

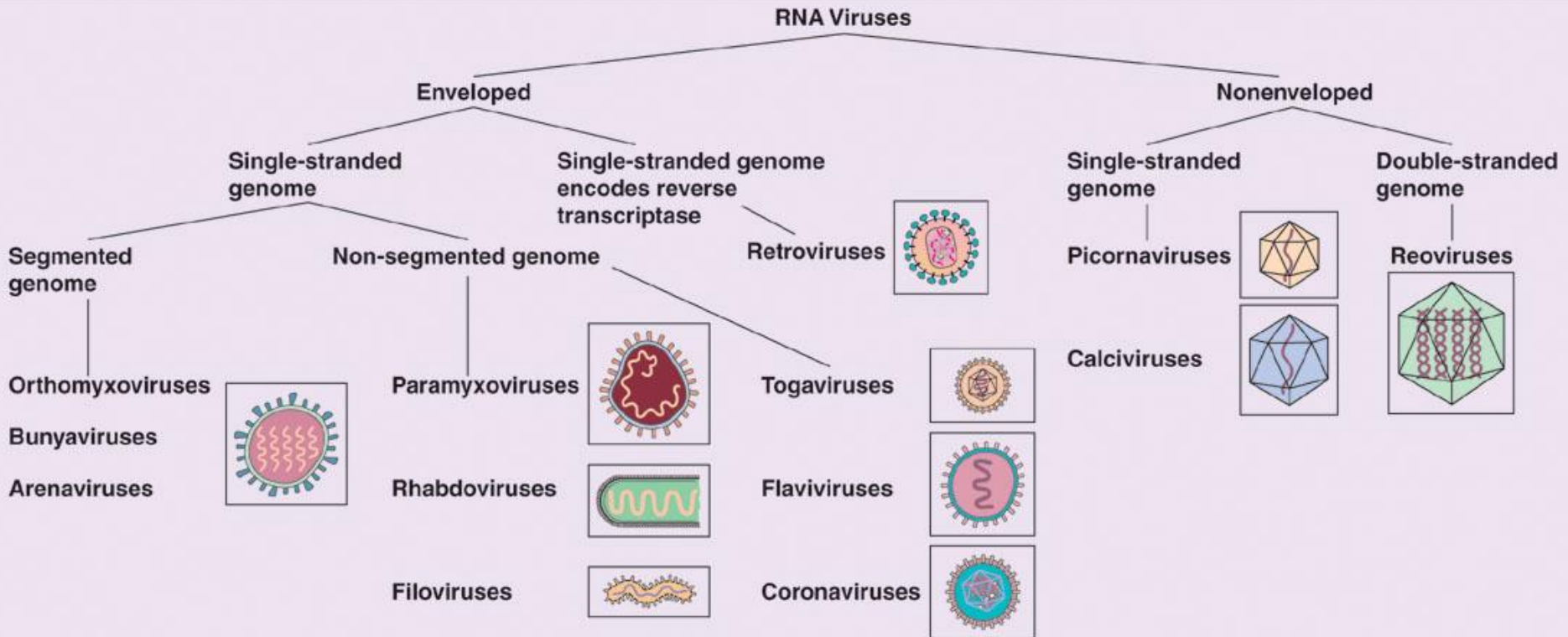


The RNA Viruses of Medical Importance

Chapter 25

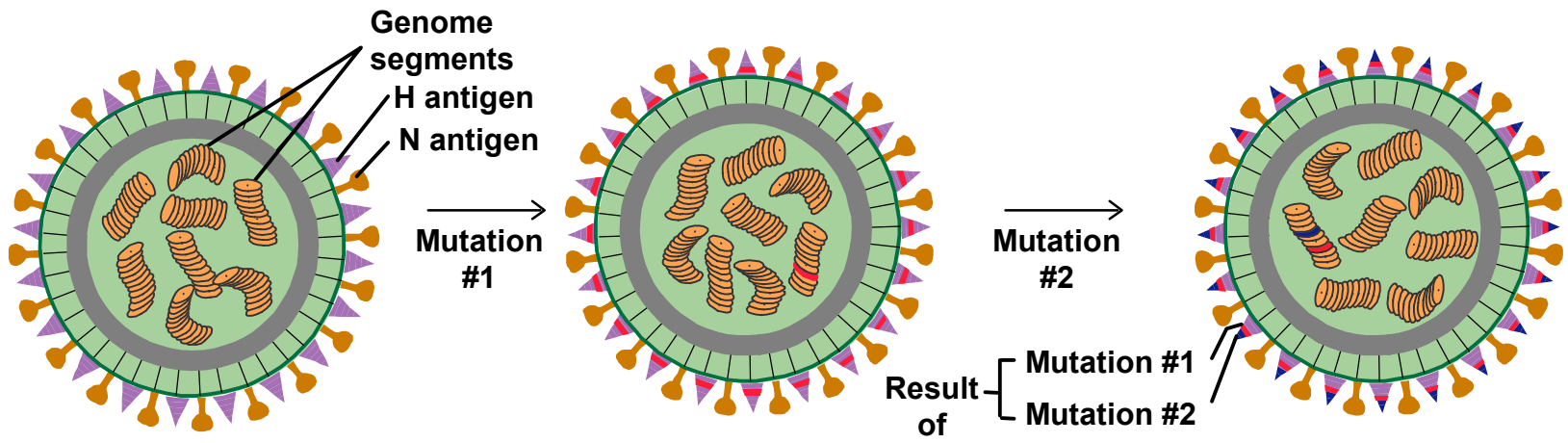
TABLE 25.1

RNA Viruses

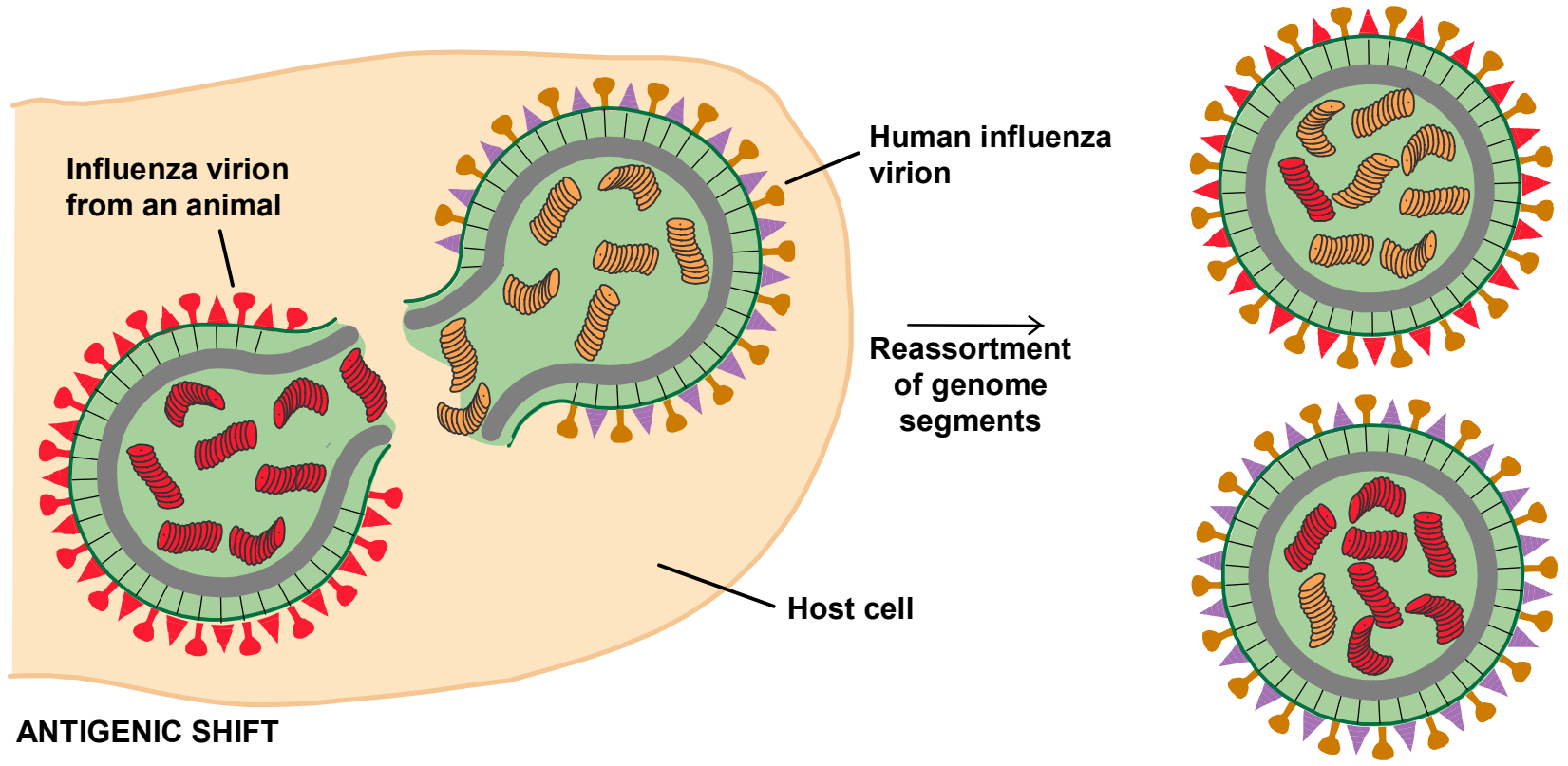


Orthomyxoviruses

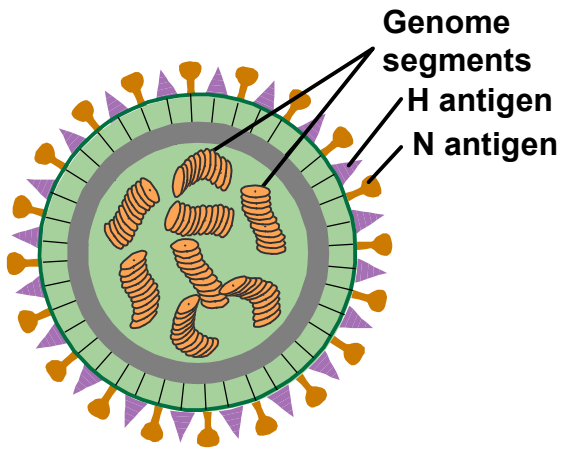
- enveloped, segmented ssRNA
- 2 types of envelope glycoprotein spikes
 - Hemagglutinin (HA) – binds to host cells
- genome constantly changes
 - Antigenic drift – minor change caused by mutations
 - Antigenic shift - major alteration occurring when segments recombine



