: infusion-related fever, chills, phlebitis, hypotension, nausea, vomiting, nephrotoxicity, hypokalemia, hypomagnesemia, hypocalcemia, anemia.

Pregnancy category B.

Caspofungin (Cancidas)

Indications: Treatment of resistant mucosal candidiasis.

Contraindications: Known hypersensitivity.

Dosage: 50 mg IV qd.

Toxicity: Rash, gastrointestinal intolerance, abnormal liver function tests. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Pregnancy category C.

Clotrimazole

Indications: Treatment of mucosal candidiasis.

Contraindications: Known hypersensitivity.

Dosage: Oral candidiasis: 10 mg lozenge dissolved in the mouth 5 times a day; vaginal candidiasis: 100 mg tablet per vagina bid x 3 days.

Toxicity: Nausea, abnormal liver function tests.

Pregnancy category C.

Fluconazole (Diflucan)

Indications: Treatment and secondary prophylaxis of mucosal candidiasis; secondary prophylaxis of cryptococcal infection.

Contraindications: Known hypersensitivity.

Dosage: Treatment of oral candidiasis: 100 mg po qd x 7-14 days; candida esophagitis: 200 mg po qd x 14-21 days; vaginal candidiasis: 150 mg po x one. Secondary prophylaxis of mucosal candidiasis: 50-200 mg po qd. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Cryptococcal infection maintenance therapy (secondary prophylaxis): 200 mg po qd. Most experts recommend initial treatment of cryptococcal infection with amphotericin B x two weeks followed by high-dose fluconazole (400 mg po qd) x 8 weeks.

Toxicity: Nausea, headache, abnormal liver function tests.

Pregnancy category C.

Itraconazole (Sporanox)

Indications: Treatment of histoplasmosis and resistant mucosal candidiasis.

Contraindications: Known hypersensitivity.

Dosage: 200 mg po qd to bid.

Toxicity: Gastrointestinal intolerance, abnormal liver function tests. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Pregnancy category C.

Nystatin

Indications: Treatment of mucosal candidiasis.

Contraindications: Known hypersensitivity.

Dosage: Oral candidiasis: 5 ml suspension to be gargled and swallowed 5 times a day x 7-14 days; vaginal candidiasis: 100,000 unit tab intravaginally 1-2 times a day x 7-14 days.

Toxicity: Nausea, vomiting, diarrhea

Pregnancy category C.

Posaconazole (Noxafil)

Indications: Treatment of resistant mucosal candidiasis.

Contraindications: Known hypersensitivity.

Dosage: 400 mg po bid.

Toxicity: Gastrointestinal intolerance, abnormal liver function tests. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Pregnancy category C.

Voriconazole (Vfend)

Indications: Treatment of resistant mucosal candidiasis.

Contraindications: Known hypersensitivity.

Dosage: 200 mg po or IV bid.

Toxicity: Rash, gastrointestinal intolerance, peripheral edema, abnormal liver function tests. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Pregnancy category D.

Chronic Hepatitis C Treatment

Daclatasvir (Daklinza)

Drug Class: NS5A inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotype 3, in combination with other agents.

Contraindications: Known hypersensitivity, concurrent use with strong CYP3A inducers.

Dosage: 60 mg once daily with sofosbuvir. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Fatigue, headache.

Elbasvir- grazoprevir (Zepatier)

Drug Class: Elbasvir NS5A inhibitor, grazoprevir NS3/4A protease inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1 and 4.

Contraindications: Known hypersensitivity to any component, moderate or severe hepatic impairment (Child-Pugh Class B or C), concurrent use of organic ion transporter polypeptide 1B (OATP1B inhibitors), strong CYP3A inducers and efavirenz.

Dosage: Fixed-dose combination of elbasvir 50 mg and grazoprevir 100 mg once daily. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Fatigue, headache, increased ALT.

No data are available regarding use in pregnancy.

Glecaprevir-pibrentasvir (Mavyret)

Drug Class: Glecaprevir NS3/4A protease inhibitor, pibrentasvir NS5A inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1, 2, 3, 4, 5, and 6.

Contraindications: Known hypersensitivity to any component, severe hepatic impairment (Child-Pugh Class C), coadministration with atazanavir or rifampin

Dosage: Fixed-dose combination of glecaprevir 300 mg and pibrentasvir 120 mg given once daily with food. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Fatigue, headache, nausea

Adverse events not observed in animal studies with glecaprevir or pibrentasvir as individual agents

Ombitasvir-paritaprevir-ritonavir and dasabuvir (Viekira Pak)

Drug Class: Ombitasvir NS5A inhibitor, paritaprevir Ns3/4A protease inhibitor, dasabuvir non-nucleoside NS5B polymerase inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1A and 1B.

Contraindications: Known hypersensitivity to any component, severe hepatic impairment.

Dosage: Fixed-dose combination of ombitasvir 12.5 mg, paritaprevir 75 mg, and ritonavir 50 mg and packaged with dasabuvir 250 mg. Dosing schedule is dependent on genotype and presence or absence of cirrhosis. For patients with genotype 1A, it is given with ribavirin twice daily with food.

