HIV Basics for Health Professionals

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Learning objectives
Review and Understand...

1. Global Epidemiology of HIV
2. Economic Impact of HIV/AIDS
3. History of HIV/AIDS, including treatment
4. International Programs and Funding
5. HIV in popular culture
6. Pathophysiology
7. Transmission
8. Diagnostics
HIV and AIDS: Definitions

- HIV (Human Immunodeficiency Virus): A retrovirus which primarily infects and damages human immune system cells such as CD4 T-cells, dendritic cells and macrophages and leads to a dysfunctional immune system and a condition called AIDS.

- AIDS (Acquired Immunodeficiency Syndrome): is defined by a CD4 count of less than 200 and/or a set of symptoms and infections resulting from a damaged immune system due to HIV infection.
Adults and Children estimated to be living with HIV, 2007

Total: 33 million (30 – 36 million)

HIV Prevalence, 2004

Note huge difference between high and low income countries!
HIV and AIDS Deaths, 2004

Territories are sized in proportion to the absolute number of people who died from HIV/AIDS in one year.
According to the UNAIDS 2008 Report on the Global AIDS Epidemic, the global proportion of women versus men who are infected has remained at approximately 50% since the late 1990's. They report that the number of women infected is increasing in each region.
Children living with HIV globally, 1990-2007

This bar indicates the range of the estimate


According to the UNAIDS report, it is estimated that more than 90% of children living with HIV acquired the virus via maternal to child transmission— at birth or during breastfeeding. Only a small percentage was infected by other means— tainted transfusion, contaminated injections, sexual abuse or sexual intercourse. The number of new infections peaked in 2000-2002 and has since declined as a result of prevention and treatment with pregnant women. It is also important to note that in 2007, there were approximately 270,000 children under age 15 who died of AIDS related illness and 90% of those deaths were in sub-Saharan Africa. The number of AIDS deaths 6 December 2012 also has started to decline since 2003. Please see module 30B for more information on Prevention of Mother to Child Transmission.
Economic Impact of HIV/AIDS in Africa

• Health Sector
  – Demand for care ↑
  – Number of health care workers ↓
  – Cost of care ↑, exceeding public spending capacity
  – In Sub Saharan Africa, >50% of hospital beds occupied by people with HIV-related diseases
  – Hospital stays longer
  – Shortage of beds
  – Provision of ARVs can strain system further

Economic Impact of HIV/AIDS in Africa

- Household Burden
  - Caregiver/family burden
  - \( \downarrow \) Income
  - \( \downarrow \) Spending on basic necessities, education
  - \( \uparrow \) Number of orphans
  - Strain of healthcare costs and funerals

CASE: Esther is a 28 year old woman living in Kenya. Her husband has been sick and unable to work for the past year. She has 2 children, ages 7 and 10. What do you think the impact of the husband’s illness has been on this family?

Economic Impact of HIV/AIDS in Africa

• Educational Sector
  – Decrease in school enrollment
    • Children as caretakers of those sick with HIV
    • Children in the workforce to make up for lost income
    • Illness and death of teachers
• Damage to enterprise, business and agricultural sectors
• Declining life expectancy

CASE: Esther’s oldest daughter, Sarah, is 10 years old. Sarah has been taking care of her father while Esther sells vegetables in the market. She has stopped going to school. What impact will this have on Sarah’s future?

Notes on Economic Impact of HIV/AIDS in Africa.

In many countries of sub-Saharan Africa, AIDS is erasing decades of progress in extending life expectancy. According to the UNAIDS Report on the Global AIDS Epidemic, the life expectancy at birth in Southern Africa has declined to levels last seen in the 1950s. For the entire sub-region, the life expectancy at birth is less than 50 years and in Zimbabwe, it is less than 40. While the death rates are on the rise for people in their most productive years (20-49), there has also been a decline in total fertility rates in the hardest hit regions.

