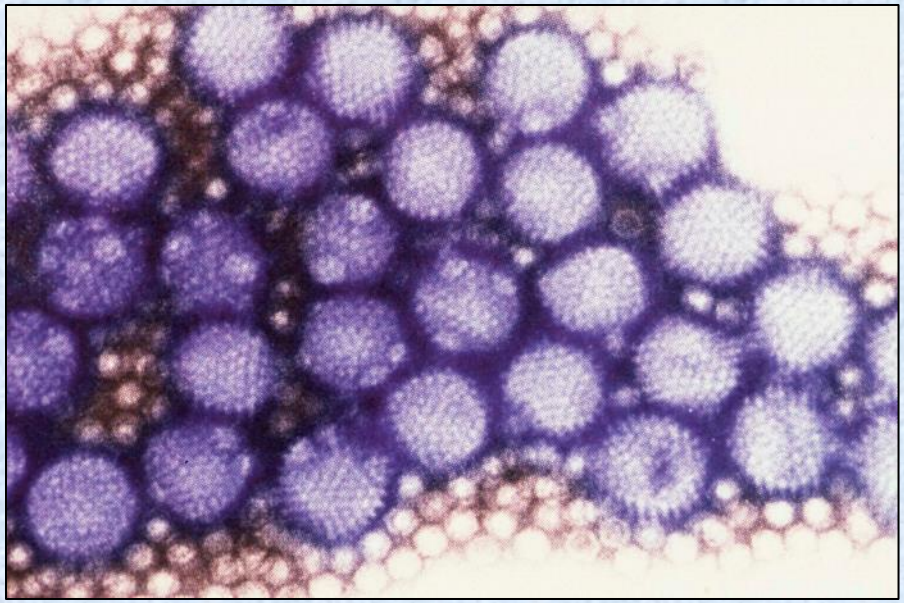
Viruses

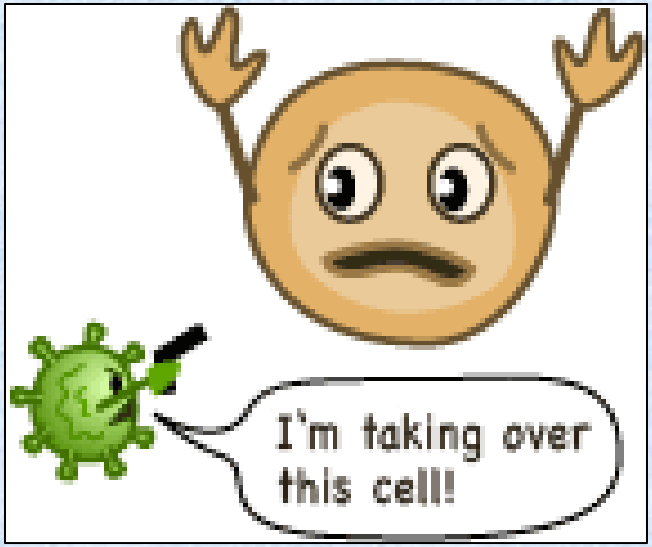


Adenovirus

Ebola

Definition of a Virus

- Sub microscopic entity
- Single nucleic acid surrounded by a protein coat
- Capable of replication only within the living cells of bacteria, animals or plants



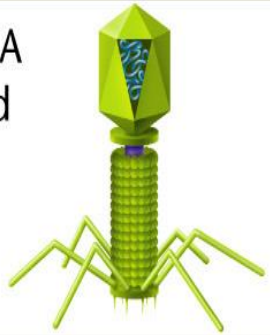
Definition of a Virus

- Viruses need a living cell to survive
- Viral genome is released inside the cytoplasm of the host cell
- Virus genomes are made of DNA or RNA
  - Not both
  - Single stranded (ss) OR double stranded (ds)

Viruses – Living or Non-living?

- Cannot exist independently from the host cell, so aren't considered living things
- However, since they can direct life processes they are often considered more than lifeless molecules
- Referred to as infectious particles, either active or inactive
- Obligate intracellular parasites

Viruses - Living or Not?

Viruses and Cells		
Characteristic	**Virus**	**Cell**
Structure	DNA or RNA core, capsid 	Cell membrane, cytoplasm; eukaryotes also contain nucleus and organelles 
Reproduction	only within a host cell	independent cell division either asexually or sexually
Genetic Code	DNA or RNA	DNA
Growth and Development	no	yes; in multicellular organisms, cells increase in number and differentiate
Obtain and Use Energy	no	yes
Response to Environment	no	yes
Change Over Time	yes	yes

Viruses – found almost everywhere, all organisms

Viruses infect:

- **Humans**

Smallpox [1]

- **Other vertebrates**

Foot and mouth disease [2]

- **Invertebrates**

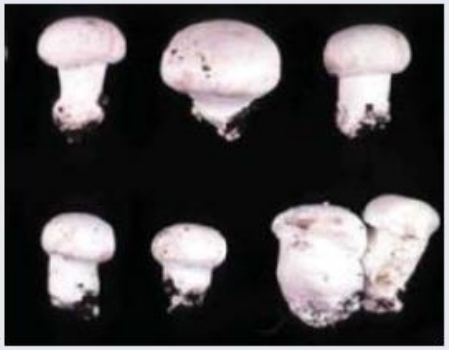
Leatherjackets infected with *Tipula* iridescent virus

- **Plants**

Delayed emergence of potato caused by tobacco rattle virus infection [3]

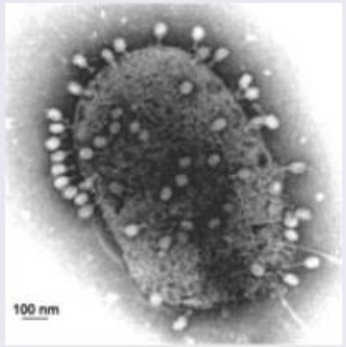
Damaged potato (spraing) caused by tobacco rattle virus infection [3]

- **Fungi**



Mushroom virus X [4]

- **Bacteria**

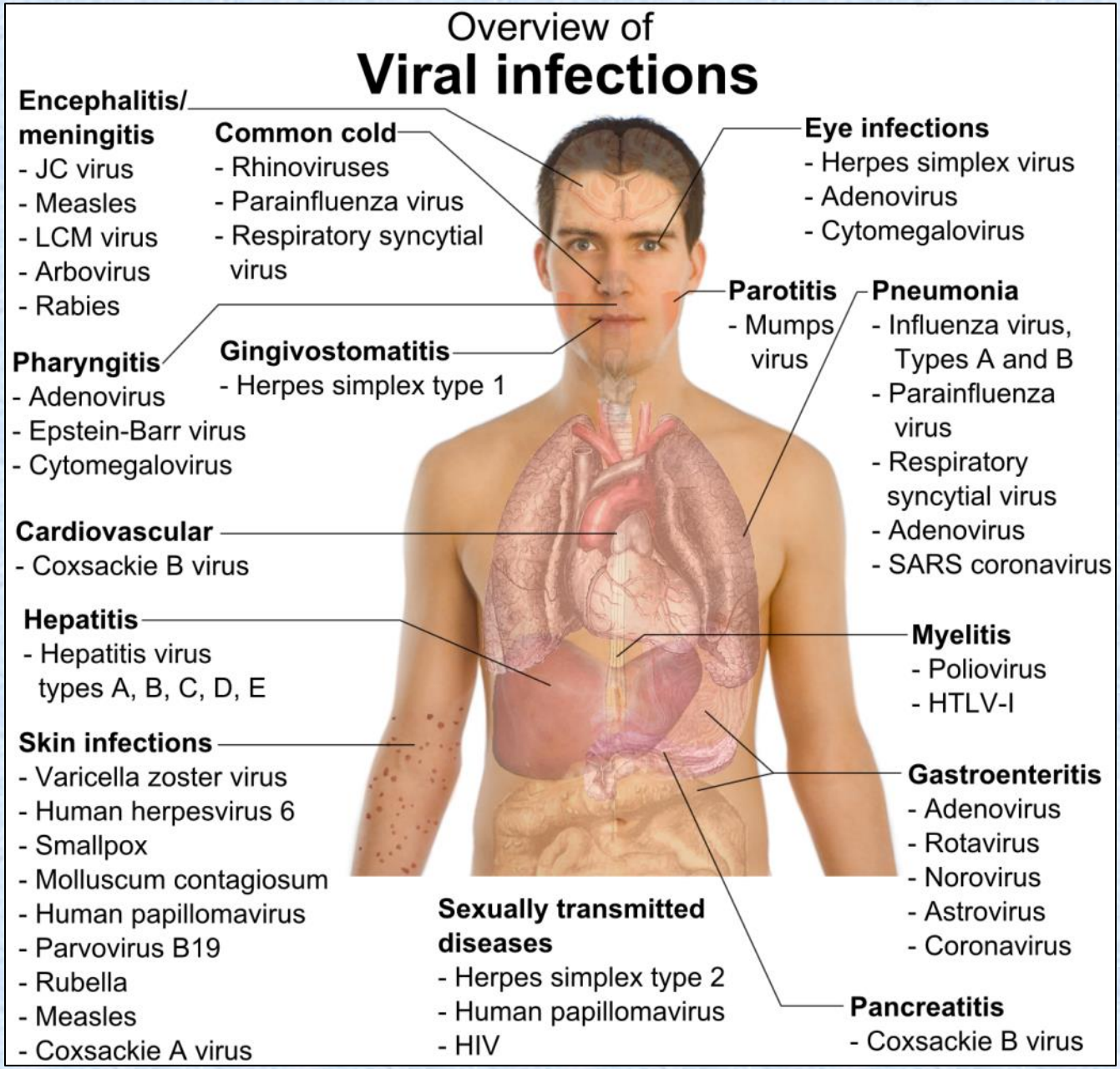


Escherichia coli cell with phage T4 attached [5]

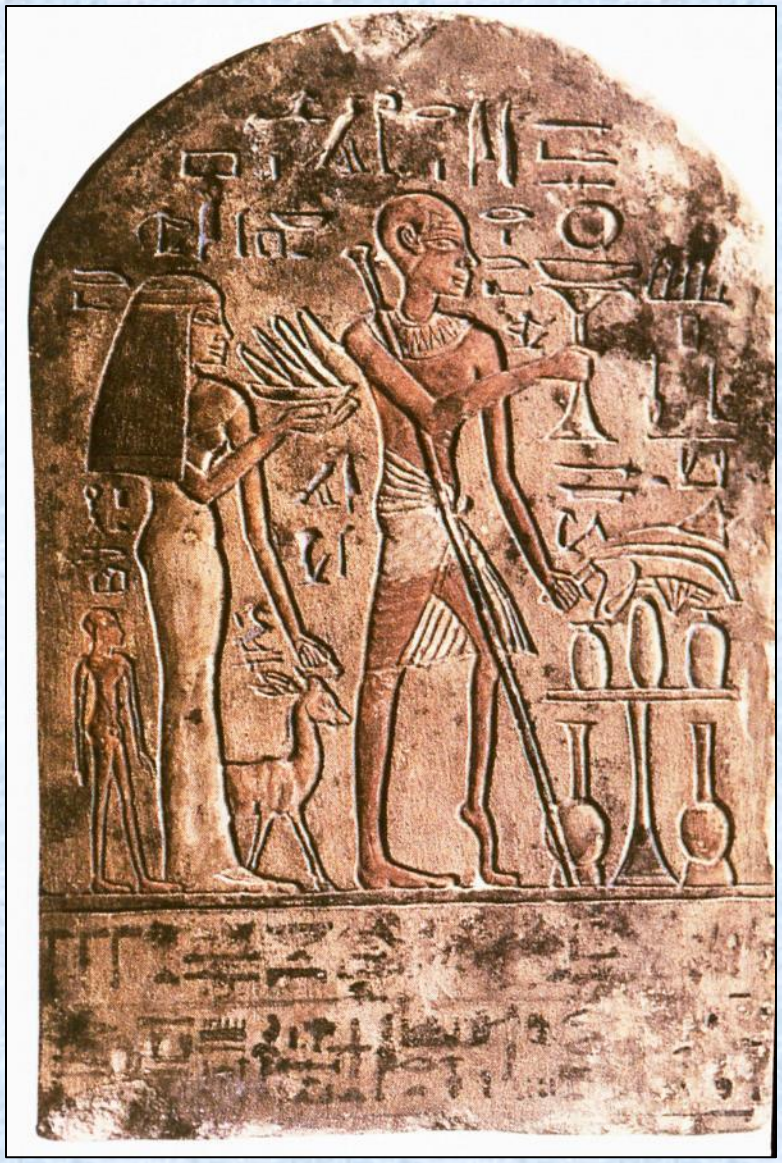
Viruses – cause many human diseases

Category	Disease
Sexually transmitted diseases	AIDS (HIV), genital warts, genital herpes
Childhood diseases	Mumps, measles, chickenpox, German measles
Respiratory diseases	Common cold, influenza, severe acute respiratory syndrome (SARS)
Skin diseases	Warts, fever blisters, shingles
Digestive tract diseases	Gastroenteritis, diarrhea
Nervous system diseases	Poliomyelitis, rabies, encephalitis
Other diseases	Smallpox, hemorrhagic fevers, cancer, hepatitis, mononucleosis, yellow fever, dengue fever, conjunctivitis, hepatitis C

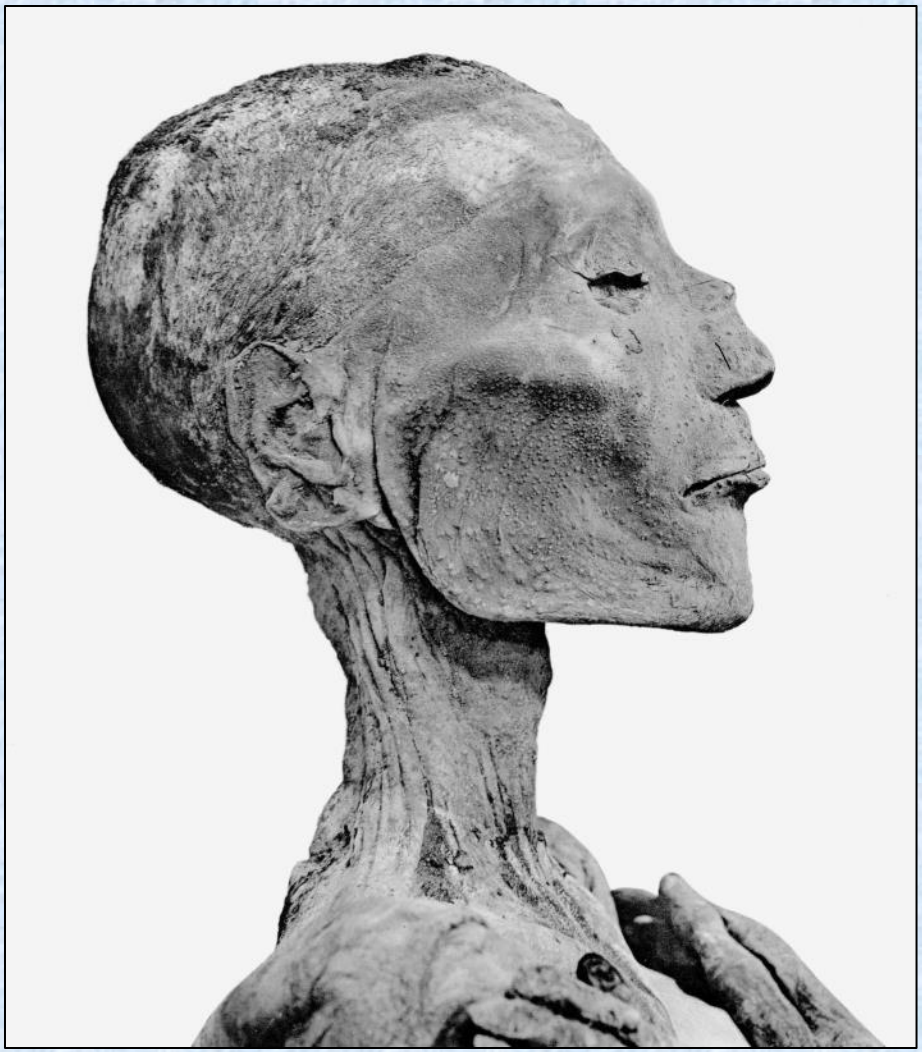
Viruses and Human Health



Egyptian with Polio

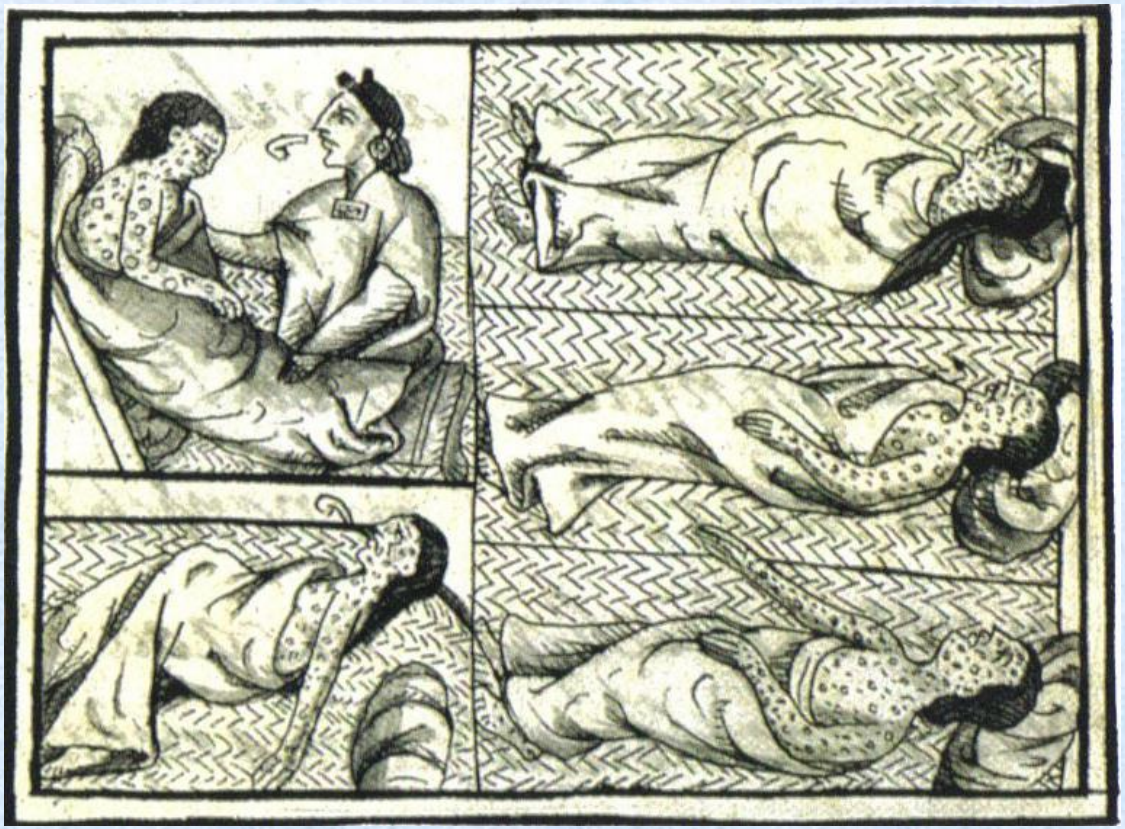


Ramses V with smallpox lesions



Smallpox –

- Egyptians, Greeks, Romans, and European civilizations all encountered various epidemics throughout their history
- decimated Native Americans



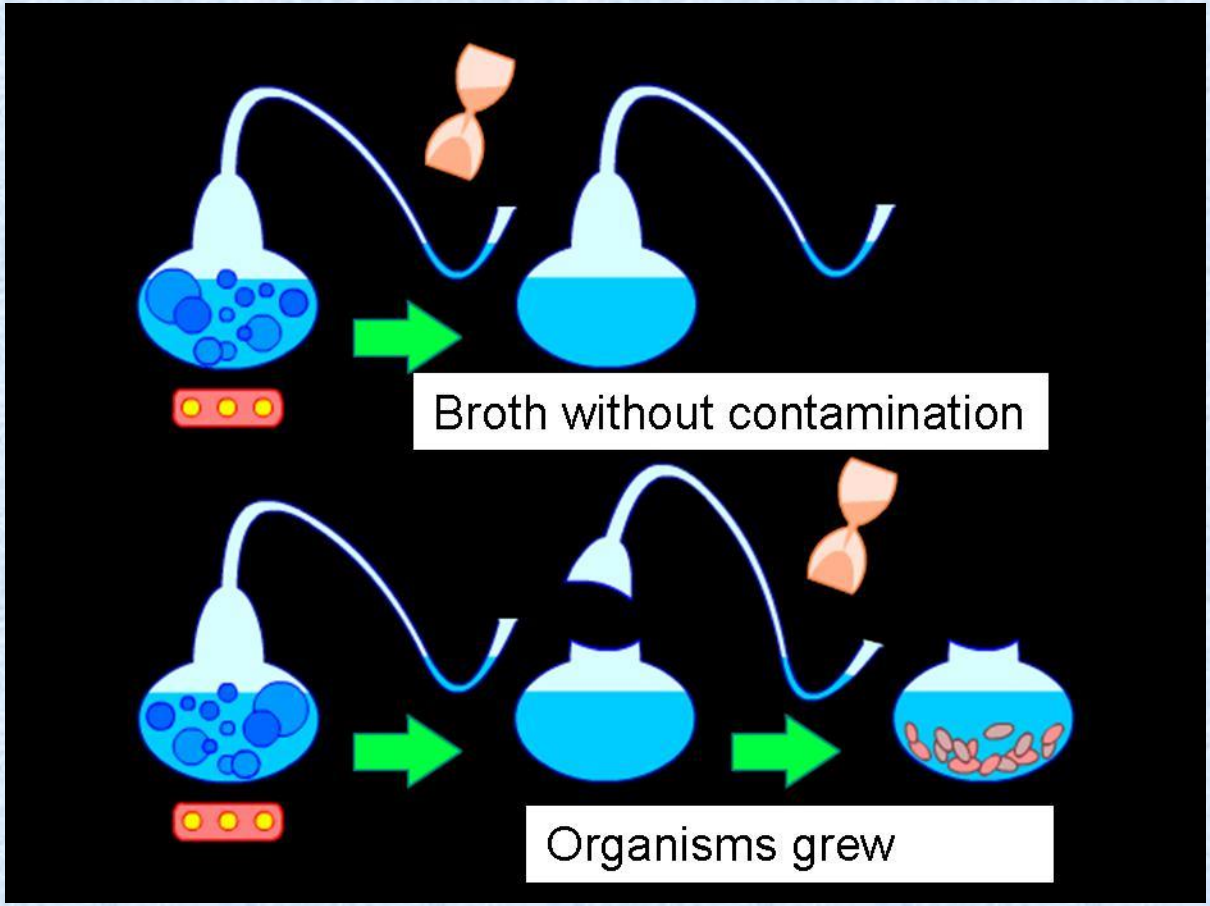
Smallpox Vaccine

- Variolation – treatment with scabs of smallpox victims, unsafe method.
- Edward Jenner, 1798
- Milkmaids got cowpox from cows, did not get smallpox
- Demonstrated inoculation with cowpox could protect against smallpox
- Brought the first hope that the disease could be controlled.

Louis Pasteur, 1822–1895

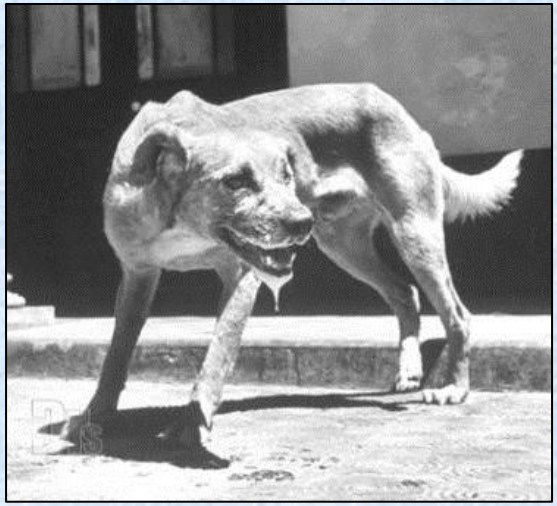
- Experiments on spontaneous generation,
- “Pasteurization”, heating liquids prevents spoiling
- Demonstrated microbes involved in disease

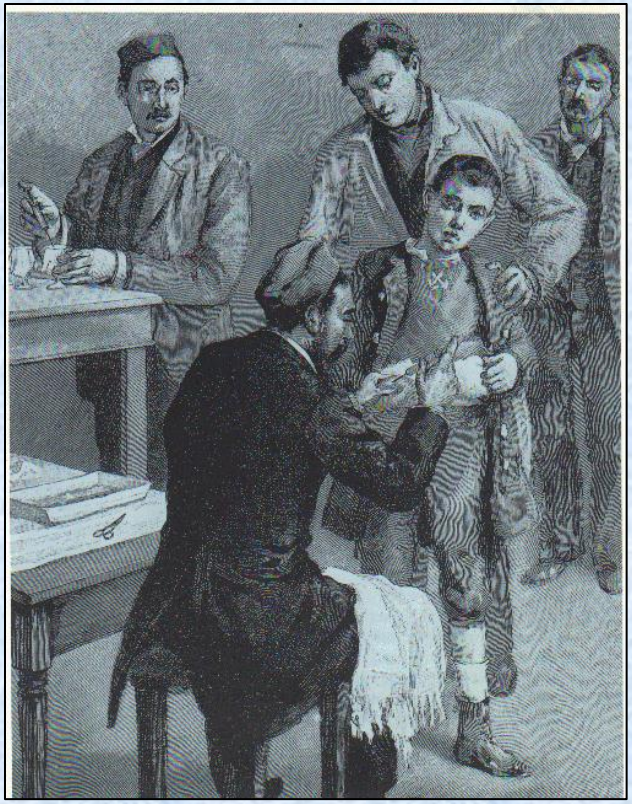
Coined word “virus”



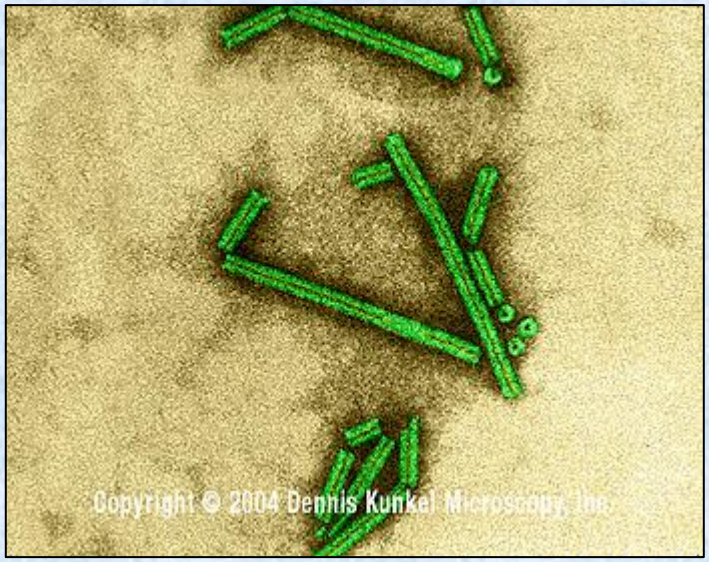
Pasteur - Rabies vaccine

- Suggested something smaller than bacteria caused rabied.
- Produced weakened “attenuated” forms of the virus.
- Louis Pasteur’s first human test subject for the rabies vaccine was a young boy who had been bitten repeatedly by a rabid dog, brought him to Pasteur’s laboratory





