AETC AIDS Education & Training Center Program
National Coordinating Resource Center

Special Issues

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents

January 2016
AETC NCRC Slide Set

About This Presentation

These slides were developed using the April 2015 guidelines, and updated in July 2016. The intended audience is clinicians involved in the care of patients with HIV.

Because the field of HIV care is rapidly changing, users are cautioned that the information in this presentation may become out of date quickly.

It is intended that these slides be used as prepared, without changes in either content or attribution. Users are asked to honor this intent.

– AETC NCRC

Special Issues: Contents

- Early HIV Infection
- Adolescents
- Women
- Illicit Drug Users
- HIV-2 Infection
- Hepatitis B or C Coinfection
- *Mycobacterium* Tuberculosis
- Preventing Secondary Transmission

Early HIV Infection

- Acute HIV infection
  - Initial phase of infection; HIV RNA and p24 Ag are present but anti-HIV antibodies are undetectable
- Recent infection
  - The phase up to 6 months after infection; anti-HIV antibodies are detectable

Early HIV Infection: Acute Retroviral Syndrome

- 40-90% have symptoms of acute retroviral syndrome but acute HIV often not recognized
- Maintain high level of suspicion in patients with compatible clinical syndrome plus risks
  - Fever
  - Lymphadenopathy
  - Pharyngitis
  - Rash
  - Myalgia or arthralgia
  - Diarrhea
  - Headache
  - Nausea and vomiting
  - Hepatosplenomegaly
  - Weight loss
  - Thrush
  - Neurological symptoms

Acute HIV Infection: Diagnosis

- Usually, detectable HIV RNA or p24 antigen with negative or indeterminate HIV antibody test result
- Combination HIV Ag/Ab tests
  - Detect HIV-1 and HIV-2 and HIV-1 p24 Ag
  - Recommended by CDC as preferred assay for HIV screening, including for possible acute HIV-1
  - Reactive specimens should be tested with assay that differentiates HIV-1 and HIV-2
  - If reactive on Ag/Ab test but negative or indeterminate on Ab differentiation test: retest with quantitative or qualitative HIV-1 RNA test
    - If negative on RNA test: Ag/Ab was falsely positive
    - If positive: likely acute HIV-1; consider ART
      - Confirm HIV-1 infection with subsequent testing to document HIV Ab seroconversion

Acute HIV Infection: Diagnosis (2)

- If initial testing done with assay that tests only HIV Ab:
  - If Ab is negative or indeterminate but acute HIV is suspected:
    - Check HIV RNA: if positive, presumptive diagnosis is acute HIV-1
    - Low-positive HIV RNA (<10,000 copies/mL) may be false positive – repeat test on different specimen
  - If diagnosis is made by HIV RNA testing, confirm diagnosis with subsequent Ab testing

Early HIV Infection: Treatment

- ART recommended for all persons with HIV, including early HIV infection
- Limited outcome data from clinical trials

Early HIV Infection: Treatment (2)

Possible benefits:

- Decrease severity of acute disease
- Lower viral “set point”
- Reduce viral reservoir
- Delay disease progression
- Enhance CD4 cell recovery
- Reduce rate of viral mutation
- Lower risk of HIV transmission
- Lessen loss of GI lymphoid tissue

Early HIV Infection: Transmitted Resistance

- Transmitted virus may be resistant to ≥1 ARV drugs in up to 16% of patients with acute HIV infection
- Perform resistance testing at baseline to guide ARV selection (genotype)
  - Treatment initiation should not be delayed pending genotype results (regimen can be modified if indicated)

Early HIV Infection: Treatment Regimen

- ARV regimen recommendations and monitoring are same as for chronic infection
- If treatment is begun before resistance test results are available, use boosted PI (transmitted resistance is uncommon, and new resistance emerges slowly)
  - May consider dolutegravir (DTG) + TDF/FTC
    - Data on transmission of integrase resistance and on efficacy of this regimen in acute infection are limited
  - If early infection in person taking TDF/FTC as PrEP, also consider boosted PI or DTG while genotype results are pending

