



INTERNATIONAL
SOCIETY
FOR INFECTIOUS
DISEASES

GUIDE TO INFECTION CONTROL IN THE HOSPITAL

CHAPTER 25:

HIV Infection & AIDS in Low- and Middle-Income Countries

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KEY ISSUES

- More than thirty years after it was first recognized in Africa, HIV infection and its consequences are amongst the leading cause of adult deaths in many cities in low- and middle-income countries (LMICs), and have significantly increased childhood mortality. Despite considerable efforts to control the epidemic, HIV continues to spread at a rapid pace in under-resourced countries. Of an estimated 36.7 million people infected by HIV worldwide (as of December 2016), 2.1 million were children less than 15. For the sole year 2016, new HIV infections were 1.7 million in adults and 160,000 in children¹. Although the yearly number of newly acquired infections continues to decline, most people newly infected with HIV live in sub-Saharan Africa. An estimated 1.0 million people died of HIV infection during 2016¹.
- In the last decades, the development of new antiretroviral (ARV) drugs (see *Tables 25.1* and *25.2*) and the extended access to Antiretroviral Therapy (ART) for HIV-infected patients have been accompanied by a dramatic reduction in HIV-associated mortality and of HIV incidence. Today, for those who have access to ARV drugs, HIV infection has to be considered as a manageable chronic illness. In 2016, the World Health Organization estimated that 19.5 million people received ART worldwide, representing 53% (39-65%) of people living with HIV in 2016¹. The coverage of antiretroviral drugs for preventing mother-to-child transmission (MTCT) of HIV has also steadily increased over the last years and was estimated to be 76% (60-88%) in 2016¹. The global challenge remains to scale up access to ARV drugs for all HIV-infected individuals together with preventing the acquisition of new infections².

KNOWN FACTS

- Both HIV type 1 (HIV-1) and HIV type 2 (HIV-2) are circulating in LMICs. HIV-2, which is mostly spread in West Africa where it co-exists with HIV-1, is less transmissible and less pathogenic than HIV-1. HIV-2 and HIV-1 group O are naturally resistant to non-nucleoside reverse transcriptase inhibitors.
- All groups of HIV-1 (group M, N, O, and P) as well as all genotypic subtypes of HIV-1 group M and recombinant circulating forms (CRFs) are cocirculating in LMICs but regional distribution of groups, subtypes, and CRFs varies considerably.
- Transfusion of HIV contaminated blood is still responsible for about 10% of overall transmission events.
- Blood banking organization, selection of blood donors, and HIV testing of blood donations are effective in preventing transfusion-associated infections.
- Sexual transmission remains by far the most frequent route of transmission in adults. Sexually transmitted infections (STIs) are facilitating HIV transmission by sexual intercourse.
- Control of STIs at the community level is a cost-effective strategy to prevent sexual transmission of HIV.
- MTCT of HIV involves almost exclusively HIV-1 and can occur *in utero*, during labor and delivery, and postnatally by breastfeeding. MTCT rate is estimated 20-30% in breastfeeding populations in the absence of prophylaxis and HIV care.
- Prevention of MTCT by treating HIV-infected pregnant or breastfeeding women and their neonates with antiretrovirals is highly efficacious, with early (6 weeks) transmission rates frequently below 2%. However, breastfeeding is responsible for a significant residual transmission.
- Susceptibility to acquisition of HIV and clinical course of HIV disease are highly variable and may be determined at the individual level by the

existence of genetic factors such as deletions on the genes coding for cellular cofactors for viral entry (such as CCR5) or their promoters.

- More than 85% of fatal overwhelming infections associated with HIV as well as the first five causes of mortality in HIV-infected African patients are potentially amenable to a simple, effective, and affordable anti-infectious treatment or prophylaxis, such as the use of cotrimoxazole³. The most devastating public health impact of HIV-1 infection on other endemic diseases is on tuberculosis. In sub-Saharan Africa, the annual incidence of tuberculosis is more than 15-fold greater in HIV-infected individuals than in HIV-uninfected individuals. In patients eligible for ART with active TB, antiretroviral therapy should be initiated shortly (2 weeks) after the initiation of TB treatment⁴.
- Clinical management of HIV-infected patients is based on access of healthcare quality services: diagnosis and treatment of tuberculosis and of other infectious diseases (pneumococcal disease, bacteraemia). The June 2016 WHO guidelines recommend that lifelong ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count². The preferred first line regimen is TDF + 3TC (or FTC) + EFV as a fixed-dose combination. Also, ART should be promptly initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count².
- As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count ≤ 350 cells/mm³.
- HIV is highly sensitive to physic and chemical environment and to widely used disinfectants. Reinforced hospital hygiene measures are of practical importance to minimize the risk of exposure to HIV-containing blood and body fluids in the healthcare settings. Post-exposure prophylaxis by means of a combination of ARV [generally three drugs given as soon as possible after exposure, for one month] is highly efficacious in preventing acquisition of HIV-1 infection after accidental exposure to the virus in the healthcare setting⁵. An adjustment of