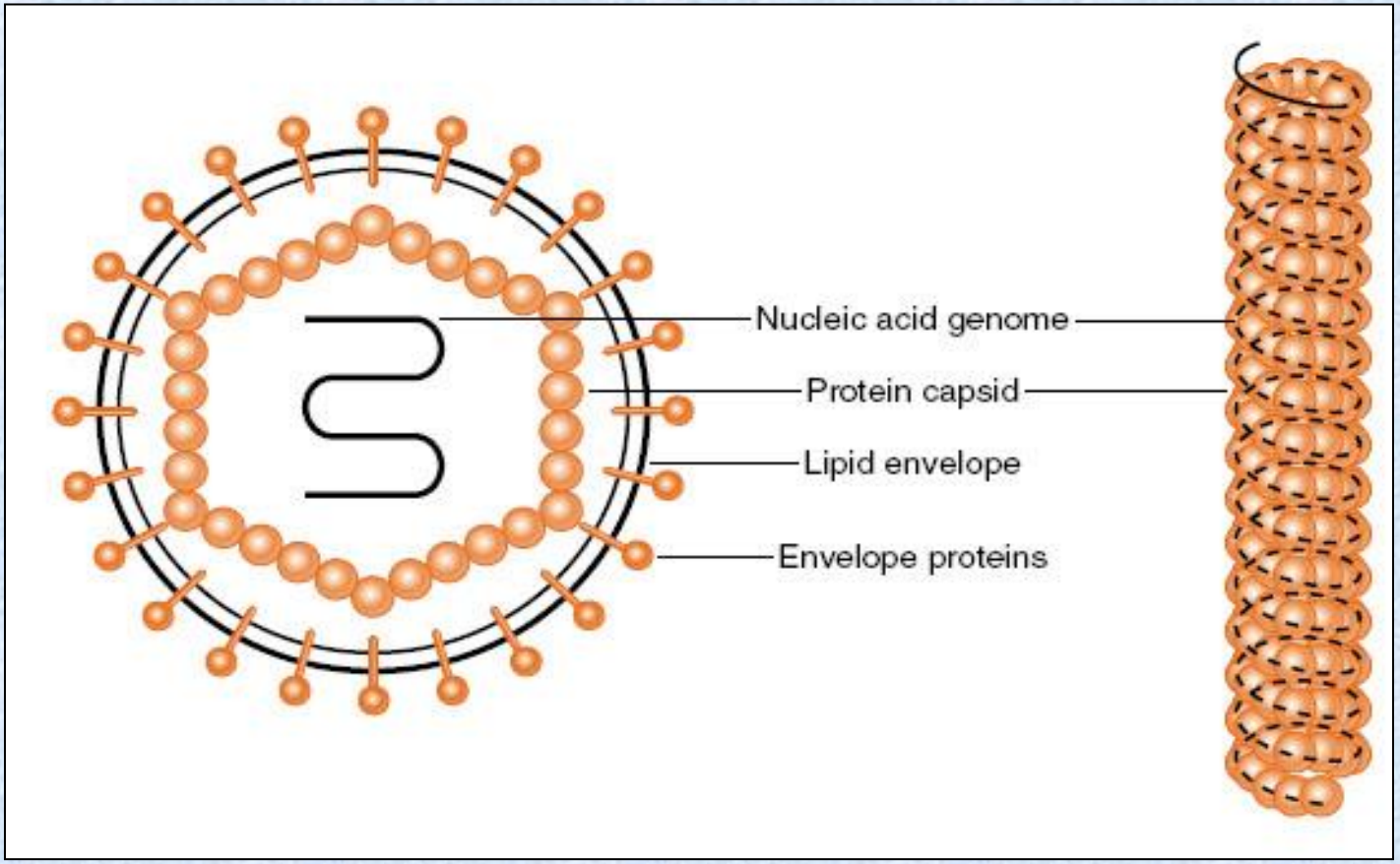
Plant Viruses - Tobacco Mosaic Virus - TMV



- 1892 – Dmitri Ivanowsky showed disease-causing agent passed right through the finest porcelain designed for bacteria, and could still reproduce and cause disease.
- 1935 – Wendall Stanley purified TMV and showed it could be crystalized

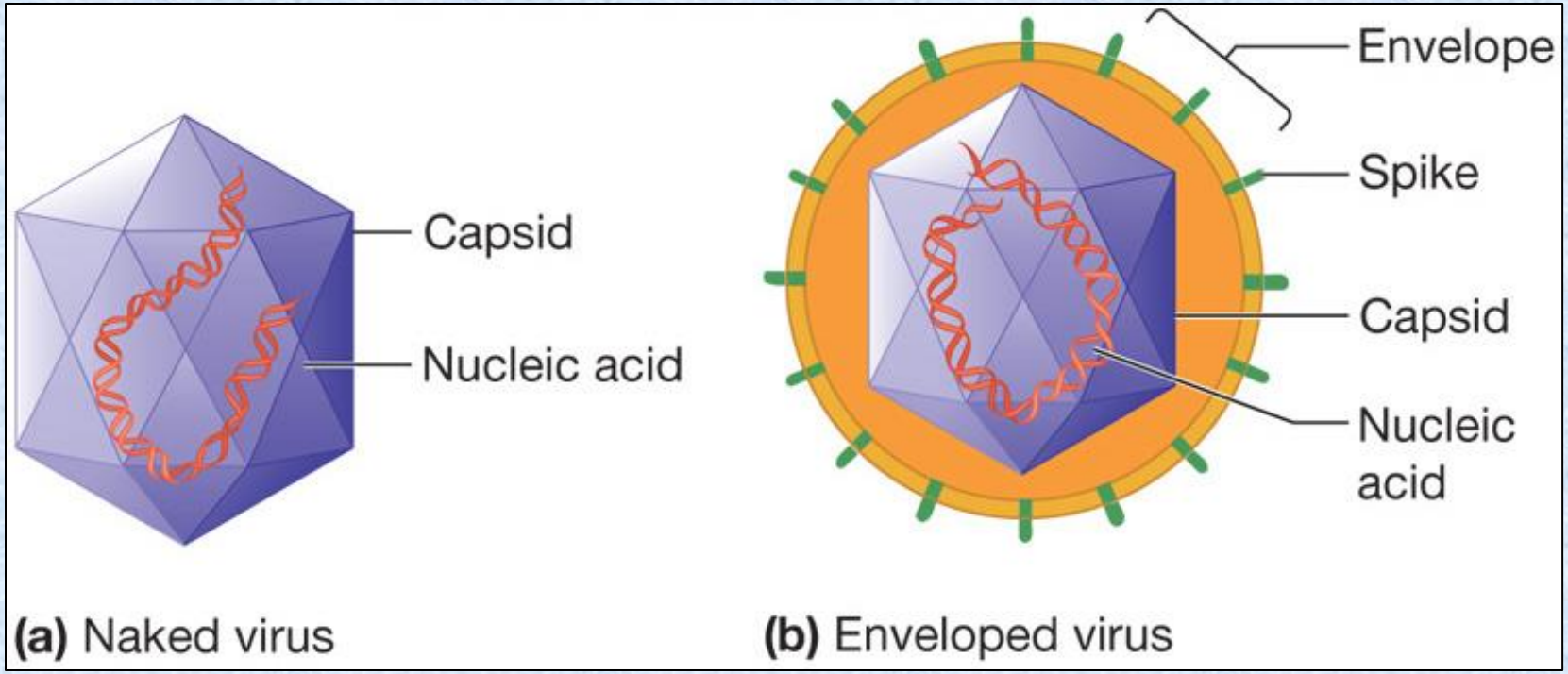
Nature of Viruses

Nucleic acid core, surrounded by a protein coat (capsid), some have in addition an **outer envelope** containing lipids and proteins.

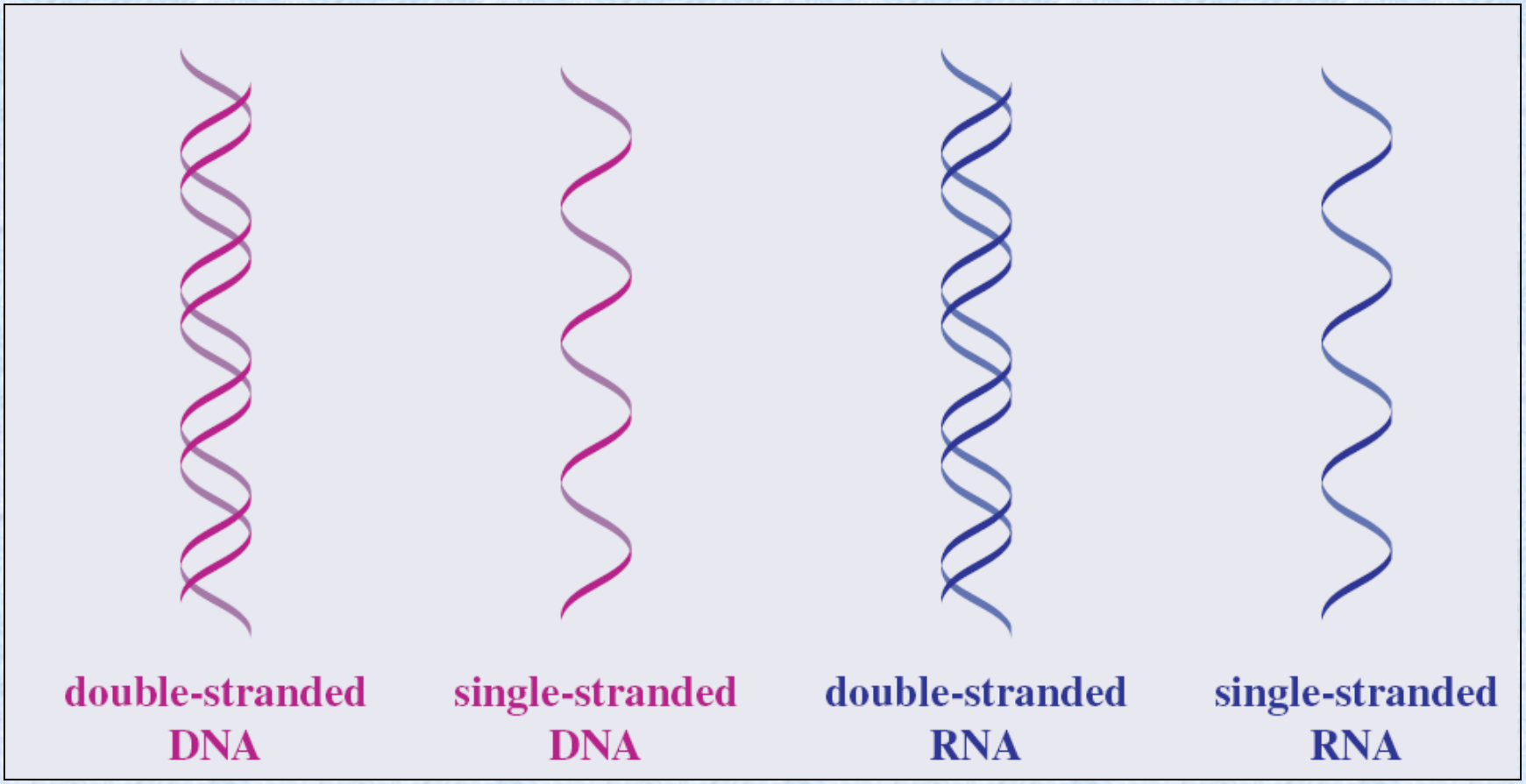


Viral genome is packaged in protein coat

…Generalized Structure of Viruses



Virus Genomes – DNA or RNA, but not both

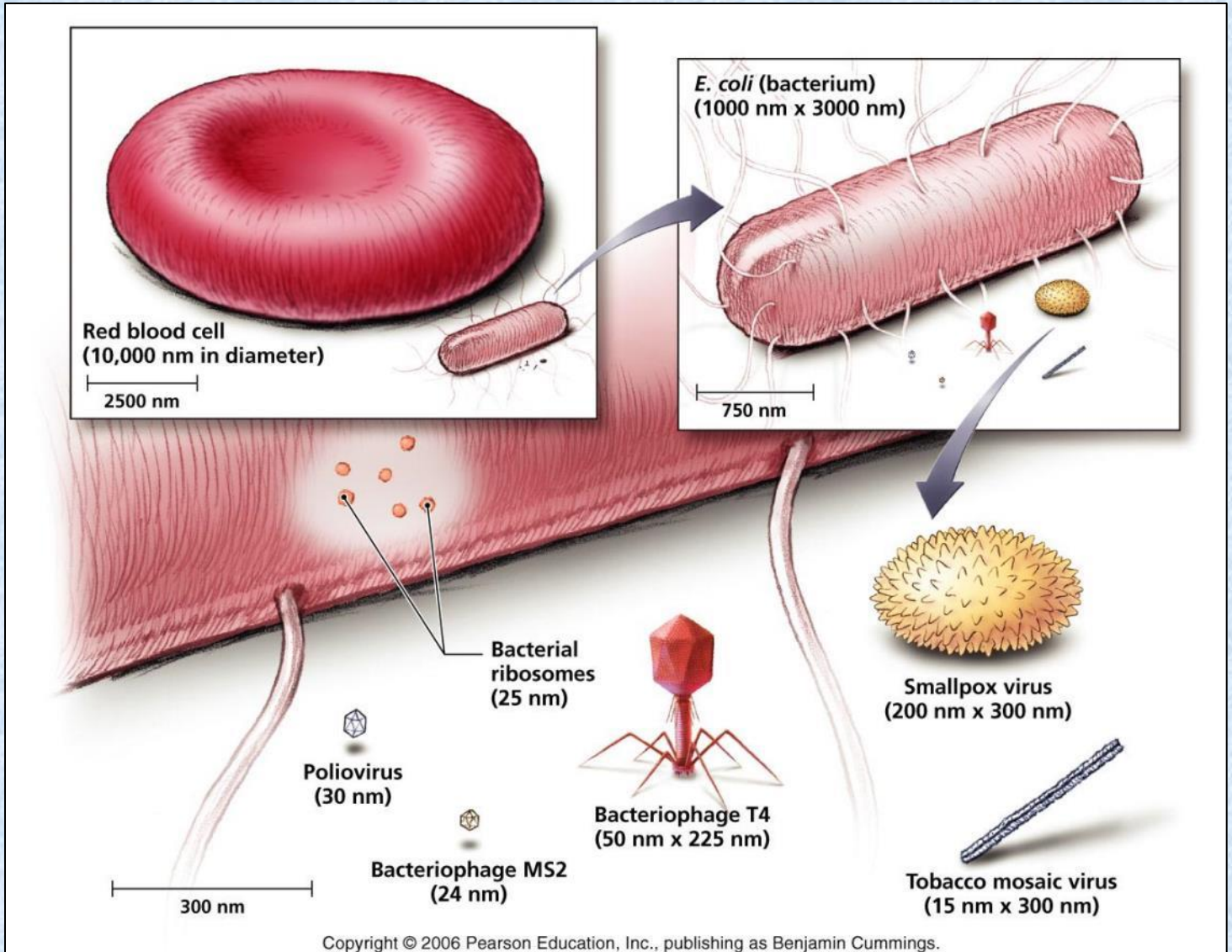


The genetic material specifies virus proteins

Some viruses may also have enzymes

Virus Size –

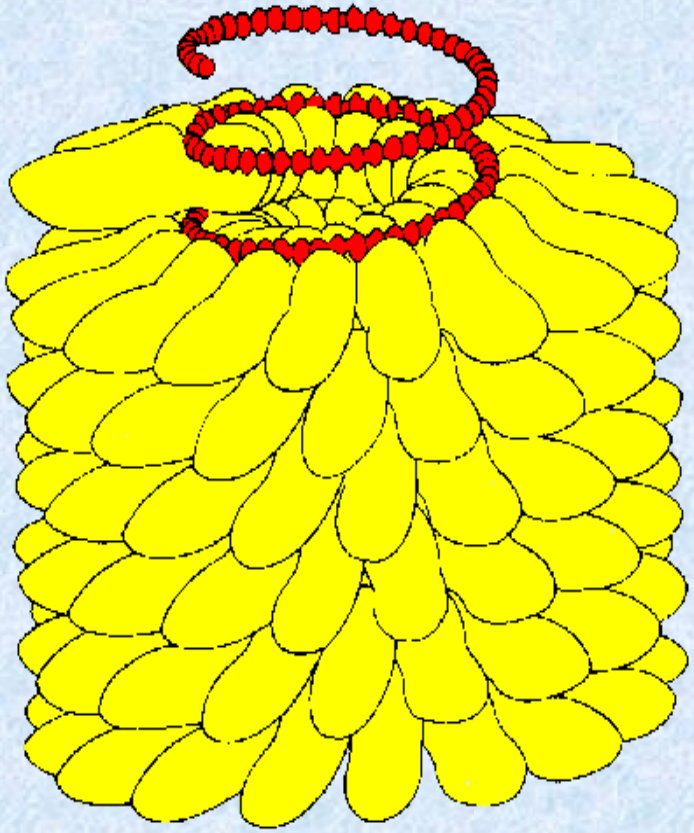
- Generally 10-400 nm (1 nm = 1 millionth millimeter)
- Most can only be seen with an electron microscope



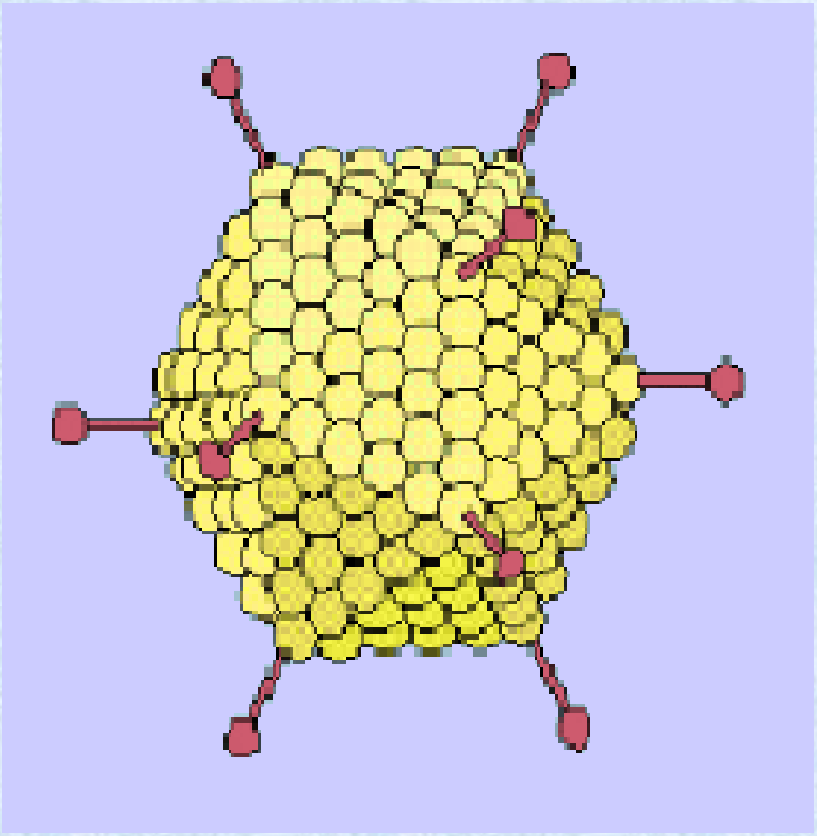
Virus Morphology

- Simple Structure
- Repetitive Structure
- High Level of Redundancy

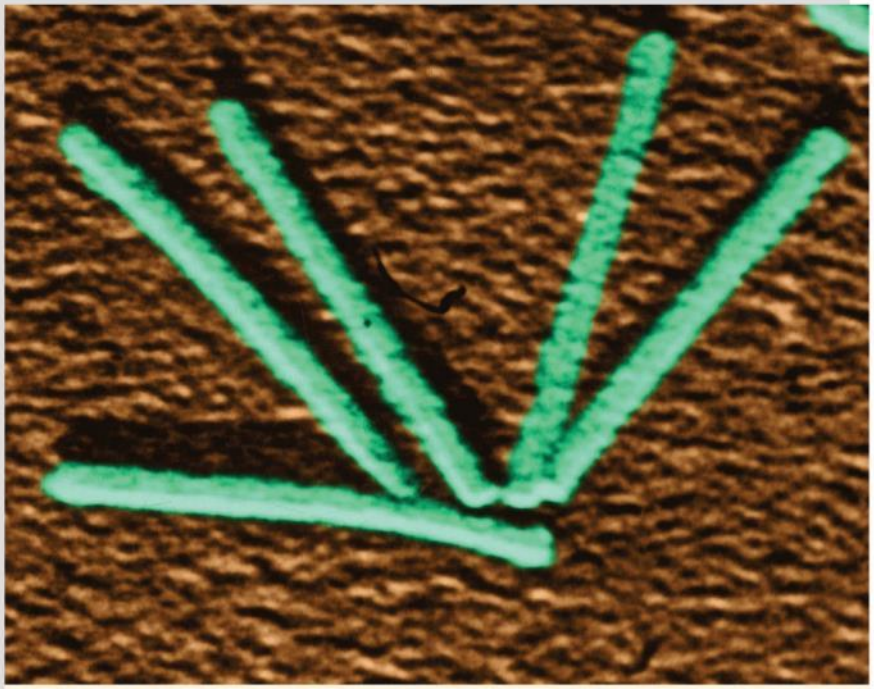
Virus Morphology



Helical

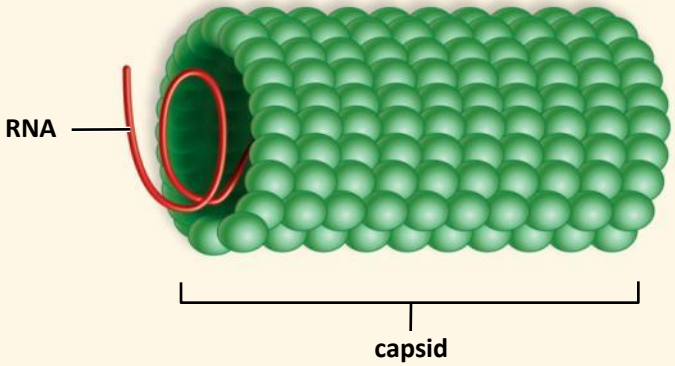


Icosahedral

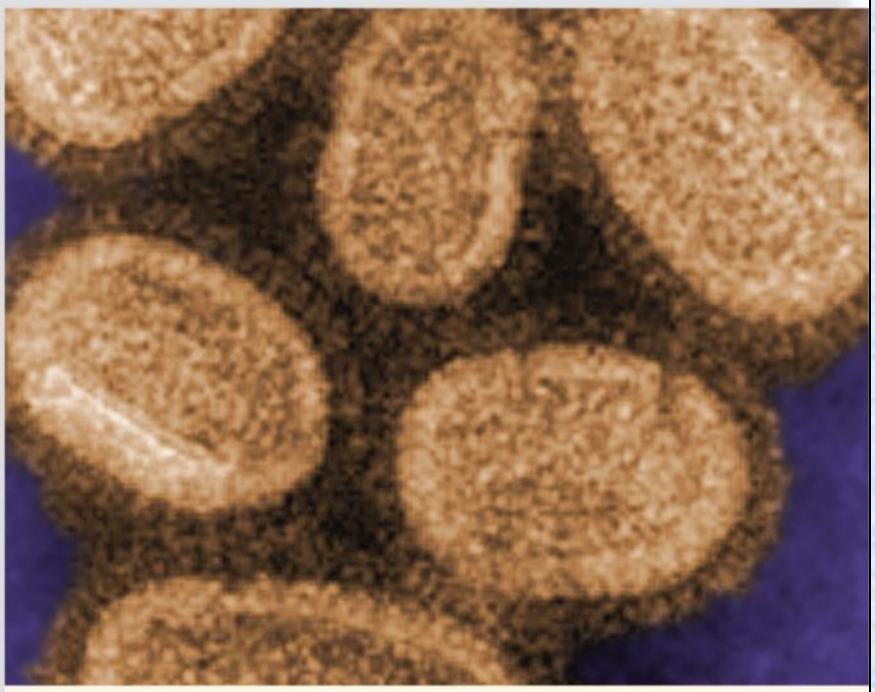


TEM 44,000×

Tobacco mosaic virus: RNA virus with a helical capsid.

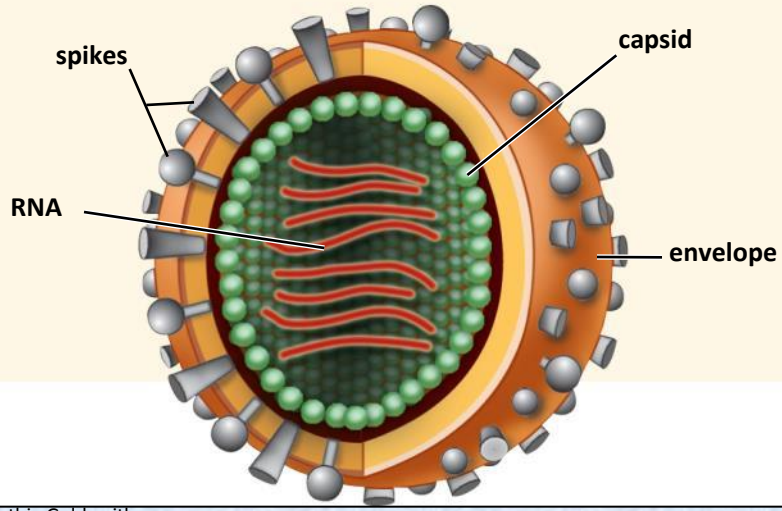


c.



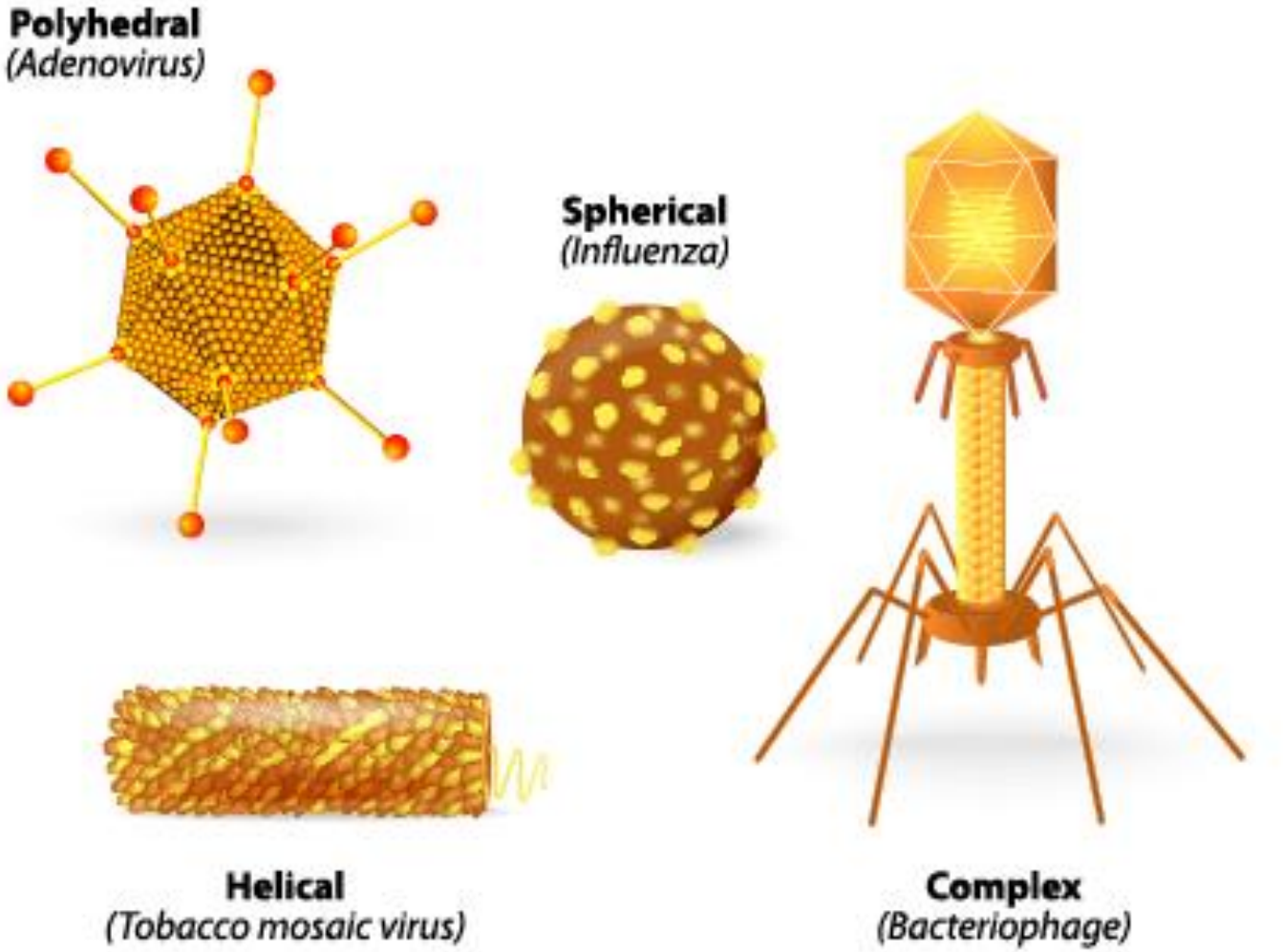
TEM

Influenza virus: RNA virus with a spherical capsid surrounded by an envelope with spikes.

