SACRAMENTO STATE
Leadership begins here.

# Chapter 10+: Viruses

Exam #3 on Wednesday
This lecture will NOT be on exam #3

Dr. Amy Rogers

## AIDS

- **Acquired immunodeficiency syndrome**
  - Caused by human immunodeficiency virus (HIV) (two main types, **HIV-1 & HIV-2**)
- HIV is a **retrovirus**
  - ssRNA genome; reverse transcribed into dsDNA; this DNA then integrates into a host chromosome as a provirus

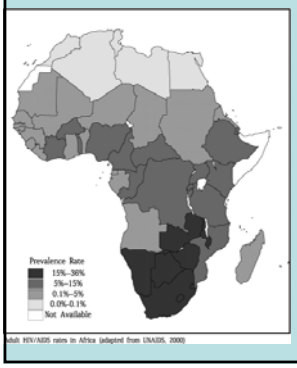
## HIV infects CD4+ cells

- HIV causes an immunodeficiency disease by **killing CD4+ $T_H$ cells**
  - Disease progression monitored by counting number of $T_H$ cells in blood
  - Slow (months to years) but relentless
  - **Macrophages** are an important reservoir of HIV infection
- AIDS patients are not killed by HIV; they die of **opportunistic infections**
  - Many such infections are rare or unusual; this contributed to the initial recognition the AID syndrome
  - or **unusual malignancies** (cancers)

## HIV epidemiology

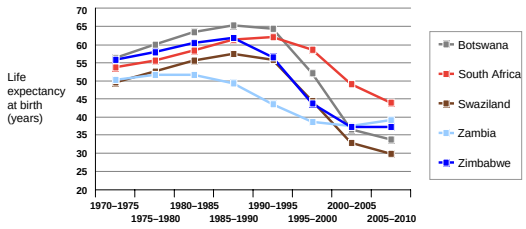
- In U.S., originally transmitted primarily by homosexual contact and contaminated blood products
  - All blood products are now screened for HIV and "universal precautions" are used by all health care workers to protect themselves from needlesticks or other contact with infected fluids
- Now, globally, HIV is transmitted primarily by heterosexual sex, and by IV drug abuse
  - Also from mother to baby (*in utero*, during delivery, or while breast feeding)

## AIDS is killing southern Africa




Botswana, Swaziland, Zimbabwe, Lesotho
- All have HIV infection rates **over 30%**

**Impact of AIDS on life expectancy in five African countries, 1970–2010**




Source: United Nations Population Division (2004). World Population Prospects: The 2004 Revision, database.

- In many populous countries (Russia, China, India, Thailand) the challenge is to prevent an explosion of the epidemic into the heterosexual population
  - Needle exchange programs; condom distribution; abstinence education
- Cultural challenges:
  - In South Africa, President Thabo Mbeki questions that AIDS is caused by HIV
  - Ignorance of how HIV is spread
    - Sex with a virgin will cure you!

## Encouraging news

- New efforts at **treatment** in Africa
  - World Health Organization (WHO) "3 by 5" campaign
    - To treat 3 million people in low income countries by 2005
      - » Didn't happen, but significant progress was made
    - Availability of therapy encourages people to get tested
    - Inexpensive generic drugs now available
- Gates Foundation & others pouring money into vaccine development

## HIV vaccine?

- First field test of an AIDS vaccine showed no benefit
- Many challenges particular to HIV that will make production of an effective vaccine difficult
  - HIV's **reverse transcriptase** enzyme is highly inaccurate (for a polymerase); the virus has a **high mutation rate**, its **antigens frequently change**

## Hantavirus

- 1993 "Four Corners" area of southwest U.S. (AZ, CO, NM, UT)
  - Sudden outbreak of rapidly fatal lung disease in healthy adults
- Public health system was activated (CDC, USAMRIID)
- **New virus** identified in Hantavirus group
  - Previously, many other hantaviruses were known, but none in U.S.
- **Transmitted by rodents**
  - Contact with urine, dried feces, saliva
  - 1993 outbreak attributed to 10-fold increase in deer mouse population after the end of a long drought

>50% mortality rate
*Sin nombre* virus (originally named after a location, but the residents objected…)
Hantaviruses have now been identified throughout the U.S.