The HIV-Infected Adolescent

- Heterogeneous group in numerous respects
- Most acquired HIV though sexual risk behaviors
  - 26% of new HIV infections in United States are estimated to occur in youth aged 13-26 (2010)
    - 57% of these are in young black/African Americans
    - 75% in young MSM
  - In 2010, CDC estimated that 60% of HIV-infected youth were undiagnosed
- Some infected perinatally or via blood products
  - Usually heavily treatment experienced

The HIV-Infected Adolescent (2)

- ART recommended for all
- Readiness and ability to adhere to ART should be carefully considered
- Support is needed to reduce barriers to adherence and maximize ART success

The HIV-Infected Adolescent (3)

- Adult guidelines for ART usually appropriate for postpubertal adolescents
- Dosing should be based on sexual maturity rating (SMR)/Tanner stages
  - Use adult dosing schedules for those in late puberty
- Youth have lower rates of viral suppression, higher rates of virologic rebound and loss to follow-up

The HIV-Infected Adolescent (4)

Challenges to adherence:

- Denial and fear of HIV infection
- Misinformation
- Distrust of the medical establishment
- Fear and lack of belief in the effectiveness of medications
- Low self-esteem
- Unstructured and chaotic lifestyles
- Lack of familial and social support
- Unavailable or inconsistent access to care

The HIV-Infected Adolescent (5)

Special considerations:

- Preventing (and screening for) STDs (including HPV)
- Family planning counseling
- For females, gynecologic care, contraception (including interactions with ARVs); avoid EFV
- For transgender youth, sensitive psychosocial and health supports
- Prevention of HIV transmission

The HIV-Infected Adolescent (6)

Transitioning care:

- Recognize differences between many adolescent and adult HIV care models
- Consider issues of independence, autonomy, decisional capacity, confidentiality, consent, medical insurance
- Recognize different biomedical and psychosocial needs of perinatally infected vs behaviorally infected youth

The HIV-Infected Adolescent (7)

Facilitators to successful transitioning:

- Optimize communication between adolescent and adult providers, including multidisciplinary case conferences
- Address patient/family resistance (eg, owing to knowledge deficits, stigma, disclosure, differences in practice styles)
- Prepare youth for life-skills development (eg, appropriate use of care providers, medication management)
- Identify optimal clinic model
- Evaluate success of care model
- Include interventions that improve outcomes (eg, support groups and mental health consultation)
- Incorporate a family planning component

HIV-Infected Women

- ART recommended for all HIV-infected women, for their health and to reduce transmission to HIV-uninfected sex partners
- In general, no sex differences in virologic efficacy of ART
- Some evidence of sex differences in metabolism and response to some ARVs
- Increased risk of certain ARV adverse effects:
  - NVP-associated hepatotoxicity (especially if initiated at CD4 count >250 cells/μL); NVP not recommended
  - Lactic acidosis: d4T + ddI; these are not recommended
  - Metabolic complications: eg, lipoaccumulation, elevated triglycerides, osteopenia/osteoporosis

HIV-Infected Women (2)

- Women of childbearing potential
  - Offer preconception counseling and care
  - Offer effective counseling and contraception to prevent unintended pregnancy
  - For HIV-infected women who wish to conceive: inform as to options for preventing sexual transmission of HIV while attempting conception
  - Interventions include:
    - Screening and treatment for STDs (both partners)
    - ART and virologic suppression
    - PrEP (Pre-exposure prophylaxis) for uninfected partner
    - Male circumcision
    - Self-insemination with HIV-uninfected male partner's sperm

HIV-Infected Women (3)

Efavirenz

- Teratogenic in nonhuman primates
- Risk of neural tube defects occurs during the first 5-6 weeks of pregnancy, and pregnancy usually is not recognized before 4-6 weeks of pregnancy
- Do pregnancy test before starting EFV (women of childbearing potential)
- Counsel about potential risk to fetus and desirability of avoiding pregnancy while on EFV
- Consider alternative ARV agent in women who are trying to conceive or who are not using effective contraception, if feasible