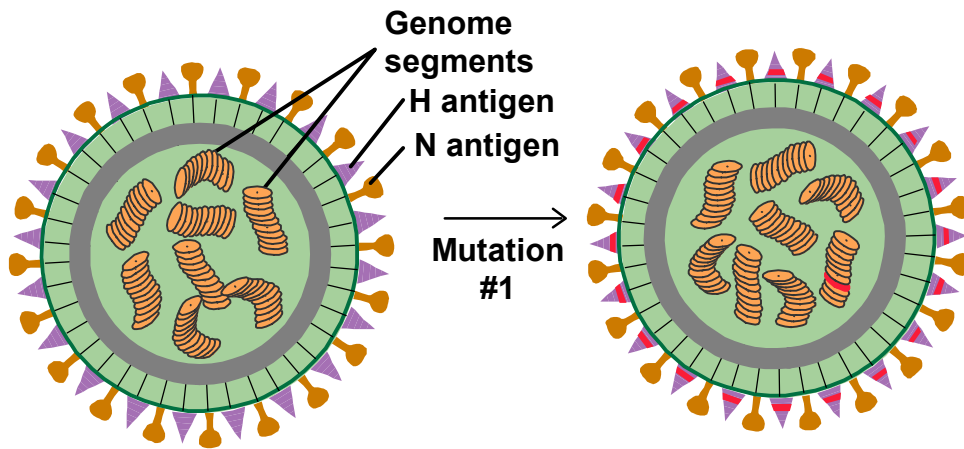
ANTIGENIC DRIFT



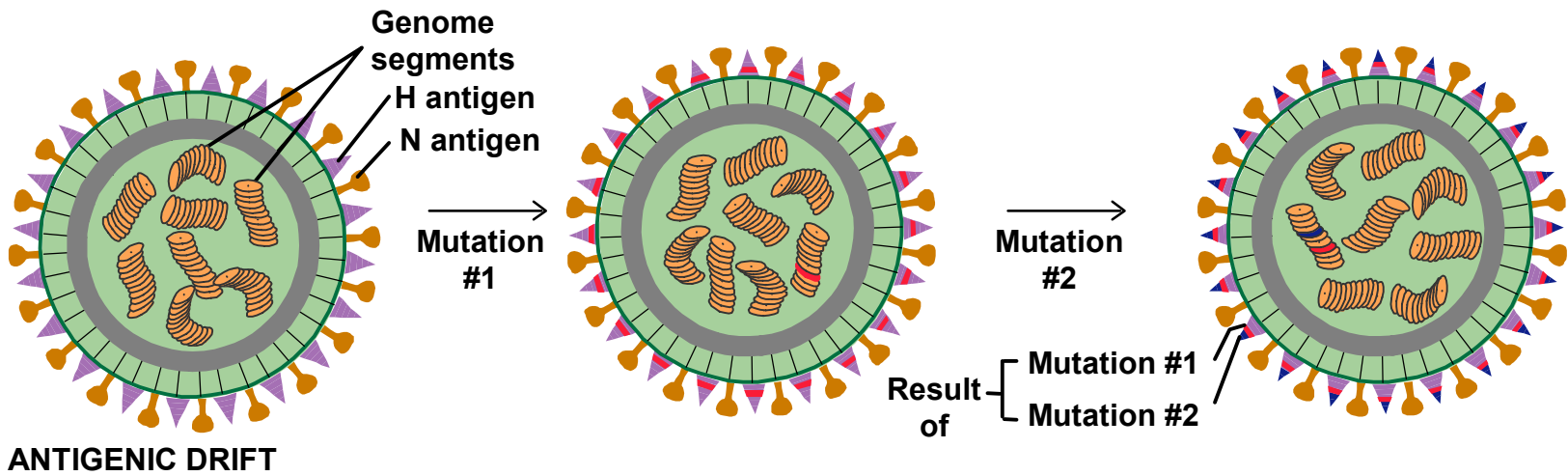
ANTIGENIC SHIFT

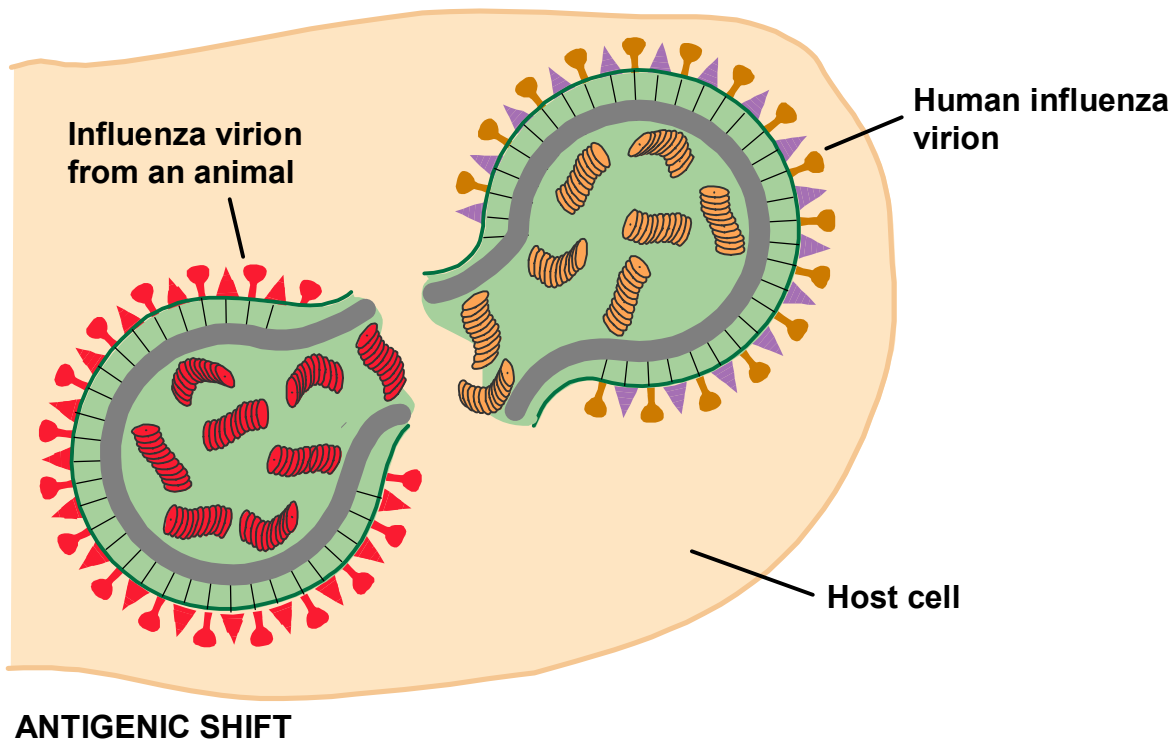
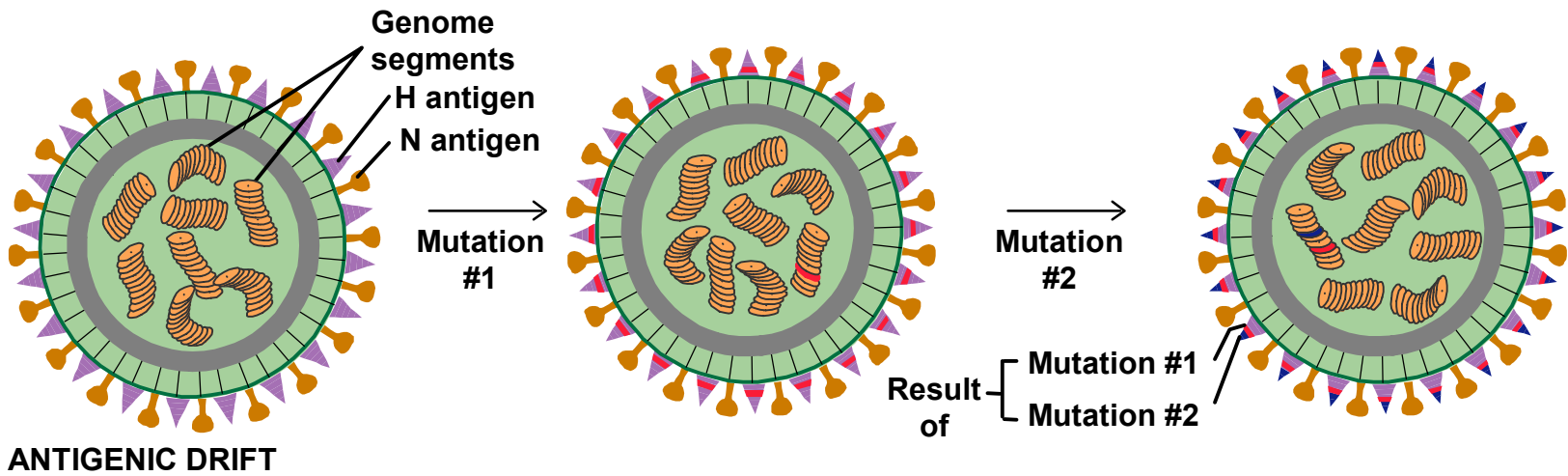


