Africa

- Africa, is the origin of the HIV epidemic
- HIV has caused immense suffering
  - AIDS causes households to dissolve
  - AIDS strips families of their assets and income earners
  - The epidemic adds to food insecurity in many areas
  - It is hard to overemphasize the trauma and hardship that children are forced to bear ( orphaned, responsibility )
  - Professional class of teachers, healthcare workers, missing
  - Biggest increase in deaths has been among adults aged between 20 and 49 years (60%)
- **Africa had the first epidemic, and it has by far the worst epidemic**
  - As of 2011, the HIV prevalence rate in Swaziland was the highest in the world at 26.0 percent of persons aged 15–49

**Causes:**
- Incursion of humans into natural habitats of non-human primates
- European colonialism and exploitation
- Poverty
  - Lack of education
  - Lack of disposable needles
  - Lack of women’s rights
- **Concurrency in sexual relationships**
- Male circumcision or lack thereof
- Violence against women
- Each day in Africa (2011):
  - 3300 people die of AIDS.
  - 5000 people are infected with the HIV virus.
- Overall prevalence = 4.9%
- Although many governments
  - in Sub-Saharan Africa denied that there was a problem for years, they have now begun to work toward solutions
African incidence of HIV, year 2000

Percentage of the Adult (ages 15-49) population with HIV/AIDS [darker is higher incidence]
S. Africa, the last of the African nations to adopt widespread ART, and the last to begin Life Expectancy recovery

President Thabo Mbeki was an HIV-AIDS denier*, whereas the new President, Jacob Zuma has instituted a policy of early and extensive ART treatment. The results have been dramatic.

*during almost a decade in office Mbeki had questioned whether H.I.V. causes AIDS and suggested that antiretroviral drugs could be harmful

Harvard researchers estimated, in 2008 that the delay by Mr. Mbeki’s government in using antiretroviral drugs to prevent women from infecting their newborns earlier this decade led to the deaths of 35,000 babies, and that 330,000 people died prematurely for lack of treatment
• HIV incidence has fallen by more than 25% between 2001 and 2009 in 22 sub-Saharan countries.

The general state of genital health is an important variable between countries and cultures; concurrent infections that increase inflammation or create lesions in the vaginal or rectal tissues facilitate HIV-1 transmission.

Epidemiological studies strongly indicate that transmission is linked to viral shedding, that is, the amount of infectious virus that is present in genital fluids. This is in turn linked to the disease stage, and is highest during ACUTE INFECTION and late-stage AIDS.

Acutely infected individuals pose a particularly profound risk, which is why epidemics usually spread explosively when they strike a new population; highly viraemic people unaware of their newly infected status are at high risk for transmitting the infection to new individuals who then become highly viraemic while remaining sexually active — a vicious spiral.
High rates of HIV in sub-saharan Africa:

- As of 2000, heterosexual transmission accounted for around 90% of transmission.
- Why the high rate of heterosexual transmission in Africa, when the probably of transmission is thought to be so low?

Consider:

- Lack of male circumcision—4-5-fold difference in HIV between southern and western Africa (correlative geographic evidence).
- Confounding effects—all Muslims, only 6% of non-Muslims circumcised.
- Three randomized controlled trials in Africa demonstrated that adult medical male circumcision (MMC) is effective in reducing HIV acquisition by 50–60%.
- Reduction in HIV target cell populations through removal of mucosal foreskin.
- Increased keratinization of penile skin other than the foreskin.
- Doesn’t explain why spread in southern Africa is so much higher than India or Europe.
As the most common causative agent of GUD worldwide, HSV has an important role in HIV infections.

HIV-1 RNA was detected in ulcer swabs in 25 of 26 men with symptomatic HSV-2 infection, and the levels exceeded 10,000 copies ml$^{-1}$ of swab sample.

The levels of HSV shedding correlate with HIV plasma viral levels. Even asymptomatic HSV shedding was found to be associated with increased HIV shedding.

Correlation is men, not women.