There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.

Toxicity: Dermatologic reaction, headaches, fatigue, pruritus, diarrhea, abnormal liver function tests (particularly in the first 4 weeks of treatment).

Pregnancy category B.

Pegylated Interferon (PEGASYS, PEG-Intron)

Drug Class: Interferon.

Indications: Treatment of chronic hepatitis C infection in combination with ribavirin.

Contraindications: Known hypersensitivity.

Dosage: Pegylated interferon alfa-2a (PEGASYS) 180 mcg SC weekly with ribavirin 400 mg po bid.

Pegylated interferon alfa-2b (PEG-Intron) 1.5 mcg/kg SC weekly with ribavirin 400 mg po bid.

Toxicity: Constitutional symptoms, depression, leukopenia, thrombocytopenia and injection site reactions.

Pregnancy categories C (PEGASYS) and X (PEG-Intron).

Ribavirin (Copegus, Rebetol, Ribasphere)

Drug Class: Nucleoside analog.

Indications: Treatment of chronic hepatitis C infection in combination with other agents.

Contraindications: Known hypersensitivity, severe anemia, pregnancy.

Dosage: 800-1400mg per day, divided into two doses, dependent on regimen. Always dose with food. *There are many potential drug interactions, some of which require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Rash, hemolytic anemia, neutropenia, leukopenia, thrombocytopenia.

Pregnancy category X.

Simeprevir (Olysio)

Drug Class: NS3/4A protease inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotype 1, in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 150 mg po qd with food. Dosing schedule is dependent on genotype, presence or absence of cirrhosis, and prior drug treatments. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Rash, photosensitivity, liver decompensation, pruritus, nausea, myalgia, dyspnea, increased bilirubin level.

Pregnancy category C (X for use with pegylated interferon and ribavirin).

For patients without cirrhosis, regardless of prior treatments, simeprevir should be given with sofosbuvir for 12 weeks.

For patients with cirrhosis, regardless of prior treatments, simeprevir should be given with sofosbuvir for 24 weeks.

Sofosbuvir (Sovaldi)

Drug Class: NS5B polymerase inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1-6, in combination with other agents.

Contraindications: Known hypersensitivity.

Dosage: 400 mg po qd. Also available as Harvoni, fixed-dose combination of sofosbuvir 400 mg and ledipasvir 90 mg given once daily. Dosing schedule is dependent on genotype, presence or absence of cirrhosis, and prior drug treatments. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Fatigue, headache, insomnia, fever, chills, myalgia, rash, pruritus, gastrointestinal intolerance, anemia, neutropenia.

Pregnancy category B (category X for use with pegylated interferon and ribavirin).

Sofosbuvir-ledipasvir (Harvoni)

Drug Class: Sofosbuvir Ns5B inhibitor, ledipasvir Ns5A inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1, 4, 5, and 6.

Contraindications: Known hypersensitivity to any component, coadministration with amiodarone or P-glycoprotein inducers.

Dosage: Fixed-dose combination of ledipasvir 90 mg and sofosbuvir 400 mg given once daily. Dosing schedule is dependent on genotype, presence or absence of cirrhosis, and prior drug treatments. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Headache, weakness.

Pregnancy category B.

Sofosbuvir-velpatasvir (Epclusa)

Drug Class: Sofosbuvir Ns5B inhibitor, velpatasvir Ns5A inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1, 2, 3, 4, 5, and 6.

Contraindications: Known hypersensitivity to any component, coadministration with amiodarone or P-glycoprotein inducers.

Dosage: Fixed-dose combination of velpatasvir 100 mg and sofosbuvir 400 mg given once daily. Dosing schedule is dependent on genotype, presence or absence of cirrhosis, and prior drug treatments. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Headache, fatigue.

Pregnancy category B.

Sofosbuvir-velpatasvir-voxilaprevir (Vosevi)

Drug Class: Sofosbuvir Ns5B inhibitor, velpatasvir Ns5A inhibitor, voxilaprevir NS3/4A protease inhibitor.

Indications: Treatment of chronic hepatitis C infection, genotypes 1, 2, 3, 4, 5, and 6 previously treated with a hepatitis C regimen containing an NS5A inhibitor.

Contraindications: Known hypersensitivity to any component, coadministration with rifampin

Dosage: Fixed-dose combination of velpatasvir 100 mg, sofosbuvir 400 mg and voxilaprevir 100mg given once daily. Dosing schedule is dependent on genotype, presence or absence of cirrhosis, and prior drug treatments. *There are many potential drug interactions, some of which may require dosage modification or preclude its co-administration with other agents; see Physicians Desk Reference or package insert for more information.*

Toxicity: Headache, fatigue, diarrhea, nausea, increased serum bilirubin.

Adverse events not observed in animal reproduction studies using individual components.

Miscellaneous Therapeutic Agents

Dronabinol (Marinol)

Indications: Appetite stimulant for treatment of AIDS wasting syndrome.

Contraindications: Known hypersensitivity, significant cognitive dysfunction.

Dosage: 2.5 mg po bid.