History of HIV

HIV/AIDS: episodes in an evolving epidemic

- 1980: First cases of unusual immune deficiency identified among gay men in USA
- 1982: Acquired Immunodeficiency Syndrome (AIDS) first defined
- 1983: Human Immunodeficiency Virus (HIV) identified as cause of AIDS
- 1984: African heterosexual AIDS epidemic revealed
- 1985: First HIV antibody test approved in USA. HIV screening of blood donations starts
- 1986: Cases of HIV/AIDS now reported in all world regions
- 1987: First HIV prevalence begins among pregnant women in Uganda
- 1988: WHO launches Special Programme on AIDS
- 1989: First decline in HIV prevalence begins among pregnant women in Uganda
- 1992: Highly Active Antiretroviral Therapy (HAART) first discussed
- 1994: First treatment developed to reduce mother-to-child transmission
- 1995: Brazil provides antiretroviral therapy through its public health system
- 1996: UNAIDS created
- 1997: Outbreak in eastern Europe detected among injecting drug users
- 1998: First efficacy trial of a potential HIV vaccine starts in Thailand
- 1999: UN Security Council holds its first discussion of HIV/AIDS
- 2000: UN Secretary-General Kofi Annan calls for creation of a global fund on AIDS and health
- 2001: UN General Assembly adopts HIV/AIDS Declaration of Commitment
- 2002: Launch of Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM)
- 2003: WHO backs “3 by 5” target of ARV treatment for 3 million people by 2005
- 2004: WHO declares ARV treatment gap a global health emergency

Source: WHO/UNAIDS
History of HIV: The early epidemic in Africa

- *Early 20th Century*: Transfer of an ancestral virus from chimpanzees to humans
- 1960s: Approximately 2000 total people infected
- 1970s: First signs of epidemic in Kinshasa, Congo
  - Increase in opportunistic infections
    - Cryptococcal Meningitis, Kaposi’s Sarcoma, Tuberculosis and pneumonias
- 1980s: Uganda identifies rise in “slim disease,” later known as AIDS wasting

History of HIV Medications

- **1987**: AZT approved by FDA
- **1992**: Combination Therapy arrives with addition of first Nucleoside Reverse Transcriptase Inhibitor (NRTI)
- **1995/6**: First Protease Inhibitor (saquinavir) and Non-NRTI (nevirapine) are approved.
  - “Triple Therapy” initially brings hope of elimination of the virus.
  - Death rates in developed countries decrease by 84% over next four years at a cost of $10,000-$15,000 USD per year per patient
- **1997**: AZT used in pregnancy and delivery reduces transmission to infant by nearly 30%.
Generic Antiretrovirals (ARV)

- Generics are bioequivalent to brand name drugs
- Dosage, strength, route of administration, quality, performance and intended use are all the **SAME**
- Price is greatly decreased
- Generic producers do not cover costs of drug discovery or safety and efficacy trials
- Pharmaceutical companies argue:
  - Reduced profits decrease funding for drug R&D
  - Patents give pharmaceutical companies the exclusive rights to make and sell a drug so that they can recover costs
  - Patents last approximately 20 years
- The Agreement on Trade Related Aspects of Intellectual Property (TRIPS) gives companies 20 years of exclusive patent rights

Oxfam UK Cut the Cost Campaign, 2001
Avert, AIDS, Drug Prices and Generic Drugs, 2008
Notes on Generic Antiretrovirals (ARV).

TRIPS was introduced in 1995. TRIPS introduced intellectual property law into the international trading system for the first time and applies to all members of the World Trade Organization (WTO). Because the implementation of TRIPS was to have a huge impact on generic drug production, the majority of developing countries were given a ten-year transition period in which to comply. This means that developing countries (such as India) were able to continue developing generic drugs until 2005, whilst least developed countries have until 2016.

History of Generic ARV: ↓ Pricing

- 5 years after highly active antiretroviral therapy (HAART) was introduced in the US, only 8,000 people in Sub-Saharan Africa were on ARV

Cost Prohibitive!

- 2000 - Indian Drug Company began production of generic ARV
  - Increased competition for major pharmaceutical companies
  - Clinton foundation negotiation of decreased prices
- Mid-2001 - Triple combination therapy available for as low as $295/year
- 2004-2007 - ARV price for low and middle income countries decreases 30-64%
  - Most common regimen 3TC/D4T.NVP - $87 USD per patient/year
Notes on History of Generic ARV: ↓ Pricing.

As a result of international criticism and pressure (from Doctors Without Borders, OXFAM, Clinton Foundation and others), five major pharmaceutical companies agreed to reduce the cost of AIDS medications in 2000. By 2003, drug manufacturers had reduced the price of ARVs for resource poor countries, however the price offered was still high above the price of generics.

For more information on pricing of ARVs in developing countries, see MSF, “Untangling the Web of Price Reductions; A pricing guide for the purchase of ARVs for developing countries,” 10th ed., 2008.