HIV-Infected Women: Contraception

- ARV interactions with hormonal contraceptives:
  - Oral agents: PIs, EFV, and elvitegravir/cobicistat may increase or decrease levels of ethinyl estradiol, norethindrone, and norgestimate, and may cause contraceptive failure or estrogen or progestin adverse effects
    - Consider alternative or additional contraceptive method if used with interacting ARVs
  - Few data on transdermal patch, vaginal ring: cautions as above
  - DMPA: few data; no significant interactions with EFV, NVP, LPV/r, NFV, NRTIs
  - Implants: EFV may decrease levonorgestrel and etonogestrel levels and cause contraceptive failure
- IUD: safe and effective

HIV-Infected Women: Contraception (2)

- Hormonal contraception and HIV infection risk:
  - Conflicting data; in one study of serodiscordant couples, DMPA associated with risk of acquiring HIV (for HIV-uninfected women) and transmitting HIV (for HIV-infected women); no significant association with oral contraceptive use (small numbers); no participants were on ART
  - Other studies have not observed association of hormonal contraception and HIV transmission or acquisition

HIV-Infected Women: Contraception (3)

- Consistent use of condoms (male or female) recommended to reduce risk of HIV transmission and STD acquisition, regardless of contraceptive use
- ART and suppression of HIV viremia is recommended to reduce HIV transmission risk

Treatment for Pregnant Women*

- Combination ART recommended for all HIV-infected pregnant women, regardless of CD4 count, HIV viral load, or clinical status
- Counsel on known benefits and risks of ART during pregnancy

* See also the U.S. Public Health Services Task Force *Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States*.

ART for Pregnant Women (2)

To reduce risk of perinatal transmission:

- Combination ART, with maximal and sustained suppression of HIV RNA levels during pregnancy
- Perform resistance testing before starting ART, and for women on ART with detectable HIV RNA
  - ART initiation should not be delayed pending resistance test results; modify ARV regimen if indicated based on test results

ART for Pregnant Women (3)

Regimen considerations:

- Potential PK changes caused by pregnancy, different dosing requirements
- Potential adverse effects of ARVs on pregnant women
- Potential short- and long-term ARV effects on the fetus and newborn

ART for Pregnant Women (4)

Efavirenz

- Risk of neural tube defects in first 5-6 weeks of pregnancy
- Because pregnancy is rarely recognized before 4-6 weeks of pregnancy, and changes in ARVs may increase risk of loss of viral control and risk of perinatal transmission, EFV can be continued in pregnant women who present in the first trimester on a virologically suppressive regimen that includes EFV

ART for Pregnant Women (5)

Zidovudine:

- IV ZDV infusion recommended during labor if maternal HIV RNA is ≥1,000 copies/mL (or is unknown) near time of delivery

ART for Pregnant Women (6)

- Report cases of prenatal ARV exposure to the Antiretroviral Pregnancy Registry (http://www.apregistry.com)
- See U.S. PHS Task Force *Guidelines for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women*

Postpartum Management

- Continue ART after delivery, as for all HIV-infected persons
- Note that ART adherence may worsen postpartum; specifically address and support adherence
- Breast-feeding is not recommended, owing to risk of postnatal transmission
- HIV-infected women should avoid premastication of food for the infant: associated with HIV transmission to child

HIV and the Older Patient

- In the U.S., approximately 30% of HIV-infected persons are ≥50 years of age
- Aging-related comorbidities may complicate management of HIV
- HIV may increase risk of comorbidities and may accelerate the aging process
- Limited data on effects of ARVs in older persons (eg, adverse effects, drug-drug interactions)

HIV and the Older Patient:
HIV Risk, Diagnosis, and Prevention

- Reduced mucosal and immunologic defenses and changes in risk behaviors may lead to increased risk of HIV acquisition and transmission
- HIV screening rates in older persons are low
- Older persons may have more advanced HIV at presentation and ART initiation
  - Screen for HIV per CDC recommendations
  - Sexual history, risk-reduction counseling, screening for STIs (as indicated) are important to general health care for HIV-infected and HIV-uninfected older persons