regimen according to the index patient profile of antiretroviral resistance may be necessary.

SUGGESTED PRACTICE

- Scaling up access to ART in LMICs, and monitoring it in terms of adherence, efficacy, tolerance, and sustainability remain major challenges. Adherence is critical for treatment success and the best ways for optimizing adherence are under scrutiny. The most optimal way to follow up the biological efficacy of ART in LMICs remains debatable. Point of care tests for HIV diagnosis (including molecular tests for infant diagnosis) and for monitoring HIV viral load are available and advisable for prompt ART initiation and follow up.
- In HIV infected individuals, co-infections with hepatitis C (HCV) or B (HBV) viruses are frequent. Although considerable progress has been accomplished in treating these co-infections with HIV, the access to anti-HCV (directly acting antivirals, DAA) and some anti-HBV drugs remains problematic in many LMICs.
- Access to second and third lines of ART remains extremely problematic in many LMICs. The best combinations to propose in second and third lines are under evaluation.
- The interactions between HIV infection and other tropical diseases, such as malaria, other parasitosis, or malnutrition, remain largely undetermined. Also, the complex interactions between HIV disease progression and reactivations of chronic infections, such as infections with herpesviruses, and immune activation remain to be clarified.
- Pre-exposure prophylaxis (PrEP) defined as the continuous or intermittent administration of an antiretroviral drug or drug combination to an exposed uninfected person to prevent HIV acquisition has been successfully implemented in men who have sex with men (MSM) with almost 90% protection if the prophylaxis is effectively taken⁶. Recently,

WHO has recommended offering access to PrEP to any population exposed to HIV having an expected incidence of HIV infection above 3 per 100 person-years^{2,7}. However, very few PrEP programs exist that offer this service in highly exposed populations other than MSM, such as transgender women, injecting drug users, serodiscordant heterosexual couples, commercial sex workers pregnant women from very high incidence areas, or infants exposed to HIV by breastfeeding.

- The recent WHO guidelines on prevention of MTCT of HIV have the ambition to eliminate the MTCT of HIV – elimination being defined as less than 50 new HIV infections per 100,000 live births and less than 5% of overall MTCT rate – and recommend that all pregnant and breastfeeding women infected with HIV initiate ART which should be maintained lifelong. Several studies on prolonged maternal ARV prophylaxis during breastfeeding are ongoing in order to determine if this can achieve elimination of breastfeeding transmission of HIV-1. It is likely that in some settings, high residual transmission by breastfeeding would justify rescue interventions (by infant PrEP or passive immunoprophylaxis).
- Treatment as prevention (TasP) strategy, consisting as administering ART to all HIV infected individuals regardless of their CD4 T cell count or HIV viral load with the aim of both interrupting transmission and universalizing ARV treatment for the individual's own benefit, is attractive⁸. In practice, the sustained individual and societal benefits and the cost-effectiveness of this strategy remain controversial.
- Although some encouraging results have been obtained in recent years, a preventive HIV vaccine has remained elusive. Various existing preventive strategies, including PrEP and vaginal microbicides combined in comprehensive packages are presently under investigation.

