Lecture 30
AIDS

Discovery: 1979-1981
- Los Angeles physician, Joel Weisman
- symptoms
  - mononucleosis-like syndrome, fever, weight loss, swollen lymph nodes
  - oral and anal infestations, called thrush (yeast infection)
  - reduced population of lymphocytes in blood, cause by the disappearance of helper T cells
  - rare bronchial pneumonia, *Pneumocystis carinii* pneumonia (PCP)
- five patients, all homosexuals

Cause?
- All had cytomegalovirus (CMV)
- Possible association with Epstein-Barr virus

NY City
- More hospitals, cases spread around
- Noticed requests for pentamidine, drug used to treat drug resistant cases of PCP
- 9 requests in early 1981 raised concern
- Also Kaposi's sarcoma, relatively rare skin cancer/disorder

Announcement of the disease:
- March 1981, first patient died
- June 5, 1981, CDC described five Los Angeles cases in weekly bulletin, the *Morbidity and Mortality Weekly*
- conclusion: "all the above observations suggest the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections...."

Early stories
- July, 4 1981, second CDC article, linked to Kaposi's sarcoma
- July 3, 1981, first public notice in *New York Times*, very brief article on an inside page
- November 1981, had over 150 cases
- early 1982, passed 200 and climbing
Response?
- Clarify the situation
- If a new disease, find out what is causing it
- Find ways to prevent
- Did not even have terminology
- Called gay disease, gay syndrome, gay plague, etc.

Centers for Disease Control
- Founded 1942, to track malaria
  - 1946, Communicable Diseases Center
  - 1951, Epidemic Intelligence Service (EIS)
  - 1961 began *Morbidity and Morality Weekly Report* (MMWR)
  - 1976, Swine flu

Patient zero, 1981-1983
- Looked intensively at first 250 cases reported
- Two foci, Los Angeles and New York
- Identified one patient in New York
- Initial information

Naming and further clarification
- 1982, AIDS, for Acquired Immune Deficiency Syndrome
- French used SIDA, Syndrome d'Immuno-Deficience Acquise
- ARC, AIDS-related complex
- LAS, Lymphadenopathy Syndrome
- 1983, AIDS entered in Cumulated Index Medicus as "acquired immunodeficiency syndrome"

Tracking the spread of AIDS, 1982-1984
- major locations, New York, Los Angeles, San Francisco, in that order
- sexually transmitted, how not yet certain
- Hemophiliacs, 1982
- March 1981, AIDS spread during caesarian section, given blood transfusions
- June, 1983, wife of hemophiliac diagnosed with AIDS

By end of 1983

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450 mid-1982  
750 end of 1982  
1800 mid-1983  
3000 end of 1983  
20,000 prediction for 1985

Discovery of the cause of AIDS
- AIDS is a "syndrome"
- Cytomegalovirus (CMV) commonly present
- Kaposi's sarcoma, brings in cancer
- Various hepatitis viruses associated
- Various animal pathogens produced similar complexes, such as feline leukemia

Developments in virology
- 1950s, first report of "slow viruses,"
- Oncogenic viruses -- viruses that cause cancer
- DNA --> RNA --> proteins
- Discovery of reverse transcriptase

Robert Gallo, HTLV-I
- Focus on leukemia
- Found a factor that stimulated the growth of white blood cells
- Eventually were able to trace to a growth factor, interleukin-2, and then to a retrovirus, HTLV-1
- HTLV-1 = Human T-cell Leukemia Virus
- Later, L = lymphoma, or lymphotropic
- Results announced in 1980

Discovery of the AIDS virus, 1982-1984
- NCI, laboratory of Robert Gallo
- Pasteur Institute, Luc Montagnier
- September, 1983, Cold Springs Harbor meeting
- 1984, Gallo gives up his HTLV thesis

Test for AIDS
- December, 1983, French file patent request
• April 1984, NIH files patent on behalf of Gallo
• patent is not granted until 1986, U.S. given preference over French
• 1984, finally agreed that LAV and HTLV-III are one virus, which will eventually be called HIV virus

1984-1986, mechanism of HIV infection
• RNA, retrovirus
• affinity for T4-lymphocytes
• upon entering cell, RNA transcribed to DNA
• upon reactivation (cause still uncertain) destroys host T-cell and also other T-cells

Estimates, 1991
206,392 Americans diagnosed
133,232 Americans died
73,160 Americans living with AIDS.
took 8 years to reach 100,000 cases, just 26 months to double that number.

