

MMG 301 Lec 34 Viral Diseases

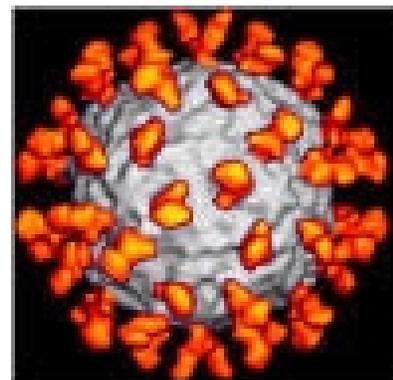
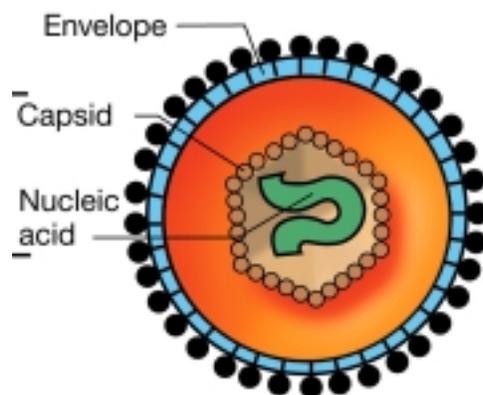
Questions for today

1. How does the life cycle of a virus infecting eukaryotic cells differ from that of bacteriophage?
2. What are the major viral respiratory diseases?
3. What are the major sexually-transmitted viral diseases?
4. What are other key viral diseases?
5. What do we know about emerging viral diseases?

[for more information, see the Centers for Disease Control and Prevention web site at: <http://www.cdc.gov/>]

Life Cycle of Viruses that Infect Eukaryotes

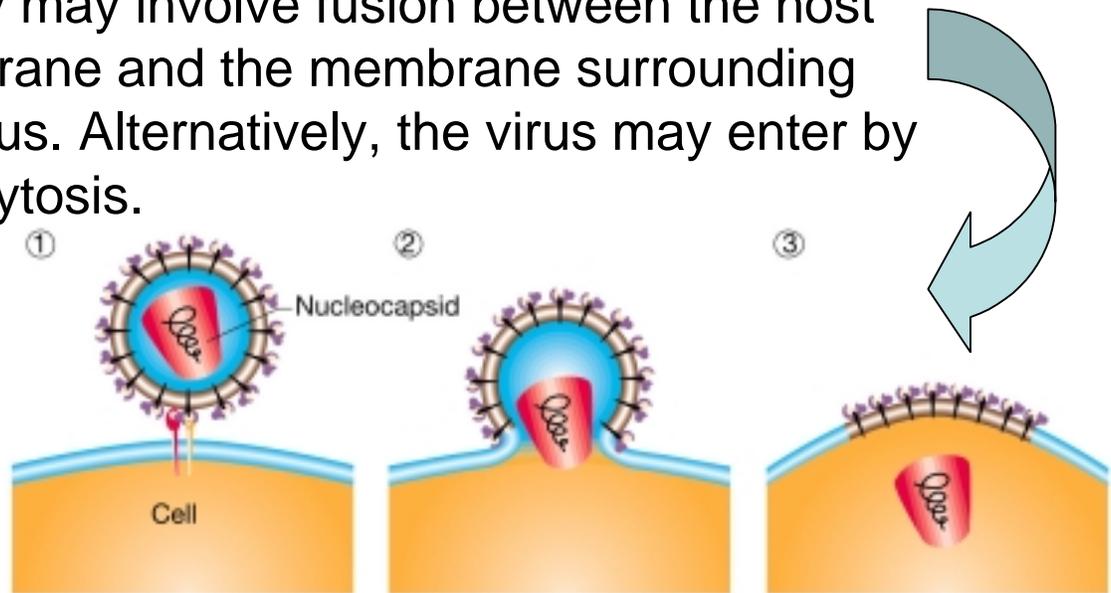
Most eukaryote-specific viruses are enveloped, often with virus-encoded proteins embedded in the lipid bilayer.