Toxicity: Neuropsychiatric symptoms, gastrointestinal intolerance.

Pregnancy category C.

Human Growth Hormone [Somatropin] (Serostim)

Indications: Hormonal treatment of AIDS wasting syndrome.

Contraindications: Known hypersensitivity, presence of an actively growing intracranial tumor.

Dosage: For patients > 55 kg, dose is 6 mg SC qd; for patients 45-55 kg, dose is 5 mg SC qd; for patients 35-45 kg, dose is 4 mg SC qd.

Toxicity: Arthralgia, edema, hypertension, hyperglycemia.

Pregnancy category B.

Human Growth Hormone-Releasing Factor [Tesamorelin] (Egrifta)

Indications: Hormonal treatment of HIV-related lipodystrophy.

Contraindications: Known hypersensitivity, active malignancy, pregnancy.

Dosage: 2 mg SC once daily.

Toxicity: Injection site reaction, arthralgia, edema, rash.

Pregnancy category X.

Megestrol Acetate (Megace)

Indications: Appetite stimulant for treatment of AIDS wasting syndrome.

Contraindications: Known hypersensitivity, pregnancy.

Dosage: Oral suspension: 400-800 mg po qd; tablets: 80 mg po qid up to 800 mg/day.

Toxicity: Hypogonadism, adrenal insufficiency, diarrhea, impotence, rash, hyperglycemia.

Pregnancy category D.

Oxandrolone (Oxandrin)

Indications: Anabolic steroid for treatment of AIDS wasting syndrome.

Contraindications: Known hypersensitivity, history of breast or prostate cancer, significant hepatic dysfunction, nephrosis, pregnancy.

Dosage: 5-10 mg po bid.

Toxicity: Edema, hypertension, virilization, glucose intolerance, hyperlipidemia, abnormal liver function tests.

Pregnancy category X.

Testosterone

Indications: Treatment of hypogonadism; treatment of AIDS wasting syndrome.

Contraindications: Known hypersensitivity, history of male breast or prostate cancer, pregnancy.

Dosage: 200-400 mg IM q 2 weeks. Topical treatment is also available: 1) gel preparation (Androgel) 5 g topically qd; and 2) transdermal systems via non-scrotal patch including Androderm and Testoderm.

Toxicity: Coagulopathy, cholestatic jaundice, increased libido, edema, flushing, priapism, local reaction with patches.

Pregnancy category X.

Thalidomide (Thalomid)

Indications: Treatment of refractory aphthous ulcers; treatment of refractory AIDS wasting syndrome.

Contraindications: Known hypersensitivity, pregnancy.

Dosage: 50-200 mg po qd. Physicians and pharmacists must be registered in the REMS program at 1-888-423-5436 to prescribe thalidomide. Female patients must have a negative pregnancy test within 24 hours of starting therapy, weekly pregnancy tests in the first month of therapy, monthly pregnancy tests thereafter, and agree to use two forms of contraception. Male patients must use a condom for contraception.

Toxicity: Peripheral neuropathy, drowsiness, orthostatic hypotension, fever, rash, neutropenia.

Pregnancy category X.

Footnotes

Consultation with expert clinicians is recommended in the areas of antiretroviral therapy, tuberculosis management, and chronic hepatitis C treatment.

* Lactic acidosis, rarely with hepatomegaly and steatosis, has been associated with all drugs in this class.

** Hyperlipidemia, glucose intolerance/diabetes mellitus, and alterations in body fat distribution have been associated with combination antiretroviral therapy, especially regimens containing protease inhibitors.

*** Drugs for TB can also be administered as directly observed therapy (DOT) in different dosage regimens.

+ For primary prophylaxis, see PCP Treatment and Prophylaxis section.

++ Cidofovir and foscarnet also have activity against HSV and VZV and may have a role in the treatment of resistant strains. Valacyclovir, an acyclovir analogue, has been associated with cases of thrombotic thrombocytopenic purpura (TTP) in patients with advanced HIV disease.

Pregnancy Categories: A: Controlled studies show no risk; B: No evidence of risk in humans; C: Risk cannot be excluded; D: Evidence of risk; X: Contraindicated in pregnancy.

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Web Sites

1. AETC National Resource Center
<http://www.aids-ed.org>
2. AIDSinfo: Department of Health and Human Services
<http://www.aidsinfo.nih.gov>
3. Centers for Disease Control and Prevention
<https://www.cdc.gov/hiv/default.html>
4. Hepatitis C Guidelines
<http://www.hcvguidelines.org>
5. Hepatitis Drug Interactions
<http://www.hep-druginteractions.org>
6. The Johns Hopkins HIV Guide
http://www.hopkinsguides.com/hopkins/ub/index/Johns_Hopkins_HIV_Guide/All_Topics/A
7. National HIV/AIDS Clinician Consultation Center
<http://nccc.ucsf.edu>
8. National HIV Curriculum
<https://www.hiv.uw.edu>
9. The Online TST/IGRA
<http://www.tstin3d.com>
10. The Stanford HIV Drug Database
<http://hivdb.stanford.edu>