The Current State of the Epidemic
HIV & AIDS in the United States

AIDS deaths in the U.S. decreased by 42% from 1996 - 97

In 2005:

> 1,000,000 Men, Women & Children are infected with HIV

> 45,000 new infections

Women accounted for ~ 30% of new HIV diagnoses in U.S. adults
U.S. HIV & AIDS by Race/Ethnicity

- Among new AIDS cases in men, 60% were in African Americans and Hispanics
- Among new AIDS cases in women, 80% were in African Americans and Hispanics
- AIDS is now the #1 killer of African American women age 25 - 34
- HIV incidence among African Americans is 8 times higher than among Caucasians

Proportion of US AIDS cases among adults and adolescents, by race/ethnicity and year of diagnosis 1985-2003

U.S. versus GLOBAL HIV NUMBERS

> 40 million are now HIV-infected

→ 5 million infected in 2005 @ a rate of > 11,000/day

  ~ 1500 in children < 15 years old
  ~ 10,000 in persons 15 - 49 years old (50% women)

→ ~ 1% of sexually active adults are infected

→ 90% of the infected don’t know it!

→ >3 million died from AIDS in 2005

  > 33% were adult women
  ~ 20% were under 15 years old
HIV in Sub-Saharan Africa

- 8% of 15-49 years old are infected
- In Botswana, Zimbabwe, Nigeria 25 - 35% of adults are infected
- In South African provinces 25 - 45% of pregnant women are infected
Twenty African nations have suffered severe human development reversals in the past decade (health, education, economic wealth).

**First Reports of the Disease**

**October 1980 - May 1981**

Michael Gottlieb, physician in Los Angeles
Noted 5 young male patients, all with a rare pneumonia

→ Caused by a single-cell protozoan: *Pneumocystis carinii pneumonia* (PCP)

→ Rare condition previously linked with failure of the immune system

→ All had other active viral and fungal infections

→ All were sexually active gay men

What is the Cause of the Disease?

Environment & Behavior? NO
In 1981: Described as Gay-related Immune Deficiency (GRID)
   Early proposed cause: Recreational use of amyl nitrate

Genetics? NO
No evidence of familial linkage between affected individuals

Pathogen? YES
In 1981 and 1982:
   Observed clustering of patients linked by sexual contact
      (heterosexual & homosexual)
   Appearance in intravenous drug users
   Appearance among blood transfusion recipients and hemophiliacs
   → Transmissible agent present in the blood and a subset of body fluids
   → Renamed Acquired Immune Deficiency Syndrome

The Discovery of Human Immunodeficiency Virus Type-1

Françoise Barré-Sinoussi & Luc Montagnier

Begins in Jan. 1983:
Lymph node biopsy from the neck of Frederic Brugiere

Virus was successfully cultured from these cells and infected healthy immune system cells upon exposure

Virus appeared to target a specific type of human T-cell

Shown to be a Retrovirus based on a specific enzymatic activity
The societal context of AIDS produced many early theories for the origin of the disease

**Major questions:**
- Is AIDS a new or old disease?
- Where did it first arise?
- Where did the virus come from?

**Simian Immunodeficiency Viruses**

There are several SIV strains specific to certain species of monkey

- SIVagm - African green monkey
- SIVmnd - Mandrill ape
- SIVsm - Sooty Mangabey monkey

Under normal conditions, each strain only infects a specific species and does not infect humans

Only chimpanzees can be infected with HIV
HIV came from a strain of Simian Immunodeficiency Virus

In 1999: Isolations of SIVcpz from chimpanzees in captivity
   → Nearly identical to HIV-1
   → Probably entered humans in the early 20th C

*Pan troglodytes troglodytes* chimp species found in Cameroon, West equatorial Africa, Central Africa

The natural habitat of these chimpanzees directly coincides with the geographical pattern of the early HIV-1 epidemic

The Zoonosis of HIV-1

Chimpanzees have been infected with SIVcpz for thousands years, but rarely display illness

Cross-species transmission of SIV has been frequent

But up until about 40 - 50 years ago infected individuals rarely left the region → probably confined the infection to local areas

Bush-meat trade along new roadways has increased exposure to SIVcpz

Facilitates the movement of infection into urban areas

→ Chimpanzees are the natural host reservoir for HIV-1
Molecular Components of HIV

RNA
Protein
Lipid

Why does HIV need our cells?

HIV-infected human T-cell
DNA is the primary information archive of living systems.

Genetic information is a linear chemical code.

Central Dogma of Molecular Biology

Addresses the...
Transfer of genetic information from one macromolecule to another

&

Utilization of genetic information to synthesize functional macromolecules.
DNA must be accurately copied for genetic information to be passed on.

**DNA REPLICATION** is the essential first step in genetic inheritance.

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The functional expression of genetic information begins with an intermediary macromolecule: **RNA**.

**TRANSCRIPTION** is the process of using DNA as a template to guide RNA synthesis.

The linear code stored in DNA is preserved in a modified form in RNA.
The Basics of Information Transfer in the Cell

Proteins are the macromolecular workhorses of living systems.

**TRANSLATION** is the synthesis of proteins based on the genetic information as expressed in RNA.

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F0F1 ATP synthase

*Dale Muzzey & Robert Lue, BioVisions*
Viruses have nucleic acid genomes but no means to harness energy to replicate or build macromolecules.

Viruses require the machinery of the host cell to replicate.
What is the enemy: understanding the causal agent of AIDS

- The current state of the epidemic
- The AIDS epidemic in the United States
- The global AIDS epidemic
- The AIDS epidemic in Africa and the societal impact

- Emergence of a new disease and the uncovering of the enemy
  - First reports of the disease and how it is transmitted
  - Is the cause environmental, genetic, or pathogenic?
  - The discovery of Human Immunodeficiency Virus Type-1

3. The origin of HIV and AIDS
   - Simian Immunodeficiency Viruses
   - Zoonosis of HIV-1

   - The basics of information transfer and why HIV needs the cell
     - Cells and Viruses share common macromolecules
     - Why does HIV need our cells?
     - The Central Dogma of information transfer