Enveloped virus

Viral Attachment and Penetration

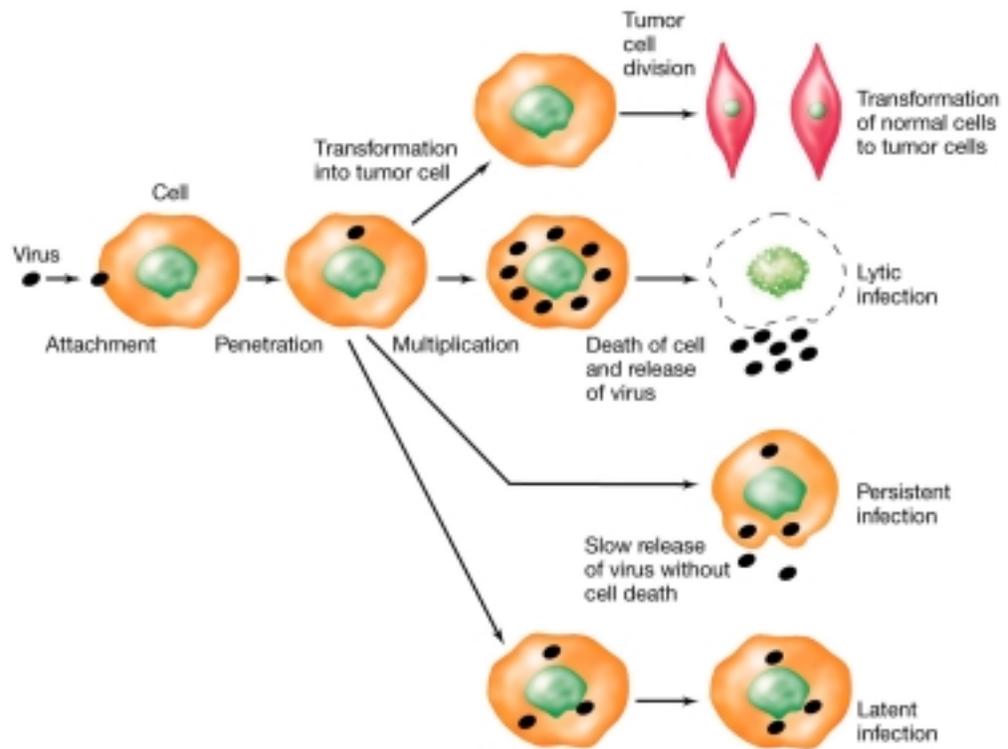
- Attachment involves specific interactions between (typically protein) components on the virus and the host cell.
- In contrast to bacteriophage, the entire virus typically enters the eukaryotic cell.
- Entry may involve fusion between the host membrane and the membrane surrounding the virus. Alternatively, the virus may enter by endocytosis.



Replication of viruses in Eukaryotes

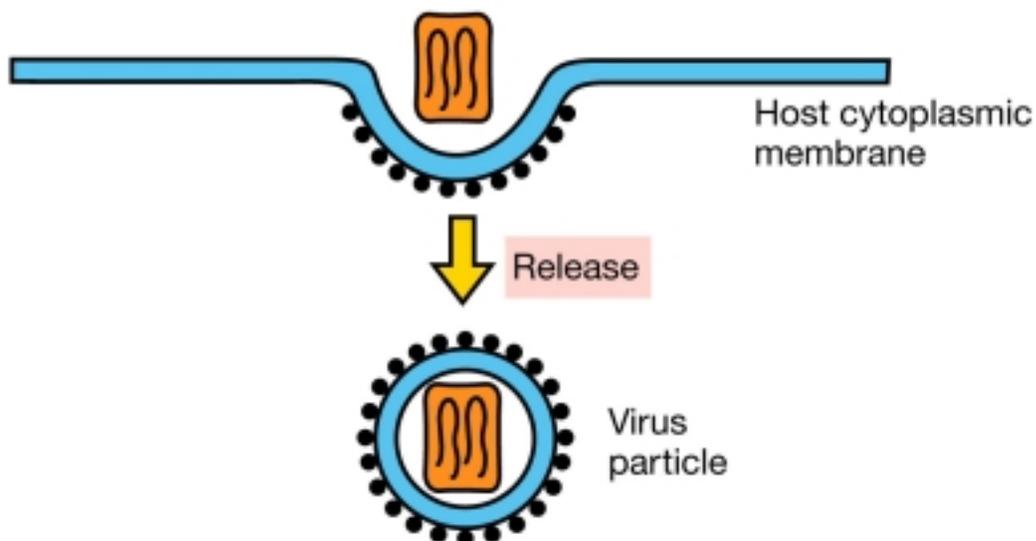
- Typically much more complicated than for bacteriophage due to cell compartmentation (eukaryotic DNA synthesis occurs in nucleus, protein synthesis in cytoplasm).
- Some viruses replicate in nucleus while other replicate in the cytoplasm.
- Splicing and RNA modifications are often found.
- Reverse transcriptase (a polymerase using RNA as the template to make DNA) is critical to some RNA viruses.