HIV and the Older Patient: ART

- "ART is recommended in patients >50 years of age, regardless of CD4 cell count" (BIII)
- Older persons have decreased immune recovery and increased risk of non-AIDS events
- No data on specific ARVs in older persons; individualize ARV selection
- Monitor ART effectiveness and safety per general guidelines, but give special attention to renal, liver, cardiovascular, metabolic, and bone health

HIV and the Older Patient: ART (2)

- CD4 cell recovery on ART may be less robust in older patients (though virologic response appears to be the same as in younger patients)
- Starting ART at younger age may result in better outcomes (immunologic and perhaps clinical)
- Interactions between ARVs and other medications, as well as polypharmacy, may complicate care

HIV and the Older Patient: ART (3)

- Adherence:
  - Some data suggest older HIV-infected patients may be more adherent to ART than younger patients
  - However, many issues (eg, complex dosing requirements, cost, limited health literacy, neurocognitive impairment) may impact adherence
  - Assess adherence regularly; facilitate adherence

HIV and the Older Patient: Complications and Comorbidities

- Non-AIDS illnesses (eg, cardiovascular disease, liver disease, cancer, bone fragility, and neurocognitive impairment) may have increased disease burden in aging HIV-infected persons
- Current primary care recommendations advise to identify and manage risks in HIV-infected as in HIV-uninfected individuals

Illicit Drug Users

- Transmission via injection drug use is second most common HIV transmission route in U.S.
- Noninjection illicit drug use may facilitate sexual transmission of HIV
- HIV infection most associated with heroin and stimulants (eg, cocaine and amphetamines); amyl nitrate and other club drugs also associated

Illicit Drug Users (2)

- HIV-infected injection and noninjection drug users
  - Often have multiple comorbidities
  - Increased morbidity and mortality
  - Increased risk of overdose than HIV-uninfected drug users
  - Decreased access to HIV care
    - Less likely to receive ART

Illicit Drug Users: Efficacy of HIV Treatment

- In drug users who are not actively using, efficacy similar to that of other populations
- Active drug use may interfere with adherence and ART success
- In some patients, substance abuse treatment may be required for ART success
- Many other support mechanisms may be effective
- Injection drug users may have more ARV-related adverse effects

Treatment of Opioid Addiction: Interactions with ARVs

- Methadone: may interact significantly with ART
  - NRTIs: no significant effects on methadone levels; ZDV levels increased
  - NNRTIs: EFV and NVP decrease methadone levels
  - PIs: may decrease methadone levels; methadone decreases amprenavir levels
  - Integrase inhibitors: no significant effects on methadone levels (except EVG + PI/r may decrease levels)

Treatment of Opioid Addiction: Interactions with ARVs (2)

- Buprenorphine: limited data; interacts with some PIs and NNRTIs
  - ATV and TPV/r levels decreased, do not use with unboosted ATV
  - Buprenorphine levels increased by ATV/r, DRV/r (effect of cobicistat not studied)
  - Buprenorphine levels decreased by EFV, modestly by ETR
- Naltrexone: no expected interactions with PIs or NNRTIs

HIV-2 Infection

- Endemic in West Africa, and rates are high in countries with strong socioeconomic ties to West Africa (eg, France, Spain, Portugal, Brazil and other former Portuguese colonies)
  - Consider in persons who originated in these areas or who have had sex or needle-sharing partners from these areas

HIV-2 Infection (2)

- Compared with HIV-1:
  - Usually longer asymptomatic stage, lower plasma HIV-2 RNA levels, lower mortality rates
- Can progress to AIDS
- Coinfection with HIV-1 and HIV-2 is possible; consider if patient is from a high-prevalence area
- Also consider (in appropriate epidemiologic setting) if:
  - Atypical serologic findings (eg, positive screening test with indeterminate HIV-1 Western blot)
  - Low or undetectable HIV-1 RNA
  - Declining CD4 count despite apparent virologic suppression on ART

HIV-2 Infection (3)