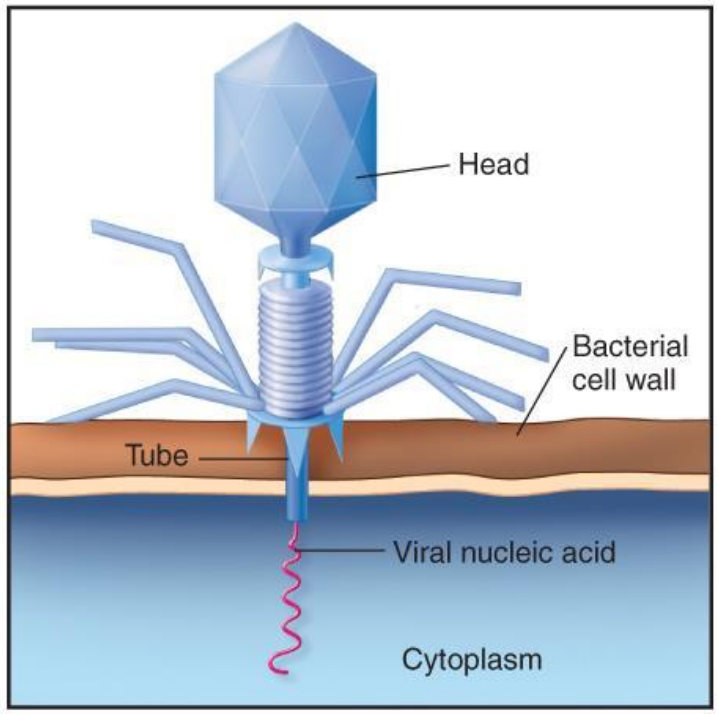


d.

VIRAL SHAPES



Bacteriophage



(a)

(b)

- Viruses that infect bacteria
- Complex – have head, neck, tail, base plate and tail fibers

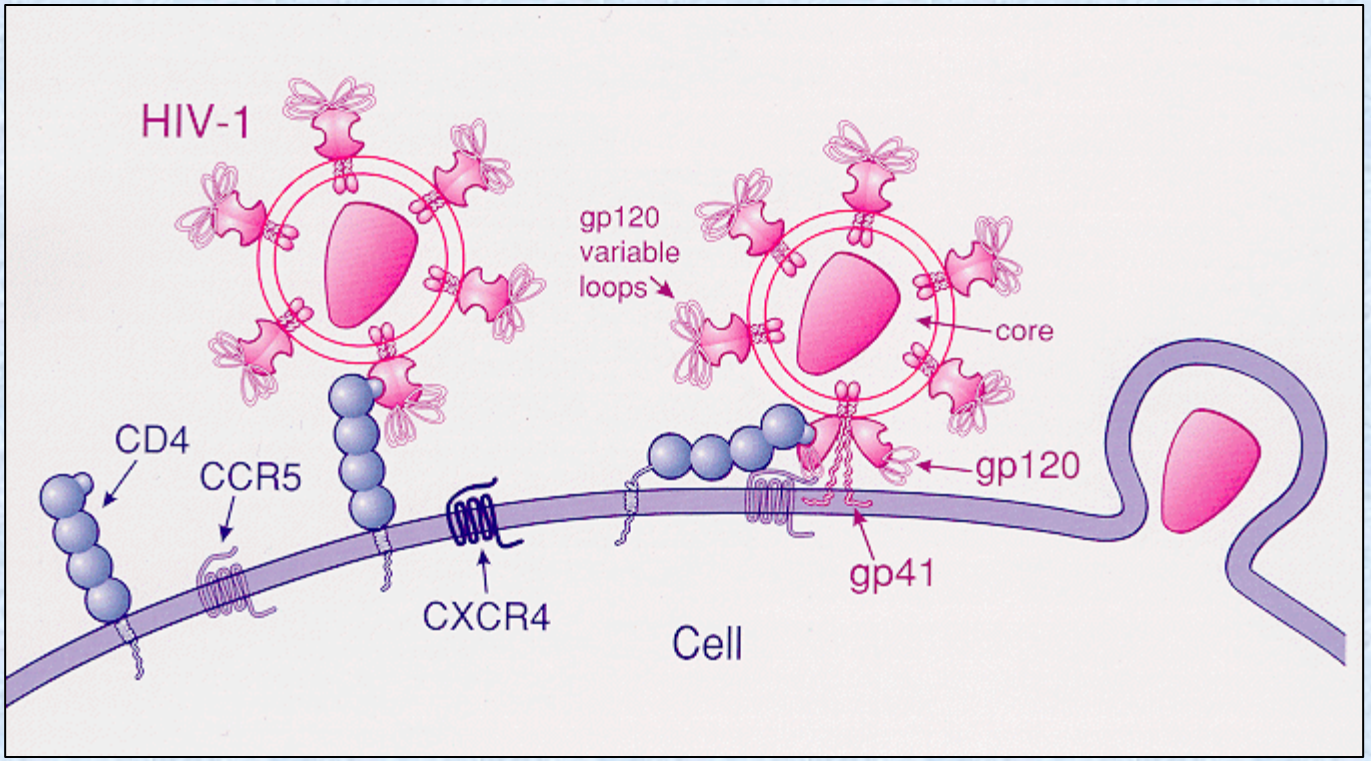
Origin of Viruses?

Viruses appear to be polyphyletic
– they have many evolutionary origins

- Leftover from the RNA World? Pre-cellular?
  -RNA viruses only organisms today with just RNA
- Fragments of plant or animal genomes
  -Some large viruses genomes resemble cell DNA
  -Many viruses take host DNA
- Escaped bacterial plasmids
- Degenerate cells?

Host Specificity

- A specific virus infects only reproduce in a specific organism
- Some viruses are specific to certain tissue types
- Specificity determined by receptors on coat, lock and key fit



Attachment of HIV to cell

Classification - viruses are classified by a number of characters, probably related to the origin of these groups.

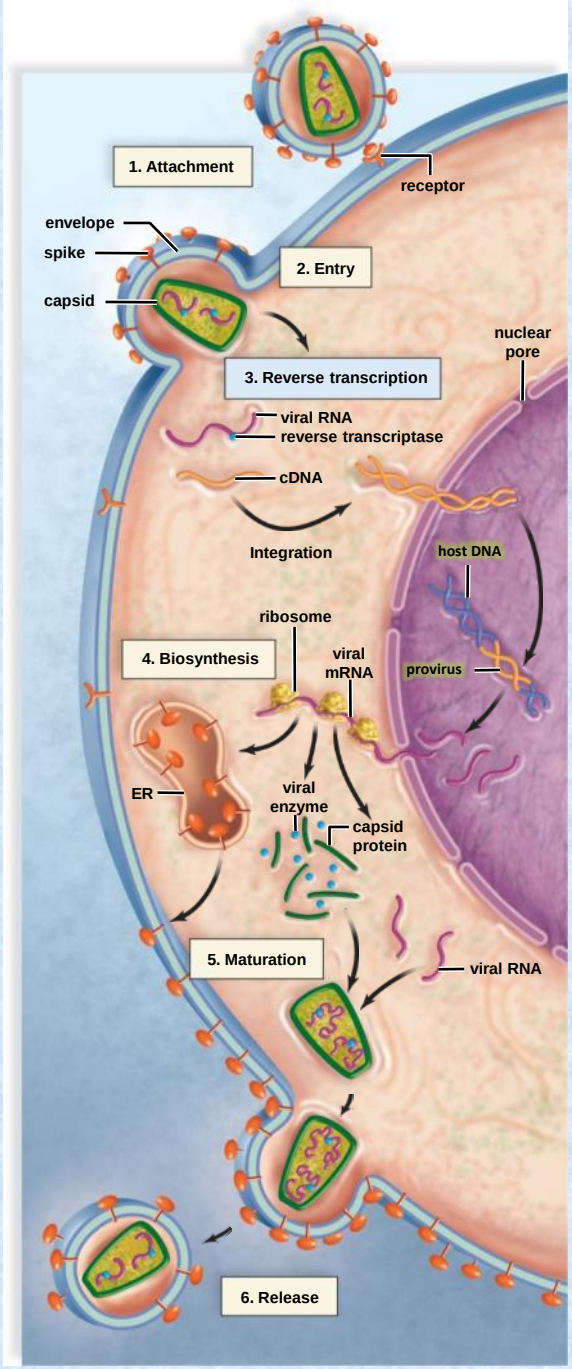
- Nucleic acid - RNA or DNA
- Single stranded or double stranded
- Plus-strand (ss RNA acts directly as mRNA), or Minus-strand (ss RNA is transcribed to make mRNA)
- Large or small genomes, size
- Presence or absence of envelope
- Shape - icosahedral, helical, brick
- Host - plants, animals, arthropods, bacteria

Types of Viruses

- **Animal viruses**: Rabies, Polio, Mumps, Chicken pox, Small pox, and Influenza.
- **Plant Viruses**: Tobacco mosaic virus (TMV), Banana streak virus, Carrot thin leaf virus
- **Bacterial Virus**: Bacteriophages (T1, T2, T3, and T4.)
- SPECIFIC in what type of cell and what type of organism they infect
  - Polio – human nerve cell
  - T4 – only certain strains of *E. coli*

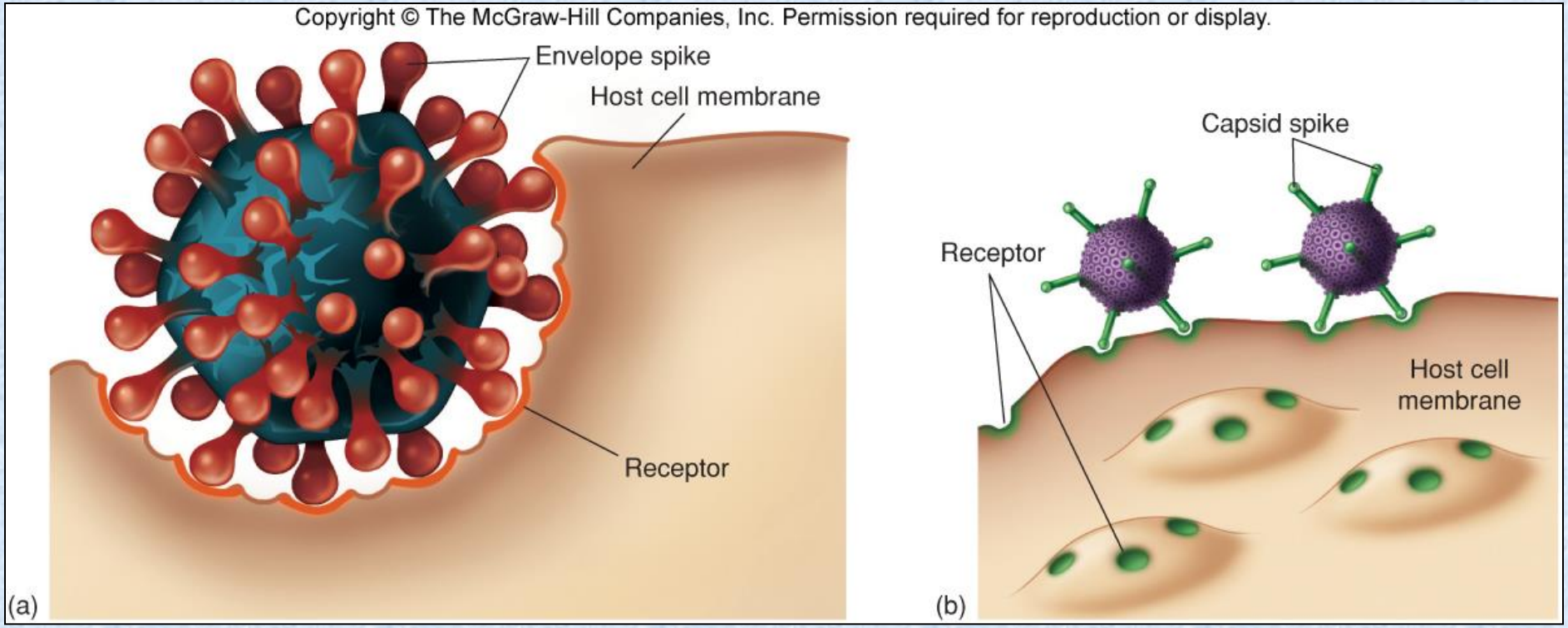
Virus Reproduction

1. Attachment
2. Penetration - Uncoating
3. Biosynthesis
4. Maturation - Assembly
5. Release



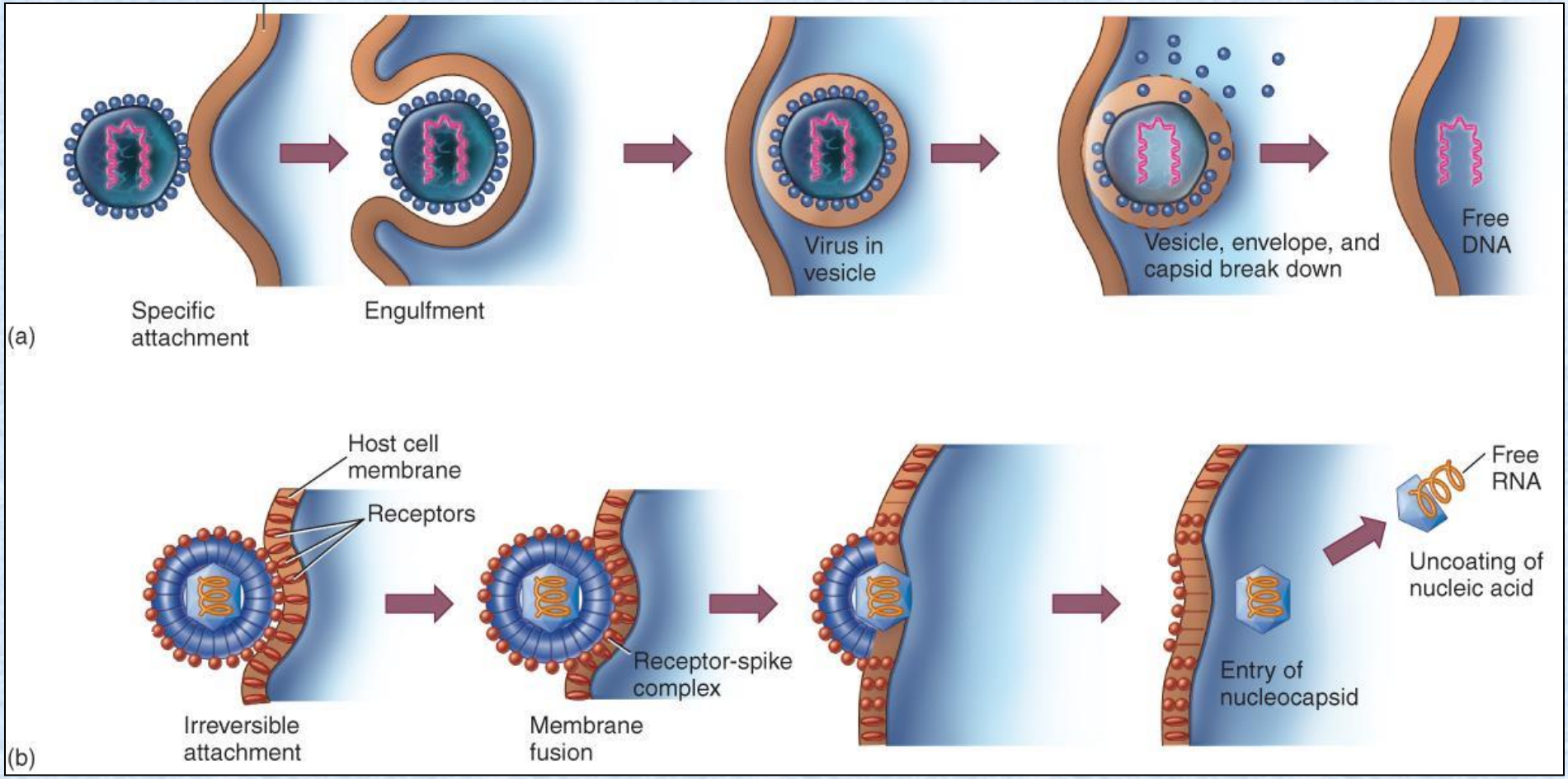
Attachment - Adsorption

- Virus encounters susceptible host cells
- Adsorbs specifically to receptor sites on the cell membrane
- Because of the exact fit required, viruses have a limited **host range**



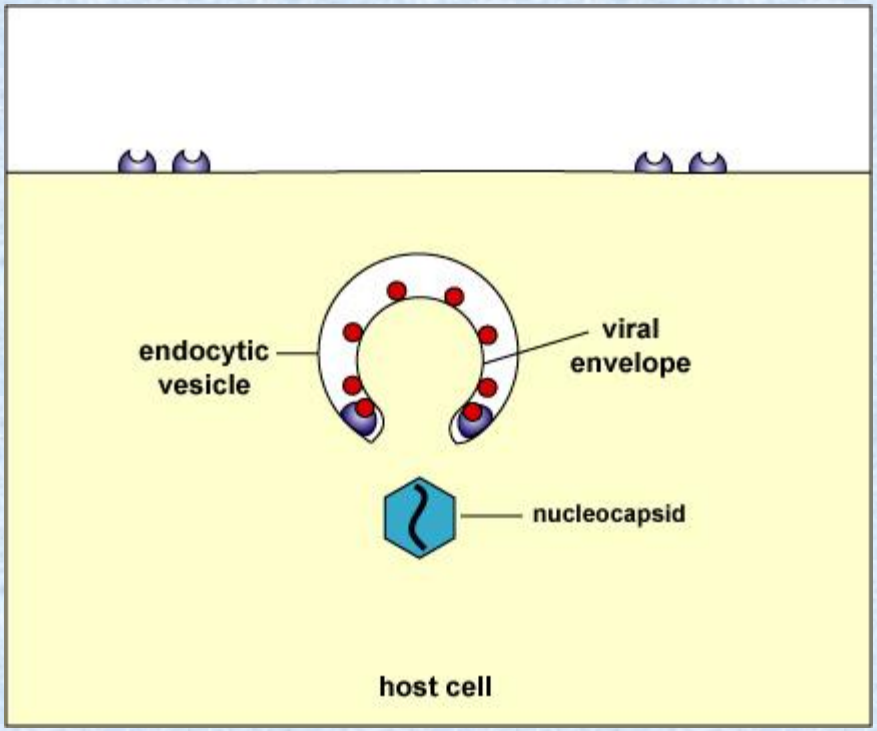
Penetration

- Host cell engulfs virus
- Flexible cell membrane of the host is penetrated by the whole virus or its nucleic acid.
- Endocytosis or membrane fusion



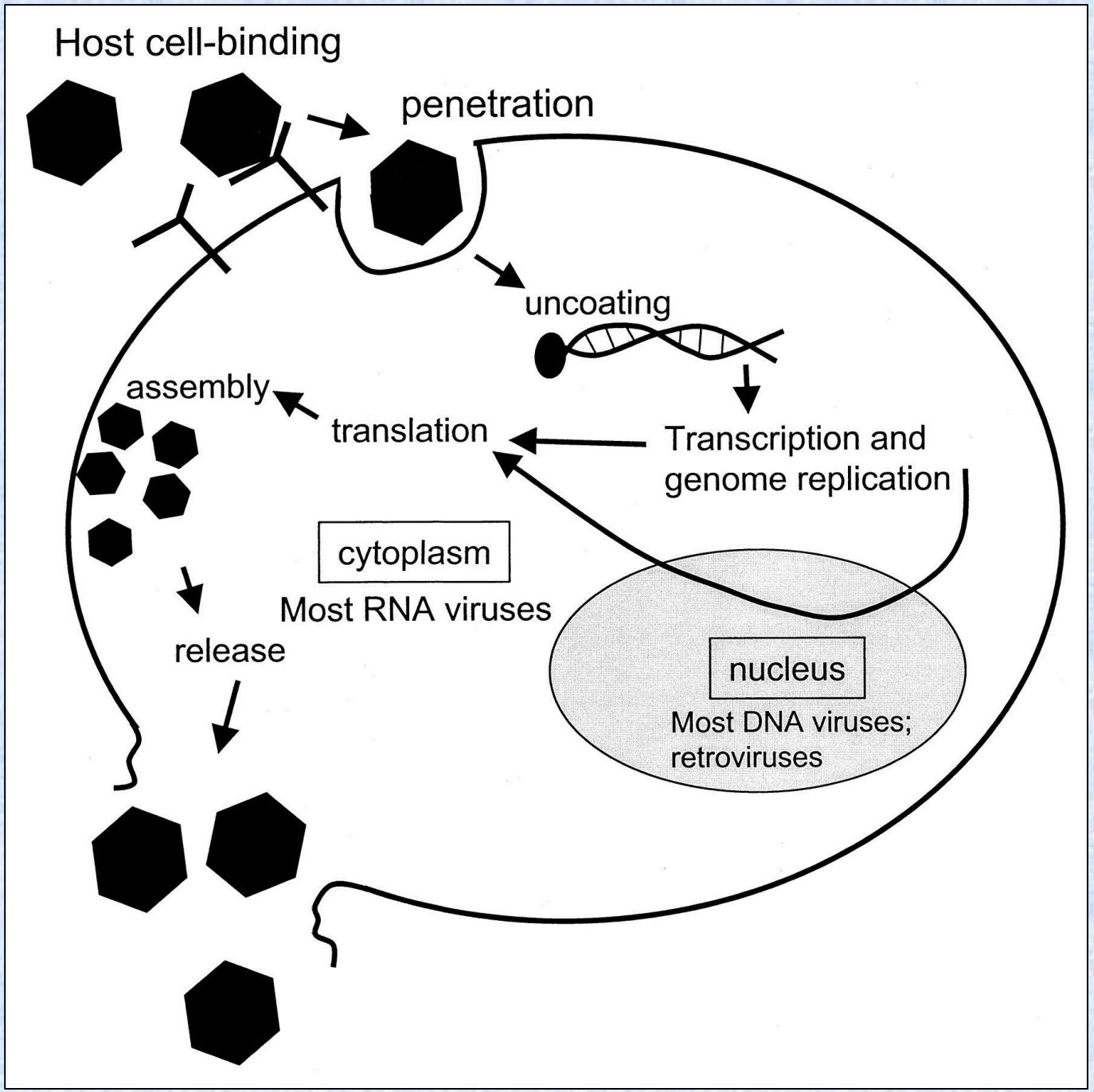
Penetration - Uncoating

- Enzymes in the vacuole dissolve the envelope and capsid
- The virus is now **uncoated**



Biosynthesis

- Viral nucleic acid takes control over the host's synthetic and metabolic machinery
- DNA viruses- enter host cell's nucleus where they are replicated and assembled
  - DNA enters the nucleus and is transcribed into RNA
  - The RNA becomes a message for synthesizing viral proteins (translation)
  - New DNA is synthesized using host nucleotides
- RNA viruses- replicated and assembled in the cytoplasm

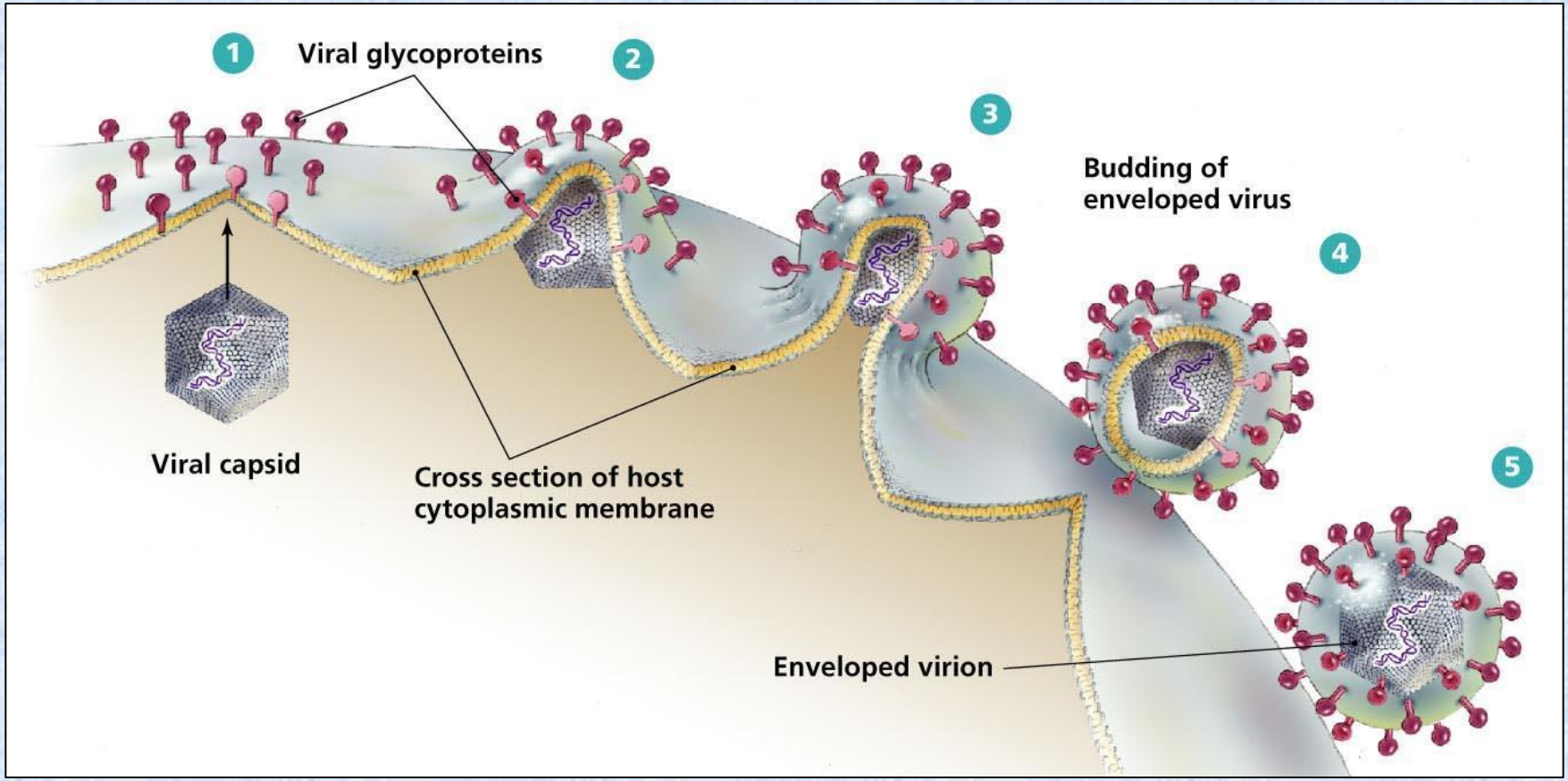

Host cell-binding
penetration
uncoating
assembly
translation
Transcription and
genome replication
cytoplasm
Most RNA viruses
release
nucleus
Most DNA viruses;
retroviruses