The ADJUSTED-RISK RATIO for HIV acquisition for a person with GUD ranges from 2.2 to 11.3, whereas non-ulcerative STDs show adjusted-risk ratios of 3–4.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Aetiological agents</th>
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<tbody>
<tr>
<td>Systemic infections without mucosal disease</td>
<td>HIV, hepatitis B, cytomegalovirus</td>
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<tr>
<td>Genital ulcers</td>
<td><em>Haemophilus ducreyi</em>, herpes simplex virus 1 and 2, <em>Treponema pallidum</em></td>
</tr>
<tr>
<td>Mucosal inflammation</td>
<td><em>Neisseria gonorrhoeae</em>, <em>Chlamydia trachomatis</em>, <em>Trichomonas vaginalis</em></td>
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<td>Changes in epithelial cells</td>
<td>Human papillomavirus</td>
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</table>
Female and male genitalia and susceptibility points for HIV infection

The protective effect of MMC against HIV acquisition did not change when adjusting for baseline and incident HSV-2 or GUD. However,

- incident HSV-2 infection more than tripled the risk of HIV acquisition
- GUD during follow-up increased the risk of HIV acquisition by seven-fold
Stratified cervicovaginal epithelium in women; inner foreskin, penile glans in men

Stratified cervicovaginal epithelium In line with their protective function, stratified genital epithelial cells are not susceptible to HIV-1 infection and do not transcytose viral particles

But, Epithelial micro-abrasions can be detected in 60% of women following consensual intercourse, and are also frequently observed on the inner foreskin and penile glans

the outermost, apical surface of the genital epithelial barrier comprises a superficial layer of dead epithelial cells that is impervious to the virus and is renewed every three days
Unlike its vaginal counterpart, the rectal epithelium provides little or no physical protection against potential trauma during intercourse.

The rectum, unlike the genital tract, is populated with organized lymphoid tissues (lymphoid follicles) that contain specialized microfold cells (M CELLS) that are capable of binding and presenting HIV-1 to the underlying lymphoid tissue (seems to be X4 virus only).

Intestinal epithelial cells can themselves transcytose HIV-1 particles to the underlying lamina propria when exposed to infected seminal leukocytes (macrophages or T cells).
Sub-epithelial dendritic cells (DCs) express mannose C-type lectin receptors (CLR), including DC-SIGN, that function as highly efficient virus-attachment factors.

Only a small proportion of DCs are vulnerable to productive HIV-1 infection.

DCs can bind HIV-1 particles efficiently and then internalize the virus into intracellular endocytic vacuoles.

This is a natural process; the role of DCs as sentinel cells is to sample incoming pathogens or their antigens, transport them to regional lymph nodes and, once there, present them to T and B cells and initiate adaptive immune responses.

HIV-1 can remain infectious within the DCs for up to five days without infecting the cell.

DCs interact with, and activate, CD4+ T cells in T-cell-rich regions of the lymph nodes, the virus is in a perfect environment for its rapid and efficient amplification.

The migration of the DCs to the draining lymph nodes has transported the internalized virus to where it wants to be — the 'Trojan Horse' scenario.

HIV-1 might also be disseminated to the draining lymph nodes by migrating CD4+ T cells. A similar phenomenon also occurs in herpes simplex virus infection.
Does violence against women explain the increased incidence of heterosexual spread?

Lancet 2010; 376: 41–48

Interpretation: Relationship power inequity and intimate partner violence increase risk of incident HIV infection in young South African women. Policy, interventions, and programmes for HIV prevention must address both of these risk factors and allocate appropriate resources.
Does concurrency explain the high rates of heterosexual transmission in Africa?

HIV transmission in most Asian countries remains strongly associated with particularly high-risk activities—ie, injection-drug use, male-male sex, prostitution and, in China, paid donation of plasma.

Infection rates in adults in South Africa, Botswana, Zimbabwe, and western Kenya range from 20 to 40%, roughly an order of magnitude higher than anywhere else in the world (2004, before the increased access to ART).