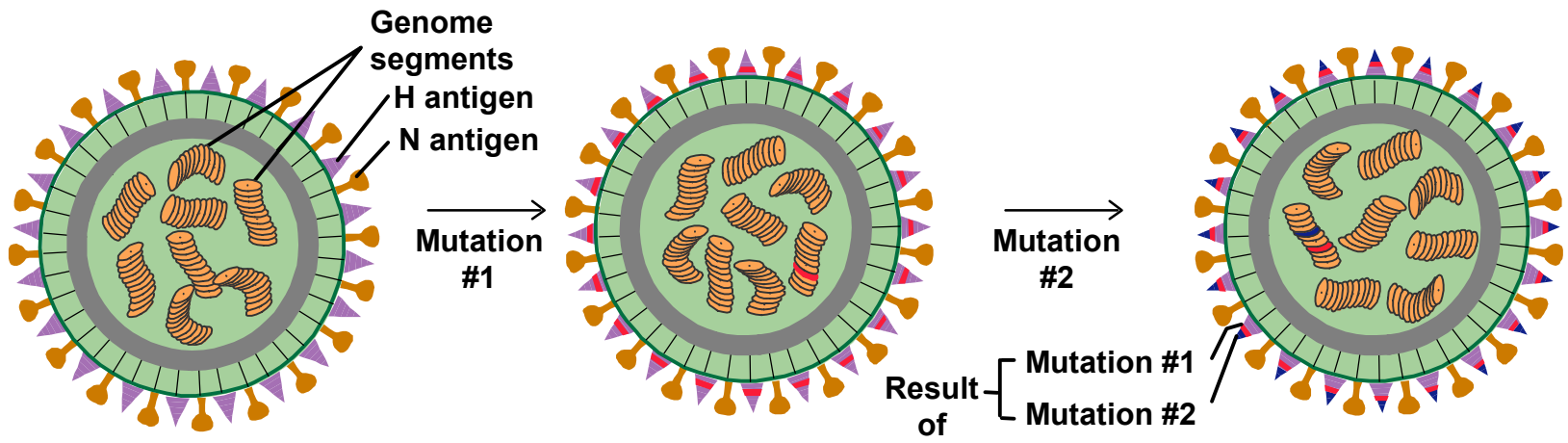
ANTIGENIC DRIFT



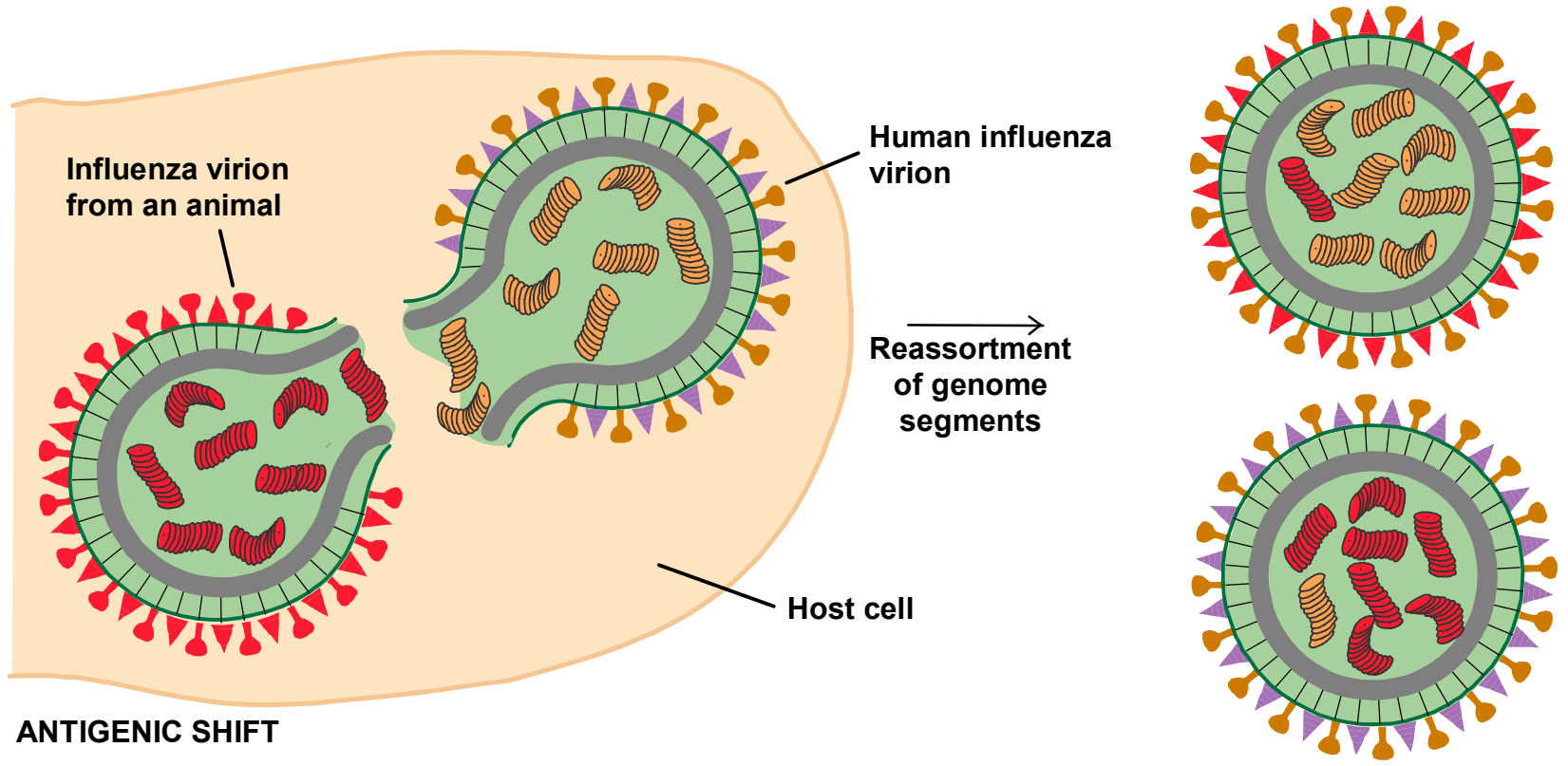
ANTIGENIC DRIFT







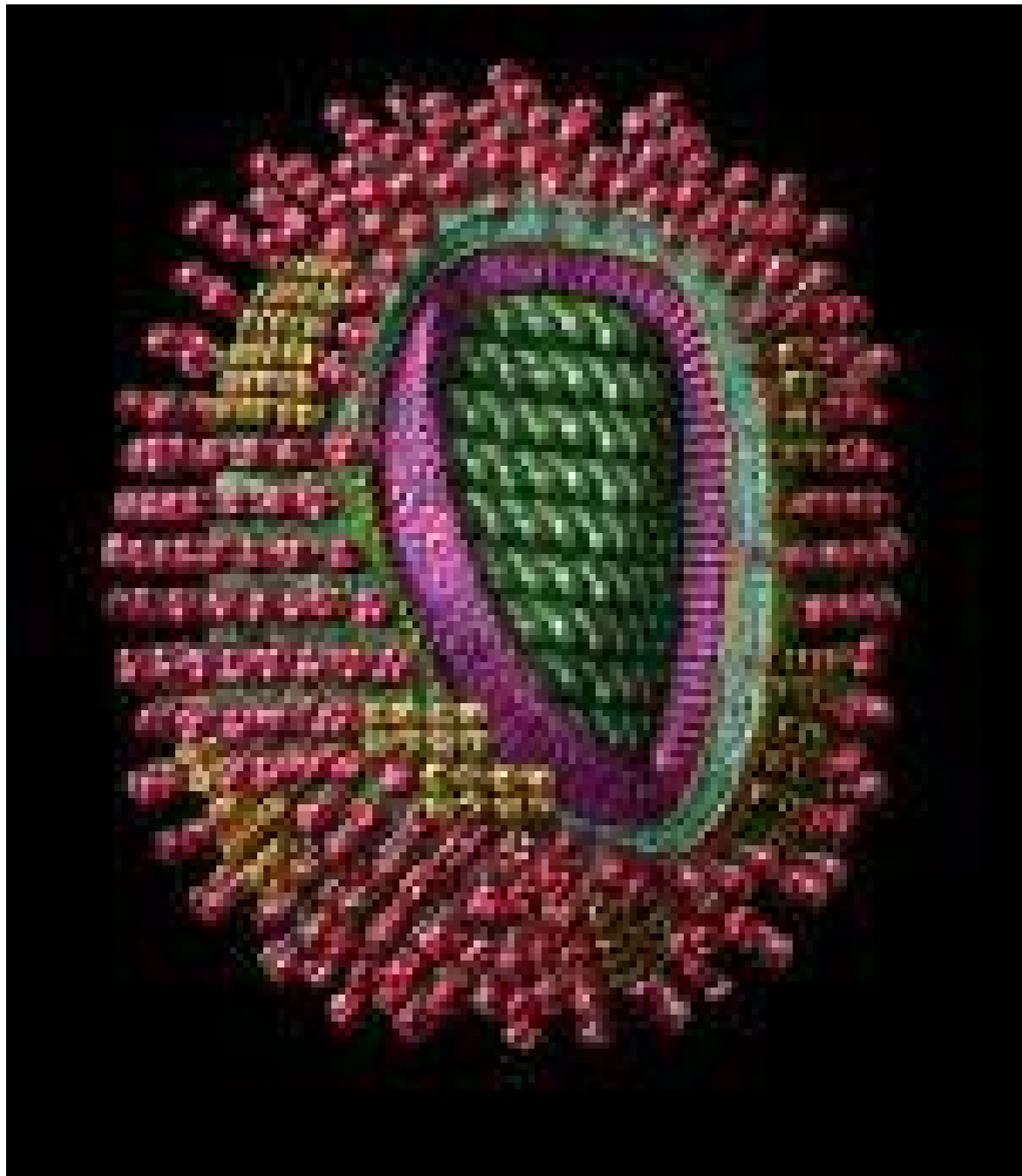
ANTIGENIC DRIFT



ANTIGENIC SHIFT

**Artist's
cutaway
Image of
Influenza
virus**

Video



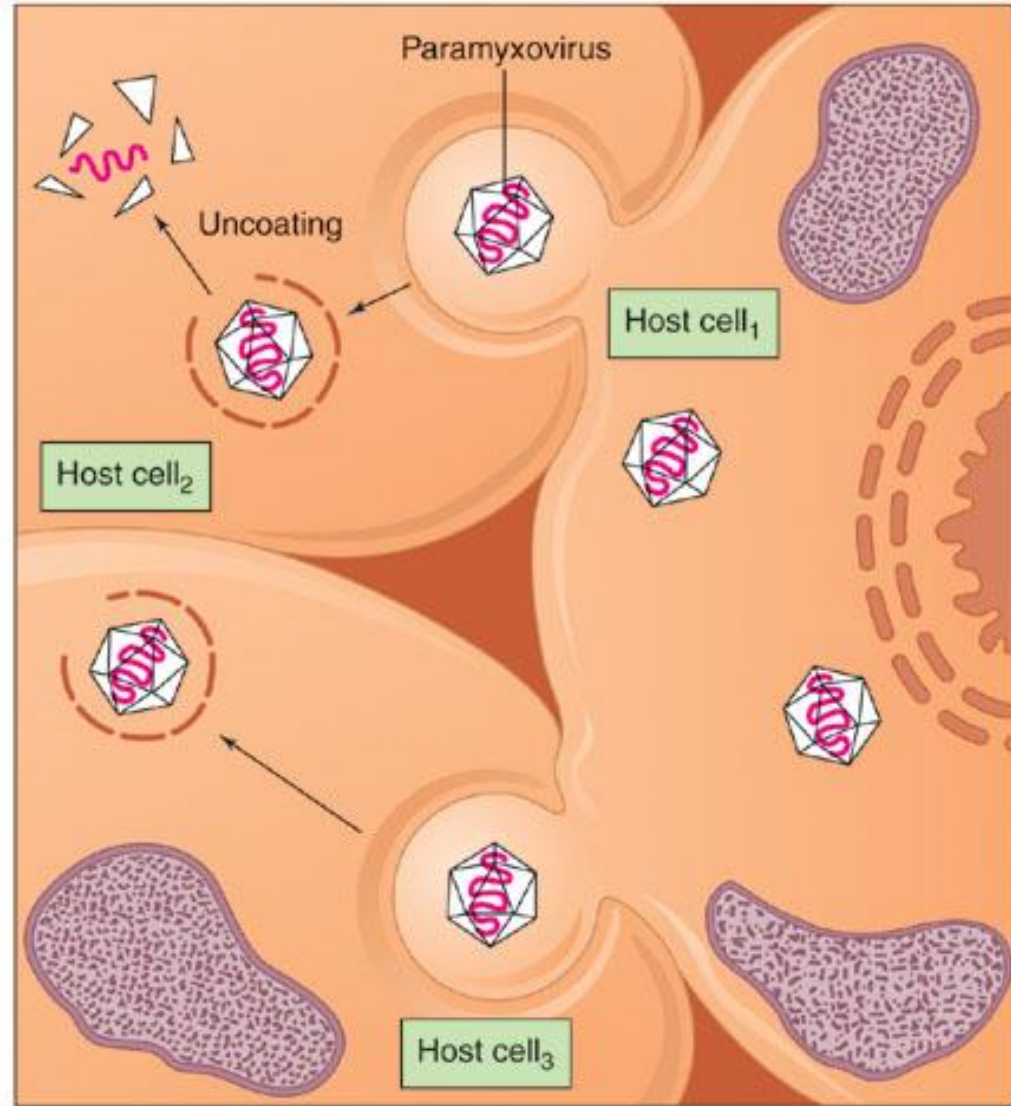
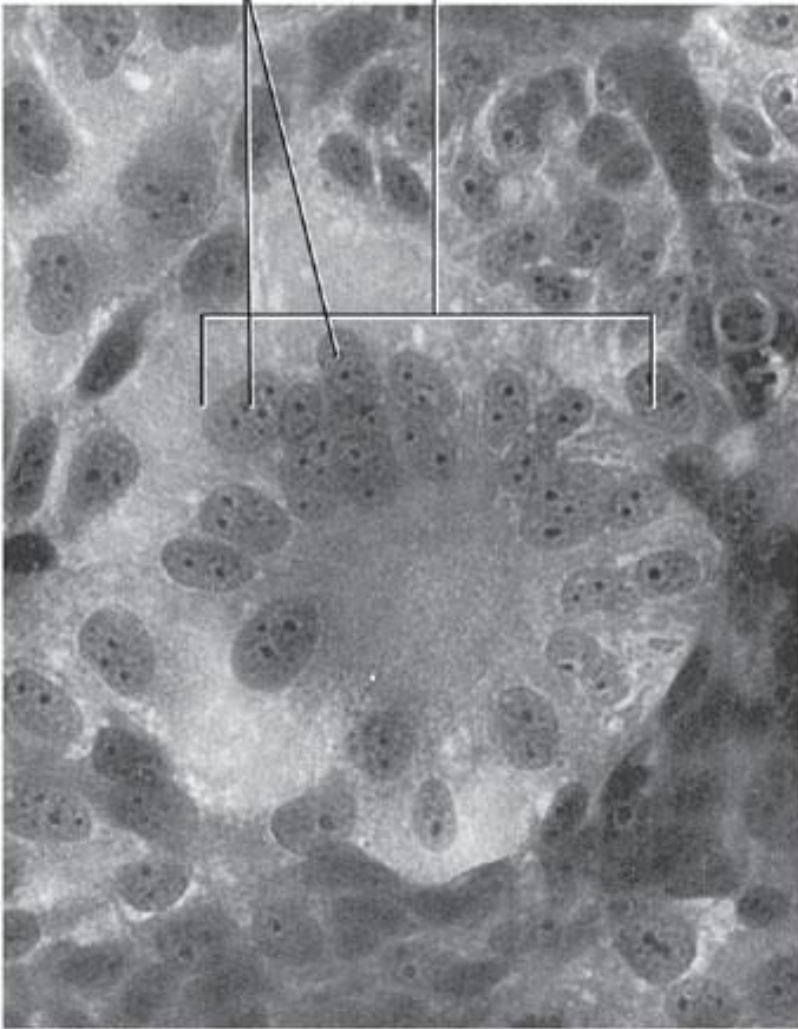
Influenza type A

- acute, highly contagious respiratory illness
- seasonal, pandemics
- among top 10 causes of death in US
- respiratory transmission
- binds to ciliated cells of respiratory mucosa
- causes rapid shedding of cells, stripping the respiratory epithelium, severe inflammation
- fever, headache, myalgia, pharyngeal pain, shortness of breath, coughing
- treatment: amantadine, rimantadine, zanamivir & oseltamivir
- annual trivalent vaccine

Paramyxoviruses

- enveloped ssRNA
 - Paramyxoviruses (parainfluenza, mumps virus)
 - Morbillivirus (measles virus)
 - Pnuemonovirus (respiratory syncytia virus)
- respiratory transmission
- envelope has HN & F spikes
- virus causes infected cells to fuse with neighboring cells – syncytium or multinucleate giant cells form

Nuclei Giant cell



(a)

(b)

Parainfluenza