The Effect of Generic Competition

Sample AIDS triple combination: Lowest world prices per patient, per year

According to the UNAIDS 2008 Report on the Global AIDS Epidemic, the global proportion of women versus men who are infected has remained at approximately 50% since the late 1990’s. They report that the number of women infected is increasing in each region.
Fixed Dose Combinations (FDC)

• Manufacture and export of generics led to advances in drug combinations
  – 2001 Indian generic pharmaceutical company. Cipla, produced a ONE-PILL combination of three ARVs patented by different pharmaceutical companies
  – Not obligated by TRIPS or patent laws
• FDCs have decreased number of pills taken each day
  – Increased adherence and decreased resistance
• Heat resistant forms of drugs produced

Kaplan, WHO, 2003
Generic ARVs in 2008

- India is the largest exporter of generic ARVs, sending nearly two-thirds of their production internationally
- Brazil, South Africa, Zambia, Ghana, Tanzania, Uganda, Ethiopia, and Zimbabwe are all in various phases of starting generic production
- The majority of countries now have policies regarding generic use
- President’s Emergency Plan for AIDS Relief (PEPFAR) and the Clinton Foundation both distribute generics
- Pharmaceutical companies offer tiered pricing, with lower prices available for poor countries
Notes on Generic ARVs in 2008.

In 2006, UNITAID was established. UNITAID is an international drug purchase facility that is intended to “provide long-term, sustainable and predictable funding to increase access and reduce prices of quality drugs and diagnostics for the treatment of HIV/AIDS, malaria and tuberculosis in developing countries.” UNITAID has helped to negotiate a system of tiered pricing with pharmaceutical companies. Tiered pricing means that the price at which the these companies sell their drugs is calculated using formulas based on average income per head, leading to lower prices in poor countries.

For more information on UNITAID: [http://www.unitaid.eu/](http://www.unitaid.eu/)
TRIPS and Second Line ARVs

• Patents are required on all new medications produced in member countries of the WTO (India, Brazil, Thailand, etc)
• Many patents have expired on first line drugs, but second line, or more recent drugs, are still under patent
  – 2nd line drugs are easier to take, less toxic, more effective and are needed in cases of toxicity or resistance
• 2007 cost of 2nd line regimen was US$1214 in low-income and US$3306 in middle-income countries
• Poor countries must wait for patents to expire or apply for an exception
  – Voluntary licensing or compulsory licensing
Notes on TRIPS and Second Line ARVs. Voluntary licensing: A government, an individual, or an organization can request a voluntary license from a patent holder (usually a large pharmaceutical company) to allow generic drugs to be supplied during a public health emergency, either through imports or by local production. A number of voluntary licenses have been granted to date including a license granted by Merck for South African generic producer Aspen Pharmacare to produce Efavirenz (a non-nucleoside reverse transcriptase inhibitor, or NNRTI).

A compulsory license is a government license that enables someone other than the patent holder to copy patented products and processes without fear of prosecution. Governments can issue them if a patent owner abuses their rights by, for example, failing to offer their product on the market, or offering it at a price that is too high for potential buyers to afford. Following the 2001 Doha agreement, a country can issue a compulsory license for a drug that treats a disease causing a severe health emergency in that country without royalties being paid, though production quantities are limited by this agreement.

The WTO paragraph 6 waiver which allows members who are unable to produce pharmaceuticals at home and are suffering a serious health crisis to import generics from other nations under compulsory licenses.
Notes on TRIPS and Second Line ARVs, cont. Licensing agreements have caused problems for some countries. Thailand has issued a number of compulsory licenses for antiretroviral drugs, including Sustiva, produced by Merck pharmaceuticals and Kaletra by Abbott pharmaceuticals. Unfortunately, this move by the Thai government provoked controversy with Abbott. As a result, Abbott announced that it would not be applying for licenses to sell seven of its newest products in Thailand (one of which was a new once-a-day heat resistant form of Kaletra which would have been extremely useful in the hot Thai climate) (AIDSMap, 2007). This controversy was difficult for Thailand, but subsequently, the price of Kaletra has dropped by half in many developing countries. In 2007, Brazil issued a compulsory license to produce a lower-cost, generic version of Merck's antiretroviral Efavirenz. Recognizing the repercussions that Brazil may face, President Luiz Inacio Lula da Silva said: *Between our trade and our health, we have chosen to look after our health.*” (AFP, 2008). To see the article about Thailand’s experience with compulsory licensing, see: Alcorn, K. (2007). “Abbott to withhold new drugs from Thailand in retaliation for Kaletra compulsory license,” AIDSMap. Available online at: http://www.aidsmap.com/en/news/00C7641B-57F5-4AB8-8876-9040425D4464.asp To see the above mentioned article about Brazil, see: Brazil: AFP (2008). “Brazil's success in AIDS fight depends on cheap drugs.” Available online at: http://afp.google.com/article/ALeqM5ieT0IHsJgOHEPjVBfKCZg75I0CRQ
HIV/AIDS Program Funding: A few examples