1992
• killed 170,000 Americans, 'nearly three times more than died in the Vietnam War.'
• More and more, HIV infection results from unprotected teenage sexual activity and drug abuse.
• Gay men still account for most AIDS cases.
• Women now account for 11 percent of cases, with the percentage increasing each year

1994
• 800,000 and 1.2 million HIV-infected individuals in the United States.
• Through September 1993, the total cases of AIDS diagnosed and reported to CDC in the United States was 339,250."

WHO Press 1 Jul 1994
• Estimated number of AIDS cases worldwide up 60% since this time last year
• Global estimate of the number of AIDS cases
• Largest number -over 2.5 million in sub-Saharan Africa

1996
• 28 million HIV infected
• 93% in developing countries
• More women than men infected in sub-Saharan Africa
• 68% of new cases in sub-Saharan Africa

1997
• Improved treatment using “drug cocktails”
• Death rate drops
• Mortality rates
• Actual number of deaths
  
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AIDS 2001
• ~40 million people worldwide infected with HIV virus
• ~20 million have died from AIDS
• 2001, 5 million newly infected, 3 million died
• 1/3rd living with HIV/AIDS are 15-24
• 70% of infected live in sub-Saharan Africa
• 38% of adults in Botswana are infected
• AIDS pandemic orphaned 14M, 92% Africa
• 7 m in Asia & Pacific living with HIV/AIDS
• Women account for 50% percent HIV/AIDS-infected adults

Future?
• US
  Infection rate constant (40,000/year)
  African-Americans & women disproportionately affected
• World situation
  90% of all cases in developing countries
  Major burden, sub-Saharan Africa
  Growing problem in Asia
• Treatment
  Drugs suppress, do not cure
  Supply falls short of demand (10x or more)
Hemorrhagic fevers
- Soul Hantaan (Hantaan fever)
- 1962-64, Bolivian Hemorrhagic Fever
- Late 1960s, Lassa Fever, Nigeria
- Mid 1970s, Ebola Fever, Zaire

Other “New” Diseases
- 1986, Mad Cow Disease
- 1999, West Nile Virus (human encephalitis)
- 2002, SARS

Major policy questions:
- Basic science vs. clinical/applied
- Priorities
  - US health
  - World health
  - Prevention vs. cure
  - Basic treatment for all vs. high end of insured
- How much can we afford to spend on health care?
  - US health costs = 13.9 % GDP, ($4,887/person).
  - US lags behind in key indicators of health.

AIDS Death by country

1. India 310,000 (1999 est.)
2. South Africa 300,000 (2000 est.)
3. Ethiopia 280,000 (1999 est.)
4. Nigeria 250,000 (1999 est.)
5. Kenya 180,000 (1999 est.)
6. Zimbabwe 160,000 (1999 est.)
7. Tanzania 140,000 (1999 est.)
8. Mozambique 114,111 (2001 est.)
9. Uganda 110,000 (1999 est.)
10. Zambia 99,000 (1999 est.)
11. Congo, Democratic Republic of the 95,000 (1999 est.)
12. Cote d'Ivoire 72,000 (1999 est.)
13. Malawi 70,000 (1999 est.)
14. Thailand 66,000 (1999 est.)
15. Cameroon 52,000 (1999 est.)
16. Burma 48,000 (1999 est.)
17. Burkina Faso 43,000 (1999 est.)
18. Rwanda 40,000 (1999 est.)
20. Benin 37,000 (2002)
21. Ghana 33,000 (1999 est.)
22. Botswana 24,000 (1999 est.)
23. Central African Republic 23,000 (1999 est.)
24. Haiti 23,000 (1999 est.)
25. United States 20,000 (1999 est.)