- widespread as influenza but more benign
- respiratory transmission
- seen mostly in children
- minor cold, bronchitis, bronchopneumonia, croup
- no specific treatment available

Mumps

- epidemic parotitis
- self-limited, associated with painful swelling of parotid salivary glands
- humans are the only reservoir
- 40% of infections are subclinical
- 300 cases in US/year
- incubation 2-3 weeks fever, muscle pain & malaise, classic swelling of both cheeks
- in 20-30% of infected males, epididymis & testes become infected; sterilization is rare
- live attenuated vaccine **MMR**



Measles

- caused by *Morbillivirus*
- also known as red measles & rubeola
- different from German measles
- very contagious
- transmitted by respiratory aerosols
- humans are the only reservoir
- less than 100 cases/yr in US
- virus invades respiratory tract
- sore throat, , dry cough, headache, conjunctivitis, lymphadenitis, fever, **Koplik** spots – oral lesions
- rash

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TABLE 25.2

The Two Forms of Measles

	Synonyms	Etiology	Primary Patient	Complications	Skin Rash	Koplik's Spots
Measles	Rubeola, red measles	Paramyxovirus; <i>Morbillivirus</i>	Child	SSPE,* pneumonia	Present	Present
German Measles	Rubella, 3-day measles, rubeola	Togavirus: <i>Rubivirus</i>	Child/fetus	Congenital defects	Present	Absent

**Subacute sclerosing panencephalitis.*

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Koplik's spots



(b)

(a)

measles

- most serious complication is subacute sclerosing panencephalitis (SSPE), a progressive neurological degeneration of the cerebral cortex, white matter & brain stem
- 1 case in a million infections
- involves a defective virus spreading through the brain by cell fusion & destroys cells
- leads to coma & death in months or years
- attenuated viral vaccine **MMR**

RSV

- also called *Pneumonvirus*
- infects upper respiratory tract & produces giant multinucleate cells
- most prevalent cause of respiratory infection in children 6 months or younger; most susceptible to serious disease
- epithelia of nose & eye portal of entry
- replicates in nasopharynx
- rhinitis, wheezing, otitis, croup
- treatment: synagis, a monoclonal antibody that blocks attachment, **ribavirin**

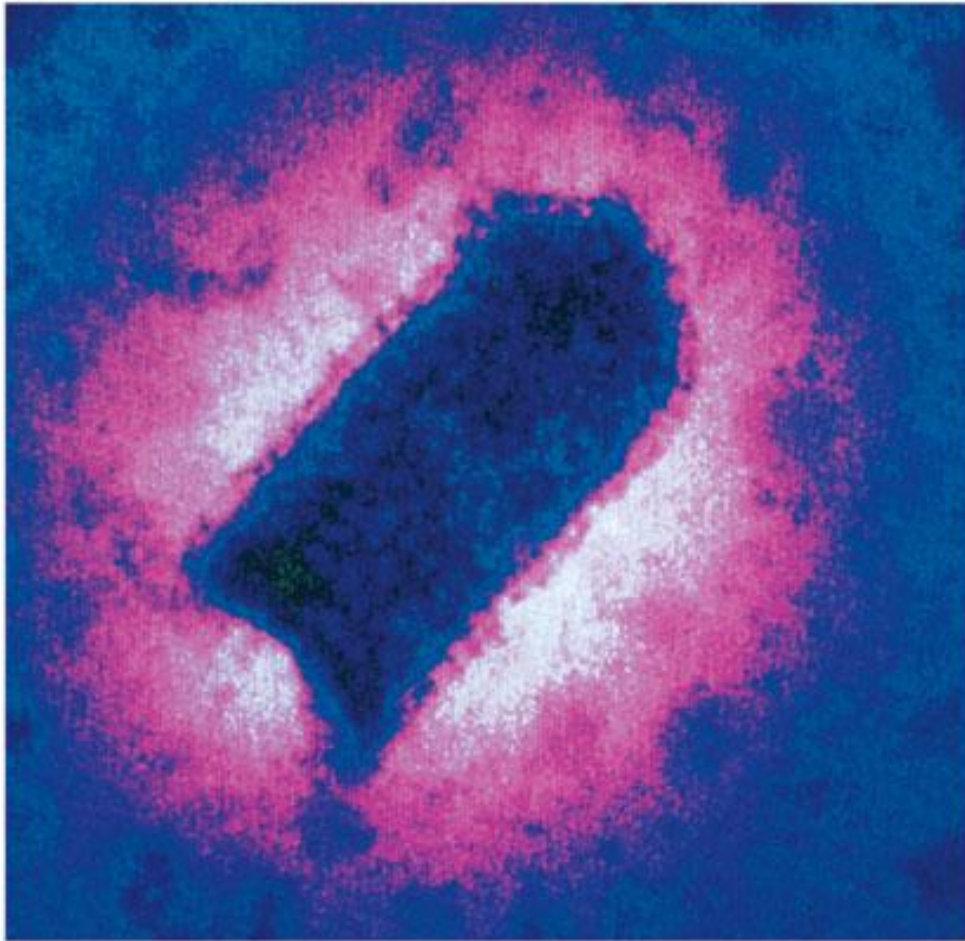


THIS
VIRUS SCAN
SAYS I HAVE A
COLD!!