- Testing:
  - CDC recommends initial test with HIV-1/HIV-2 Ag/Ab immunoassay, and subsequent testing with HIV-1/HIV-2 Ab differentiation immunoassay
    - Multispot HIV-1/HIV-2 Rapid Test is approved for differentiating HIV-1 and HIV-2
  - Commercially available HIV-1 viral load assays do not reliably detect or quantify HIV-2
  - HIV-2 RNA assays are available from University of Washington and N.Y. State Department of Health
    - Approximately 1/4-1/3 of untreated HIV-2-infected patients will have HIV-2 RNA levels below the limits of detection; some may have CD4 decline and clinical progression
  - No validated HIV-2 genotype or phenotype assays

HIV-2 Infection: ART

- Optimal treatment strategy not defined: no randomized controlled trials on when to start ART or on specific ARVs
  - ART should be started before there is clinical progression
  - Activity of some ARVs is different in HIV-2 infection

HIV-2 Infection: ART (2)

- ARV activity
  - NRTIs: active, though lower barrier to resistance than with HIV-1 (in vitro data)
  - NNRTIs and enfuvirtide: HIV-2 is intrinsically resistant; do not use
  - PIs: DRV/r, LPV/r, SQV/r have greatest activity; others should be avoided
  - INSTIs: potent activity
  - CCR5 antagonist (MVC) appears active against some isolates, but:
    - No approved assays to determine HIV-2 coreceptor tropism
    - HIV-2 uses multiple minor coreceptors in addition to CCR5 and CXCR4

HIV-2 Infection: Treatment Considerations

- Limited controlled trial data on initial ART options: use 2 NRTIs + HIV-2-active boosted PI or INSTI, pending availability of further data
- Use HIV-2 RNA levels, CD4 count, clinical status to assess treatment response
- CD4 recovery on ART may be poor
- Resistance-associated mutations develop commonly on ART
  - Genotype interpretation algorithms may not be applicable to HIV-2
- In the event of treatment failure, consult with an expert in HIV-2 management

HBV/HIV Coinfection

- 5-10% of HIV-infected persons in the United States have chronic HBV infection
- Progression of HBV is faster with HIV coinfection (cirrhosis, ESLD, hepatocellular carcinoma [HCC])
- HBV does not alter progression of HIV infection or efficacy of ART
- In HBV/HIV-coinfected patients, liver toxicity from ARVs and flares of HBV may complicate HIV treatment

HBV/HIV Coinfection and ART

Considerations in ART:

- FTC, 3TC, TAF, and TDF are active against both HIV and HBV
  - Discontinuation may cause HBV flares
- HBV resistance to 3TC monotherapy
  - 40% at 2 years, 90% at 4 years
  - 3TC or FTC should be used in combination with other anti-HBV drugs
- Entecavir has activity against HIV; may select for M184V mutation, conferring cross-resistance to 3TC and FTC
  - Use only with fully suppressive ARV regimen

HBV/HIV Coinfection and ART (2)

- Immune reconstitution may result in transaminase elevation
  - Patients with immune reconstitution may have loss of envelope antigen (HBeAg), associated with HBV flare
- Some ARVs may increase transaminase levels; ARV toxicity may be difficult to distinguish from HBV flare (and possible precursor to HBeAg seroconversion)

HBV/HIV Coinfection: Treatment Recommendations

For all HBV/HIV-coinfected patients:

- Counsel avoidance of alcohol
- Vaccinate against hepatitis A (if not immune)
- Advise on methods to prevent HBV transmission
- Evaluate severity of HBV infection

HBV/HIV Coinfection: Treatment Recommendations (2)

For all with positive HBsAg:

- Quantitative test for HBV DNA before ART initiation
- If already on ART with HBV-active agents, quantitative HBV DNA test every 6-12 months to monitor HBV treatment efficacy

HBV/HIV Coinfection: Treatment Recommendations (3)

If not yet on treatment and HBV *or* HIV treatment is needed:

- Treat *both* infections by starting an ARV regimen that includes TDF/FTC or TAF/FTC (or TDF + 3TC) as NRTI backbone
  - Avoid HBV monotherapy, to avoid HBV resistance
  - TAF appears to cause less renal toxicity and less loss of bone mineral density than TDF