- Multilateral Agencies:
  - Global Fund to Fight AIDS, TB, and Malaria
  - World Bank

- National Government Initiatives:
  - PEPFAR (see slides 14, 15)
  - DFID (UK)

- Private Donors
  - Includes corporate donors, individual philanthropists, religious groups, charities and non-governmental organizations (NGOs)
    - Bill and Melinda Gates Foundation
    - William J. Clinton Foundation
Global Fund to Fight AIDS, TB and Malaria

• April 2001, United Nations Secretary General Kofi Annan called for the creation of a global fund

• Selected goals of the Fund are:
  – Provide funds, but not implement programs
  – Support programs that reflect national ownership
  – Awards based on disease burden and lack of resources
  – Support comprehensive programs that include prevention/treatment

• To date, Global Fund has spent $1.3 billion in 136 countries
Presidential Emergency Plan for AIDS Relief (PEPFAR)

PEPFAR: The US initiative to combat global HIV/AIDS
  – First initiative signed in 2003: 15 billion USD over 5 years for 15 focus countries (see notes).
  – Actual spending: 18.8 billion USD
  – Recently renewed for 2009-2013

- Goals 2004-2009 “2-7-10”
  - Prevent 7 million new AIDS infections
  - Treat at least 2 million people
  - Provide care for 10 million people with AIDS and orphans

- Goals 2009-2013
  - Prevent 12 million new HIV infections
  - Treat at least 3 million people
  - Provide care for 12 million people, including 5 million orphans
  - Plus… Expanded initiatives
Notes on PEPFAR. PEPFAR Focus countries are: Botswana, Cote d'Ivoire, Ethiopia, Guyana, Haiti, Kenya, Mozambique, Namibia, Nigeria, Rwanda, South Africa, Tanzania, Uganda and Zambia. Vietnam was added later to make a total of 15 countries. In 2003, the initial agreement gave recipients specific spending criteria.

- 55% for treatment of individuals with HIV/AIDS
- 15% for palliative care of individuals with HIV/AIDS
- 20% for HIV/AIDS prevention
- 10% for orphans and vulnerable children.

The 2008 reauthorization act does not specify in such detail how the money should be spent. Guidelines in the 2008 reauthorization include:

1. Over half of the funds are to be spent on treatment, including antiretroviral treatment, care for associated opportunistic infections and nutritional support for people living with HIV/AIDS.
2. In countries with generalized HIV epidemics, at least half of all funds for the prevention of sexual transmission should be allotted to: abstinence, delay of sexual debut, monogamy, fidelity, and partner reduction.
Notes on PEPFAR, continued.

3. 10% for helping orphans remains the same.

Expanded initiatives of the 2009-2013 plan include:

- Providing at least 80% of the target population with services including counseling, testing and treatment to prevent mother-to-child transmission of HIV
- Ensuring the proportion of children receiving treatment for HIV/AIDS is relative to the overall infected proportion
- Training at least 140,000 new health care workers
- Prevention activities have been expanded to include: diagnosis and treatment of other sexually transmitted infections, engaging vulnerabilities of women and girls, addressing stigma and discrimination
- In addition, the 2008 act calls for some broader interventions, including: strengthening health systems and collaborating with programs that address malaria, tuberculosis, child and maternal health, clean water, food and nutrition, education, and other needs.
- For more information and a PDF version of PEPFAR’s 2005 plan, please see PEPFAR’s website:

http://www.pepfar.gov/
PEPFAR: Limitations and Controversy

- Coordination difficulties amongst both U.S. and non U.S. agencies
- U.S. government policy constraints (see notes)
  - Regulations on quality standards slowed generics approval
  - A-B-C Priorities (Abstain – Be faithful – Condoms)
  - No needle exchange
  - Anti-Prostitution Clause
  - Global Gag Rule (no U.S. assistance to any NGO that uses funds from other sources to refer to or perform abortions)
- Shortages of qualified health workers in focus countries
- Focus country government restraints
- Weak infrastructure, including data collection and reporting systems, and drug supply systems.
PEPFAR: Limitations and Controversy.

