

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 Mortality 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-Deficiencie 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

200 end of 1981

| | |
|--------|---------------------|
| 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**

1994 42,114 (15.4/100K)
1995 42,500 (15.4/100K)
1996 36,865
1997 16,865

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**

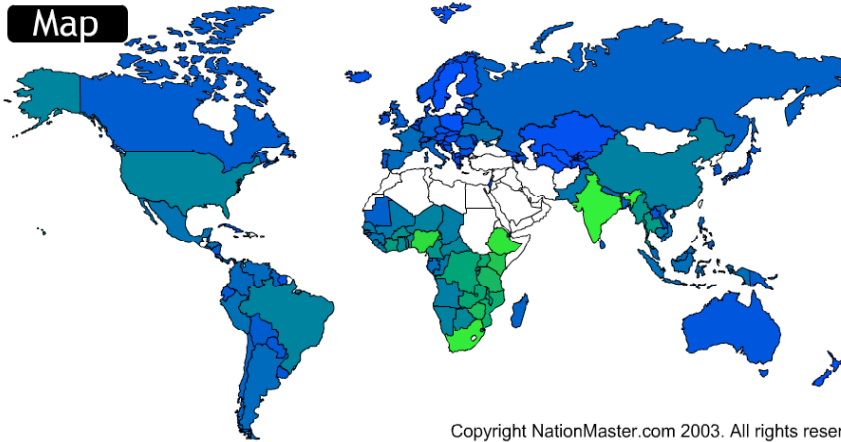
Major policy questions:

- **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

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|---|--|
| 1. India 310,000 (1999 est.) | 13. Malawi 70,000 (1999 est.) |
| 2. South Africa 300,000 (2000 est.) | 14. Thailand 66,000 (1999 est.) |
| 3. Ethiopia 280,000 (1999 est.) | 15. Cameroon 52,000 (1999 est.) |
| 4. Nigeria 250,000 (1999 est.) | 16. Burma 48,000 (1999 est.) |
| 5. Kenya 180,000 (1999 est.) | 17. Burkina Faso 43,000 (1999 est.) |
| 6. Zimbabwe 160,000 (1999 est.) | 18. Rwanda 40,000 (1999 est.) |
| 7. Tanzania 140,000 (1999 est.) | 19. Burundi 39,000 (1999 est.) |
| 8. Mozambique 114,111 (2001 est.) | 20. Benin 37,000 (2002) |
| 9. Uganda 110,000 (1999 est.) | 21. Ghana 33,000 (1999 est.) |
| 10. Zambia 99,000 (1999 est.) | 22. Botswana 24,000 (1999 est.) |
| 11. Congo, Democratic Republic of the 95,000 (1999 est.) | 23. Central African Republic 23,000 (1999 est.) |
| 12. Cote d'Ivoire 72,000 (1999 est.) | 24. Haiti 23,000 (1999 est.) |
| | 25. United States 20,000 (1999 est.) |

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