Demographic surveys suggest that African men do not have more sexual partners than men elsewhere.

A comparative study of sexual behaviour found that men in Thailand and Rio de Janeiro were more likely to report five or more casual sexual partners in the previous year than were men in Tanzania, Kenya, Lesotho, or Lusaka, Zambia.

Very few women in any of these countries reported five or more partners a year.

Men and women in Africa report roughly similar, if not fewer, numbers of lifetime partners than do heterosexuals in many western countries

HOWEVER, there is more concurrency.

in Africa men and women often have more than one—typically two or perhaps three—concurrent partnerships that can overlap for months or years.
Incidence of HIV by transmission type

* Casual HS = casual heterosexual sex
* PWID = People who inject drugs
* MSM = Men who have sex with men
Mathematical modeling to compare the spread of HIV in two populations:

- one in which serial monogamy was the norm
- one in which long-term concurrency was common

Although the total number of sexual relationships was similar in both populations, HIV transmission was much more rapid with long-term concurrency—and the resulting epidemic was ten times greater.

The effect of such concurrency on the spread of HIV is exacerbated by the fact that viral load, and thus infectivity, is much higher during the initial weeks or months after infection.

Therefore, as soon as one person in a network of concurrent relationships contracts HIV, everyone else in the network is placed at risk.

By contrast, serial monogamy traps the virus within a single relationship for months or years.

- Per-act probability of heterosexual HIV transmission is quite low, the much higher number of cumulative sexual acts—and hence the likelihood of transmission—within any given relationship was much greater in concurrency relationships.

- Although most African women in concurrent partnerships are not prostitutes, such relationships often include a quasi-transactional aspect, related to issues of gender inequality, poverty, and the globalization of consumerism.

- Because most Africans do not have exorbitant numbers of partners, they may not fully realize how dangerous, especially in regions of high HIV-prevalence, such behaviors actually are.
Uganda policy: Zero Grazing
Please view *THE AGE OF AIDS Part One: Six, The Power of Leadership*