1. A-B-C: The first PEPFAR act provided approximately two-thirds of all funds for preventing sexual transmission of HIV, specifically on abstinence and decreasing the number of partners—"be faithful" (known as "AB" strategies). One-third of the money for preventing sexual transmission was to be spent on condoms, media and outreach programs (C). In the original document, condom provision and promotion was intended only for those who practice high-risk behaviors including: "prostitutes, sexually active discordant couples [in which one partner is known to have HIV], substance abusers, and others". It is unclear if this policy will remain in the renewal document.

2. PEPFAR does not support any needle or syringe exchange programs

3. The anti-prostitution clause states that no funds will be made available to provide assistance to any group or organization that does not have a policy explicitly opposing prostitution and sex trafficking. This policy has drawn criticism from many countries and programs that would like to work with Commercial Sex Workers to reduce their risk of becoming HIV infected.

4. The "Global Gag Rule", also known as the "Mexico City Policy", denies U.S. international family planning funding to foreign non-governmental organizations that provide safe abortion services, counseling, referral, or information about safe abortion, advocate for changes in abortion law in their own country, conduct research on the effects of unsafe abortion, or otherwise work on safe abortion issues. This policy has indirectly affected some of the HIV/AIDS organizations around the world.

For more information on the successes and controversies of PEPFAR, see: AVERTing HIV and AIDS, PEPFAR, [http://www.avert.org/pepfar.htm, 2008](http://www.avert.org/pepfar.htm, 2008)
Treatment Access: The Goals

• 2003 UN General Assembly Meeting on HIV/AIDS
  – WHO, UNAIDS, and Global Fund declare the lack of access to HIV treatment a global health emergency

• 3 by 5 Initiative
  – First global initiative set by WHO in 2003
  – Called for 3 million people in developing countries to have access to treatment by the end of 2005
  – Goal not reached

• “All by 2010”
  – Goal set by G8 countries, reaffirmed by UN
  – Calls for universal access to treatment by 2010
    • Defined as: 80% of people in urgent need of treatment are receiving it
Treatment Access: The Goals
At the end of 2005, between 1.3 million people in low- and middle-income countries were receiving ARV medication. In sub-Saharan Africa, 810,000 were on treatment out of an estimated 4.7 million who needed antiretrovirals. Of the 152 countries targeted by the 3 by 5 initiative, 18 countries met the goal of providing treatment to at least half of their needy people by the end of 2005. The list included Poland, Thailand and thirteen countries from the Americas and the Caribbean. Only three African nations - Botswana, Namibia and Uganda - met their 50% targets.
As mentioned, the “all by 2010” initiative was set out by the member countries of the G8 Summit (Canada, France, Germany, Italy, Japan, Russia, the UK and the US). Reports on the progress to “All by 2010” indicate that the goal is not likely to be achieved, though significant progress is being made.
HIV and Popular Culture: TV/Movies/News

http://www.youtube.com/watch?v=iSfy4AhDDnw

Movie Trailer for Philadelphia, the story of a lawyer diagnosed with AIDS, 1993
http://www.youtube.com/watch?v=cl4B9AU45P4

Song from The Family Guy, an animated American sitcom, 2005
http://www.youtube.com/watch?v=biG957fCjpU
HIV and Popular Culture: Music

“Let’s Talk about AIDS,” by American pop band Salt-N-Pepa, 1992
http://www.youtube.com/watch?v=jPwEjhAuR8Y

“A Little Bit of Love,” Uganda All Star, 2007
http://www.youtube.com/watch?v=MNKXYtWDH5Q

HIV/AIDS Song from India
http://www.youtube.com/watch?v=IwUjEjrQdM8

HIV/AIDS Song from Argentina, 2007
http://www.youtube.com/watch?v=Xwnsu9QwY4E
Notes on HIV and Popular Culture: Music

1. Salt and Pepa altered their original song, “Let’s Talk about Sex” to incorporate the message about HIV/AIDS.

2. “A Little Bit of Love” by the Uganda All Star group was a collaboration of musicians from Uganda. It was produced by the Makerere University-Walter Reed Project (MUWRP), in collaboration with the Henry M. Jackson Foundation for the Advancement of Military Medicine and DownTown Entertainment.