Maturation - Release

- Non-enveloped and complex viruses are released when the cell lyses or ruptures
- Enveloped viruses are liberated by **budding** or **exocytosis**
- Anywhere from 3,000 to 100,000 virions may be released, depending on the virus
- Entire length of cycle- anywhere from 8 to 36 hours

Maturation - Assembly

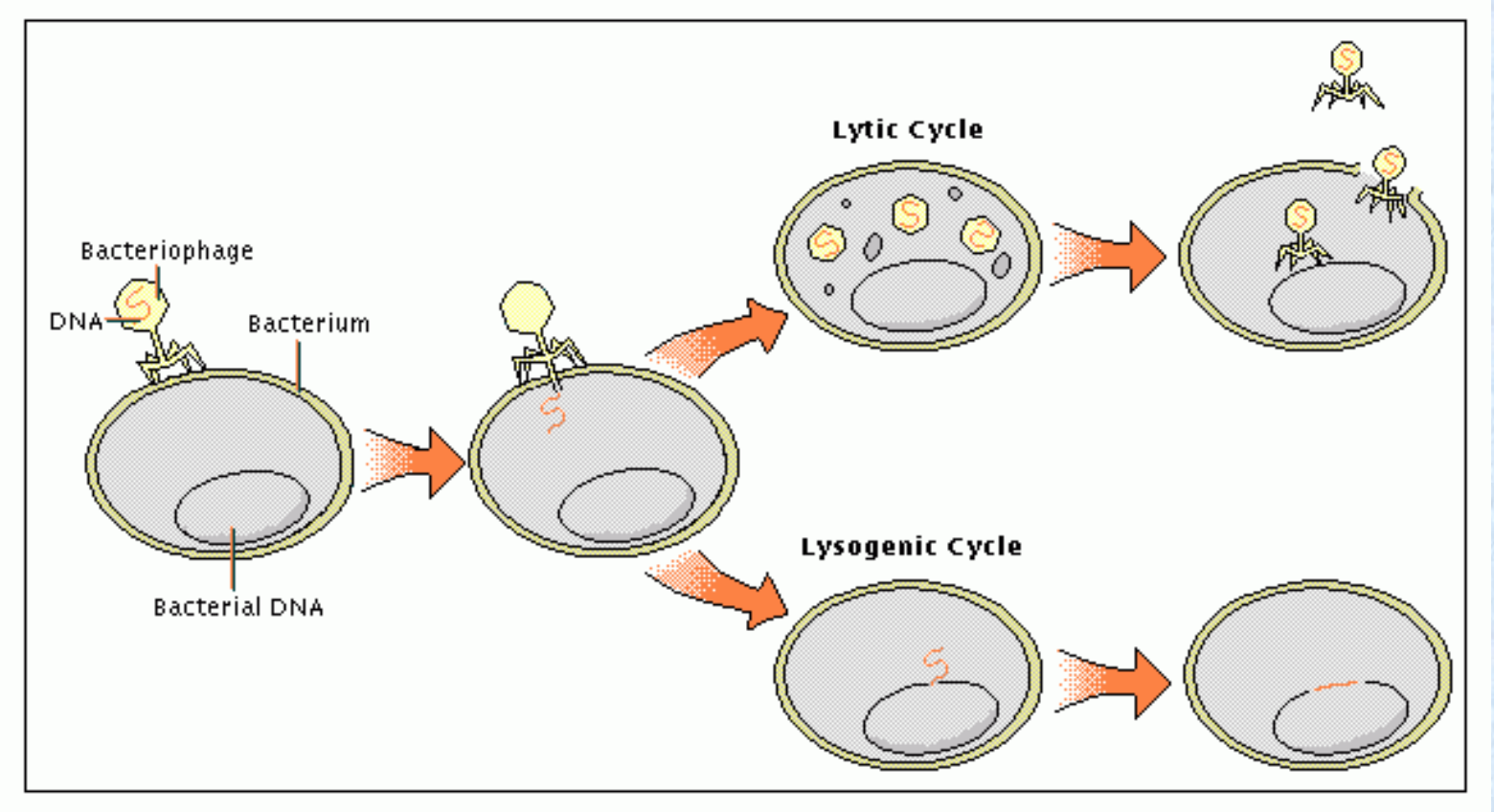
- Mature virus particles are constructed from the growing pool of parts



Lytic Versus Lysogenic Infection

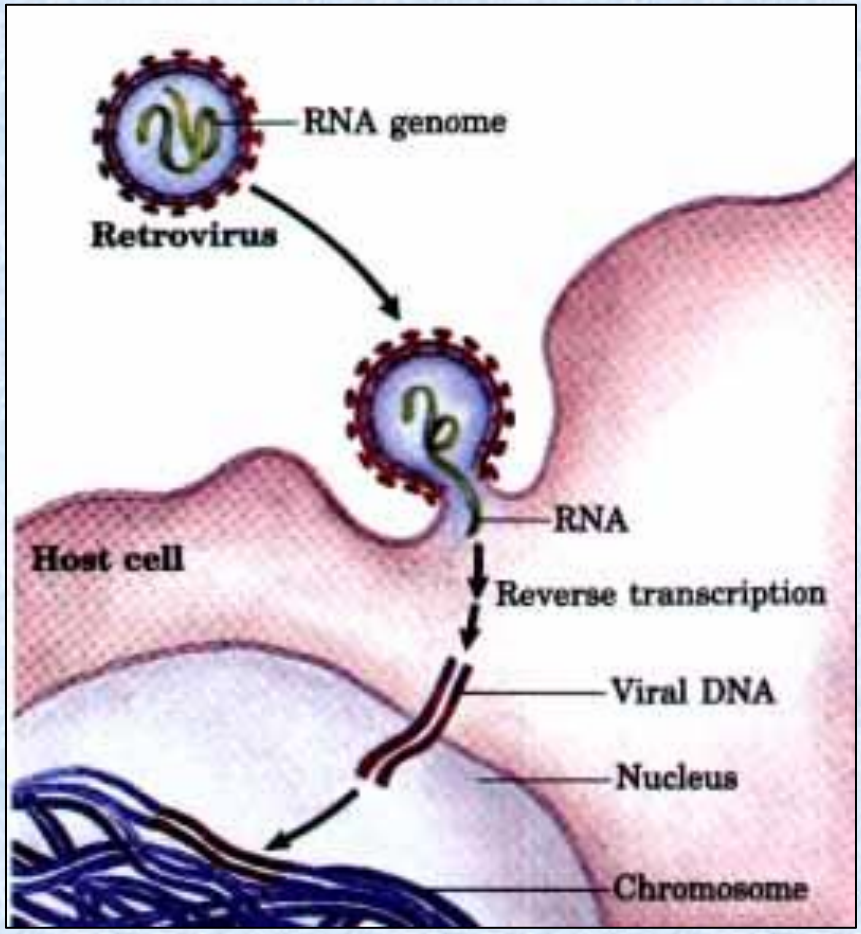
- In a lytic infection, the host cells fills with virions and bursts.
  - The result is cell death.
- Lysogenic infections are also known as latent infections.
  - The viral genome becomes incorporated into the host cell's DNA.
    - It can remain this way for an extended period.
    - The host cell lives.

- **Virulent (Lytic)** - host cell is burst open (lysis, lytic cycle), cell dies. (Ebola)
- **Temperate (Lysogeny)** - virus becomes inserted in the host cell's DNA, can **remain latent for a long time**, passed along for **many generations** to all descendants. (Herpes, HIV)

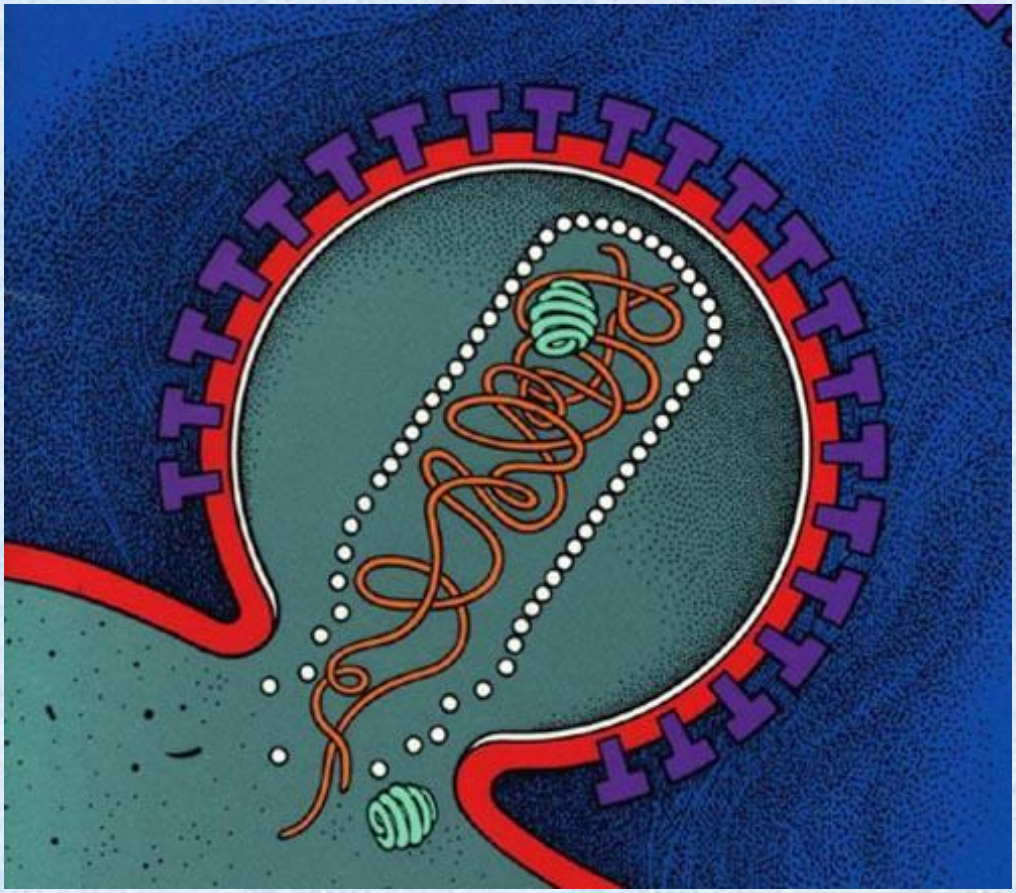


Retroviruses (e.g. HIV)

Contain **reverse transcriptase** which makes a double-stranded DNA copy of the RNA, the DNA then is integrated in the host's genome and makes copies of the viral molecule.



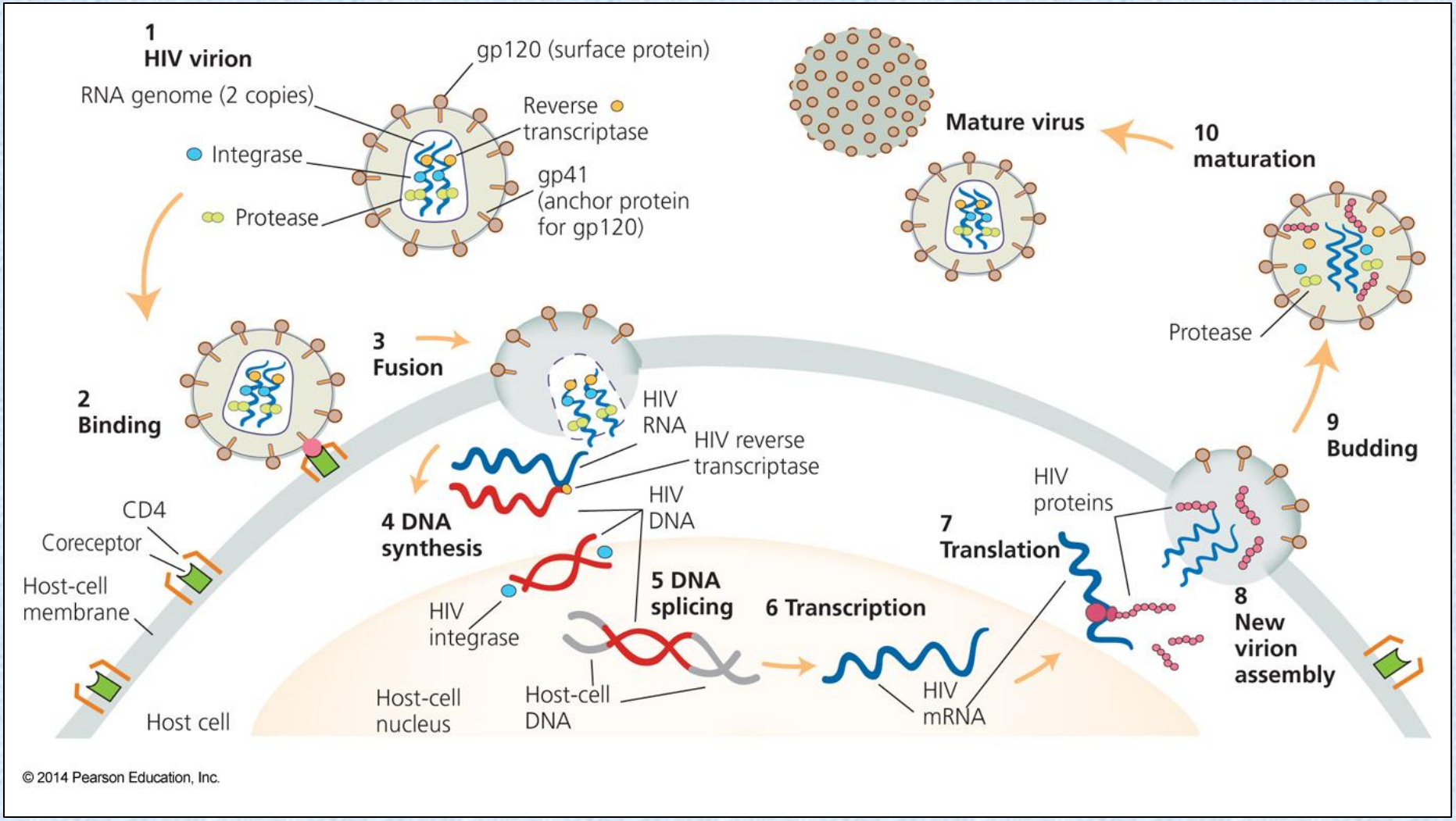
- HIV binds to two protein receptors on cell's surface : CD4 and a co-receptor, usually CCR5.
- Host cell membrane and viral coat fuse and virus contents enter cell.



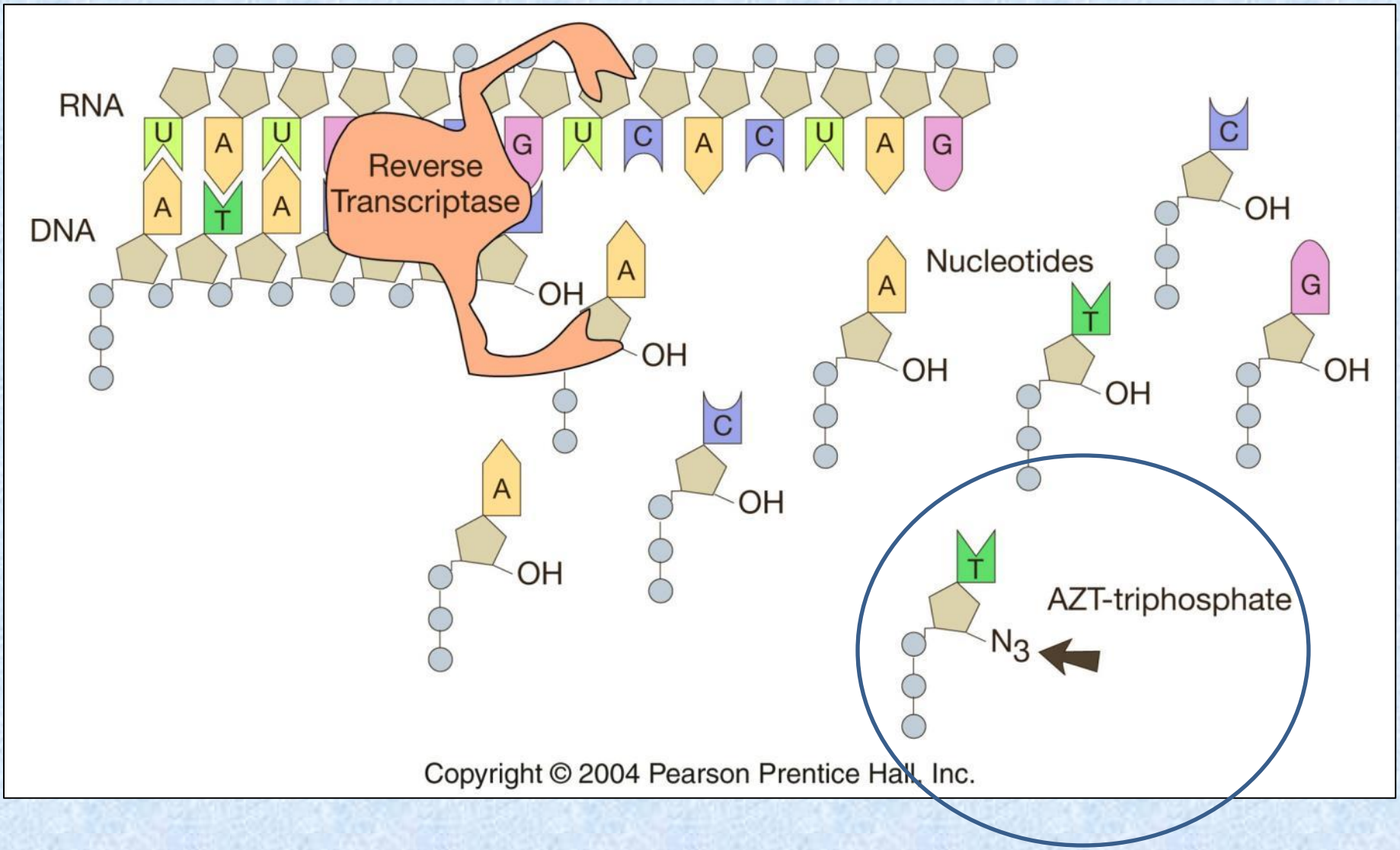
What the virus inserts

- RNA genome: codes for several proteins.
- **Reverse transcriptase**: transcribes viral RNA into DNA
- Integrase: this enzyme splices DNA into host DNA
- Protease: this enzyme involved in production of viral proteins

HIV Life Cycle



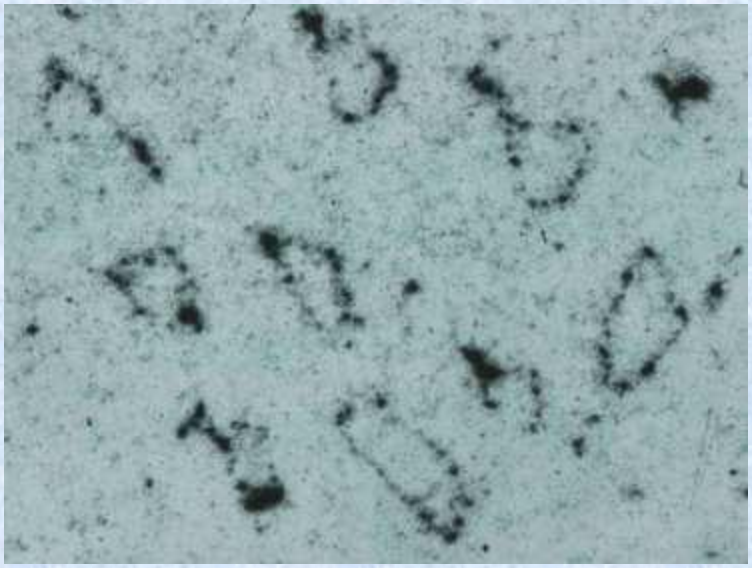
Reverse Transcriptase and AZT

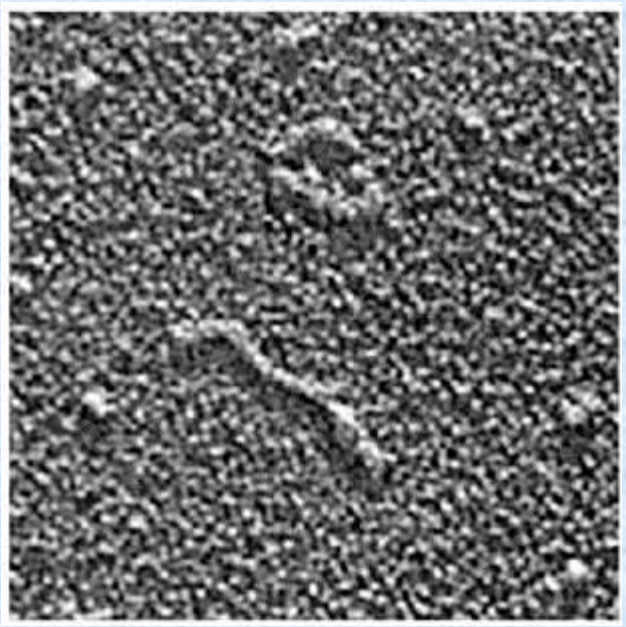


Insertion of AZT causes DNA strand formation to stop

Viroids

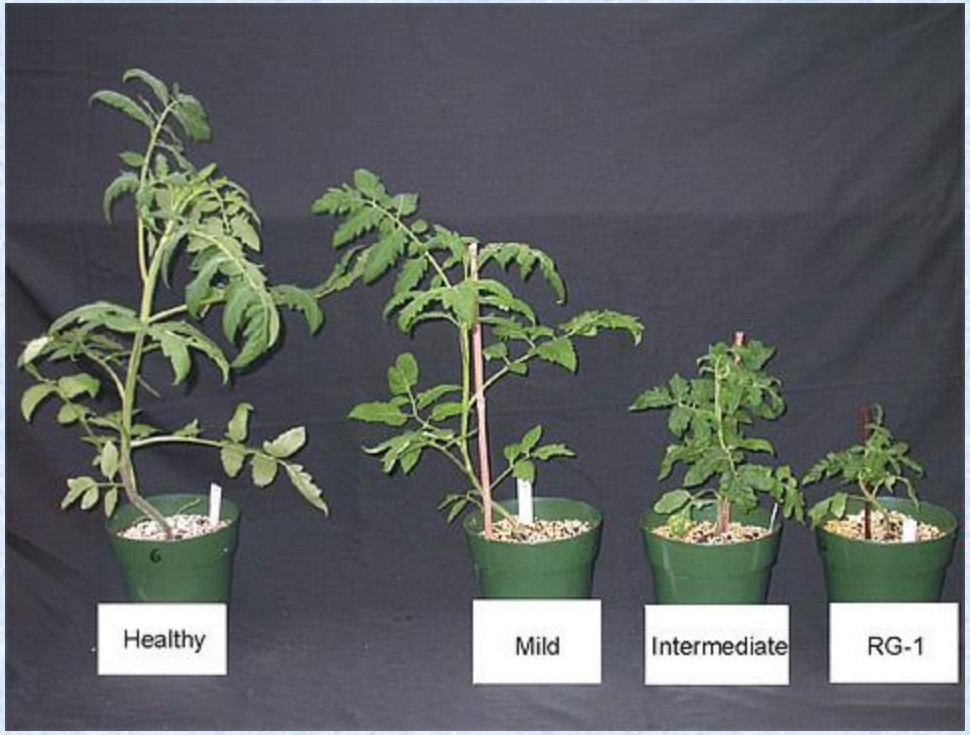
- Naked strands of RNA,
- The smallest of viruses; a plant virus with its RNA arranged in a circular chromosome without a protein coat.
- Many crop diseases





Viroids

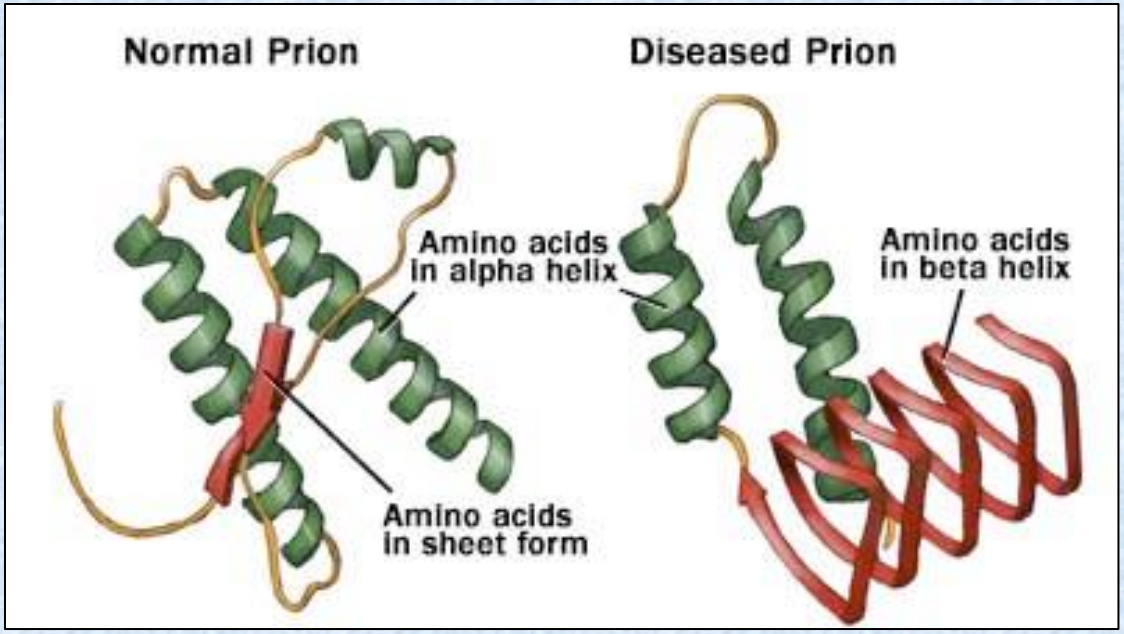
Potato spindle tuber viroid, discovered 1967



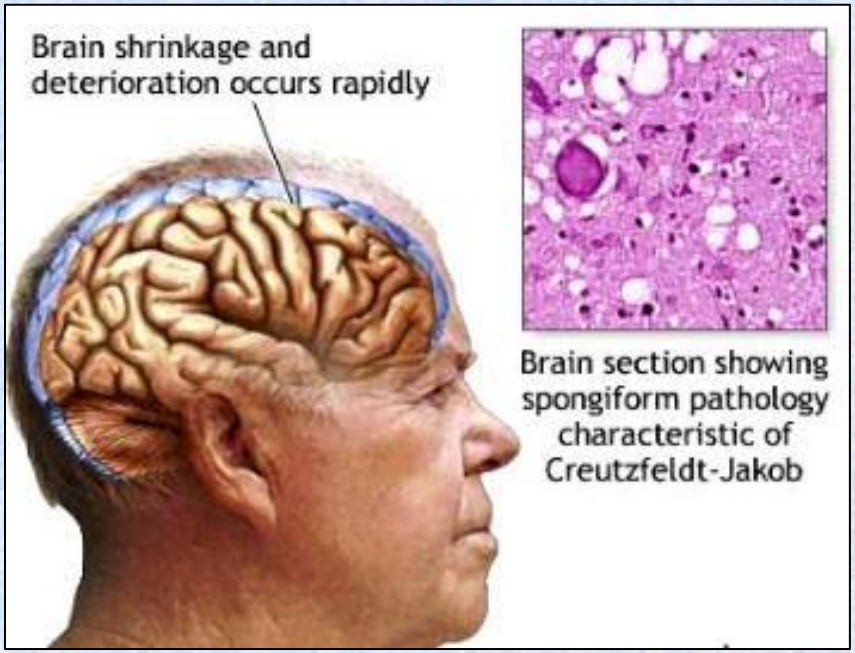
Common symptom are stunting, leaf epinasty and distortion, fruit distortion and color break, stem and leaf necrosis, and even death of the whole plant — is often dependent upon environmental conditions

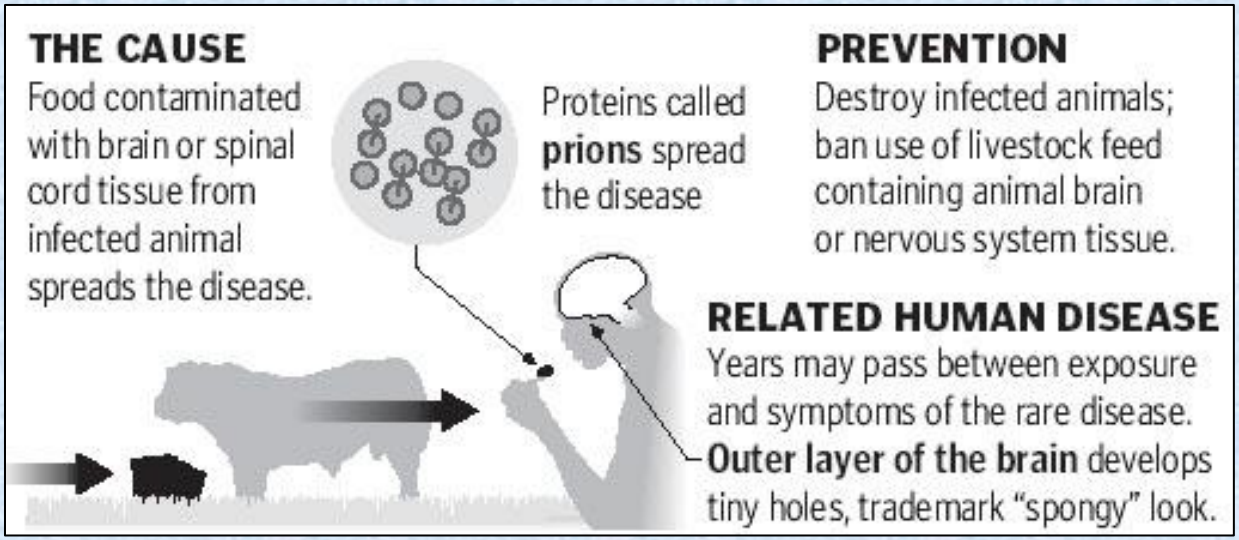
Prions

- Protein molecules with contagious tertiary structure
- Destroy nerve tissue in the brain
- Human (Kuru) and animal (Scrapie, Mad Cow)
- Some practices, including eating brains of cattle, transmitted the cattle disease (BSE or bovine spongiform encephalopathy) to humans.