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS:

- Prevention, clinical and psychosocial management, as well as a continual struggle against discrimination/stigmatisation are all integral parts of HIV/AIDS control programs. Each of these components is not sufficient in itself but all are synergistic.
- Voluntary counselling and testing for HIV is the entry point of HIV prevention and care and has to be made available widely. WHO recommends also that HIV self-testing be offered as an additional approach to HIV testing services⁹.
- In terms of prevention the following strategies should be implemented:
 1. STI diagnosis and treatment at the community level (based on well validated treatment algorithms) as well as large access to male and female condoms and, in some circumstances, male circumcision, vaginal microbicides, and PrEP.
 2. Blood bank organization, blood donors' selection and HIV testing of blood donations.
 3. Increased accessibility of mother and child to high quality healthcare services (antenatal clinics, basic obstetrical needs, nutritional education) including a thoughtful package of antenatal care. Provision of ART to breastfeeding or pregnant women as per 2016 WHO recommendations².
 4. Reinforcement of available health programs (TB control, malaria control, expanded program on immunization, maternal and child care, family planning, et cetera). Each contact with health care providers should be used to promote the offer of HIV testing, prevention and care.
 5. Access of all health professionals to post exposure prophylaxis in case of accidental exposure to blood or body fluids potentially containing HIV and hepatitis viruses.
- In terms of psychosocial and clinical management the following strategies should be implemented:

1. Skilled, acceptable, accessible, and sustainable voluntary HIV counselling and testing services.
2. Simple clinical algorithms for clinical management of HIV disease and treatment of infectious episodes by means of available essential drugs and including nutritional support.
3. Decentralised management and community support.
4. Improved integrated strategies to diagnose and treat TB.
5. As a priority, initiation of lifelong ART in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count, preferentially by means of a fixed-dose combination of antiretrovirals. The preferred first line regimen is TDF + 3TC (or FTC) + EFV, although some country programs have switched to dolutegravir in replacement of efavirenz.

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Table 25.1 Antiretroviral Drugs Used in the Treatment of HIV Infection (as of 8 September 2016)

Source: U.S. Food and Drug Administration (FDA):

<https://www.fda.gov/forpatients/illness/hivaids/treatment/ucm118915.htm>

Multi-Class Combination Products

| Brand https://www.accessdata.fda.gov/scripts/cder/daf/ | Generic Name |
|--|--|
| Atripla | efavirenz, emtricitabine and tenofovir disoproxil fumarate |
| Complera | emtricitabine, rilpivirine, and tenofovir disoproxil fumarate |
| Evotaz | atazanavir sulfate, cobicistat |
| Prezcobix | cobicistat, darunavir ethanolate |
| Stribild | elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate |

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

| Brand Name | Generic Name |
|--------------------------|--|
| Combivir | lamivudine and zidovudine |
| Emtriva | emtricitabine, FTC |
| Epivir | lamivudine, 3TC |
| Epzicom | abacavir and lamivudine |
| Hivid | zalcitabine, dideoxycytidine, ddC (no longer marketed) |

| | |
|--------------------------|---|
| Retrovir | zidovudine, azidothymidine, AZT, ZDV |
| Trizivir | abacavir, zidovudine, and lamivudine |
| Truvada | tenofovir disoproxil fumarate and emtricitabine |
| Videx EC | enteric coated didanosine, ddl EC |
| Videx | didanosine, dideoxyinosine, ddl |
| Viread | tenofovir disoproxil fumarate, TDF |
| Zerit | stavudine, d4T |
| Ziagen | abacavir sulfate, ABC |

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

| Brand Name | Generic Name |
|--|------------------|
| Edurant | rilpivirine |
| Intelence | etravirine |
| Rescriptor | delavirdine, DLV |
| Sustiva | efavirenz, EFV |
| Viramune (Immediate Release) | nevirapine, NVP |
| Viramune XR (Extended Release) | nevirapine, NVP |

Protease Inhibitors (PIs)

| Brand Name | Generic Name |
|---------------------------|--------------------------------------|
| Agenerase | amprenavir, APV (no longer marketed) |
| Aptivus | tipranavir, TPV |
| Crixivan | indinavir, IDV, |

| | |
|---------------------------|----------------------------------|
| Fortovase | saquinavir (no longer marketed) |
| Invirase | saquinavir mesylate, SQV |
| Kaletra | lopinavir and ritonavir, LPV/RTV |
| Lexiva | Fosamprenavir Calcium, FOS-APV |
| Norvir | ritonavir, RTV |
| Prezista | darunavir |
| Reyataz | atazanavir sulfate, ATV |
| Viracept | nelfinavir mesylate, NFV |

Fusion Inhibitors

| Brand Name | Generic Name |
|------------------------|-------------------|
| Fuzeon | enfuvirtide, T-20 |

Entry Inhibitors - CCR5 co-receptor antagonist

| Brand Name | Generic Name |
|---------------------------|--------------|
| Selzentry | maraviroc |