★ Hantavirus:
1. emerging viral disease in U.S.
2. zoonosis

## Herpesviruses

- Herpes simplex viruses (HSV1, HSV2)
  - Oral herpes (cold sores)
  - Sexually transmitted genital herpes
- Varicella-Zoster Virus (VZV)
  - Chicken pox
  - Shingles

## Herpesviruses & latency

All herpesviruses can become

**latent**

The virus hides out ***inside*** cells for *long* periods of time (decades)

While latent,
the virus is hidden from the immune system,
and does not cause symptoms.

## Reactivation of herpesvirus infections

★For HSV & VZV, the virus becomes latent in **neurons**

- Virus can migrate along nerves all the way to the central nervous system
- The **latent virus can reactivate**, and start a symptomatic infection again at any time
  - Some triggers are known (i.e., immunosuppression); often it is unclear why

- HSV: reactivation means a recurrence of oral or genital lesions/blisters, and active shedding of virus (highly infectious)
  - Shedding of virus also can occur *without* symptoms
- VZV:
  - **Initial infection: chicken pox**
  - ★**Reactivation: shingles**


- Shingles blisters look just like chicken pox, but are painful, and appear in distinctive patterns following the **distribution of the infected nerve**

## Viral Hepatitis

- Several viruses cause *hepatitis* (inflammation of the liver)
  - The many hepatitis viruses are **NOT** related, except that they all cause liver disease
- ★In California, Hepatitis A is common
  - **Fecal-oral transmission**
    - Point source outbreaks in restaurants
  - **Routine vaccination** of children is mandatory in CA
- Hepatitis B is a more severe hepatitis
  - spread by contact with infected blood, or by sex

## Hepatitis D virus

- Hepatitis D virus is **defective**
  - it *cannot replicate* without the help of hepatitis B virus co-infecting the same cell
- A hepatitis patient will *never* be infected only with the D virus
- Patients infected with **D** are **always infected** also with **hepatitis B**
  - Such patients have significantly worse disease than B only

## Virus eradication

- In only 10 years (1967-1977) the WHO eradicated smallpox from the earth
  - Highly infectious virus
  - 20-40% mortality rate
  - Important role in human history
  - *Demon in the Freezer:* known & secret stocks exist

Success was possible because:

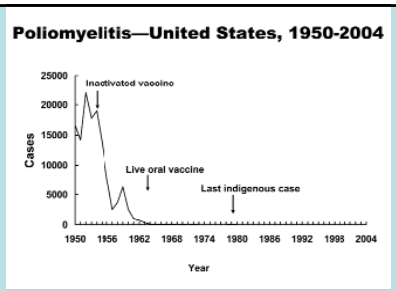
★
- Excellent vaccine available
- No reservoirs of virus outside humans
- No carrier state; symptoms appear fairly soon after exposure

## Poliovirus

- Highly infectious *enterovirus* (replicates in the gut) spread by **fecal-oral route**
- Easily spread in crowded conditions, or among young children (whose sanitary habits may leave something to be desired…)
- Vast majority of infections are asymptomatic
- Virus can invade from the gut, enter the blood and spread to motor neurons (central nervous system)
  - temporary or permanent **paralysis**
- Polio can only infect humans (**no animal reservoir**)

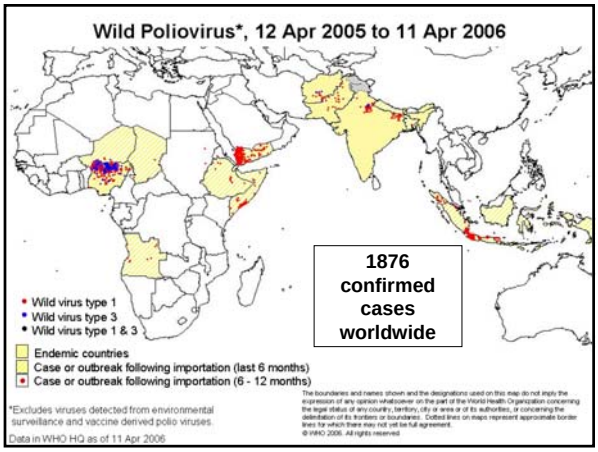
## Paralytic polio & the “Iron Lung”