Prions - Creutzfeldt-Jakob Disease (vCJD) in humans





Viruses and Human Health

Viruses – cause many human diseases

Category	Disease
Sexually transmitted diseases	AIDS (HIV), genital warts, genital herpes
Childhood diseases	Mumps, measles, chickenpox, German measles
Respiratory diseases	Common cold, influenza, severe acute respiratory syndrome (SARS)
Skin diseases	Warts, fever blisters, shingles
Digestive tract diseases	Gastroenteritis, diarrhea
Nervous system diseases	Poliomyelitis, rabies, encephalitis
Other diseases	Smallpox, hemorrhagic fevers, cancer, hepatitis, mononucleosis, yellow fever, dengue fever, conjunctivitis, hepatitis C

Emerging Viruses

New or previously uncommon illnesses.

Examples:

- AIDS
- West Nile Encephalitis
- Hantavirus pulmonary syndrome (HPS)
- Severe acute respiratory syndrome (SARS)
- Ebola hemorrhagic fever
- Hanta Virus
- Avian influenza

Events that can cause emergence of viruses

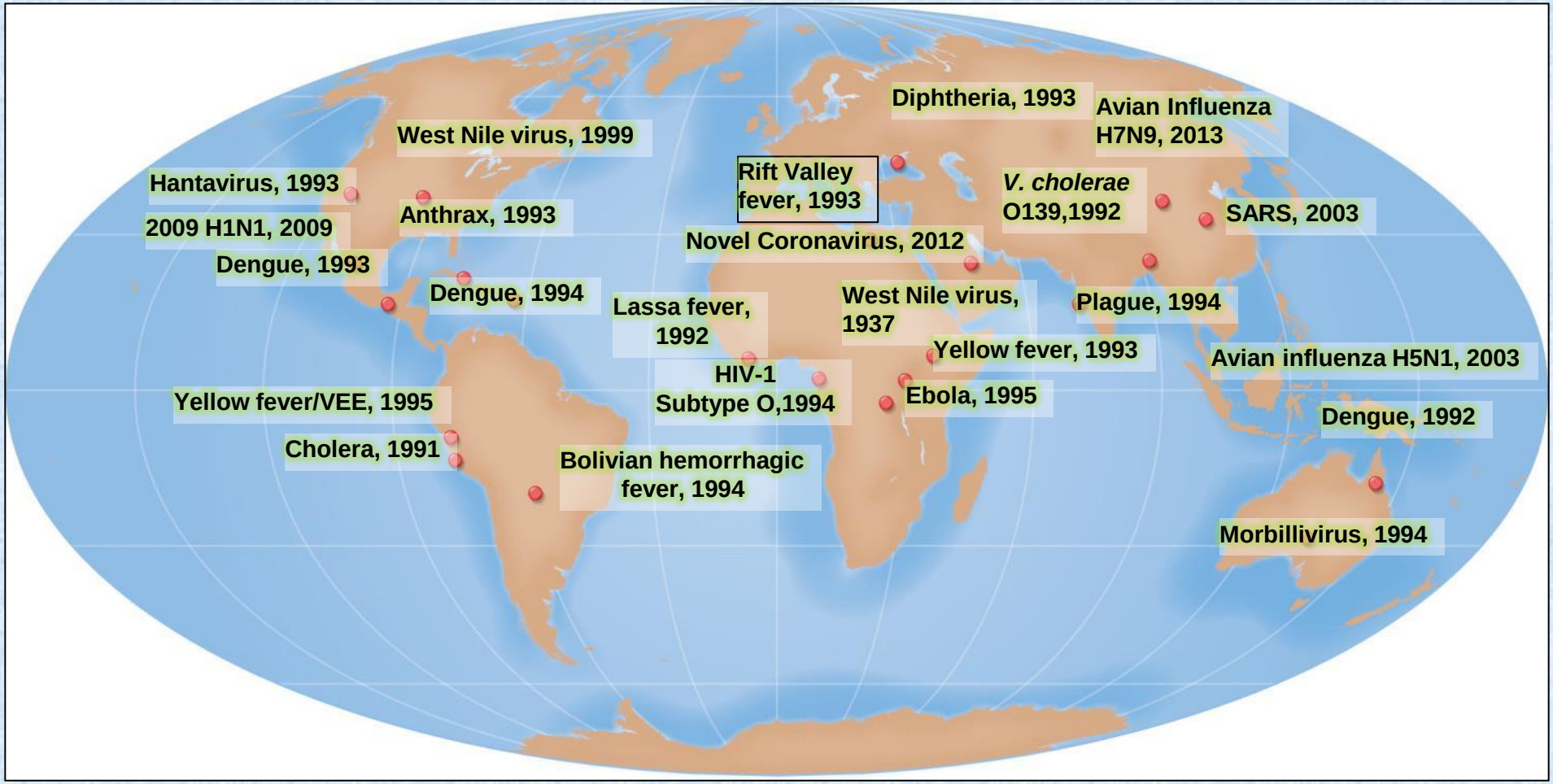
Virus may extend its range, jump to new host

- Example: West Nile was transported to US and took hold in birds and mosquitoes
- Humans come in contact with new viruses while clearing rainforest

Genetic mutation may occur

- Example: Influenza strains H5N1, H1N1, and H7N9 were created through mutation of flu viruses which only infected animals
- It is necessary to obtain flu vaccine each year due to the rapidly mutating flu virus

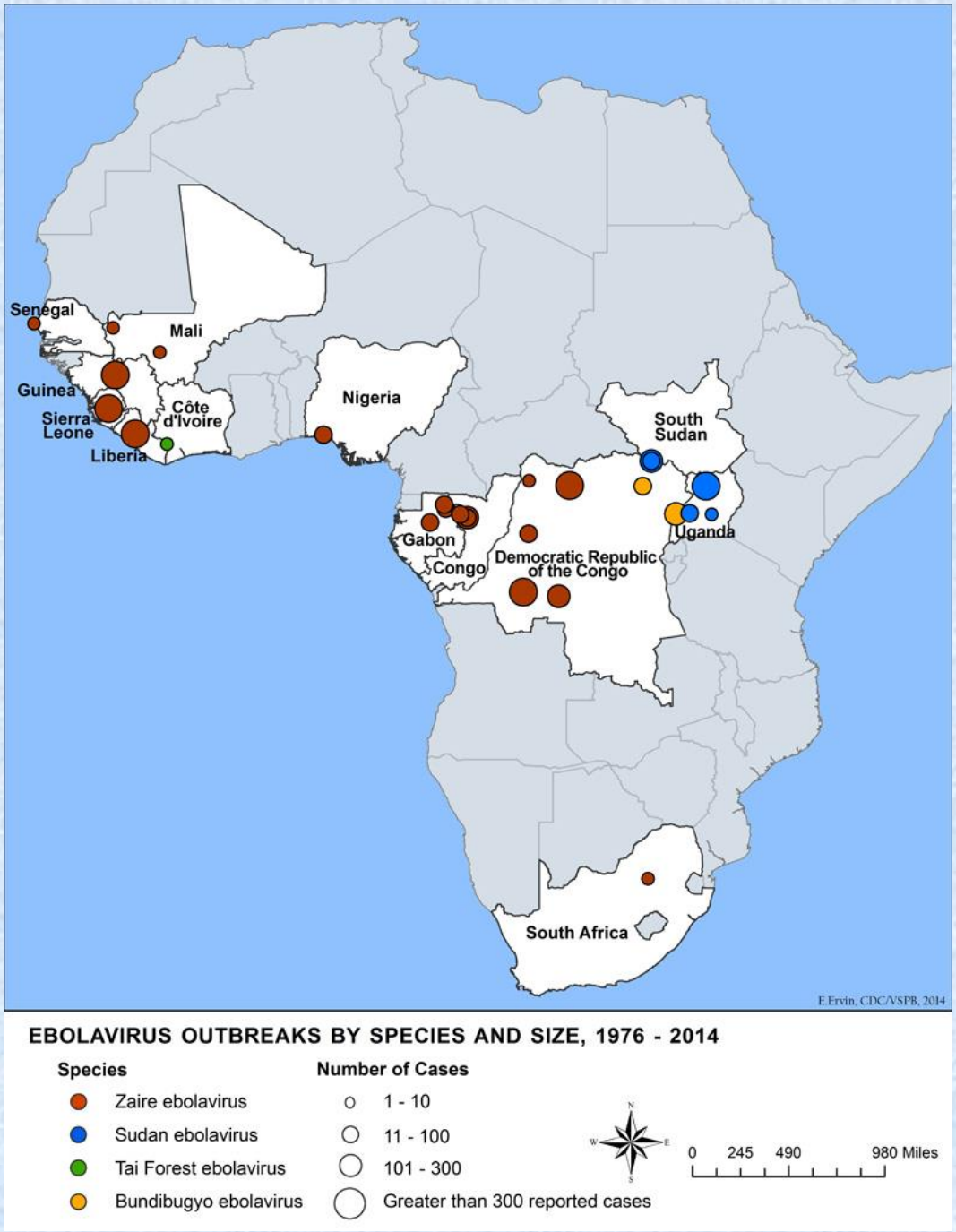
Emerging Viruses

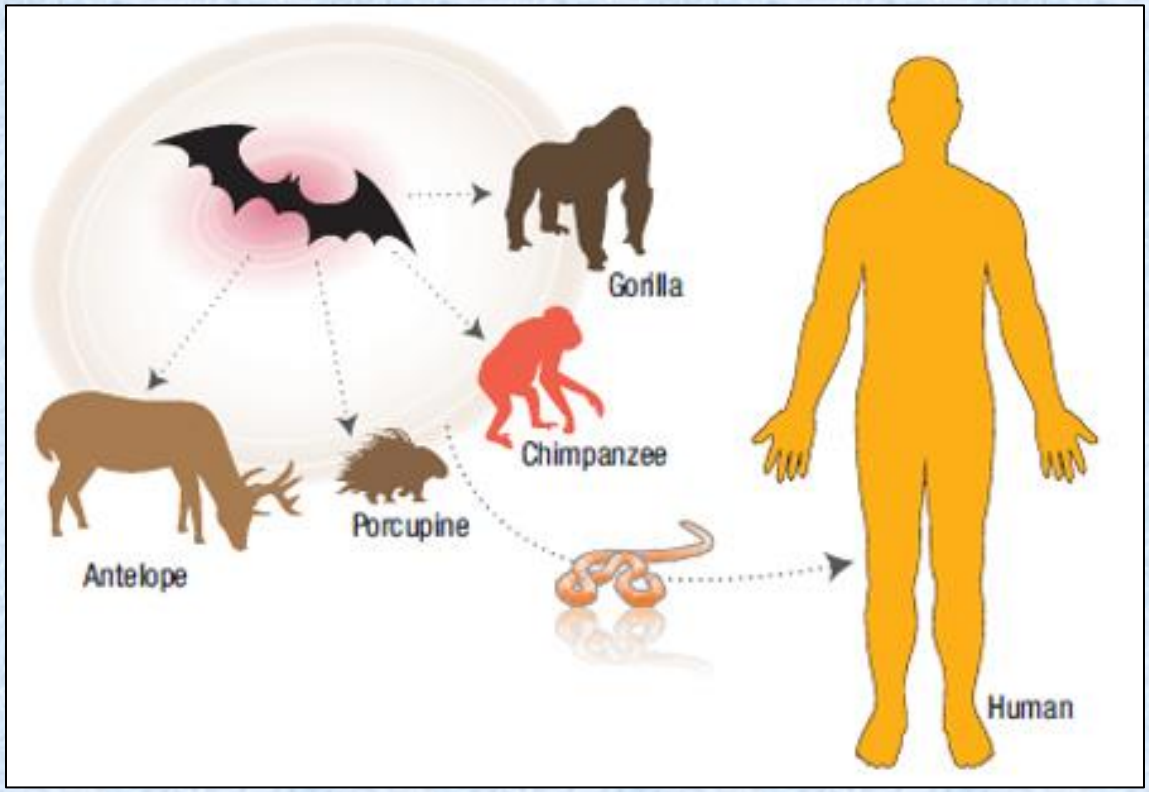


Ebola

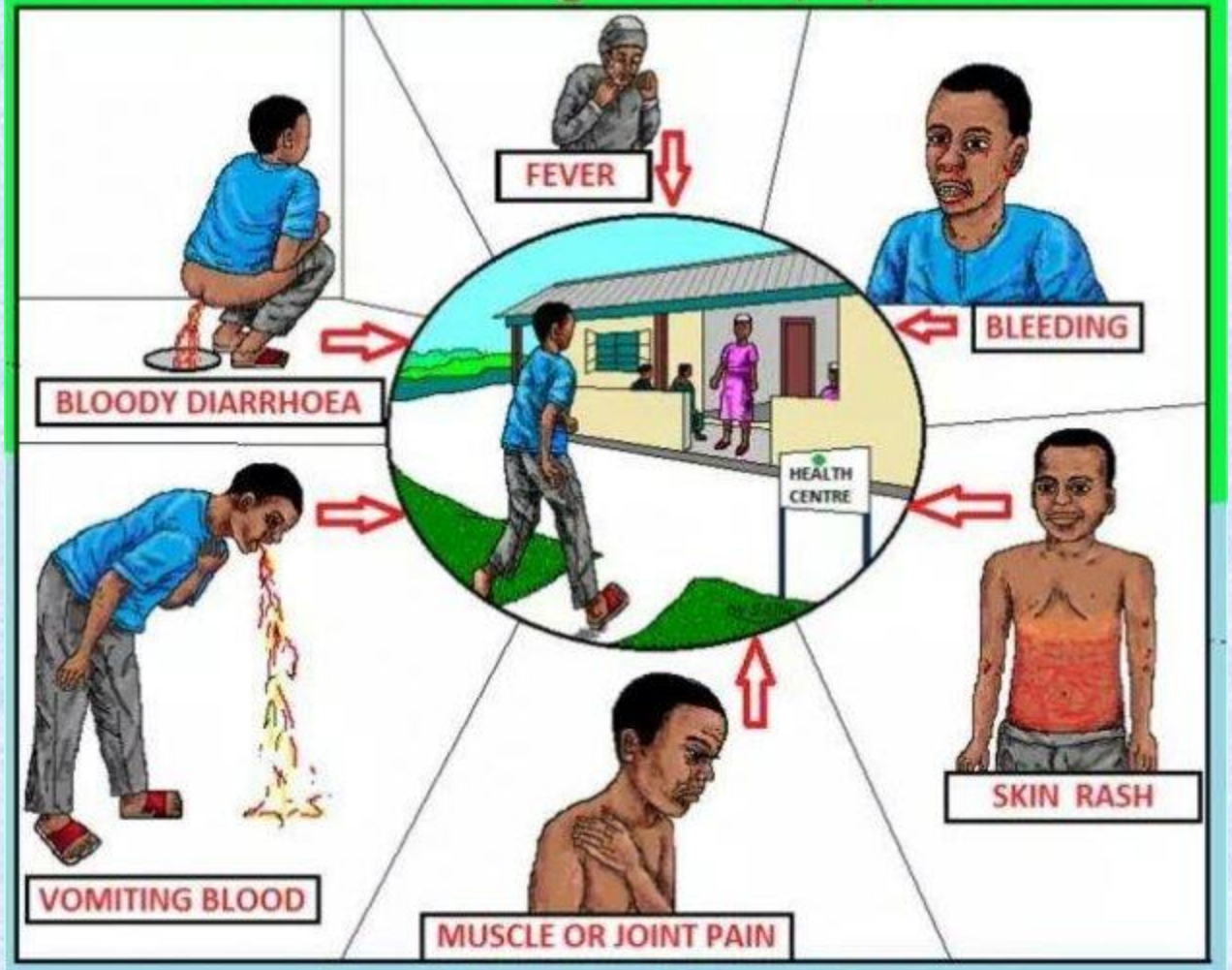
- Filoviridae, 5 species or strains
- First appeared in 1976 , Sudan, Congo; sporadic outbreaks in Africa
- Host probably fruit bats
- Transmitted to people from wild animals, blood, eating **bush-meat** (infected monkeys, bats etc)
- 2014 Ebola epidemic is the largest in history, affecting multiple countries in West Africa - Guinea, Liberia and Sierra Leone
- Often fatal, 25-90% fatality rate, average 50 %

Ebola


Senegal
Mali
Guinea
Sierra Leone
Liberia
Côte d'Ivoire
Nigeria
South Sudan
Uganda
Gabon
Congo
Democratic Republic of the Congo
South Africa
E.Ervin, CDC/VSPB, 2014
EBOLAVIRUS OUTBREAKS BY SPECIES AND SIZE, 1976 - 2014
Species
Zaire ebolavirus
Sudan ebolavirus
Tai Forest ebolavirus
Bundibugyo ebolavirus
Number of Cases
1 - 10
11 - 100
101 - 300
Greater than 300 reported cases
N
W
E
S
0 245 490 980 Miles


Gorilla
Chimpanzee
Porcupine
Antelope
Human

EBOLA - Signs and Symptoms

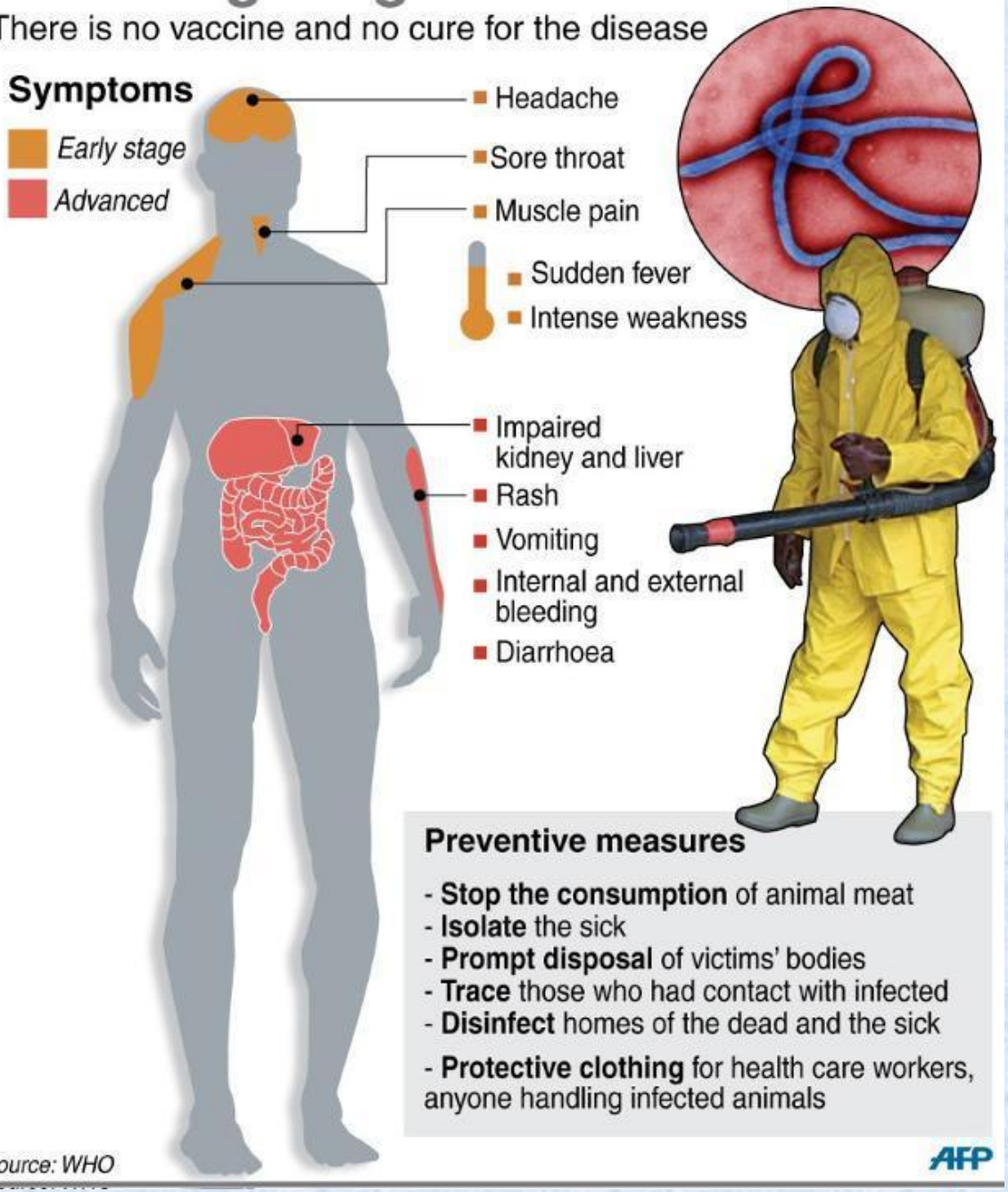


If you have any of these Signs

GO IMMEDIATELY TO THE NEAREST HEALTH FACILITY

Ebola: fighting a killer virus

There is no vaccine and no cure for the disease



Preventive measures

- **Stop the consumption** of animal meat
- **Isolate** the sick
- **Prompt disposal** of victims' bodies
- **Trace** those who had contact with infected
- **Disinfect** homes of the dead and the sick
- **Protective clothing** for health care workers, anyone handling infected animals

Source: WHO

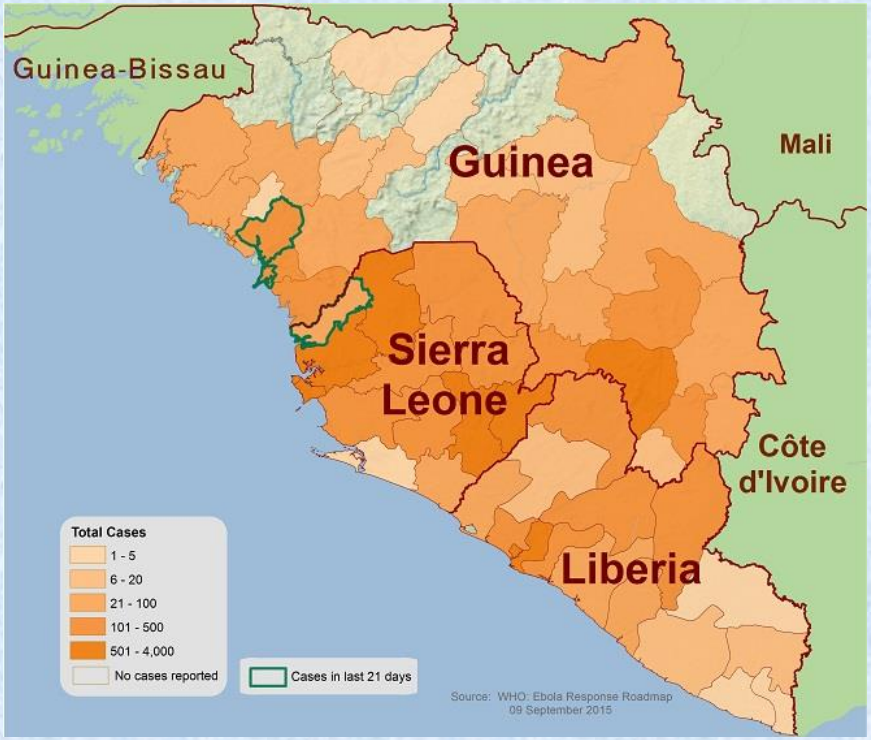
AFP

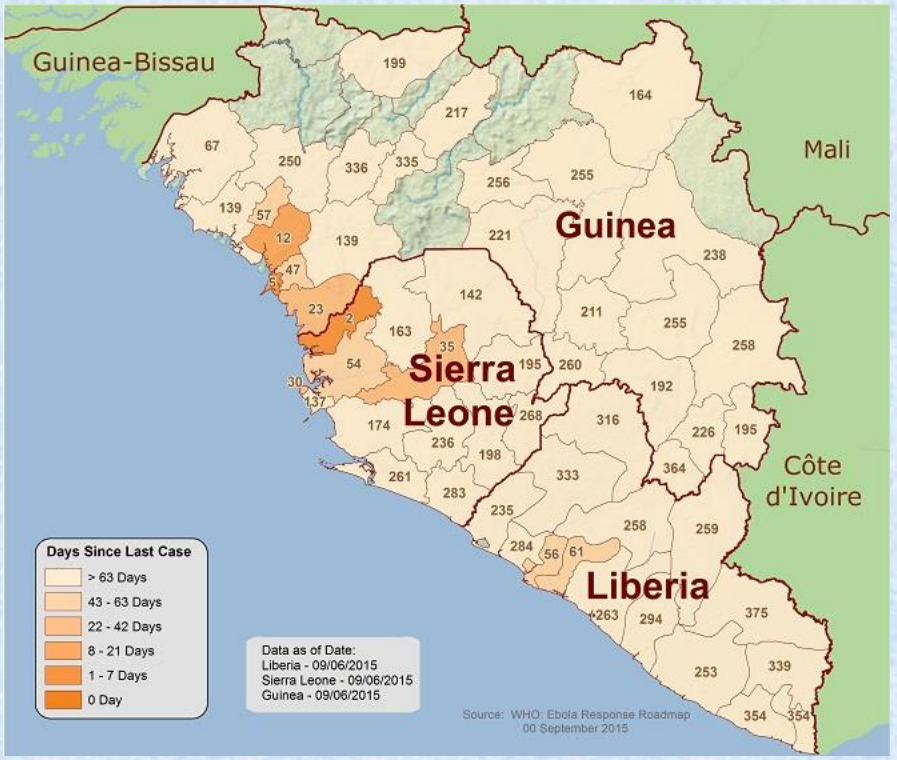
Quarantine – Temperature Monitoring at Airports

Liberia – Quarantine, Nobody leaves

Ebola in U.S.