- The government communicated a clear warning and prevention recommendation: AIDS, or “slim,” was fatal and required an immediate population response based on “zero grazing,” that is, faithfulness to one partner
- substantial HIV reductions in Uganda resulted from public-health interventions that triggered a social process of risk avoidance manifested by radical changes in sexual behaviors
- *The outcome was equivalent to a highly effective vaccine (80%) effectiveness*
- Widespread support for condom distribution using social marketing (i.e., commercial techniques to achieve social goals), voluntary testing and counseling, and improved treatment of sexually transmitted infections largely came after the initial declines in HIV incidence and prevalence
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<tr>
<td>People living with HIV</td>
<td>30.0 million [27.2-33.1 million]</td>
<td>31.0 million [28.2-34.1 million]</td>
<td>31.7 million [28.9-34.8 million]</td>
<td>32.2 million [29.4-35.3 million]</td>
<td>32.5 million [30.1-36.0 million]</td>
<td>32.8 million [30.7-36.7 million]</td>
<td>33.2 million [31.5-37.7 million]</td>
<td>33.5 million [31.9-38.3 million]</td>
<td>34.0 million [31.9-38.3 million]</td>
<td>34.4 million [31.5-37.7 million]</td>
<td>34.9 million [32.2-38.8 million]</td>
<td>35.3 million</td>
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<td>New HIV Infections (Total)</td>
<td>3.4 million [3.1-3.7 million]</td>
<td>3.3 million [3.0-3.6 million]</td>
<td>3.1 million [2.9-3.5 million]</td>
<td>3.0 million [2.7-3.3 million]</td>
<td>2.9 million [2.6-3.2 million]</td>
<td>2.8 million [2.5-3.1 million]</td>
<td>2.7 million [2.4-3.0 million]</td>
<td>2.6 million [2.2-2.9 million]</td>
<td>2.6 million [2.2-2.9 million]</td>
<td>2.5 million [2.1-2.9 million]</td>
<td>2.5 million [1.9-2.7 million]</td>
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<td>New HIV Infections (adults)</td>
<td>2.8 million [2.6-3.1 million]</td>
<td>2.7 million [2.5-3.0 million]</td>
<td>2.6 million [2.3-2.9 million]</td>
<td>2.4 million [2.2-2.7 million]</td>
<td>2.3 million [2.1-2.6 million]</td>
<td>2.3 million [2.0-2.6 million]</td>
<td>2.2 million [1.9-2.5 million]</td>
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<td>2.0 million [1.7-2.4 million]</td>
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<td>New infections (children)</td>
<td>550,000 [500,000-620,000]</td>
<td>560,000 [510,000-630,000]</td>
<td>560,000 [520,000-620,000]</td>
<td>550,000 [510,000-610,000]</td>
<td>540,000 [490,000-580,000]</td>
<td>520,000 [470,000-550,000]</td>
<td>480,000 [410,000-520,000]</td>
<td>450,000 [360,000-470,000]</td>
<td>360,000 [280,000-370,000]</td>
<td>310,000 [230,000-320,000]</td>
<td>260,000 [230,000-320,000]</td>
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<td>AIDS-related deaths</td>
<td>1.9 million [1.7-2.2 million]</td>
<td>2.1 million [1.9-2.4 million]</td>
<td>2.2 million [2.0-2.5 million]</td>
<td>2.3 million [2.1-2.6 million]</td>
<td>2.3 million [2.0-2.6 million]</td>
<td>2.2 million [1.9-2.5 million]</td>
<td>2.1 million [1.8-2.4 million]</td>
<td>2.0 million [1.7-2.3 million]</td>
<td>1.9 million [1.7-2.2 million]</td>
<td>1.8 million [1.6-2.1 million]</td>
<td>1.6 million [1.4-1.9 million]</td>
<td>1.6 million</td>
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<td>People accessing treatment</td>
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<td>1.3 million</td>
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<td>2.0 million</td>
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<td>2.9 million</td>
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<td>Resources</td>
<td>US$ 3.8 billion</td>
<td>US$ 4.6 billion</td>
<td>US$ 5.7 billion</td>
<td>US$ 7.4 billion</td>
<td>US$ 8.8 billion</td>
<td>US$ 10.5 billion</td>
<td>US$ 14.6 billion</td>
<td>US$ 15.5 billion</td>
<td>US$ 15.6 billion</td>
<td>US$ 17.1 billion</td>
<td>US$ 18.9 billion</td>
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<td>Region</td>
<td>People living with HIV 2012</td>
<td>New HIV infections 2012</td>
<td>AIDS-related deaths 2012 (total)</td>
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<td>Sub-Saharan Africa</td>
<td>25.0 million [23.5 million-26.6 million]</td>
<td>2.9 million [2.7 million-3.3 million]</td>
<td>1.6 million [1.4 million-1.8 million]</td>
<td>230 000 [200 000-280 000]</td>
<td>1.2 million [1.1 million-1.3 million]</td>
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<td>South and South-East Asia</td>
<td>3.9 million [2.9 million-5.2 million]</td>
<td>200 000 [170 000-270 000]</td>
<td>270 000</td>
<td>21 000 [16 000-32 000]</td>
<td>220 000 [150 000-310 000]</td>
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<td>East Asia</td>
<td>880 000 [650 000-1.2 million]</td>
<td>8 200 [5 800-11 000]</td>
<td>81 000 [34 000-160 000]</td>
<td>1 500 [1 000-3 300]</td>
<td>41 000 [25 000-64 000]</td>
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<td>Latin America</td>
<td>1.5 million [1.2 million-1.9 million]</td>
<td>40 000 [32 000-52 000]</td>
<td>86 000 [57 000-150 000]</td>
<td>2 100 [1 000-4 600]</td>
<td>52 000 [35 000-75 000]</td>
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<td>Western and Central Europe</td>
<td>860 000 [800 000-930 000]</td>
<td>1 600 [&lt;1 300-2 000]</td>
<td>29 000 [25 000-35 000]</td>
<td>&lt;200 [&lt;100-&lt;200]</td>
<td>7 600 [6 900-8 300]</td>
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<td>North America</td>
<td>1.3 million [980 000-1.9 million]</td>
<td>4 500 [4 000-5 800]</td>
<td>48 000 [15 000-100 000]</td>
<td>&lt;200 [&lt;200-&lt;500]</td>
<td>20 000 [16 000-27 000]</td>
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<td>Eastern Europe and Central Asia</td>
<td>1.3 million [1.0 million-1.7 million]</td>
<td>19 000 [16 000-24 000]</td>
<td>130 000 [89 000-190 000]</td>
<td>&lt;1 000 [&lt;500-&lt;1 200]</td>
<td>91 000 [68 000-120 000]</td>
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<td>Caribbean</td>
<td>250 000 [220 000-280 000]</td>
<td>16 000 [14 000-19 000]</td>
<td>12 000 [9 400-14 000]</td>
<td>&lt;500 [&lt;500-&lt;1 000]</td>
<td>11 000 [9 400-14 000]</td>
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<td>Middle East and North Africa</td>
<td>260 000 [200 000-380 000]</td>
<td>20 000 [14 000-31 000]</td>
<td>32 000 [22 000-47 000]</td>
<td>3 000 [2 000-4 600]</td>
<td>17 000 [12 000-26 000]</td>
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<td>Oceania</td>
<td>51 000 [43 000-59 000]</td>
<td>3 100 [2 400-4 100]</td>
<td>2 100 [1 500-2 700]</td>
<td>&lt;500 [&lt;200-&lt;500]</td>
<td>1 200 [&lt;1 000-1 800]</td>
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<td>Global</td>
<td>35.3 million [32.2 million-38.8 million]</td>
<td>3.3 million [3.0 million-3.7 million]</td>
<td>2.3 million [1.9 million-2.7 million]</td>
<td>260 000 [230 000-320 000]</td>
<td>1.5 million [1.4 million-1.9 million]</td>
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Reason for optimism in Africa