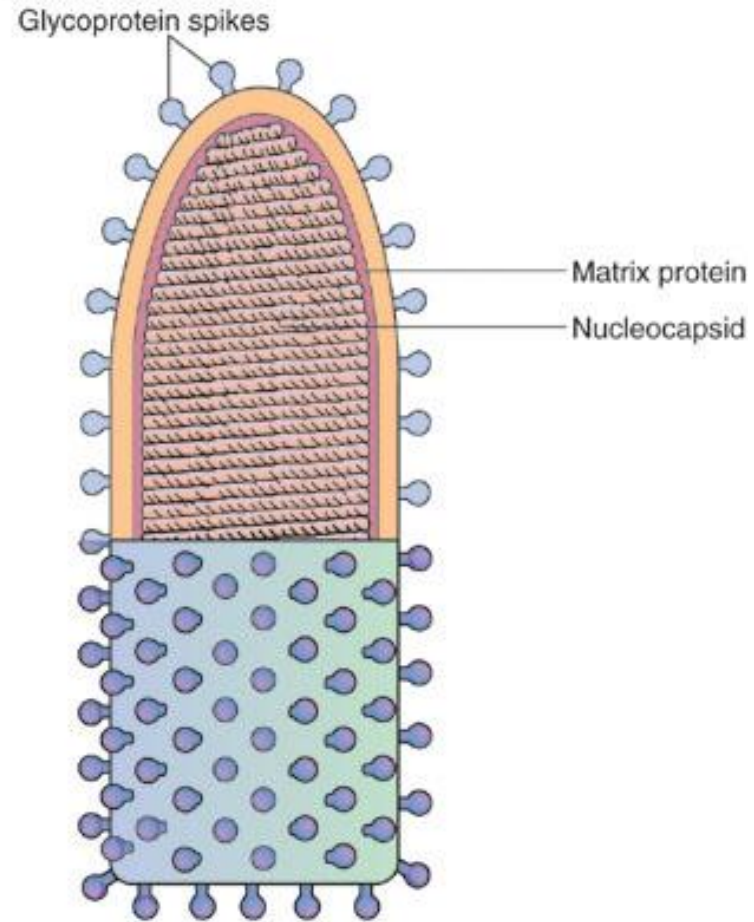
Ben Elton

rabies

- **Rhabdovirus** family
- genus Lyssavirus
- bullet-shaped virions
- enveloped
- slow, progressive **zoonotic** disease
- virus enters through bite, grows at trauma site for a week , enters nerve endings & advances toward the ganglia, spinal cord & brain
- furious form of rabies – agitation, disorientation, seizures, twitching, hydrophobia
- dumb form of rabies – paralyzed, stuporous



(a)

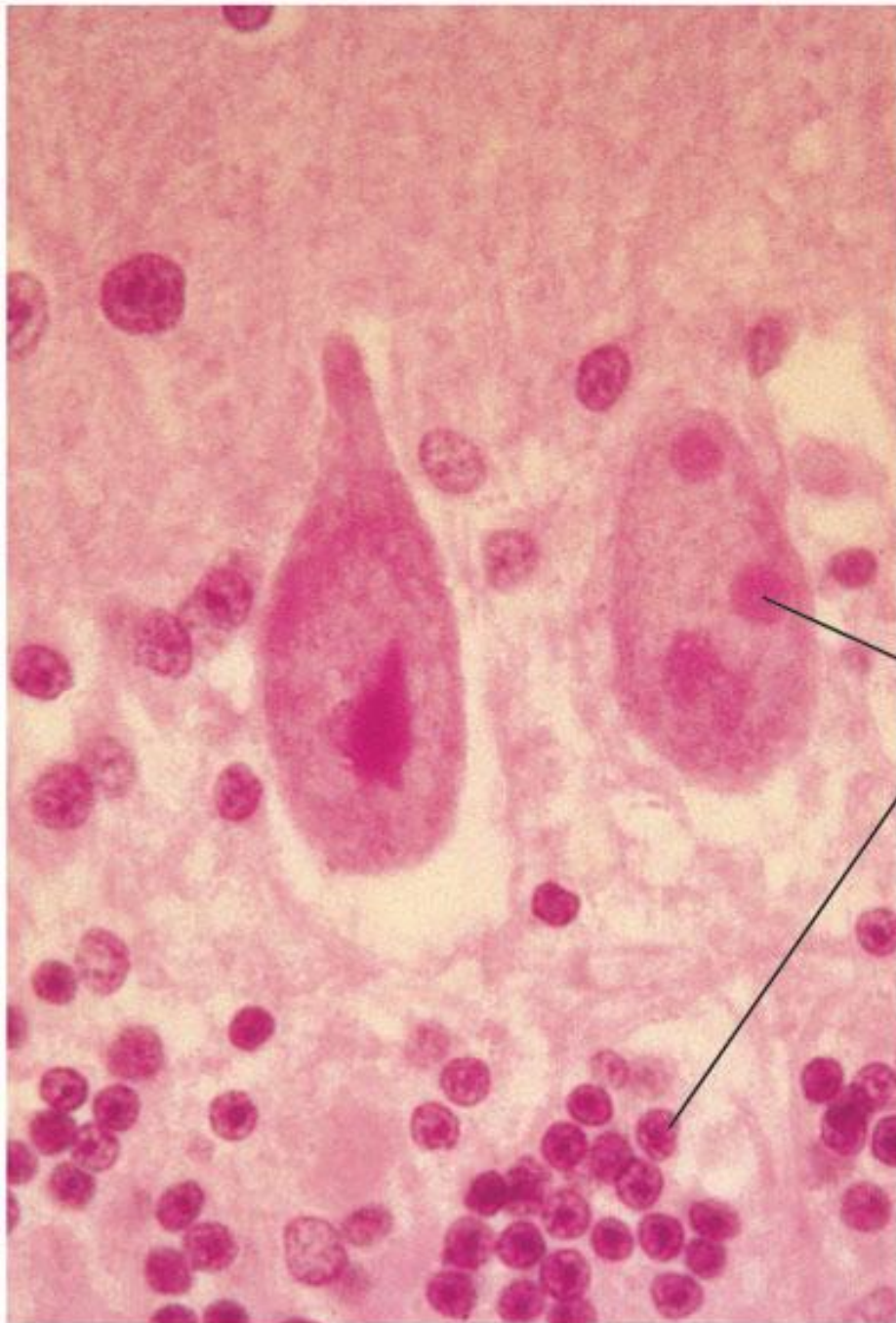


(b)



rabies

- often diagnosed at autopsy – intracellular inclusions (Negri bodies) in nervous tissue
- treatment – passive & active postexposure immunization



Negri bodies

Coronavirus

- relatively large RNA viruses with distinctively spaced spikes on their envelopes
- common in domesticated animals
- 3 types of human coronaviruses have been characterized
 - HCoV causes a cold
 - an enteric virus
 - Severe Acute Respiratory Syndrome (**SARS**)
 - airborne transmission
 - 10% of cases fatal