- 2 deaths
- Much panic





Country	Total Cases)	Laboratory -Confirmed Cases	Total Deaths
Guinea	3791	3338	2530
Sierra Leone	13701	8703	3953
Total	17492	12041	**6483**

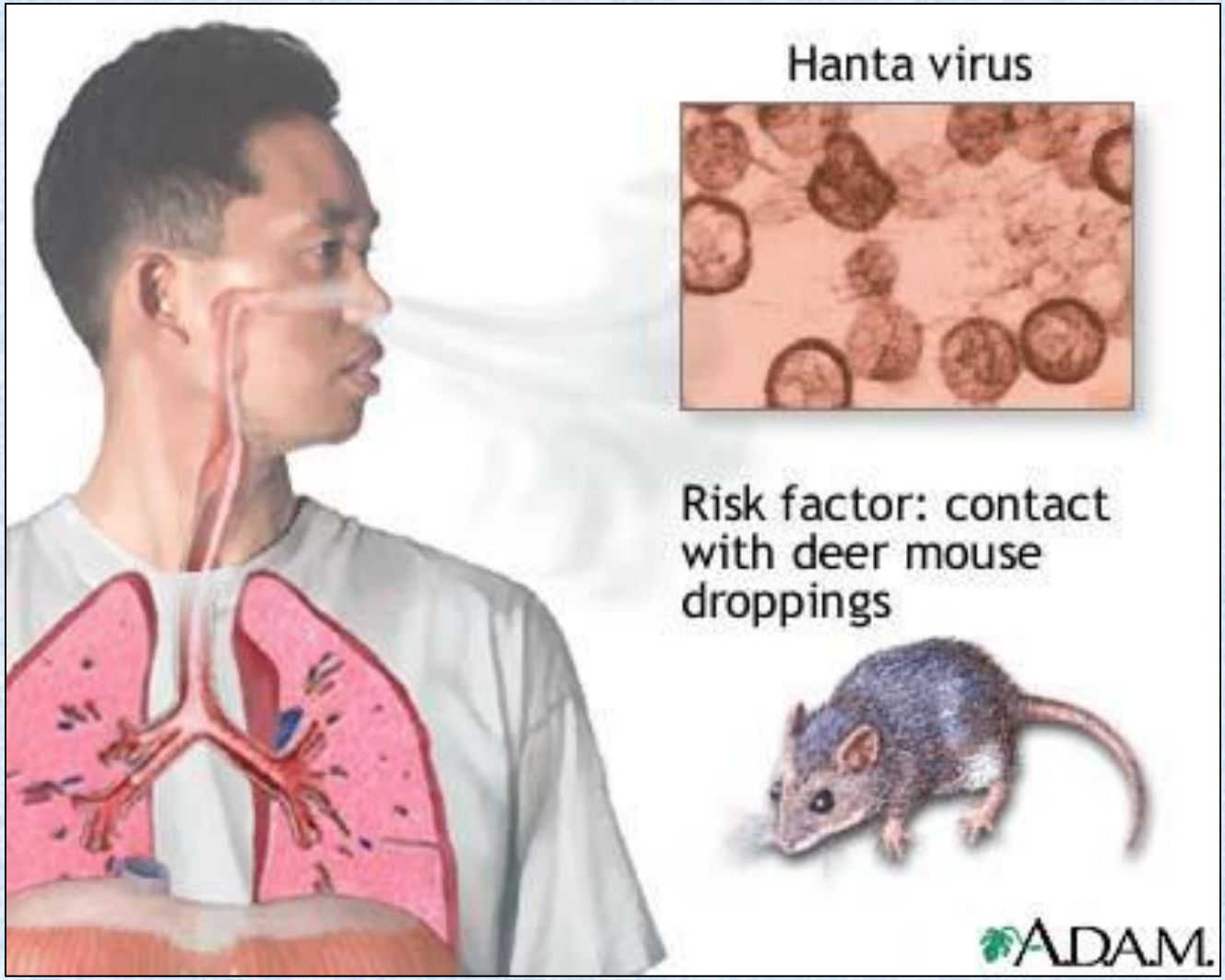
Hanta Virus

- Mice make about 70 droppings per day, a total of about 25,000 per year.
- These droppings cause allergy symptoms in many people and can also transmit food borne illnesses such as salmonella as mice often find their way into stored food.
- The most common diseases associated with rodents are Hantavirus, lymphocytic choriomeningitis (LCM), tularemia, and plague

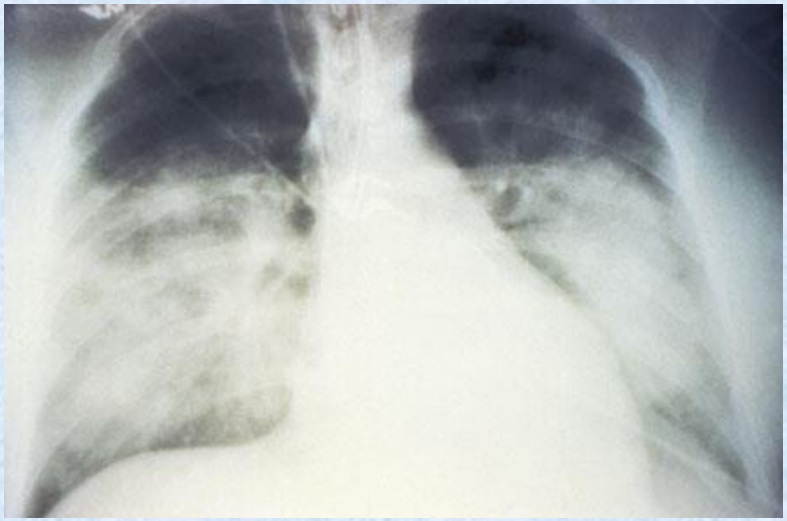
Hanta Virus

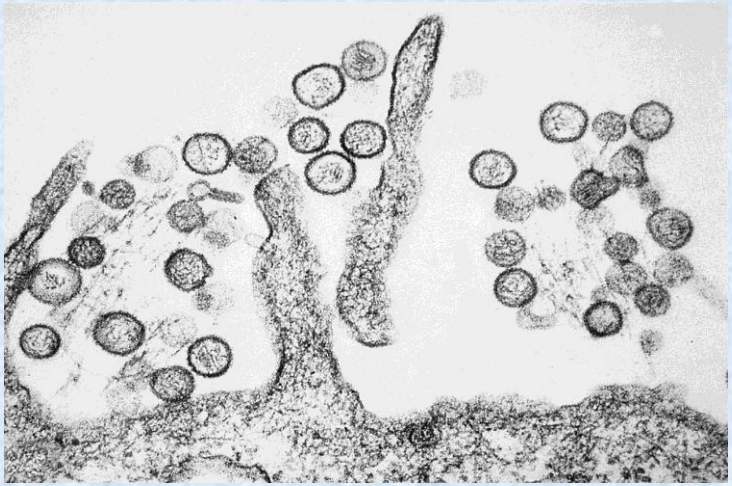
- First seen in 1950s, Korean War; UN troops developed fever, headache, renal failure
- Isolated from field mice in 1980s. Normally infect field mice.
- 1993 – outbreak in Four Corners of USA
- In SW U.S. it is spread by Deer Mouse (*Peromyscus* spp.);
- Can be spread by their urine, even when dried, and feces.
- Now in many countries, many varieties

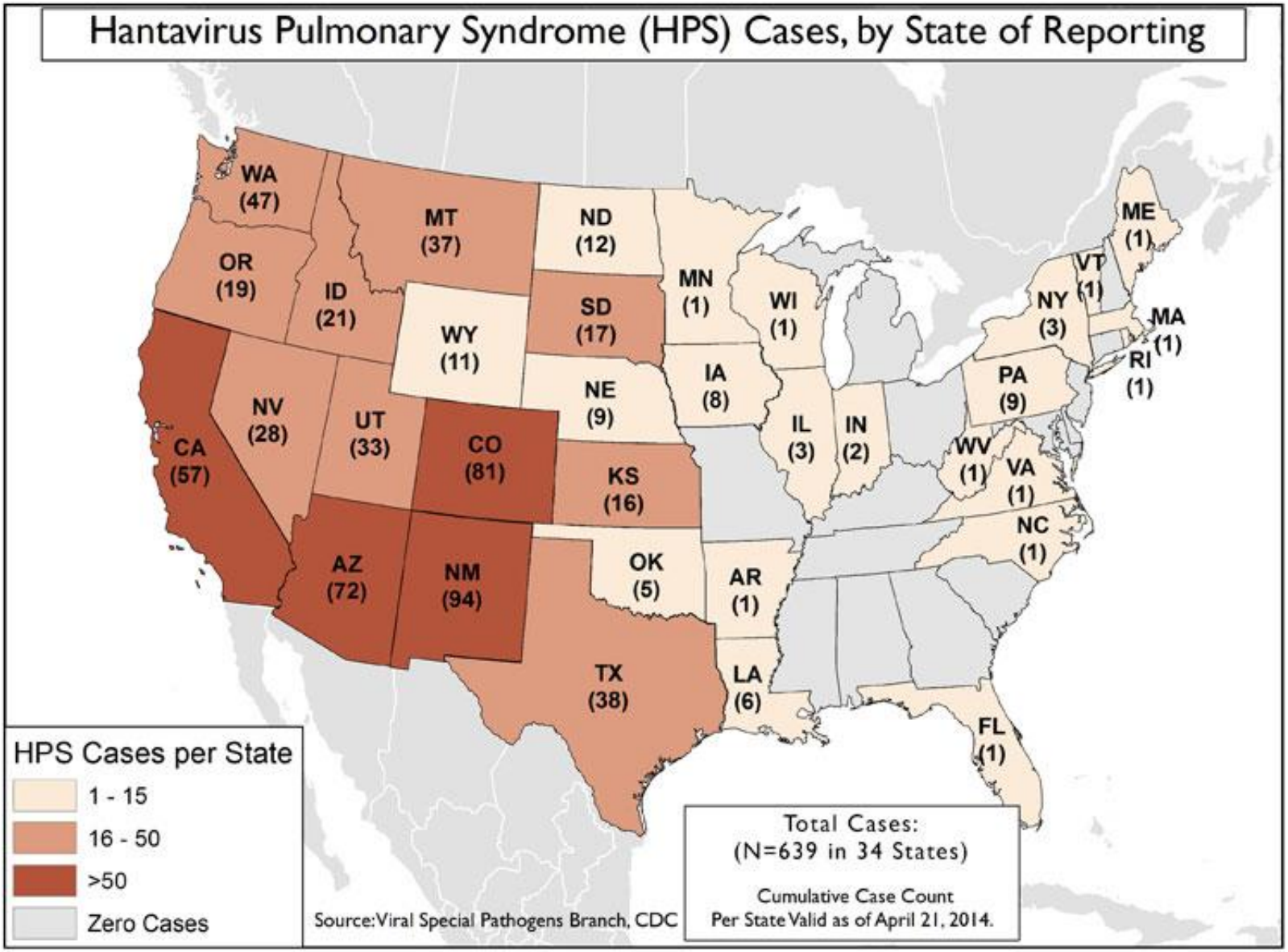
Hanta Virus


Hanta virus
Risk factor: contact with deer mouse droppings
A.D.A.M.

Hanta Virus – acute respiratory distress

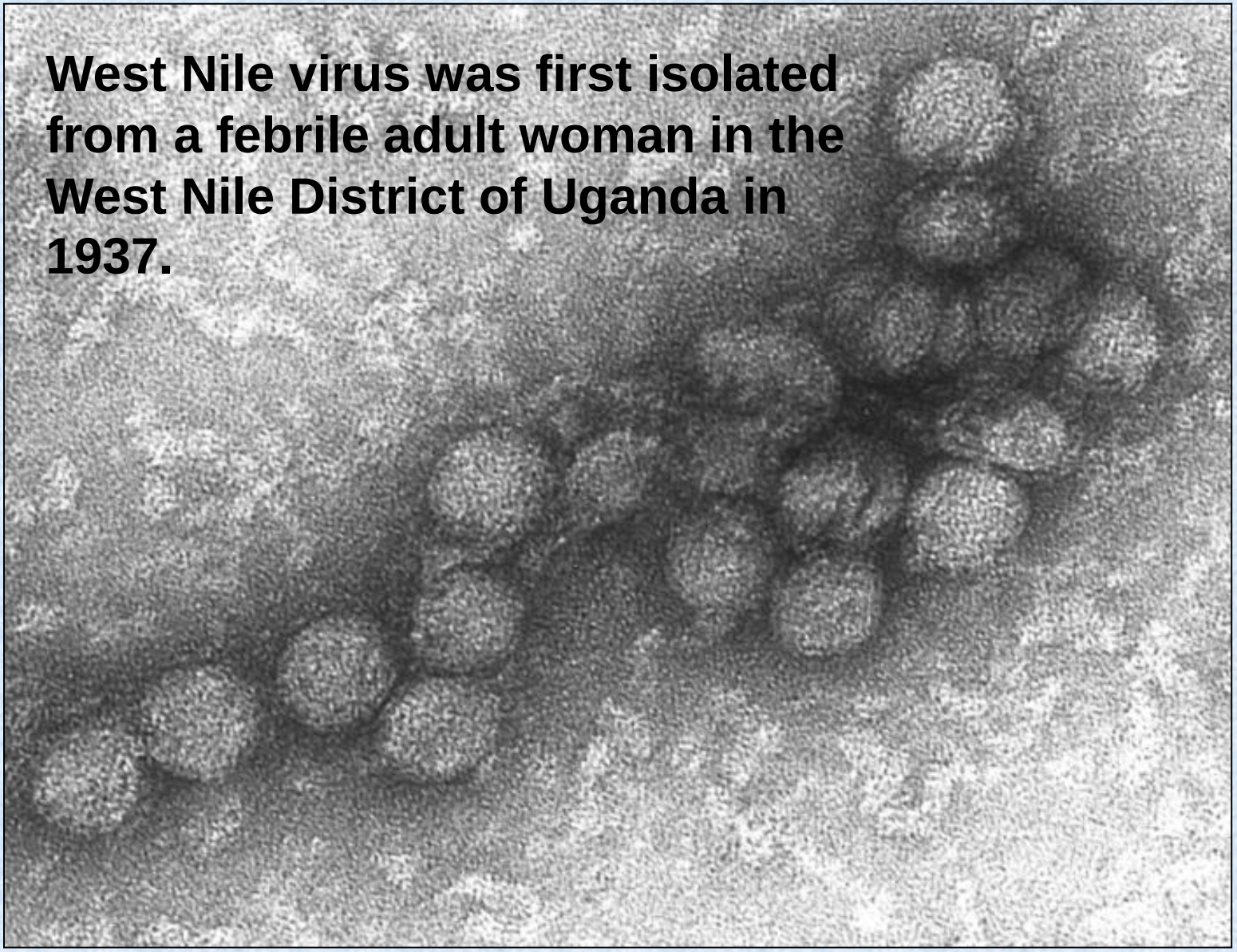






Apparently not yet in Missouri?

West Nile Virus



West Nile virus was first isolated from a febrile adult woman in the West Nile District of Uganda in 1937.

West Nile Virus

- Mosquito-borne Virus
- Causes Encephalitis or Meningitis
- Bird → Mosquito → Horse or Man
- No Treatment
- No Human Vaccine
- 1-2% Case Fatality Rate

Transmission Cycle of West Nile Virus

Horses and Humans are Accidental Dead End Hosts

Mosquito to Bird

Bird to Mosquito

About West Nile virus and humans

Human, animal immune systems usually destroy virus in bloodstream. About 80 percent of those with the virus have **no symptoms**.

About 20 percent have **mild** symptoms:

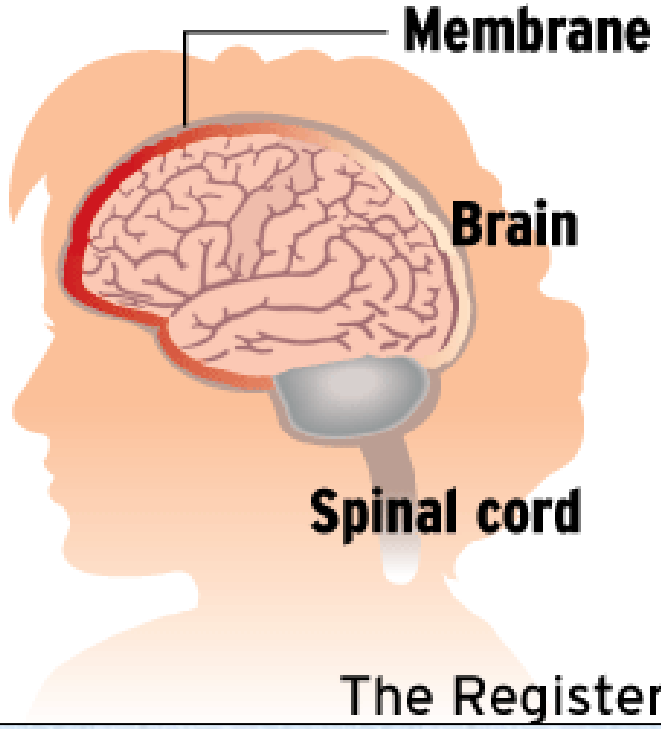
- Fever
- Headache
- Body aches
- Skin rash
- Swollen lymph nodes

A severe case, 1 in 150, can result in death. The risk is highest for elderly, children and people with impaired immune systems.

3-14

Number of days it takes for symptoms to appear after being bitten.

If virus survives in body, it can infect membranes around spinal cord and brain (encephalitis).

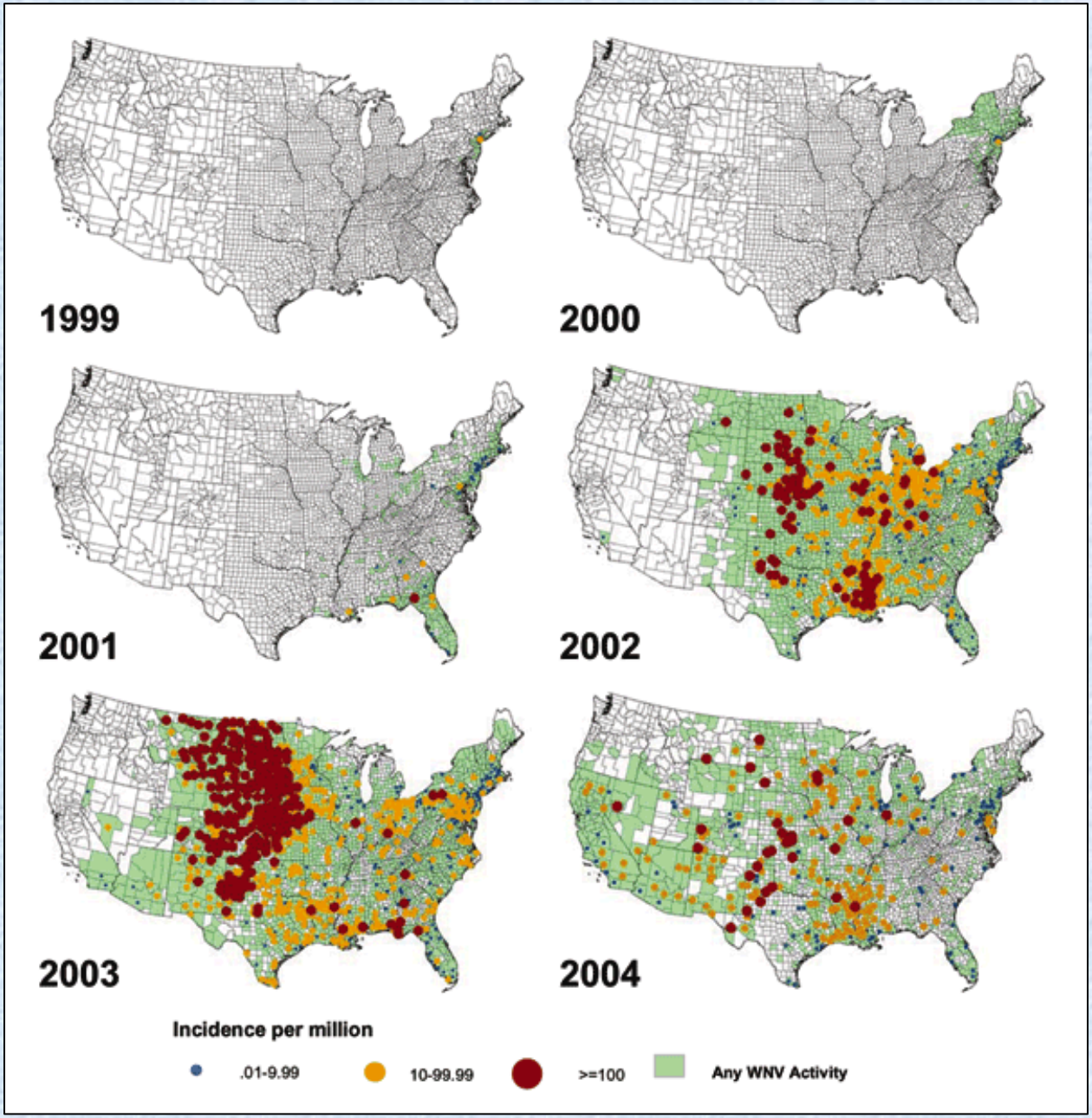


The virus is spread by mosquitoes that carry it from birds to humans.

Sources: Centers for Disease Control and Prevention

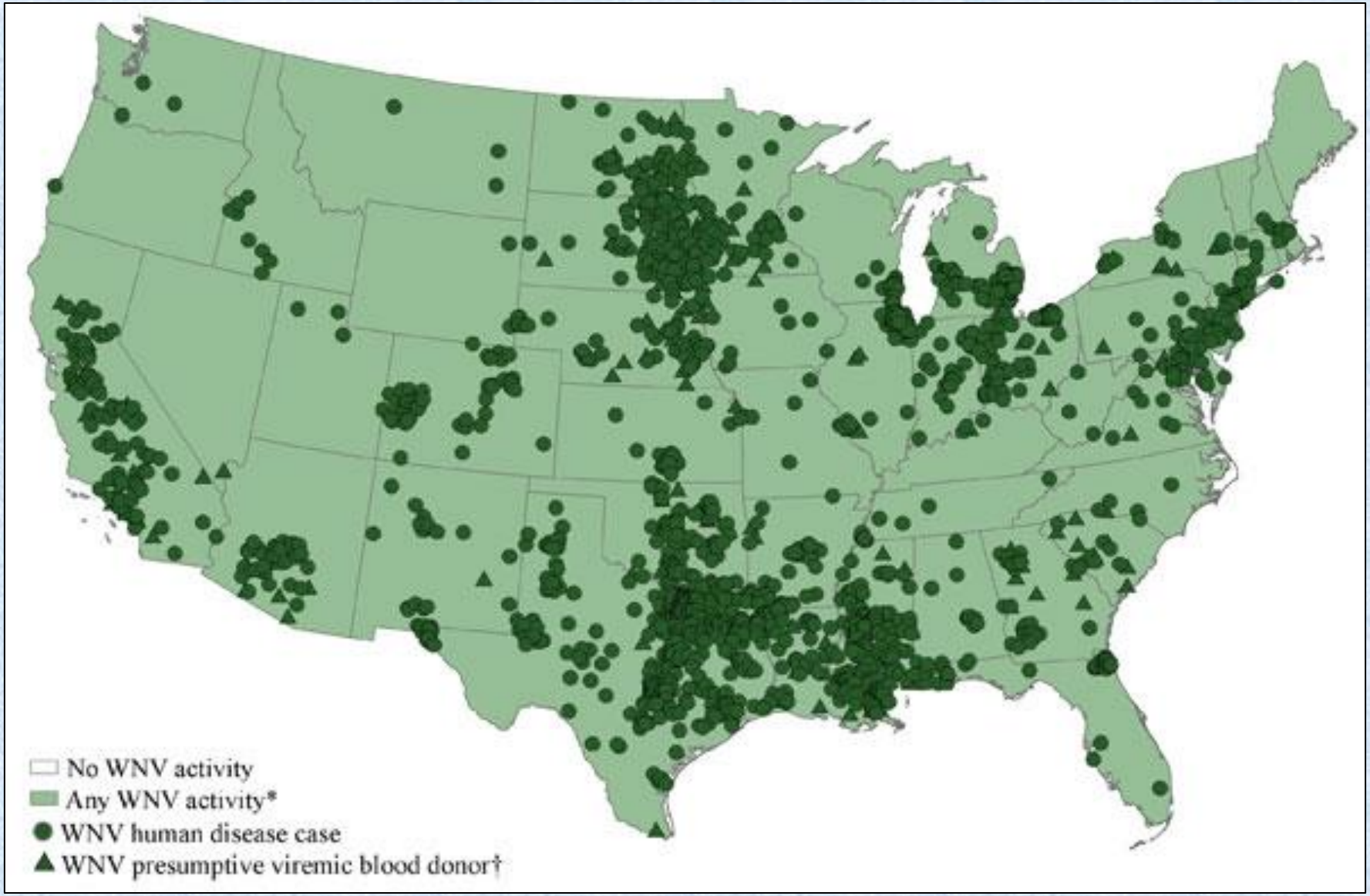
The Register

Spread of West Nile Virus – 1999 to 2004 (CDC)



Crows were hit hard

West Nile Cases – 2012 (CDC)



Remember the

"Four D's"

to defend yourself against

West Nile virus

DUSK / DAWN are the times of day you should try to stay indoors. This is when infected mosquitoes are most active.

DRESS in long sleeves and long pants when you're outside. For extra protection, you may want to spray thin clothing with repellent.

DEET (N, N-diethyl-m-toluamide) is an ingredient to look for in your insect repellent. Follow label instructions, and always wear repellent when outdoors.

DRAIN standing water in your back yard and neighborhood — old tires, flowerpots, and clogged rain gutters. These are mosquito breeding sites.