Since 2005, the number of people receiving lifesaving antiretroviral therapy (ART) has increased tenfold—from 625,000 to more than 6 million at the end of 2012. Botswana, Namibia, Rwanda, Swaziland and Zambia reached universal access to HIV treatment (80% coverage of people eligible for treatment) by the end of 2011. Kenya, Malawi, South Africa and Zimbabwe are on track to reach this goal." - UNAIDS

AIDS-related mortality has declined worldwide from an estimated 2.3 million a year in 2005 to 1.7 million in 2011, 1.2 million of those dying in 2011 in sub-Saharan Africa (http://tinyurl.com/ad9o4la). Saving 600,000 lives a year is real progress. But over a million deaths a year means the fight against AIDS is still far from over.

CHAI programs have led to more than $1 billion in cost savings since 2007 for developing countries.

http://www.clintonhealthaccess.org
6.3 million
Number of people living with HIV receiving antiretroviral therapy in eastern and southern Africa in 2012

72%
Coverage of services to eliminate new HIV infections among children in eastern and southern Africa in 2011 [64-80%]

17.1 million
Number of people living with HIV in eastern and southern Africa in 2011 [16.3-17.9 million]

1.2 million
Number of new HIV infections in eastern and southern Africa in 2011 [1.1-1.3 million]

800 000
Number of AIDS-related deaths in eastern and southern Africa in 2011 [730 000-890 000]

30%
Reduction in new HIV infections between 2001 and 2011 in eastern and southern Africa

50%
Reduction in new child infections between 2001 and 2011 in eastern and southern Africa

38%
Reduction in AIDS-related deaths between 2005 and 2011 in eastern and southern Africa
South Africa has more people with HIV than any other country in the world.

A nurse takes a blood sample from Nkosi Minenhle, 15, in a mobile clinic set up to test students for HIV at Madwaleni High School in KwaZulu Natal, South Africa.