Effects on host cells



Viral Release from Host Cell

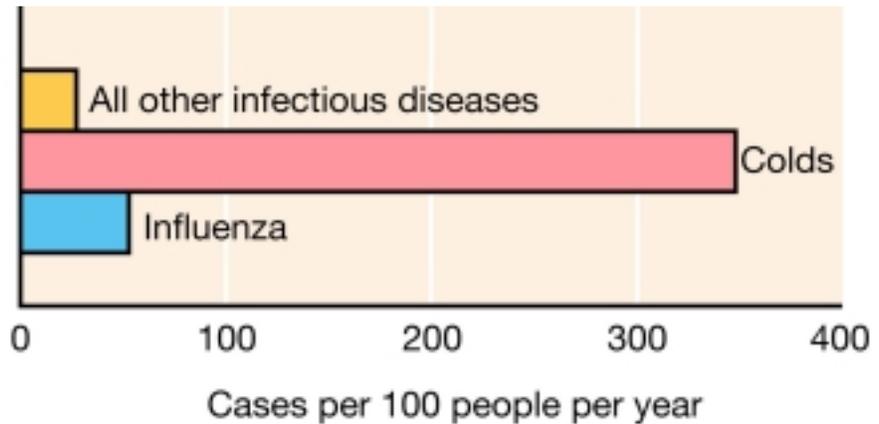
- Although lysis may occur, a more common exit strategy involves “budding” (envelope is from host)



Viral Respiratory Diseases

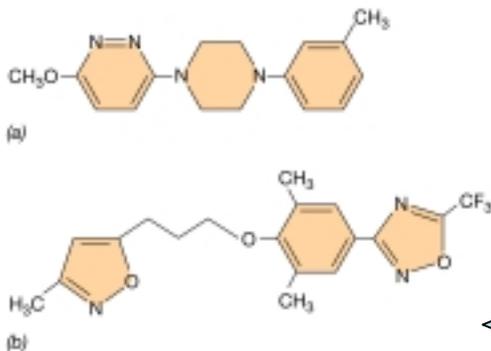
Common cold

very
common!



About 50% of cases caused by the ssRNA *rhinovirus*; remainder from other viruses

- Over 100 different serotypes (varieties identified by antigenic properties), each with varying degrees of pathogenicity
- Aerosol transmission from infected host to the next; also through contact by hands (WASH!)
- Infects upper respiratory tract to produce rhinitis (inflammation of nasal mucosal membranes), nasal obstruction and discharges, usually no fever
- Resistance to human immune defenses: virus surface contains 4 basic antigens; and 89 variants!



- Several drugs in development based on inhibiting virus uncoating and replication process

← (don't memorize!)

Influenza – ssRNA enveloped virus that can undergo *antigenic shift* to elude host immune system.

- Classified into A, B, or C groups based on the antigens in their protein coats.
- Infection in upper respiratory tract, usually through inhalation of droplets from another infected person.



- Symptoms include fever, chills, aching.
- Secondary bacterial infections can be a problem in infants and elderly.