Polio

Polio - Poliomyelitus

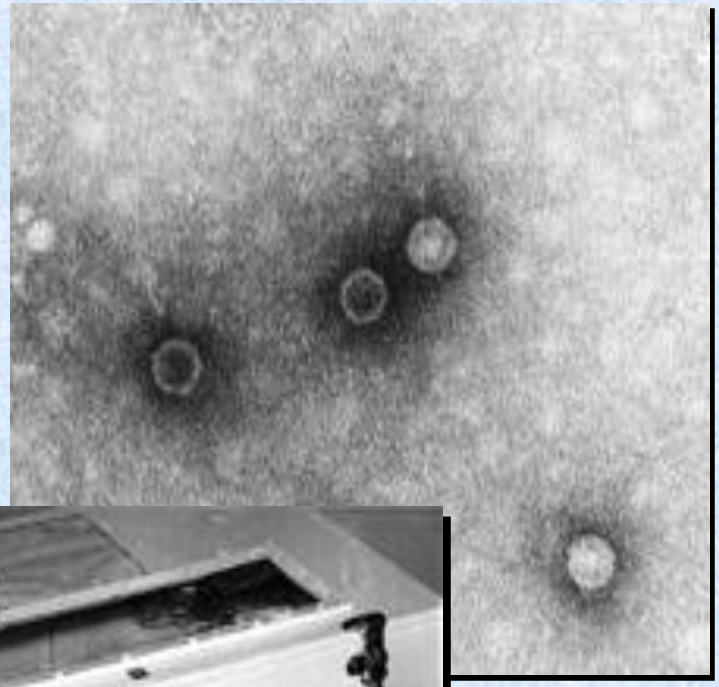
Polio Virus

- Was one of the most feared diseases in industrialized countries
- Highly infectious disease that affects only humans, paralyzed hundreds of thousands of children
- Enters the body through the mouth, via water or food contaminated with feces. Infects gastrointestinal tract, spreads to brain, other tissues
- Causes inflammation of the spinal chord and paralysis in about 2% of cases

Polio Virus

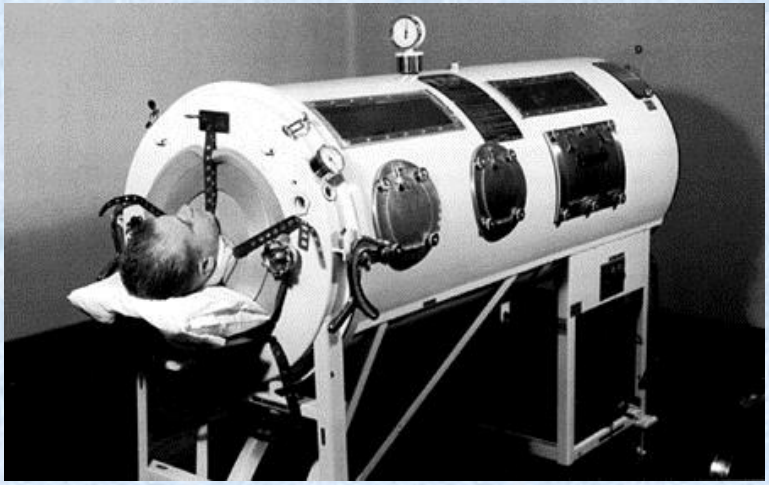
- Vaccines in the 1950s and 1960s,
  Salk, Sabine
- Brought under control and practically eliminated as a public health problem
- Still exists in a few developing countries, making comeback in others

Polio virus



Polio

Iron Lung



FDR – President Roosevelt

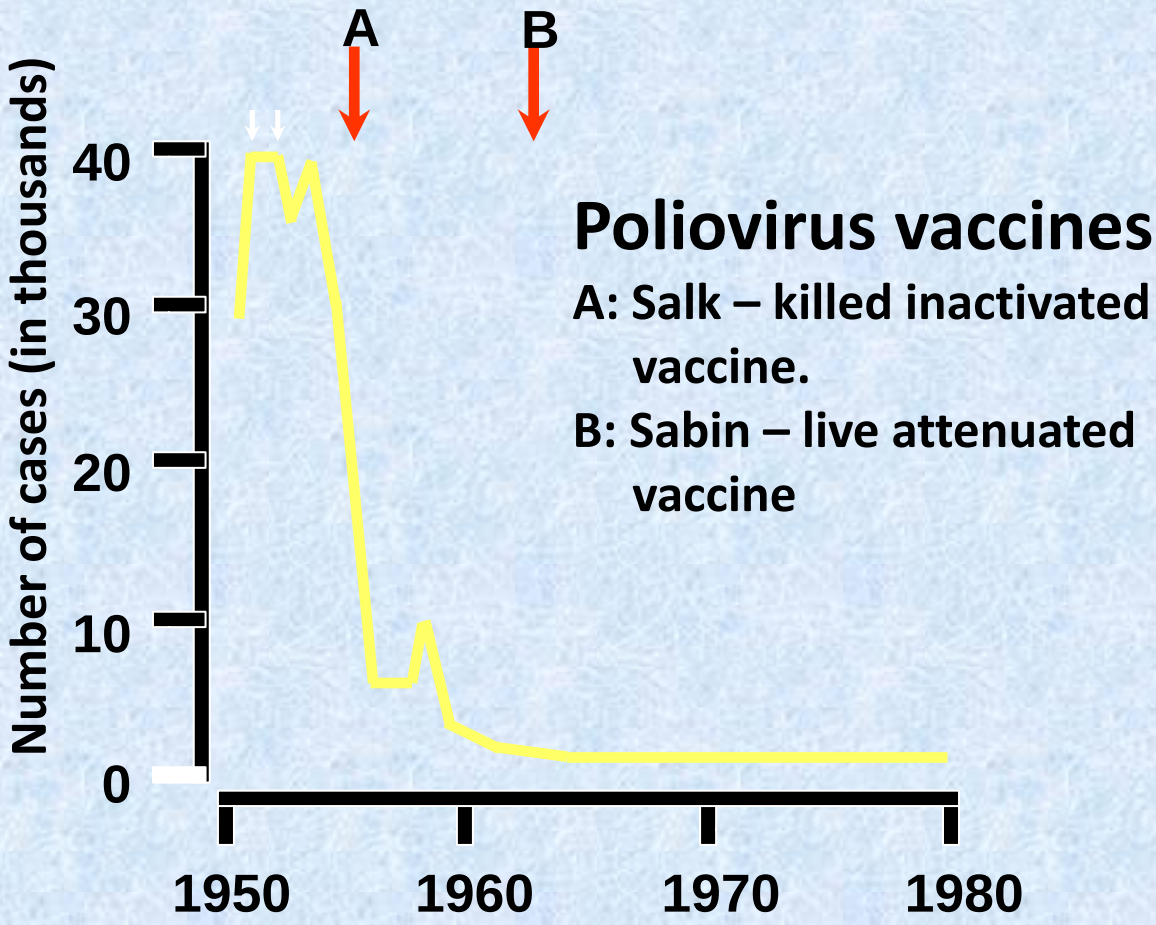
Polio Vaccines

- There is no cure for polio, but it is a highly preventable disease.
- Multiple rounds of polio vaccine protect a child for life.
- Global vaccination effort begun in 1988 has reduced the incidence of polio more than 99%

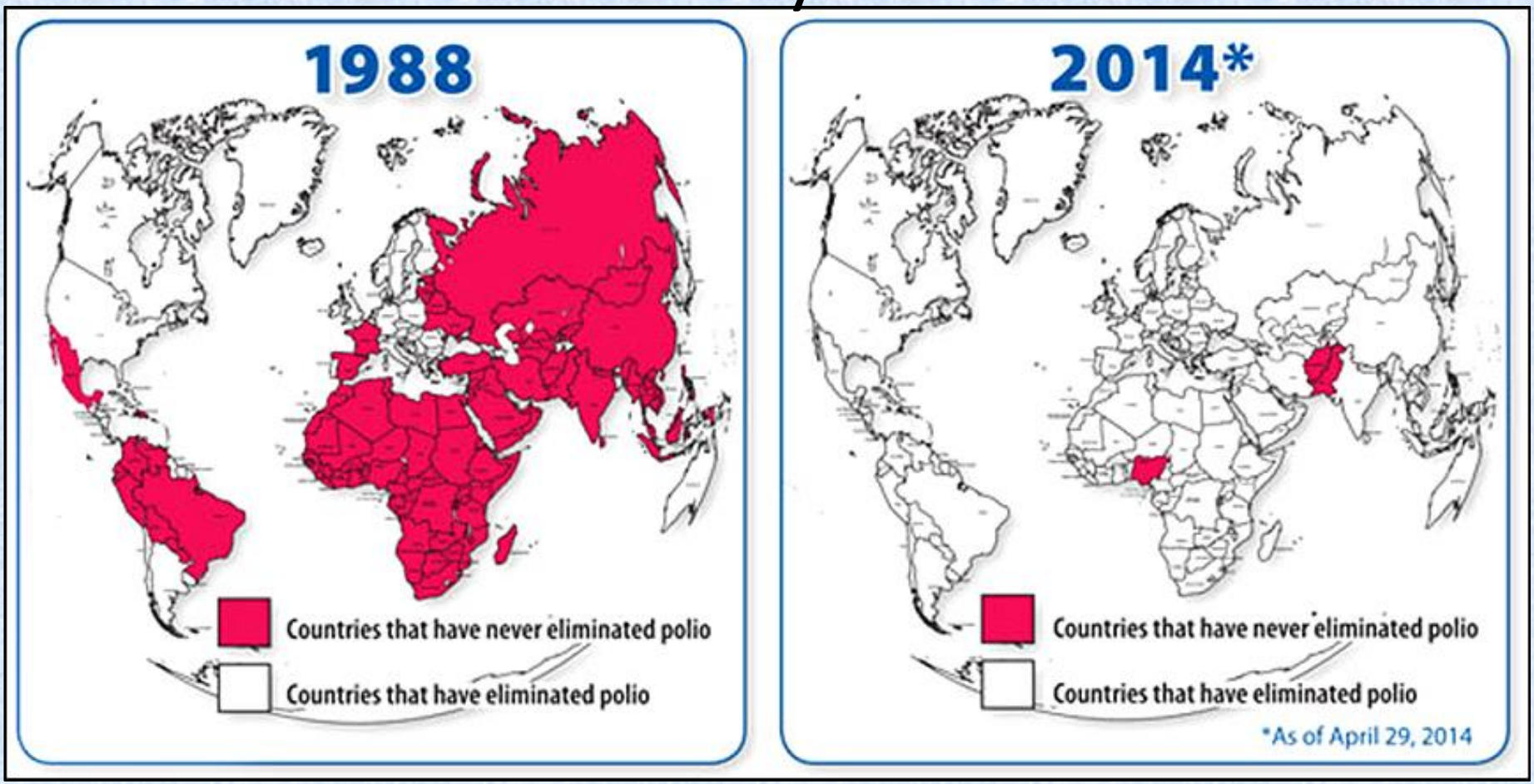
Salk Vaccine, 1950, injected, from killed virus

Sabin Vaccine, 1960, oral, from attenuated live virus

Incidence of Poliomyelitis



Polio was nearly eliminated



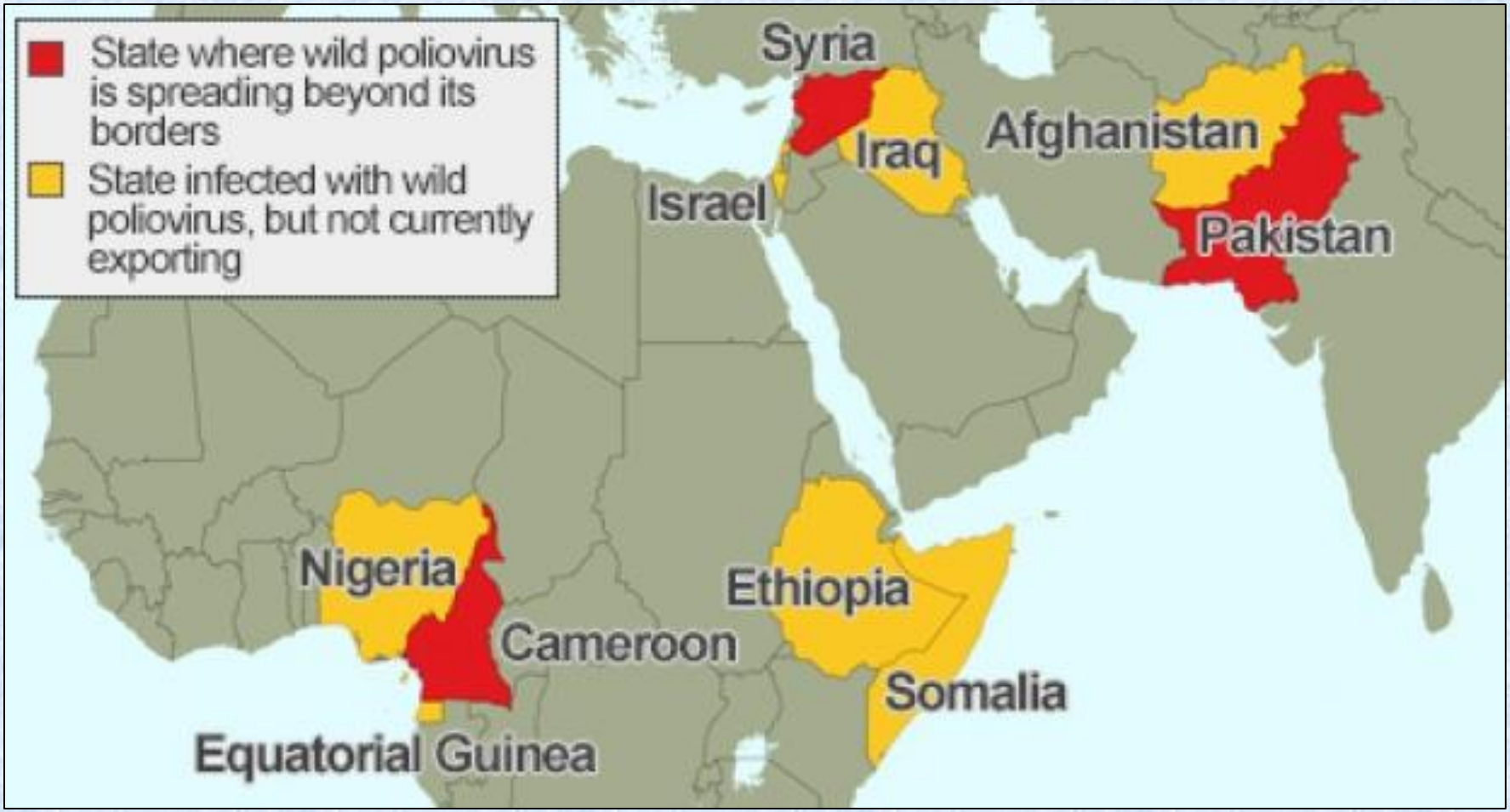
- Recent outbreaks in Africa, Asia and the Middle East have alarmed global health agencies
- Afghanistan, Cameroon, Equatorial Guinea, Ethiopia, Iraq, Israel, Nigeria, Pakistan, Somalia and Syria

Polio

Nigeria

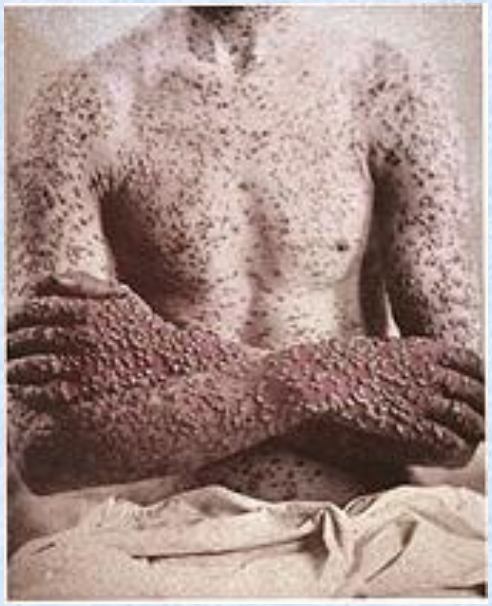
Pakistan

Polio - civil war, strife and unrest threaten the UN's goal of eradicating polio by 2018



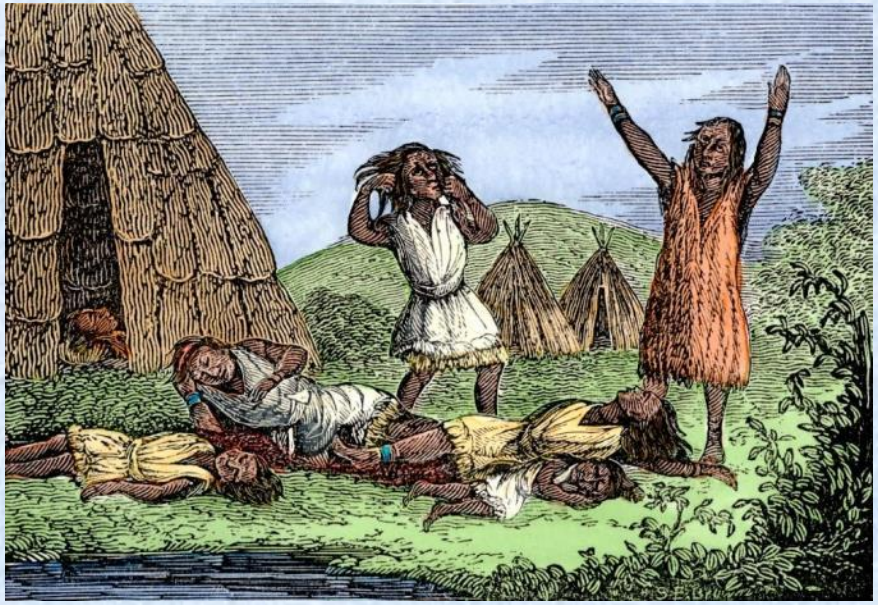
Smallpox

Smallpox - Variola



- Most likely evolved from a rodent virus between 68,000 and 16,000 years ago.
- Killed about 30% of those infected
- Leading cause of death in Europe in 18th century, killing an estimated 400,000 each year

Smallpox - Variola



- Decimated American Indians, had no previous exposure or resistance
- Killed an estimated 400,000 Europeans annually during the closing years of the 18th century
- Of all those infected, 20–60 percent—and over 80 percent of infected children—died from the disease.

Small Pox

Smallpox – killed billions of people

Youtube Videos

How we conquered the deadly smallpox virus

https://www.youtube.com/watch?v=yqUFy-t4MlQ

The Deadly Smallpox Virus - Smallpox Documentary (Great Video!)

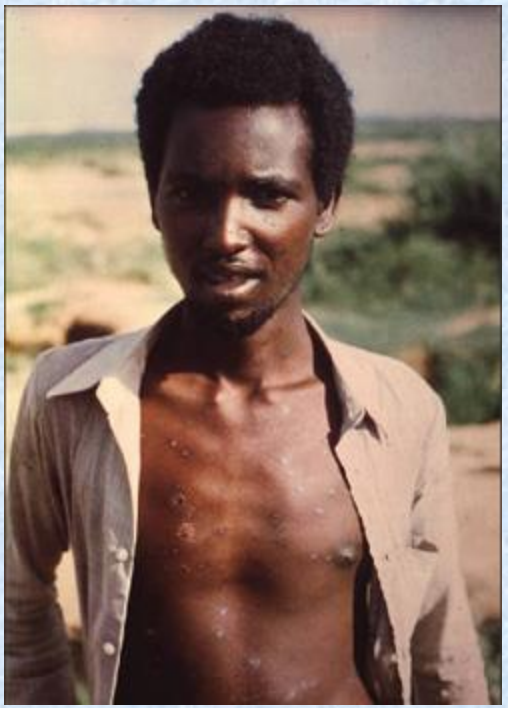
https://www.youtube.com/watch?v=gw2QiEUnt4I

Vaccination – Edward Jenner

- Noticed milkmaids who got cowpox from cows never got smallpox
- Jenner found milkmaid with cowpox, ran a needle through the sore.
- This same needle was used to inoculate an eight-year-old boy named James Phipps
- Jenner published his findings, calling his new preventative technique a “vaccine”

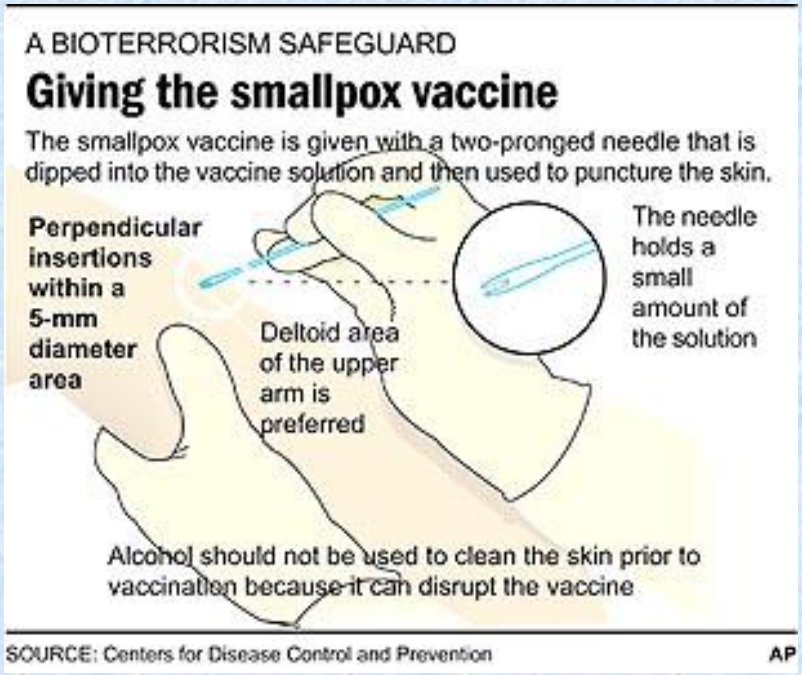
Smallpox Eradication

- Responsible for 300–500 million deaths during the 20th century
- Early 1950s estimated 50 million cases of smallpox each year.
- Last case in the U.S. was in 1949
- Last case S. Amer. 1971
- Last case was in 1977 in Somalia



The last smallpox victim. Ali Maow Maalin of Somalia is the last known individual in the world to have contracted smallpox

Smallpox Eradication

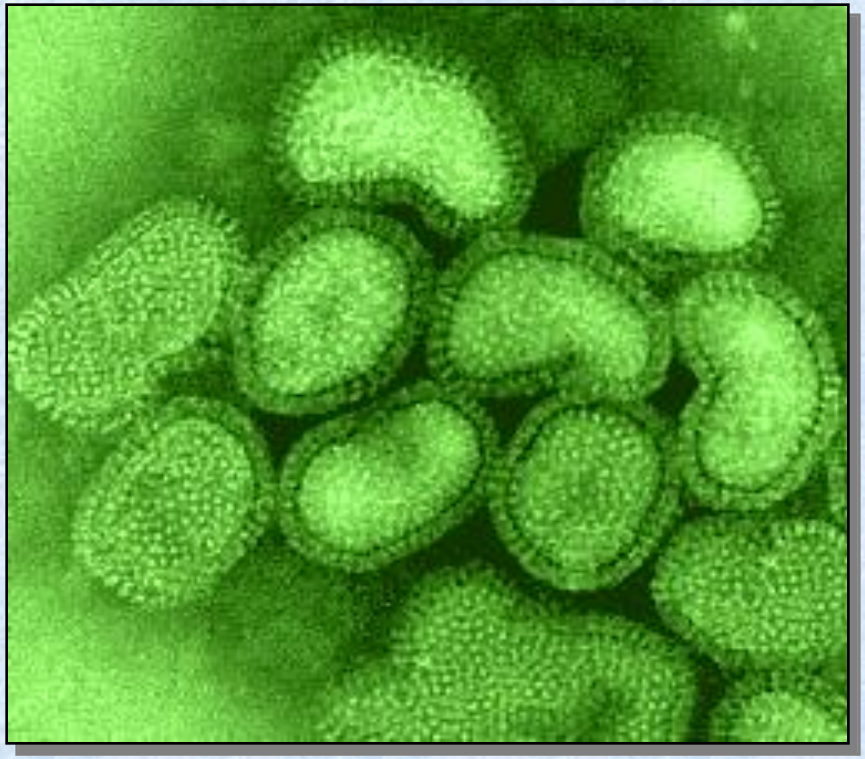


- After the disease was eliminated from the world, routine vaccination against smallpox among the general public was stopped
- Stocks still kept in Russia and U.S.
- Potential bioweapon

Influenza

Influenza A virus

- Virus that causes the flu
- Enveloped virus with a segmented RNA genome
- Infects a wide range of animals other than humans
- Major cause of respiratory infections



CDC Web Page on Influenza
http://www.cdc.gov/flu/about/disease/index.htm

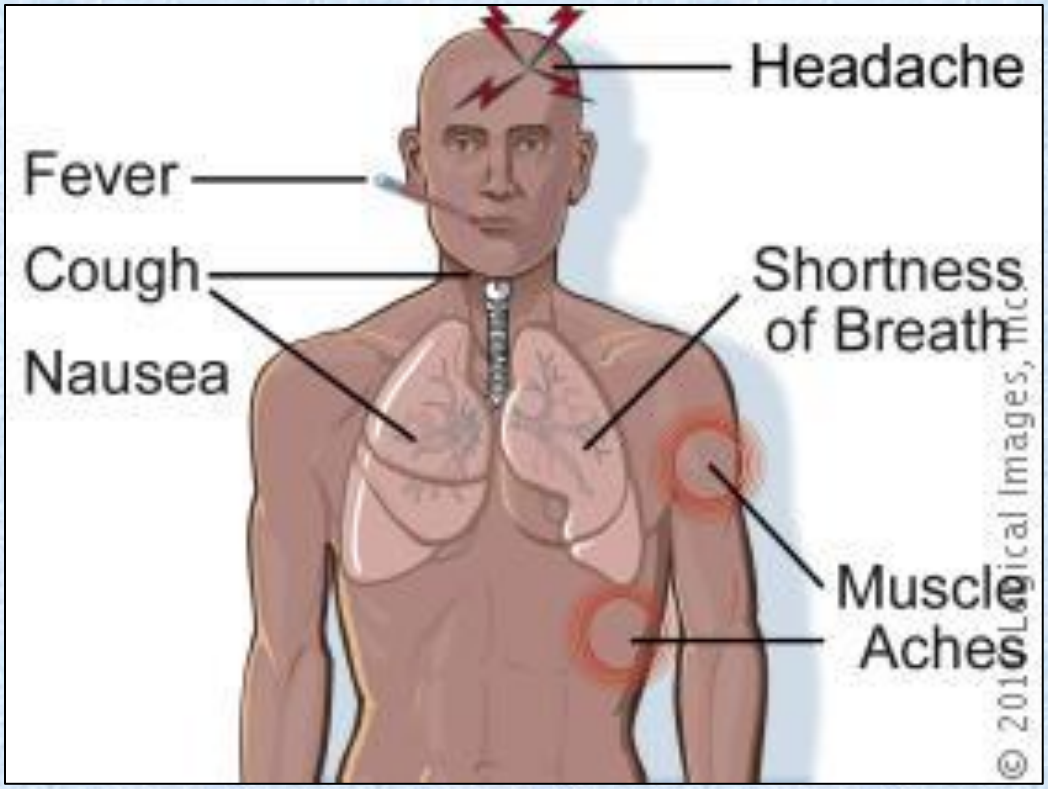
Influenza A virus

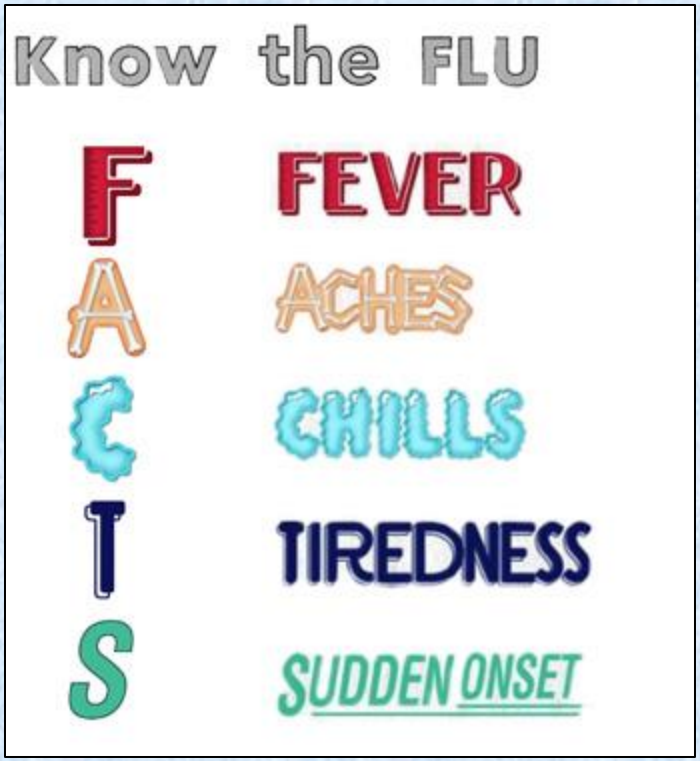
- Many variants, constantly changing
- Named various ways
  - Proteins: e.g. H5N1 = subtype that has a type 5 hemagglutinin (H) protein and a type 1 neuraminidase (N) protein
  - Species of host strain: bird (H5N1), human, swine (H1N1), equine, canine
- "Human Flu" results in approximately 36,000 deaths and more than 200,000 hospitalizations each year
- Vaccine updated every year

Influenza A

- Spread by respiratory route
- Virus infects cells of the respiratory tract
- Destruction of respiratory epithelium
  - Secondary bacterial infections

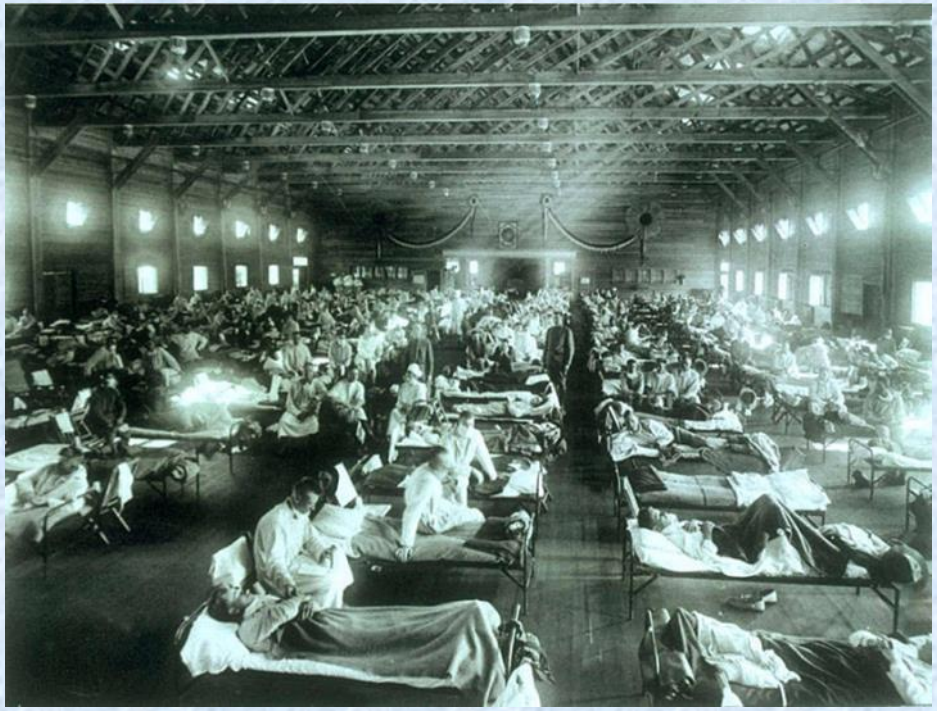
Influenza – The Flu





“Spanish” Flu (Influenza)

- World War I, a shockingly virulent strain of avian Influenza-A, swept the world
- Mass infection caused between 50 and 100 million deaths – more than all the wars of the 20th century combined!