The South African government is simplifying AIDS care, cutting treatment costs and providing antiviral drugs to almost 2 million people every day.
Nearly 350,000 South Africans died of AIDS in 2005. But in 2012, that number dropped by nearly half to about 190,000 deaths, the government

A universal HIV treatment program could have been put in place years earlier, Venter says, if there had been the political will from Mbeki. "In my view, Mbeki and his Cabinet at the time were responsible for a minimum of 330,000 deaths and probably closer to half of a million, if they had had the energy we are seeing from the current government," he says.

President Mbeki had been publicly questioning whether HIV causes AIDS. His government appeared in no rush to make antiretroviral drugs available, and his minister of health was touting garlic, beet root and lemon peel as a remedy.
South Africa Weighs Starting HIV Drug Treatment Sooner

A woman waits to get AIDS drugs on April 8 at a clinic in Ga-Rankuwa, South Africa, about 55 miles north of Johannesburg. New WHO guidelines say patients should start HIV treatment much earlier, before they become extremely sick.
2010 WHO treatment eligibility criteria, which recommended initiating ART at CD4 ≤ 350 cells/µL
The co-receptors that are most relevant to HIV-1 infection are CCR5 and CXCR4. Early in infection, CCR5-using (R5) viruses usually predominate. CXCR4-using (X4) viruses arise in a significant minority of infected individuals after several years, and are associated with accelerated disease.

X4 viruses are rarely found in early infection, but when they are, the disease course is rapid. Individuals genetically lacking CCR5 owing to homozygosity for the defective CCR5-32 allele are strongly protected from acquiring HIV-1 sexually (and also vertically and intravenously).

The absence of CCR5 might be protective at the level of transmission events in and near the genital tissues, for example, a lack of CCR5 on dendritic cells (DCs) or Langerhans cells (LCs) might be important. Alternatively, CCR5 deficiency might hinder the efficient amplification of HIV-1 in lymphoid tissues, thereby explaining why vertical and intravenous transmission are also inefficient in CCR5-32 homozygotes. In either scenario, there is a compelling argument for targeting CCR5 and the viruses that use it.

However, X4 viruses can be transmitted after vaginal inoculation in the macaque model, and some humans — including CCR5-32 homozygotes — can acquire X4 strains sexually, so, X4 viruses should not be ignored when an intervention strategy is designed.
An overwhelming body of evidence indicates that STDs that cause mucosal inflammation and ulcers contribute to the spread of HIV, by increasing infectiousness, susceptibility or both.

India, eastern European countries, Russia and China are now experiencing rapid increases in the prevalence of HIV and STDs.

In China, for example, the economic reforms of the 1980s have led to an STD epidemic and a high risk of the heterosexual spread of HIV, especially through commercial sex workers.
West Africa:

<3% in adult population
5-15% among clients of sex workers
20-75% among the sex workers themselves

South Africa:
35% of adult women are HIV-infected

Nairobi screened sex workers for Chancroid and STD which causes large and painful ulcerations of the genitalia
1981-4% sex workers were HIV positive (1400-encounters/year)
1983->67% were HIV positive

Men at STD clinic
0% were HIV positive in 1980
6% in 1982
15% in 1985
16.5 Central Asia and Eastern Europe: Hotspots in the Worldwide HIV Epidemic

• HIV incidence increased by more than 25% in 5 countries in Eastern Europe and Central Asia between 2001 and 2009.
• Primary route of transmission is intravenous drug use.
• Molecular analysis of HIV strains isolated from people in Belarus, Russia, Kazakhstan, and other former Soviet Union countries evolved from southern Ukraine.
  – Followed heroin trading routes
HIV and Heroin Drug Trafficking Routes

16.6 AIDS in China

- 48,000 new HIV infections per year
- Home to one of the largest injection drug user populations in the world
- High degree of stigmatization of people living with HIV in China
- Termination of pregnancy was recommended to pregnant women living with HIV.