“This room-sized respirator, circa 1932, could comfortably hold four patients. A fifth patient fit in the central port in times of high demand. The device was in nearly continuous use during polio epidemics through the early 1950s. (Photo courtesy of Archives of Children’s Hospital Boston) “




★Goal: Global polio eradication

World Health Organization (WHO),
Rotary International, Centers for Disease Control (CDC), UNICEF




## Some viruses cause Cancer

Viral infections may cause about 15% of all human cancers

- “onco-” means cancer
- ★**Oncogenic virus**: a virus that can cause cancer
- **(Neoplastic) Transformation**: the process of changing from a normal cell to a malignant (cancerous) cell

## What is cancer?

- Healthy cells divide only when necessary
- Cancer cells ***divide continuously***, sometimes forming a solid mass (tumor)

- Healthy cells stay where they belong
- Cancer cells ***metastasize***
  - spread to other parts of the body

## ★ What causes cancer?

- Neoplastic transformation occurs when the genes controlling cell growth & division screw up
  - Mutations (sometimes from exposure to carcinogens/mutagens like sunlight, cigarette smoke; or, errors in DNA replication or mitotic cell division)
  - Certain viral infections

## 1. How do viruses cause cancer?

★ **1. DNA tumor viruses**: Integration into host chromosome

Some DNA viruses integrate into host chromosomes.

This can cause inappropriate expression of **proto-oncogenes**

★ Proto-oncogenes are **normal** genes that ***when mutated or overexpressed*** lead to cancer.

## DNA tumor viruses affect proto-oncogenes: How?

- Viruses carry *strong promoters* that drive high-level expression of viral genes
- **If a promoter like this inserts next to a proto-oncogene**, the proto-oncogene gets inappropriately expressed.

➡ cancer (transformation)

## 2. How do viruses cause cancer?

**2. Retroviruses** (sometimes called RNA tumor viruses) bring an oncogene with them and therefore can cause cancer

**Oncogene**: a *mutated version* of a cellular proto-oncogene. Mutated protein product of the gene can lead to neoplastic transformation (cancer)

## 3. How do viruses cause cancer?

3. Death of infected cells promotes attempts to repair the damaged organ

- Surviving cells repeatedly divide
- Every time a cell divides, *there is a chance it will make a mistake in replicating its DNA*, and head down the road to cancer

★ Hepatitis B & liver cancer

## Oncogenic viruses: Hepatitis B

★In some people, Hep B establishes a **long-term (chronic) infection**

- Chronic infection is ***strongly*** associated with the development of liver cancer
  - hepatocellular carcinoma

★Cancer takes decades to appear

– Mechanism of transformation is probably slow accumulation of mutations as hepatocytes (liver cells) divide to repair liver damage

## Oncogenic viruses: Human Papilloma Viruses (HPV)

- There are perhaps 100 types
- Most do NOT cause cancer
- HPV are **sexually transmitted**
  - Cause genital warts and…

★ Several HPVs (especially HPV-16 & HPV-18) can cause **cervical cancer**

## Papilloma viruses & cervical cancer

★Cervical cancer is a sexually transmitted disease
- More than 95% of all cervical cancers are caused by HPV
  - Conversely, very few HPV infections lead to cancer
    - HPV infection is extremely common in sexually active people
- First HPV vaccine was licensed by FDA in June 2006
  - Protects against types 6, 11, 16, 18
    - which together cause 70% of all cervical cancers, and 90% of genital warts
  - Recommended for all young women and girls

- AIDS ch. 18 p. 530-535
- p. 664-667 hepatitis
- p. 556-557; 598-599 herpesviruses
- P. 276; p. 634-635; weekly news article: Hantavirus
- P 734-735 Polio
- Ch. 10 p. 293-294 (cancer & viruses)