- Responsible for annual minor *epidemics* and several *pandemics* (worldwide epidemics).



- Animals are common reservoirs as sources for new strains – often new strains originate in Asia.
- After a strain of influenza has moved through a population, most people are immune.
 - New influenza strains develop because of antigenic shift: segmented RNA genome allows shuffling and mutations of two major antigens that are on the surface of the virus envelope.

- Can get annual vaccinations for newly developing strains – epidemiologists try to keep track of which strains are coming in the next year or two.

Measles, Mumps, Rubella (MMR vaccine; lifetime immunity).

- Measles – (rubeola virus) cough, fever, nasal discharge, eventually a rash develops.
- Mumps – as with measles, is spread by airborne droplets.
 - Characterized by inflammation of salivary glands, swelling of neck.
 - Virus spreads throughout body – occasionally leading to complications like sterility, encephalitis.
- Rubella – (German measles) milder symptoms than measles; infection of fetus can result in stillbirth, heart, eye, and brain damage.

Chickenpox

- Caused by varicella-zoster virus (a Herpesvirus); highly contagious by airborne route.
- Develops characteristic lesions on face and upper trunk: erupt, fill with pus, rupture, and covered by scabs.
- Virus DNA can remain in nuclei of nerves and sensory neurons.
 - Viruses become activated later in life to develop *shingles* (e.g., Dave Letterman).

Sexually Transmitted Viral Diseases

Herpes type 1 – cold sores and fever blisters in and around mouth or lips.

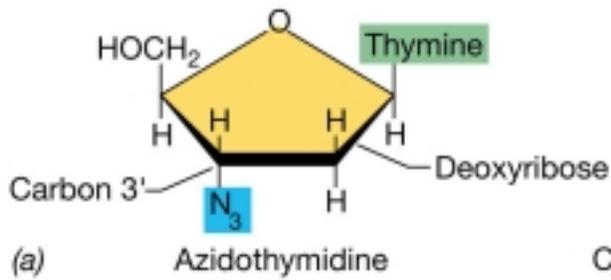
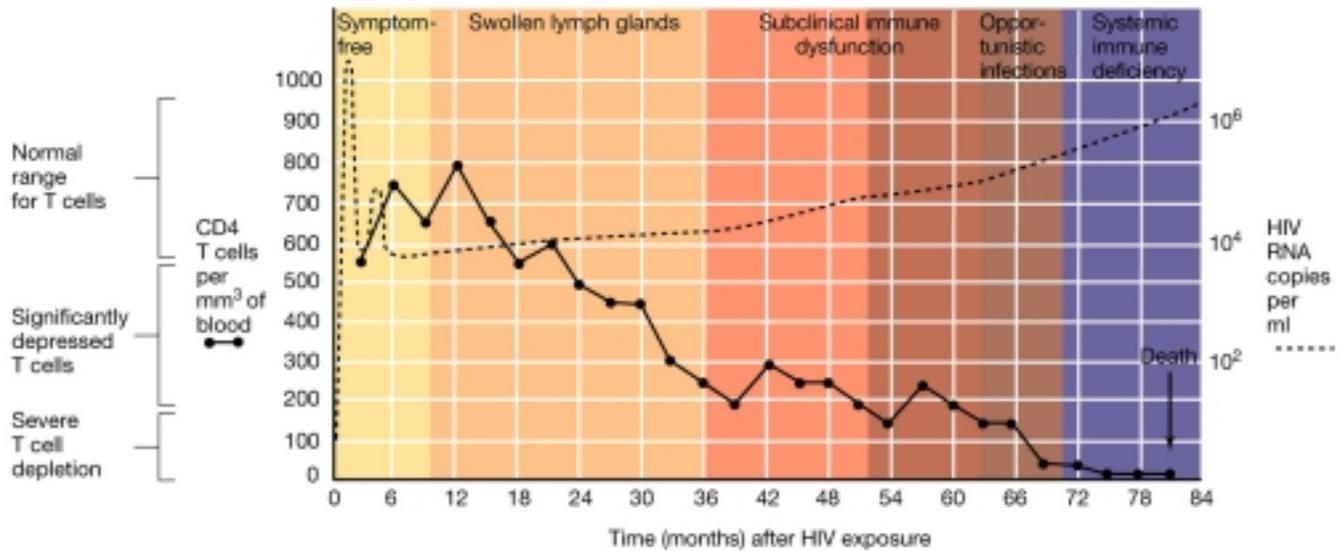
Herpes type 2 – genital lesions and blisters of penis, cervix, vulva, vagina.