HBV/HIV Coinfection: Treatment Recommendations (4)

- Alternative regimens (if TDF or TAF cannot be used safely):
  - Entecavir + a fully suppressive ARV regimen
    - Entecavir should not be considered part of ARV regimen
    - If 3TC resistance is suspected, monitor closely, increase entecavir dosage; entecavir resistance may develop quickly
  - Consider pegylated interferon-alfa for certain patients (no anti-HIV activity)
  - Adefovir and telbivudine no longer recommended for HBV/HIV coinfection
- Use in combination with suppressive ARV regimen

HBV/HIV Coinfection: Treatment Recommendations (5)

- Need to discontinue medications active against HBV
  - Severe flares of HBV possible; monitor LFTs closely
  - Consider entecavir (with suppressive ART) to prevent flares, especially if hepatic reserve is marginal
- Need to change ART because of HIV resistance:
  - If adequate HBV suppression, continue the ARVs with activity against HBV; combine with other suitable ARVs to achieve HIV suppression

HCV/HIV Coinfection

- Higher rates of progressive liver disease
- Unclear whether HCV increases HIV progression
- ART may slow progression of liver disease
- ART is recommended for all coinfected patients, regardless of CD4 count
  - If CD4 count low (eg, <200 cells/μL), start ART quickly; may delay HCV therapy until stable on ART
- For most patients, benefits of ART outweigh concerns about ARV-associated hepatotoxicity

HCV/HIV Coinfection: ART

- Recommendations for initial ARV regimens are the same as for patients without HCV infection
  - But, carefully consider potential drug-drug interactions with HCV therapies, or overlapping toxicities; some combinations are contraindicated
  - Higher risk of hepatotoxicity with some older ARVs
    - Avoid d4T, ddI, AZT, NVP, TPV if possible
  - Hepatically metabolized ARVs may require dosage modification or avoidance in patients with cirrhosis

HCV/HIV Coinfection: HCV Treatment

- Concurrent treatment of HIV and HCV is possible, but may be complicated (pill burden, drug interactions, overlapping drug toxicities)
- Evaluate all coinfected patients for HCV therapy
- Perform genotype testing and liver disease staging
  - Disease stage helps determine need for HCV treatment
- Consider potential interactions between HIV and HCV medications; modify ART if necessary

HCV/HIV Coinfection: HCV Treatment (2)

- Treatment with pegylated interferon + ribavirin (Peg-IFN/RBV) associated with poor rate of HCV clearance (sustained virologic response, SVR)
- Direct-acting antiviral (DAA) agents improve HCV response rates

HCV/HIV Coinfection: HCV Treatment (3)

- Newer DAAs
  - Simeprevir (NS3/4A protease inhibitor)
    - Cannot be given with EFV, ETR, HIV protease inhibitors, COBI, or EFG/COBI/TDF/FTC
    - Can be given with RAL, DTG, RPV, TDF
  - Sofosbuvir (NS5B nucleotide polymerase inhibitor)
    - Can be used with most ARVs, except TPV
  - Ledipasvir (NS5A inhibitor)
    - Available in fixed-dose combination with sofosbuvir
    - Compatible with most ARVs
    - Coadministration with TDF + RTV or COBI may increase TDF exposure; caution in patients with renal disease; monitor for renal toxicity

HCV/HIV Coinfection: HCV Treatment (4)

- Newer DAAs (cont.)
  - Daclatasvir (NS5A inhibitor)
    - Approved for use with sofosbuvir
    - EFV, ETR, NVP reduce daclatasvir levels; daclatasvir dosage must be increased
    - Some boosted PIs (eg, ATV/r or ATV/c) increase daclatasvir levels; daclatasvir dosage must be reduced
    - No dosage adjustment needed with boosted DRV, RPV, DTG, or RAL
  - Elbasvir (NS5A inhibitor) + grazoprevir (HCV PI)
    - Cannot be given with EFV, ETR, NVP, boosted PIs, or elvitegravir/cobicistat
    - Can be given with RPV, DTG, and RAL