3. The HIV/AIDS Song is from Secunderabad, India. It is known as “The Condom Song” and was made by Nrityanjali Academy / The International HIV/AIDS Alliance.

4. “Sin Triki Triki, No Hay Bang Bang” or “No rubber, no rumpy pumpy” was a project of a The Ministry of Health in Argentina, funded by the Global Fund.
HIV and AIDS Definitions: Review

• HIV (*Human Immunodeficiency Virus*): A retrovirus which primarily infects and damages human immune system cells such as CD4 T-cells, dendritic cells and macrophages and leads to a dysfunctional immune system and a condition called AIDS.

• AIDS (*Acquired Immunodeficiency Syndrome*): is defined by a CD4 count of less than 200 and/or a set of symptoms and infections resulting from a damaged immune system due to HIV infection.
HIV Lifecycle

1. Free Virus
2. Binding and Fusion: Virus binds to a CD4 molecule and one of two “coreceptors” (either CCR5 or CXCR4). Receptor molecules are common on the cell surface. Then the virus fuses with the cell.
3. Infection: Virus penetrates cell. Contents emptied into cell.
4. Reverse Transcription: Single strands of viral RNA are converted into double-stranded DNA by the reverse transcriptase enzyme.
5. Integration: Viral DNA is combined with the cell’s own DNA by the integrase enzyme.
6. Transcription: When the infected cell divides, the viral DNA is “read” and long chains of proteins are made.
8. Budding: Immature virus pushes out of the cell, taking some cell membrane with it.
9. Immature virus breaks free of the infected cell.
10. Maturation: Protein chains in the new viral particle are cut by the protease enzyme into individual proteins that combine to make a working virus.
Notes on HIV Lifecycle. In order for a virus, like HIV, to reproduce, it must infect a cell. In order to make new viruses, they must use the internal apparatus of a cell, and use it to make new viruses. Just as your body is constantly making new skin cells, or new blood cells, each cell often makes new proteins in order to stay alive and to reproduce itself. Viruses hide their own genetic material in the DNA of the cell, and then, when the cell tries to make new proteins, it makes new viruses as well. HIV mostly infects cells in the immune system. T cells, a type of white blood cell that normally warns the immune system about invaders, are the main immune system target of HIV. They have a large number of CD4 receptors, which allow HIV to bind easily. HIV enters into the T-cell and turns it into an HIV making factory.

2. Binding and Fusion: HIV has proteins on its envelope that are strongly attracted to the CD4+ surface receptor on the outside of the T-cell. When HIV binds to a CD4+ surface receptor, it activates other proteins on the cell's surface, allowing the HIV envelope to fuse to the outside of the cell. This process can be blocked by Entry Inhibitors.

3, 4. HIV's genes are carried in two strands of RNA, while the genetic material of human cells is found in DNA. In order for the virus to infect the cell, a process called "reverse transcription" makes a DNA copy of the virus's RNA. After the binding process, the viral capsid (the inside of the virus which contains the RNA and important enzymes) is released into the host cell. A viral enzyme called reverse transcriptase makes a DNA copy of the RNA. This new DNA is called "proviral DNA." Reverse transcription can be blocked by: Nucleoside Reverse Transcriptase Inhibitors (NRTIs), and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs).
Notes on HIV Lifecycle. 5. The HIV DNA is then carried to the cell's nucleus (center), where the cell's DNA is kept. Then, another viral enzyme called integrase hides the proviral DNA into the cell's DNA. Then, when the cell tries to make new proteins, it can make new HIVs. Integration can be blocked by integrase inhibitors.

6,7. Once HIV's genetic material is inside the cell's nucleus, it directs the cell to produce new HIV. Transcription can be blocked by antisense antivirals or transcription inhibitors (TIs), new classes of drugs that are in the earliest stage of research.