- Transmitted by direct sexual contact.
- Incurable – treatment with drugs acyclovir.
- Oral herpes – no long term effects.
- Genital herpes – linked to cervical cancer.
 - Can be passed to newborn.

Acquired Immunodeficiency Syndrome (AIDS)

- Caused by Human Immunodeficiency Virus (HIV).
- Two types now recognized:
 - HIV1 – responsible for 99% of all AIDS.
 - HIV2 – similar to HIV1 but less virulence.
- HIV infects host cells that have surface proteins called CD4 and CCR5.
 - High CD4-containing host cells found in immune system.
 - Lower CD4 cells in brain and intestinal cells.
 - The other host cell protein, CCR5, is also involved in binding of the virus and fusion.
- The *viral* protein gp120 binds to these host proteins.

- HIV is a retrovirus (thus, it requires reverse transcriptase).
- No cure – several anti-HIV drugs, when used in combination, can control virus (multiple drug therapy).
- Progression: Note the opportunistic infections.



- Reverse transcriptase inhibitors – analogs of DNA bases or inhibit in other ways.

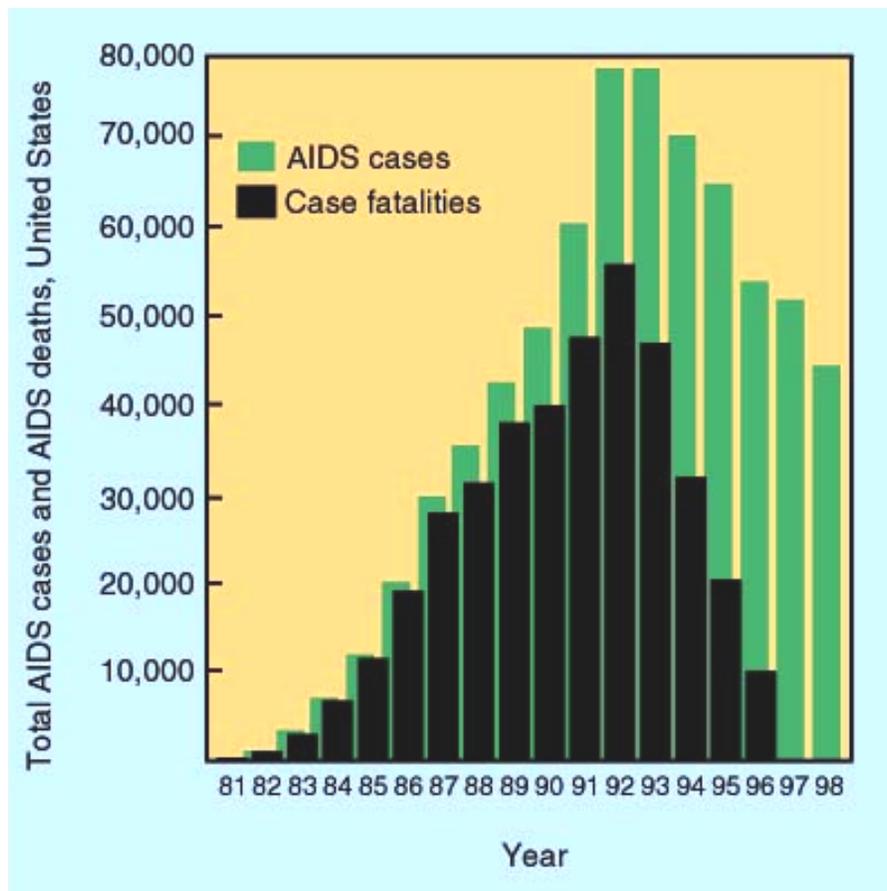


John M. Martinico and Cheryl L. Broadie

- Protease inhibitors – prevent processing of polyprotein to individual proteins and enzymes.