HIV integrase strand transfer inhibitors

| Brand Name | Generic Name |
|---|--------------|
| Isentress | raltegravir |
| Tivicay  | dolutegravir |
| Vitekta | elvitegravir |

Table 25.2 FDA Approved Generic Formulations of Nucleoside Reverse Transcriptase Inhibitors (NRTIs) Used in the Treatment of HIV Infection (as of 2 April 2014)

Source: U.S. Food and Drug Administration (FDA)

<https://www.fda.gov/ForPatients/Illness/HIVAIDS/Treatment/ucm118944.htm>

| Generic Name | Manufacturer Name |
|--|-------------------------------|
| lamivudine and zidovudine tablets USP, 150 mg/300 mg | Hetero Labs Limited |
| abacavir tablets USP, 300 mg | Mylan Pharmaceuticals, Inc. |
| nevirapine tablets USP, 200 mg | Prinston Pharmaceutical, Inc. |
| nevirapine tablets USP, 200 mg | Apotex Corporation |
| nevirapine tablets USP, 200 mg | Matrix Laboratories Limited |
| nevirapine tablets USP, 200 mg | ScieGen Pharmaceuticals, Inc |
| nevirapine tablets USP, 200 mg | Mylan Pharmaceuticals, Inc. |
| nevirapine tablets USP, 200 mg | Hetero Labs Limited, Unit-III |
| nevirapine tablets USP, 200 mg | Micro Labs Limited |
| nevirapine tablets USP, 200 mg | Strides, Inc. |
| nevirapine tablets USP, 200 mg | Cipla Limited |
| nevirapine tablets USP, 200 mg | Aurobindo Pharma Limited |
| nevirapine oral suspension USP, 50 mg/5 mL | Aurobindo Pharma Limited |
| lamivudine and zidovudine tablets, 150 mg/300 mg | Aurobindo Pharma Limited |
| lamivudine and zidovudine tablets, 150 mg/300 mg | Lupin Limited |

| | |
|---|-----------------------------|
| lamivudine and zidovudine tablets, 150 mg/300 mg | TEVA Pharmaceuticals USA |
| zidovudine Injection USP, 10 mg/mL, packaged in 200 mg/20 mL. Single-use vials | PharmaForce Inc. |
| didanosine (ddl) delayed release capsules, 125 mg, 200 mg, 250 mg, and 400 mg | Matrix Laboratories Limited |
| zidovudine 60 mg tablets for pediatric dosing † | Aurobindo Pharma Limited |
| stavudine for oral solution, 1 mg/mL | Aurobindo Pharma Limited |
| stavudine capsules (15 mg, 20 mg, 30 mg, and 40 mg) | Aurobindo Pharma Limited |
| stavudine capsules (15 mg, 20 mg, 30 mg, and 40 mg) | Hetero Drugs Limited |
| didanosine (ddl) delayed release capsules, 125 mg, 200 mg, 250 mg, and 400 mg | Aurobindo Pharma Limited |
| zidovudine oral solution USP, 50 mg/5 mL, oral solution - zidovudine, AZT, azidothymidine, ZDV (Pediatric formulation - 50 mg/5 mL) | Cipla Limited |
| zidovudine, AZT, azidothymidine, ZDV (300 mg tablets) | Matrix Laboratories, Inc. |
| zidovudine, AZT, azidothymidine, ZDV (100 mg capsules) | Cipla Limited |
| didanosine (ddl) for oral solution (pediatric powder), 10 mg/mL | Aurobindo Pharma Limited |

| | |
|--|------------------------------|
| zidovudine, AZT, azidothymidine, ZDV (100 mg capsules) | Aurobindo Pharma LTD. |
| zidovudine, AZT, azidothymidine, ZDV (300 mg tablets) | Aurobindo Pharma Limited |
| zidovudine oral solution USP, 50 mg/5 mL, oral solution - zidovudine, AZT, azidothymidine, ZDV (Pediatric formulation - 50 mg/ 5 mL) | Aurobindo Pharma Limited |
| zidovudine, AZT, azidothymidine, ZDV (300 mg tablets) | Ranbaxy Laboratories Limited |
| zidovudine, AZT, azidothymidine, ZDV (300 mg tablets) | Roxane Laboratories |
| didanosine (ddI) delayed release capsules | Barr Laboratories, Inc. |