8,9,10. The final step begins with the assembly of new virus. Long strings of proteins are cut up by a viral enzyme called protease into smaller proteins. Once the new viral particles are assembled, they bud off the host cell, and create a new virus. The virus then enters the maturation stage, which involves the processing of viral proteins. Maturation is the final step in the process and is required for the virus to become infectious. With viral assembly and maturation completed, the virus is able to infect new cells. Each infected cell can produce a lot of new viruses. Viral assembly can be blocked by Protease Inhibitors (PIs). Maturation, a new target of companies developing anti-HIV drugs, may be blocked using Maturation Inhibitors. Sources: AIDSMeds & Poz, The HIV Life Cycle, 2008

http://www.aidsmeds.com/articles/hiv_life_cycle_5014.shtml
http://www.thebody.com/content/art6021.html
CD4 and Viral Load

[Diagram showing the progression of CD4+ T lymphocyte count and HIV RNA load over time.]

- **Primary Infection**: Initially high CD4+ T lymphocyte count, with wide dissemination of virus and seeding of lymphoid organs.
- **Clinical Latency**: CD4+ T lymphocyte count decreases to normal levels, accompanied by opportunistic diseases and constitutional symptoms.
- **Death**: CD4+ T lymphocyte count continues to decline, leading to death.
HIV Transmission

Semen
Vaginal Fluid

Unprotected sex with an infected person

Blood

Contaminated needles and syringes
Tainted transfusions
Sharing unsterilized razors during cutting practices
Unprotected sex

Breastmilk

Pregnancy, Birth or breastfeeding from infected mother to child
Estimated Per-Act Risk for Acquisition of HIV, by Exposure Route

- Insertive Oral Intercourse: 0.5
- Receptive Oral Intercourse: 1
- Insertive Penile-Vaginal Intercourse: 5
- Insertive Anal Intercourse: 6.5
- Receptive Penile-Vaginal Intercourse: 10
- Percutaneous Needle Stick: 30
- Receptive Anal Intercourse: 50
- Needle-Sharing IDU: 67

Risk/10,000 Exposures
Notes on Estimated Per-Act Risk for Acquisition of HIV, by Exposure Route

These estimates of risk of transmission from sexual exposure assume no condom use. The risk for blood transfusion is approximately 9,000 per 10,000 exposures to blood contaminated with HIV.

*Refers to oral intercourse performed on a man.
HIV Prevention

- **Semen and Vaginal Fluid**
  - Condoms
  - Abstinence

- **Blood**
  - Clean needles and syringes
  - Safe blood supply
  - New or sterilized razors during cutting practices
  - Condoms

- **Breastmilk**
  - HIV testing for mom before delivery
  - HIV treatment for mom and newborn
  - Formula where water supply is clean
HIV/AIDS Diagnostic Criteria

• Laboratory Tests
  – ELISA
  – Western Blot
  – Rapid Test
  – PCR

• Staging Systems

• Clinical and Laboratory Criteria
Laboratory Testing: ELISA and Western Blot

- ELISA identifies antibodies to HIV
- Other illnesses can result in a + test (ex. Autoimmune disease, viral infection, immunizations)
- Pregnancy can cause false +
- ONLY accurate in children over 18 months old
- Window Period up to 12 weeks (during which person may be infected but without positive tests)
- Elisa test MUST be confirmed with Western Blot
Notes on ELISA and Western Blot.

Approximately 50% of ELISA tests will result positive within 22 days after HIV transmission. 95% are positive within 6 weeks. The sensitivity is >99.9%. As false positives may occur as normal biologic variants or in association with other illnesses or vaccinations, positive results must be confirmed with a confirmatory test (Western Blot). The specificity of positive results by the Western Blot combined with ELISA approaches 100%, even in low risk populations. Indeterminate Western Blot may result from early HIV infection, HIV-2 Infection, autoimmune disease, pregnancy and recent tetanus toxoid administration.

Laboratory Testing: Rapid Tests

- Rapid Tests
  - Detect HIV antibodies
  - Only accurate in children over 18 months old
  - Window period up to 12 weeks
  - MUST be confirmed
  - Results available in a few minutes to a few hours
Notes on Laboratory testing.

Blood based rapid testing, which can be done by finger stick or whole blood plasma, is 99.3% sensitive and 99.8% specific. The OraQuick Advanced saliva test has similar sensitivity and specificity, but was noted in New York City and San Francisco to have an unusually high number of false positives. This was thought to be caused by storing and handing errors.

Names of Rapid Test types: OraQuick Advance, Reveal G2, Uni-Gold Recombigen, Multispot, Sure Check

If a rapid test is positive, the standard practice is to send the sample for confirmation with Western Blot. If no Western Blot is available, two rapid tests are used to increase the sensitivity.