- AIDS is theoretically 100% preventable.

- Today, **40 million people** are estimated to be **living with HIV/AIDS**. Of these, 37.2 million are adults. 17.6 million are women, and 2.7 million are children under 15.
- An estimated **3 million** new cases in 2001, including 1.1 million women and 580,000 under age 15.
- 95% of all AIDS victims live in developing countries.



Other key viral diseases

Hepatitis [*hepaticus* = liver]

- Eight types are currently known; 5 are well characterized: A, B, C, D, E. (We will focus only on one example here).
- *Hepatitis B* – (serum hepatitis) transmitted through blood transfusions, unsterile drug users' needles, body secretions, sexually.
 - Symptoms: jaundice, fatigue, abdominal pain
 - Hepatitis B vaccine available (combined A and B forthcoming)
 - 300,000 new cases/yr in US, 5,000 deaths from cirrhosis of liver, 1,000 from liver cancer
 - 200 million infected worldwide

Viral gastroenteritis – caused by rotavirus, as well as others

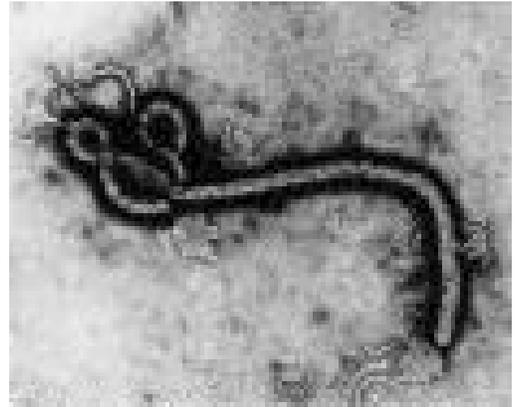
- Mainly transmitted through contaminated food (fecal oral route)
- Symptoms include diarrhea, vomiting
- Diarrheal diseases cause 5-10 million childhood deaths/yr, many are viral in origin
- Infects infants 1 mo – 1 yr in age
- 3.5 million rotavirus cases/yr in US

Emerging viral diseases/ CDC priority viruses

Viral hemorrhagic fevers

Ebola, Marburg, Hanta viruses

- Are all RNA viruses.
- Are dependent on animal or insect reservoirs.
- Most cause severe, life-threatening disease.



Marburg virus

- Earliest cases seen when West German scientists became infected with a new virus from imported monkeys from Uganda (*Marburg viral hemorrhagic fever*).
- Symptoms included bleeding (hemorrhaging) as well as blood clots, damage to retina.

Ebola virus

- First Ebola appearance (1976) infected 1,000 and killed 500; a 1995 outbreak was more quickly contained.

Hanta virus

- An outbreak in southwestern US in 1993 of a new type of hantavirus (causing hemorrhagic fevers) resulted in 30 deaths from *hantavirus pulmonary syndrome* (due to destruction of lungs).

West Nile Virus – can cause fatal encephalitis (inflammation of the brain) in humans and horses, as well as certain domestic and wild birds.

- Transmission by mosquito (no direct transmission from human or animal to human).

Severe Acute Respiratory Syndrome (SARS)

- The disease was first reported among people in Guangdong Province (China), Hanoi (Vietnam), and Hong Kong. It has since spread to other countries.
- As of April 1, more than 70 cases of SARS had been reported in the United States.
- In general, SARS begins with a fever greater than 100.4°F [$>38.0^{\circ}\text{C}$]. Other symptoms may include headache, an overall feeling of discomfort, and body aches. Some people also experience mild respiratory symptoms. After 2 to 7 days, SARS patients may develop a dry cough and have trouble breathing.
- SARS is spread by close contact between people.
- Scientists at CDC and other laboratories have detected a previously unrecognized coronavirus in patients with SARS. While the new coronavirus is still the leading hypothesis for the cause of SARS, other viruses are still under investigation as potential causes.