HCV/HIV Coinfection: HCV Treatment (5)

- Newer DAAs (cont.)
  - Ombitasvir (NS5A inhibitor)/paritaprevir (HCV PI)/RTV + dasabuvir (NS5B inhibitor): copackaged combination regimen
    - Significant and complex interactions with some ARVs: consider these carefully before administration
    - May be used with ATV, DTG, RAL
  - Approval of other DAA agents is expected soon

HCV/HIV Coinfection: Treatment (6)

- HCV treatment is evolving rapidly; consult with experts in treatment of HCV/HIV coinfection

HCV/HIV Coinfection: Other Management Issues

- Counsel patients to avoid alcohol
- Counsel on measures to reduce risk of HCV and HIV transmission to others
- Check patients for immunity to hepatitis A and B, vaccinate if not immune

TB Disease in HIV-Infected Patients

- HIV infection increases risk of progression from latent to active TB:
  - Risk increases as CD4 count declines
- TB increases HIV progression

HIV and Latent TB infection

- Treatment for latent TB infection (LTBI) reduces risk of active TB
- Management of LTBI
  - Exclude active TB disease
  - Recommended LTBI treatments:
    - Isoniazid (INH) daily or twice weekly x 9 months
      - No interactions with ARVs
    - INH + rifapentine once weekly x 12 weeks (directly observed therapy)
      - Drug-drug interactions: can be used only with EFV and RAL, and ABC/3TC or TDF/FTC (not TAF/FTC)
    - Rifampin (or rifabutin) daily x 4 months
      - Many drug-drug interactions: consult experts
- ART can prevent active TB

HIV and Latent TB infection (2)

- Immune reconstitution with ART may result in conversion of negative TST or interferon-gamma release assay (IGRA) to positive test
- Perform TST or IGRA for all patients before ART initiation
- If TST or IGRA is negative and CD4 count is <200 cells/μL, repeat TB test after CD4 count increases to >200 cells/μL on ART
- Positive test result indicates latent TB infection (absent evidence of active TB); treat all for latent TB
  - Rifapentine should not be used in persons on ART (unless through a clinical trial)

TB and HIV Coinfection: Treatment

- The treatment of TB in patients with HIV infection should follow the same principles as for the treatment of persons without HIV infection
- Initiate TB treatment immediately
  - Directly observed therapy is strongly recommended
- Initiate or optimize ART
  - Concomitant therapy for both TB and HIV shown to reduce mortality
    - Low CD4 count is risk factor for mortality
    - IRIS more common if ART is initiated early in course of TB treatment, but not associated with mortality

TB and HIV Coinfection: ART Recommendations

- Patients not on ART:
  - Immediately initiate TB treatment
  - If CD4 count <50 cells/μL: start ART within 2 weeks of starting TB treatment
  - If CD4 count ≥50 cells/μL and clinical disease is severe: start ART within 8 weeks of starting TB treatment
    - No data show harm in starting ART earlier

TB and HIV Coinfection: ART Recommendations (2)

- Pregnant women
  - Start ART as early as feasible, for maternal health and to prevent perinatal transmission
  - Consult with experts
- TB meningitis
  - Caution in starting ART early
    - In one study, immediate ART associated with higher rate of adverse events vs deferral of ART x 2 months
- Documented MDR or XDR TB
  - Optimal timing of ART initiation is not known; consult with experts

TB and HIV Coinfection: ART Recommendations (3)

- Patients on ART:
  - Continue ART (should be fully suppressive)
  - Evaluate ARV regimen for interactions with TB drugs (ie, rifamycins); may need modifications

TB and HIV Coinfection: TB Treatment Considerations

- Rifamycins should be included in TB regimens, unless TB resistance or toxicity
- Many potential drug interactions between rifamycins and ARVs

TB and HIV Coinfection: Drug-Drug Interactions

- Rifampin
  - NRTIs: not recommended with TAF
  - PIs: Do not coadminister
  - NNRTIs: Do not coadminister with ETR, RPV; can be given with EFV
  - INSTIs: Do not coadminister with EVG/COBI; increased dosage of DTG or RAL needed if given with rifampin
  - MVC: Not recommended; requires dosage increase when used with rifampin