Rapid testing is negative 90% of the time for HIV negative children at 9 months. 100% negative if the child is negative at 18 months.

Laboratory Testing: HIV Viral Load

- Polymerase Chain Reaction
  - Highly sensitive and specific for HIV
  - Amplifies HIV RNA or DNA to detect or quantify its presence
  - Used for diagnosing acute HIV
  - Used in children <18 months of age for diagnosis
  - Expensive

Photo: http://www.stanford.edu/group/parasites/ParaSites2004/Onchocerciasis/diagnosis.htm
HIV Diagnosis in Adults: Early Infection

- Acute HIV Syndrome
  - Experienced by approximately 40 - 90%
  - Within 2-4 weeks of infection with HIV
  - Non-specific symptoms: fevers (96%), enlarged lymph nodes (74%), sore throat (70%), rash (70%), sore muscles (54%)
  - High amount of virus in the blood
  - Diagnosed by HIV Viral Load testing
  - Rapid Test and/or ELISA negative or indeterminate
    - Repeat test after 3 months
  - HIV highly transmissible during acute infection

Department of Health and Human Services, 2006
Presumptive Diagnosis of AIDS in the absence of laboratory markers

- Major Signs (2 or more of the following):
  - Weight loss of at least 10% of total body weight
  - Chronic diarrhea for longer than 1 month
  - Prolonged fever for longer than 1 month
- Minor Signs (1 or more required along with major signs)
  - Persistent cough for longer than 1 month
  - Generalize pruritic dermatitis
  - History of herpes zoster
  - Oropharyngeal candidiasis
  - Chronic progressive or disseminated herpes virus infection
  - Generalized lymphadenopathy
- The presence of generalized Kaposis Sarcoma (KS) or Cryptococcal meningitis is also sufficient for the diagnosis of AIDS
HIV Diagnosis in Infants and Children <18 months

- Laboratory Diagnosis:
  - Gold standard for children <18 months is Polymerase Chain Reaction (PCR)
  - ELISA and Rapid Test not accurate
- Presumptive diagnosis of HIV in children under 18 months in the absence of lab markers
  - Clinical symptoms of 2 more more of the following:
    - Thrush
    - Sepsis and/or
    - Severe pneumonia
- Also associated:
  - Recent HIV related maternal death
  - Mother with advanced HIV, child CD4 count of <20%
Guidelines for Diagnosis and Treatment of HIV/AIDS

• World Health Organization
  – Global Priorities
  – HIV Prevention and Care
  – HIV Testing and Counseling
  – Post-Exposure Prophylaxis (PEP)
  – Antiretroviral Roll-Out and Scale-up
  – TB/HIV Co-infection

• Ministry of Health
  – Countries may choose to design their own guidelines or follow WHO guidelines

WHO, HIV/AIDS Guidelines
HIV Infection case – Esther

Esther was introduced earlier in this presentation. Her husband died and she is afraid that he might have been HIV infected.

She presents to the clinic for antenatal care in her 2\textsuperscript{nd} trimester.

She is offered an HIV test.

Follow Esther’s case in Module 113, HIV Care and Treatment
Summary

• HIV/AIDS disproportionately affects Sub-Saharan Africa.
• The HIV/AIDS epidemic is taking a devastating toll on all sectors of life, including health, education, agriculture, household and national economies.
• The history of HIV has been marked by significant scientific, medical, and public health advances.
• Strides have been made in our understanding of the virus, its origins, transmission and prevention, diagnostics and treatment.
• Controversy has surrounded the global provision of antiretroviral medications but significant advancements have been made with unprecedented international cooperation and public-private partnerships.
• The International and national efforts to fight HIV/AIDS have included large amounts of funding, public education and even popular culture.
Books and Guidelines


Weblinks


- AVERTing HIV & AIDS, PEPFAR, 2008 [http://www.avert.org/pepfar.htm]


Weblinks (continued)

  [http://www.kff.org/hivaids/timeline/hivtimeline.cfm]

- Oxfam UK, Cut the Cost Campaign Policy Papers, 2001

- Presidential Emergency Plan for AIDS Relief (PEPFAR)
  [http://www.pepfar.gov]

- UNITAID [http://www.unitaid.eu]

- World Health Organizations, HIV Guidelines
  [http://www.who.int/hiv/pub/guidelines/en]

- World Trade Organization (WTO), Fact Sheets
Credits

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