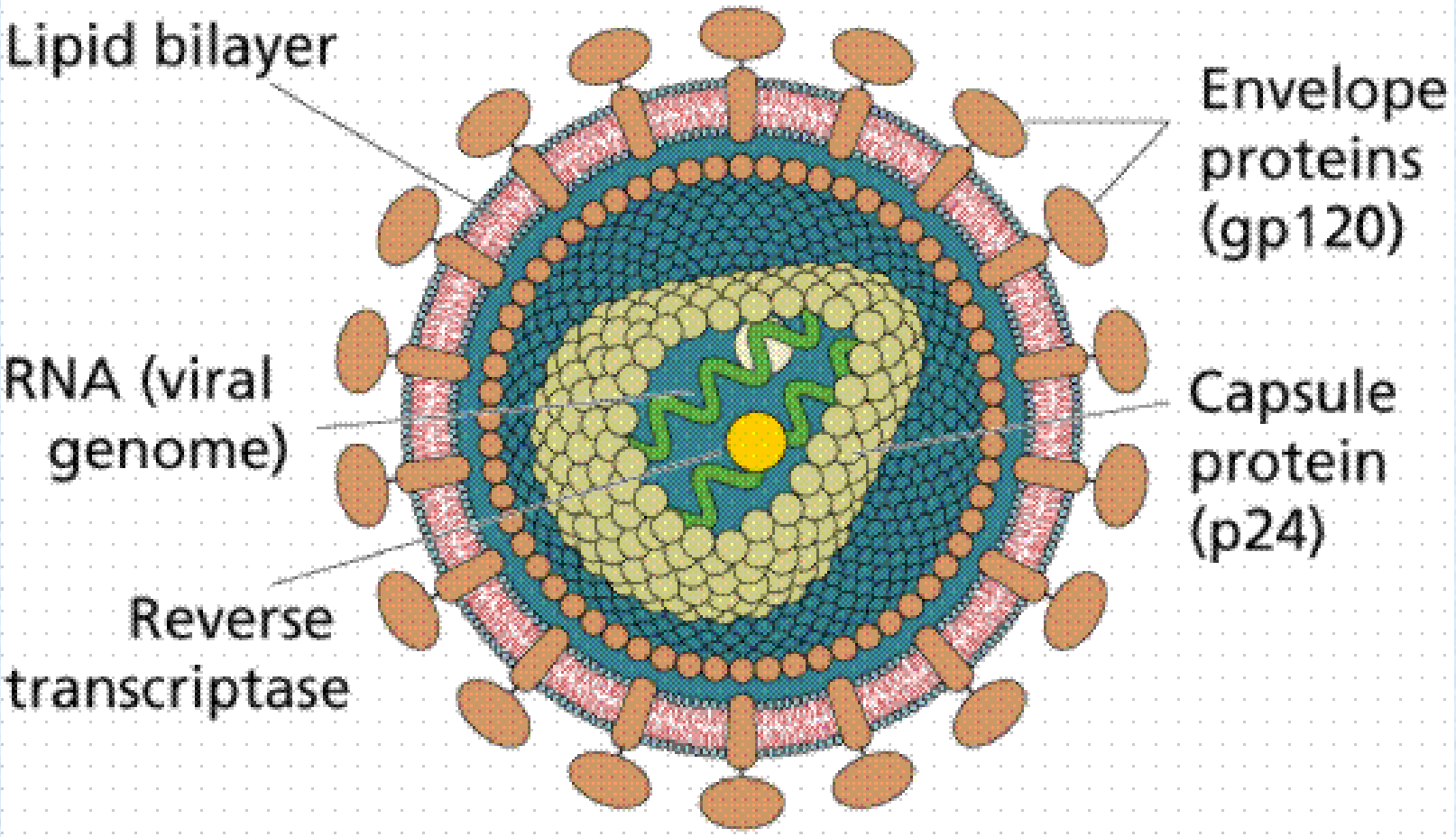
Common Misconceptions

- **The flu shot will make me sick.** *The flu shot (influenza vaccine) is comprised of inactivated viruses so one cannot contract flu from the shot.*
- **I'm healthy, I don't need the vaccine.** *Anyone can contract influenza, and the CDC recommends that all persons six months and older get the flu shot each year. It is especially important that vulnerable populations — pregnant women, individuals 65 and older, morbidly obese and persons with diabetes and high blood pressure — get vaccinated.*
- **I cannot afford the flu shot.** *The flu vaccine is free in some case; it is also covered by Medicare and many health coverage plans.*

HIV/AIDS

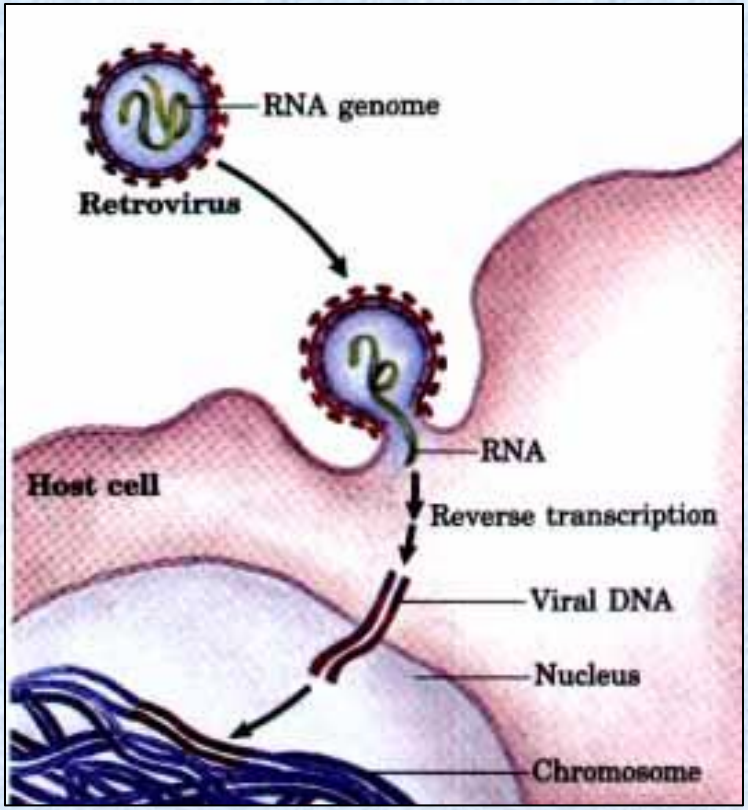
HIV/AIDS

- Acquired immune deficiency syndrome (AIDS) caused by Human Immunodeficiency Virus (HIV).
- Disease first described in 1981.
- Immune system attacked. Victim dies of secondary infections.

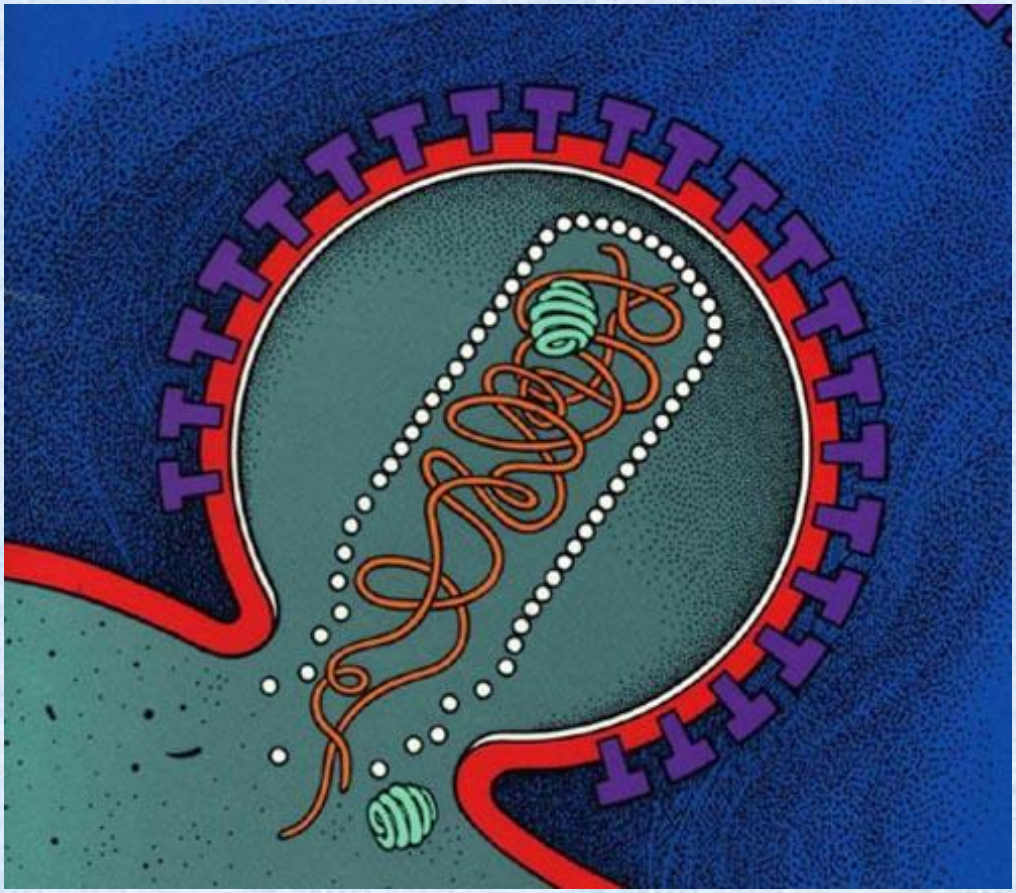

Lipid bilayer
Envelope proteins (gp120)
RNA (viral genome)
Capsule protein (p24)
Reverse transcriptase

Retroviruses

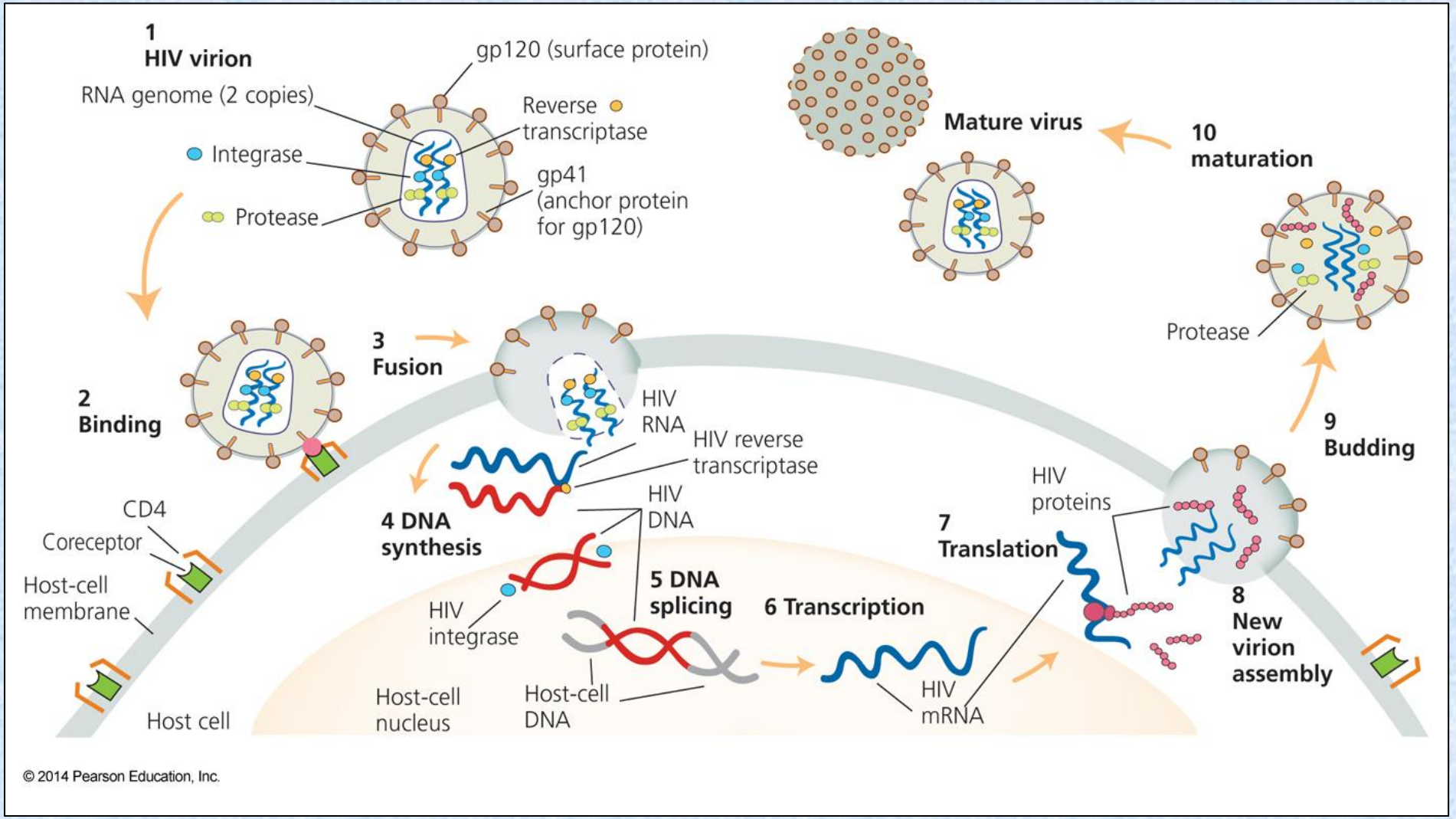
- RNA viruses that contain reverse transcriptase
- This enzyme allows RNA to produce DNA
- HIV is an example of the virus



- HIV binds to two protein receptors on cell's surface : CD4 and a co-receptor, usually CCR5.
- Host cell membrane and viral coat fuse and virus contents enter cell.



HIV Life Cycle



How HIV causes AIDS

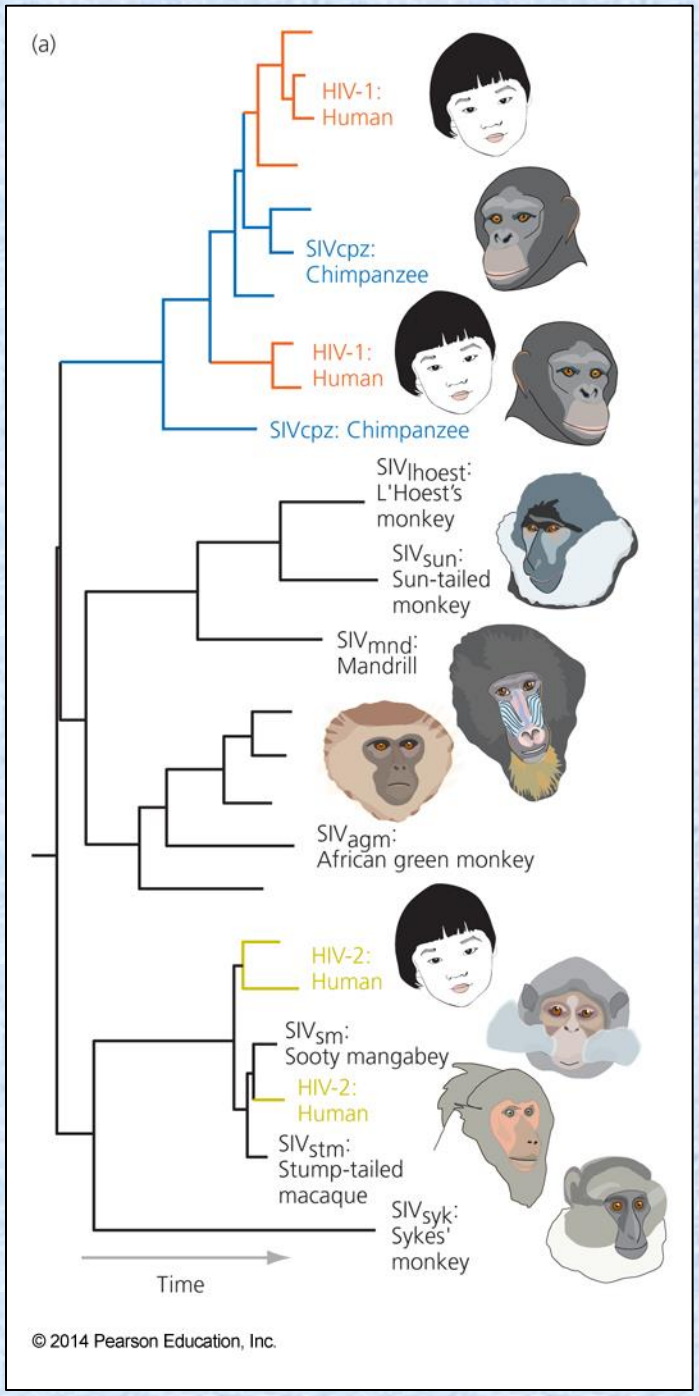
- Human body responds to infection with HIV by mobilizing the immune system.
- The immune system destroys virus particles floating in bloodstream and also destroys cells infected with virus.
- Unfortunately, the cells that HIV infects are critical to immune system function. HIV invades immune system cells especially helper T cells.
- Eventually immune system collapses and patient dies from infectious diseases, cancers (AIDS)

Origins of HIV

- Where did HIV come from?
- HIV similar to virus found in monkeys and apes called SIV (simian immunodeficiency virus).
- To identify ancestry of HIV scientists have sequenced various HIV strains and compared them to various SIV strains.

Origins of HIV

- HIV-1 is most similar to an SIV found in chimps and HIV-2 is most similar to an SIV found in a monkey called the sooty mangabey.



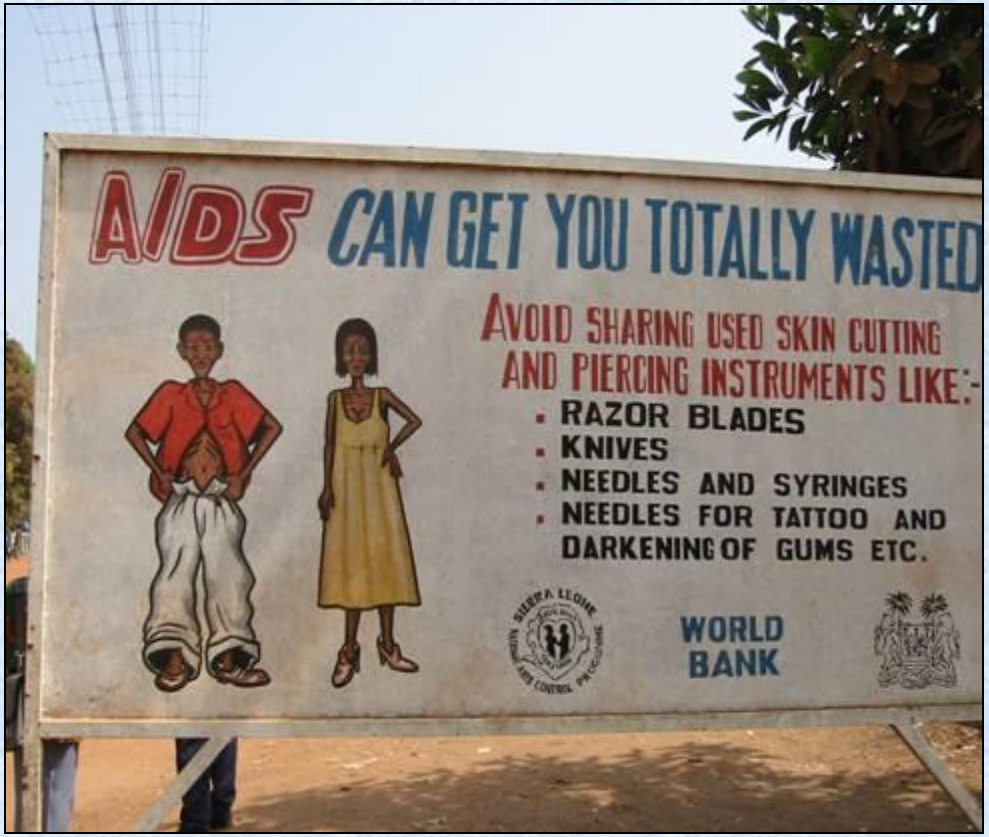
Origins of HIV

Hahn et al 2000

- Phylogenetic trees made by comparing SIV and HIV sequences.
- Suggests we got HIV-1 from Chimps, HIV-2 from monkeys

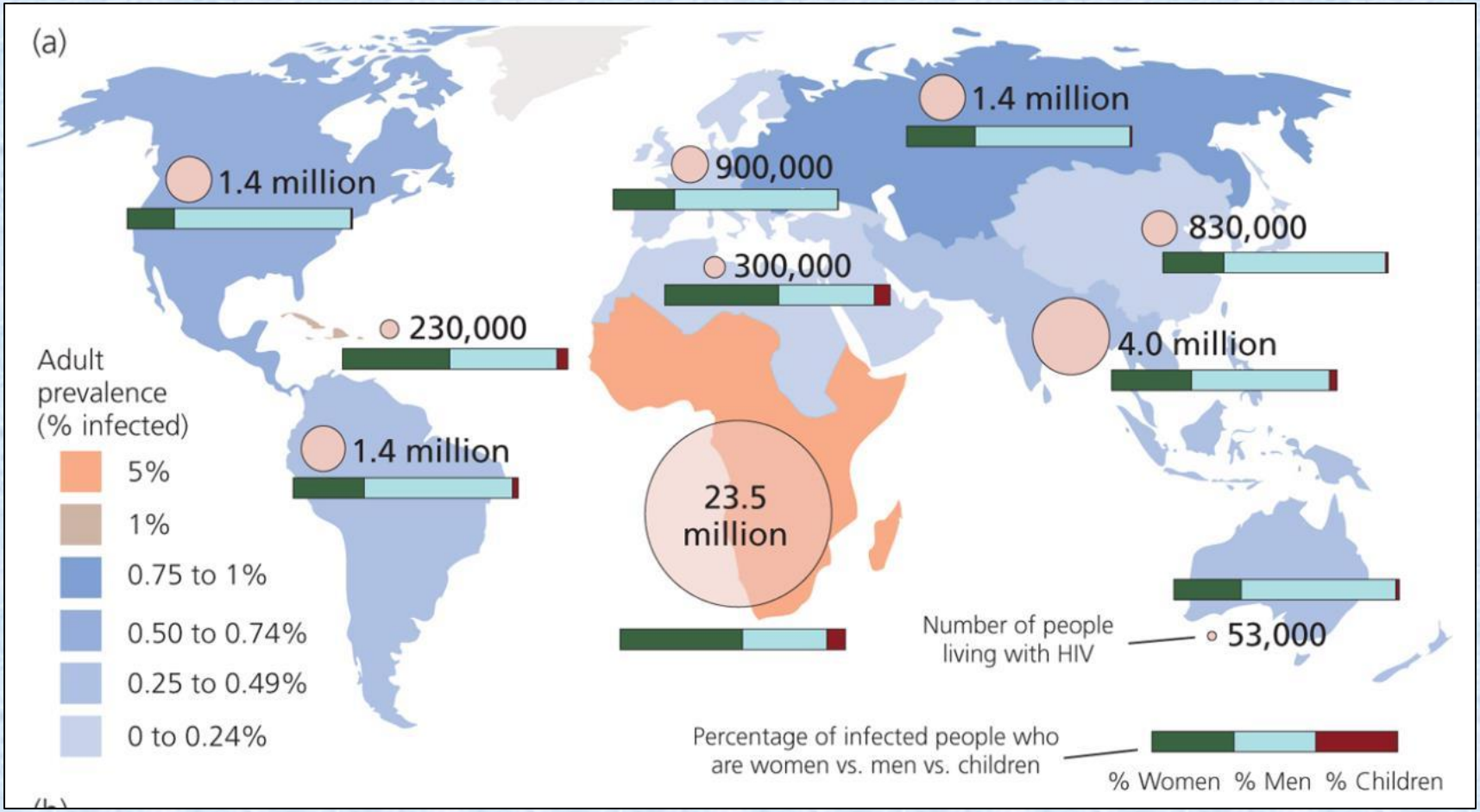
How is HIV Transmitted?

- Unprotected sexual contact with an infected partner
- Exposure of broken skin or wound to infected blood or body fluids
- Transfusion with HIV-infected blood
- Injection with contaminated needles
- Mother to child during pregnancy, birth or breastfeeding



Scale of problem

- Has infected over 65 million people
- 30 million have died
- Globally, infection rates are highest in sub-Saharan Africa, 1 in 20 adults, but also are high in southeast Asia.



Scale of problem

- About 1.2 million people in the United States were living with HIV at the end of 2012, the most recent year this information was available.
- Of those people, about 12.8% do not know they are infected.
- In the United States, about 13,712 people diagnosed with AIDS died in 2012.
- HIV disease remains a significant cause of death for certain populations. To date, an estimated 658,507 people diagnosed with AIDS in the United States have died.

HIV/AIDS Web Page – CDC
http://www.cdc.gov/hiv/

AIDS.GOV
https://www.aids.gov/hiv-aids-basics/

YouTube Videos

Transmission and Prevention of HIV (The Plain Facts)
https://www.youtube.com/watch?v=Eqxu3jjh3LE

HIV: See What We See (Medicins Sans Frontiers)
https://www.youtube.com/watch?v=OqlGFOZKC_s

End