TB and HIV Coinfection: Drug-Drug Interactions (2)

- Rifabutin
  - NRTIs: Not recommended with TAF
  - PIs: Dosage adjustment of rifabutin may be necessary
  - NNRTIs: Not recommended with RPV; can be used with EFV, ETR, NVP; dosage adjustment of rifabutin may be necessary
  - INSTIs: Do not coadminister with EVG/COBI; can be used with DTG, RAL
  - MVC: requires dosage adjustment of MVC

TB and HIV Coinfection: Drug-Drug Interactions (3)

- Rifapentine
  - NRTIs: Not recommended with TAF
  - PIs: Do not coadminister
  - NNRTIs: Do not coadminister with ETR, NVP, RPV; can be used with EFV
  - INSTIs: Do not coadminister with DTG, EVG/COBI; do not coadminister once-daily rifapentine with RAL

TB and HIV Coinfection: IRIS

- IRIS: worsening clinical status while on treatment for active TB
  - More common after ART initiation, caused by immune reconstitution
  - Occurs in 8-43% of patients with HIV/TB disease
  - Predictors: CD4 counts of <50 cells/μL, severe TB, ART initiation <30 days after start of TB treatment
  - Infrequently associated with mortality

TB and HIV Coinfection: IRIS (2)

- Management
  - Continue treatment for TB and HIV
  - NSAIDs for mild-to-moderate symptoms
  - Severe cases: corticosteroids

Preventing Secondary Transmission of HIV

Prevention interventions are a key part of HIV care

- In the United States, the rate of new HIV infections remains stable
- Risk behaviors have increased since availability of effective ART
- Sexually transmitted infections (STIs), genital irritation, substance and alcohol use, noncircumcision in men, and other conditions, can increase risk of HIV transmission
- Recent data show that ART substantially decreases risk of sexual transmission of HIV

Preventing Secondary Transmission of HIV (2)

Essential components of HIV patient care:

- Reinforce prevention messages
- Assess patient's understanding of HIV transmission
- Assess patient's HIV transmission behaviors
- Discuss strategies to prevent transmission (individualize)
- Detect and treat STIs
- For women:
  - Pregnancy prevention counseling with those who wish to avoid pregnancy
  - Preconception counseling with those who wish to become pregnant

Preventing Secondary Transmission of HIV (3)

- Tools for prevention of sexual and bloodborne HIV transmission:
  - Consistent and effective use of ART (with sustained suppression of HIV RNA)
  - Consistent condom usage
  - Safer sexual and drug-use practices
  - Detection and treatment of STIs

Preventing Secondary Transmission of HIV (4)

- Interventions in clinic settings are effective in changing sexual risk behavior
  - CDC training materials: http://www.cdc.gov/hiv/topics/research/prs/index.htm
- Interventions also effective in reducing risky injection drug-use behavior
  - Behavioral interventions and opiate substitution with methadone

Preventing Secondary Transmission of HIV: ART as Prevention

ART may reduce risk of HIV transmission

- HIV viral load directly related to probability of HIV transmission; increased ART use and lower community viral load associated with lower HIV incidence
- Observational studies show lower rates of HIV transmission among serodiscordant heterosexual couples after viral suppression on ART

Preventing Secondary Transmission of HIV: ART as Prevention (2)

ART may reduce risk of HIV transmission

- In a large RTC of HIV-discordant heterosexual couples, those on ART had 96% reduction in HIV transmission to uninfected partners
- No RTC data in MSM and IDUs
- But, HIV has been detected in genital secretions of persons with controlled plasma HIV RNA
- Belief in efficacy of ART may lead to increases in risk behavior

Websites to Access the Guidelines

- http://www.aidsetc.org
- http://aidsinfo.nih.gov

About This Slide Set

- This presentation was prepared by Susa Coffey, MD, for the AETC National Resource Center and last updated in July 2016 for the AETC National Coordinating Resource Center.
- See the AETC NCRC website for the most current version of this presentation: http://www.aidsetc.org