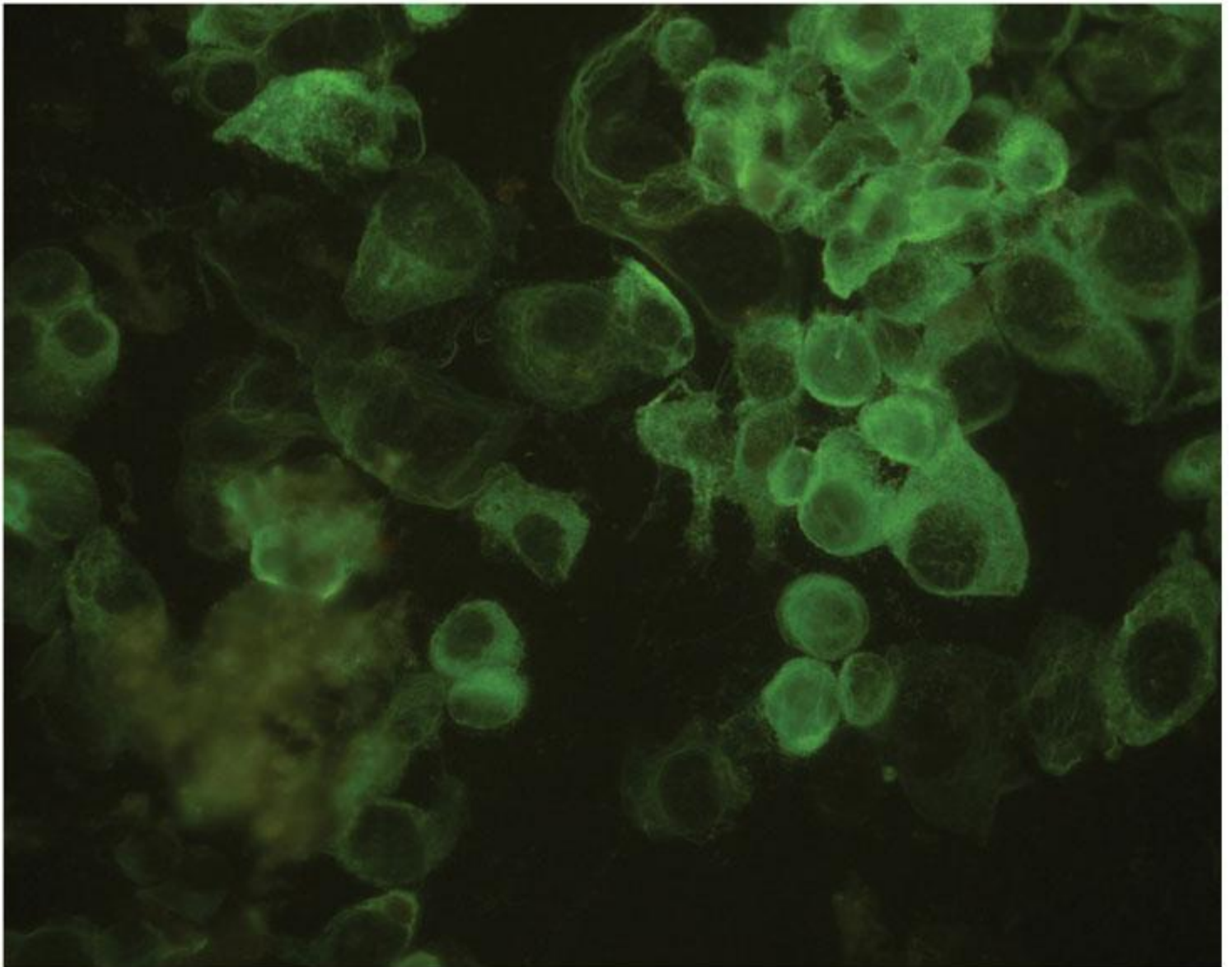
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"YES, OUR CRUISES ALLOW TRAVELERS TO CHOOSE FROM SEVERAL VIRUSES... I MEAN, PORTS OF CALL."



Rubella

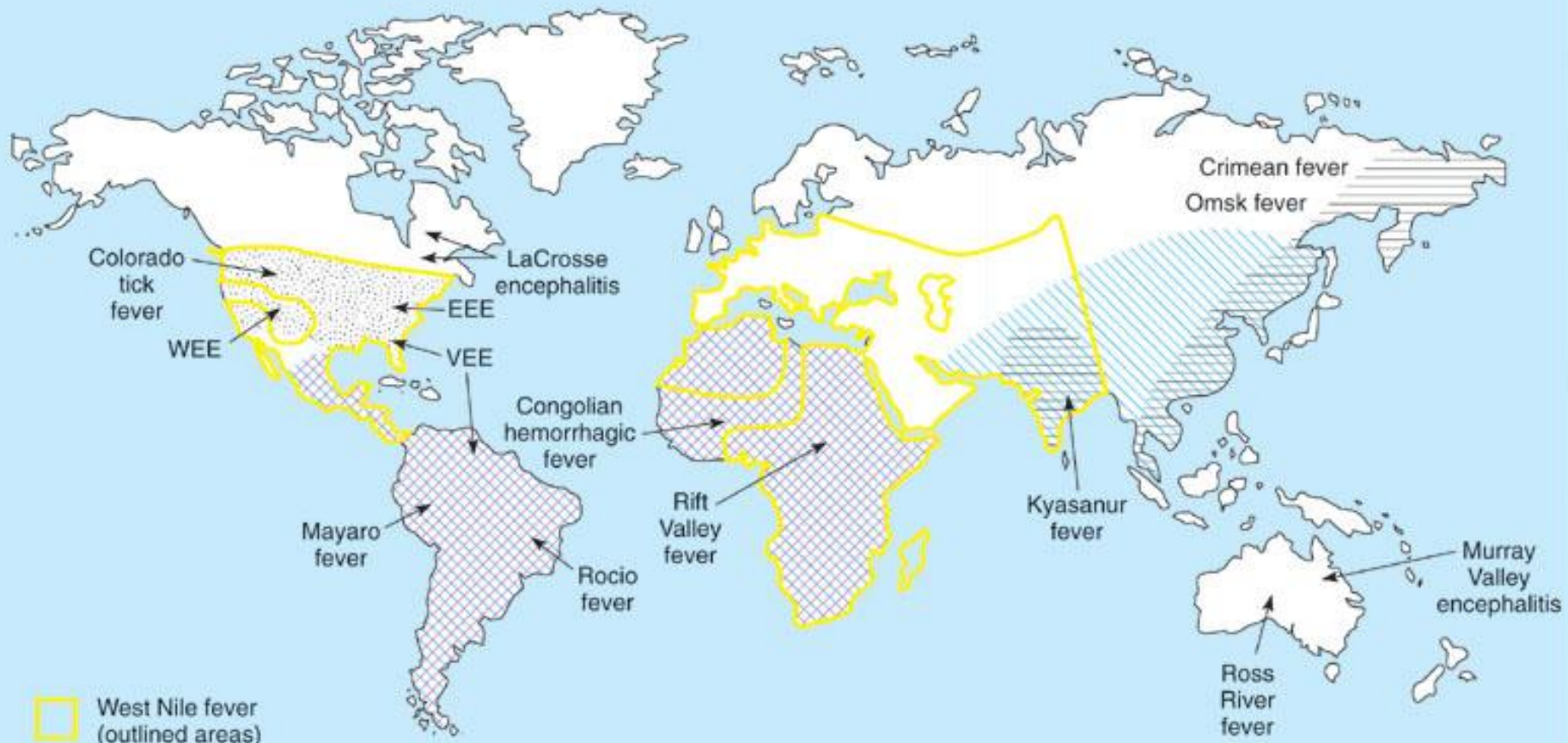
- caused by Rubivirus, a Togavirus
- ssRNA with a loose envelop
- **German measles**
- teratogenic effects- cataracts, other congenital defects
- transmitted through contact with respiratory secretions






Rubella

- postnatal rubella – malaise, fever, sore throat, lymphadenopathy, rash, generally mild
- congenital rubella – infection during 1st trimester most likely to induce miscarriage or multiple defects such as cardiac abnormalities, ocular lesions, deafness, mental & physical retardation
- attenuated viral vaccine MMR

Arboviruses

- viruses that spread by arthropod vectors – mosquitoes, ticks, flies, & gnats
- 400 viruses
- **Togaviruses, Flaviviruses, some Bunyaviruses & Reoviruses**
- most illnesses caused by these viruses are mild fevers, some cause severe encephalitis
- **dengue fever, western- & eastern equine encephalitis, yellow fever**



-  West Nile fever (outlined areas)
-  Yellow fever
-  Dengue fever
-  St. Louis encephalitis
-  Japanese encephalitis

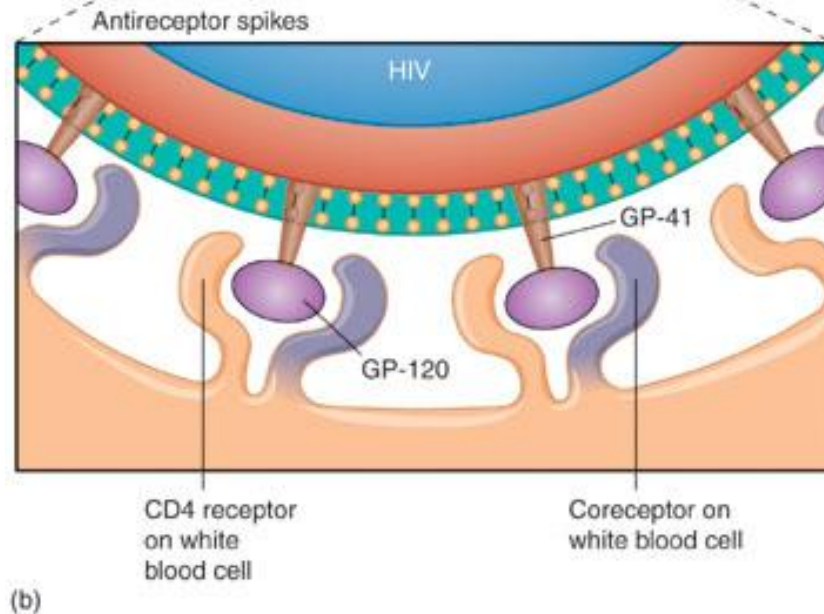
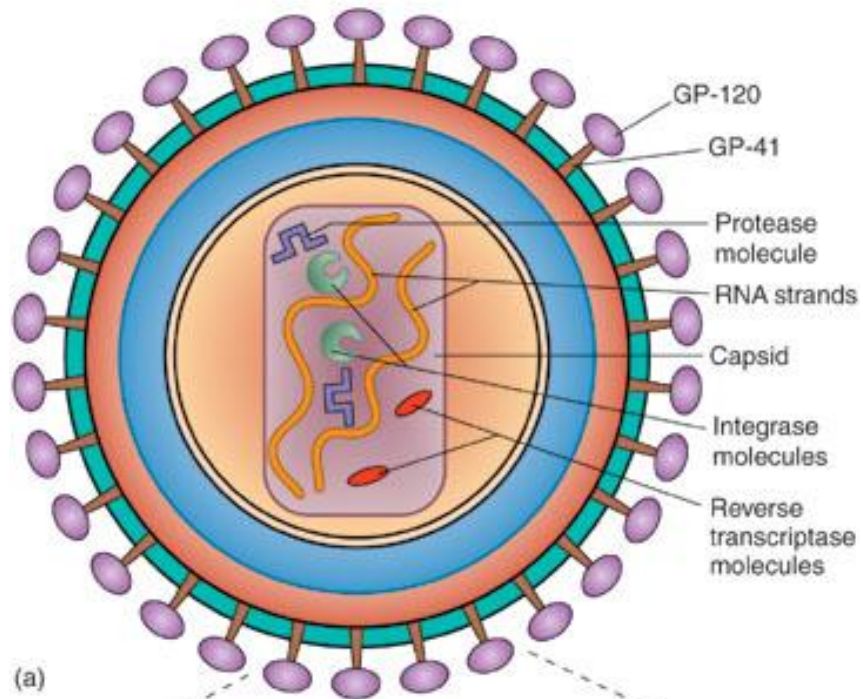
- WEE Western equine encephalitis
- EEE Eastern equine encephalitis
- VEE Venezuelan equine encephalitis

→ Shows relatively restricted distribution

Retroviruses

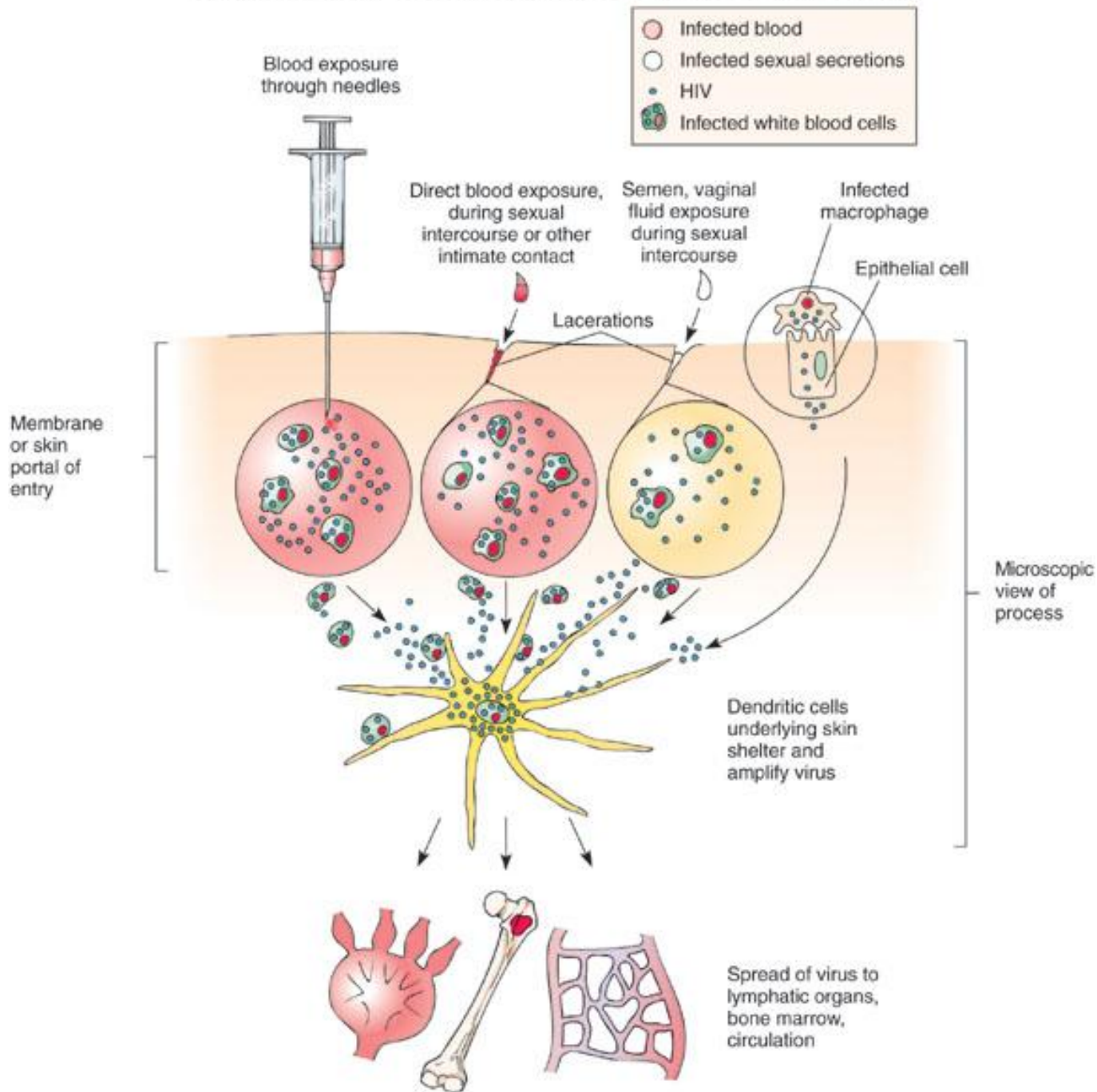
- enveloped, ssRNA viruses
- encode reverse transcriptase enzyme which makes a DNA copy of their RNA genome [Video](#)
- Human Immunodeficiency Virus (HIV) the cause of Acquired Immunodeficiency Syndrome (AIDS)
- HIV-1 & HIV-2
- T-cell lymphotropic viruses I & II - leukemia

Video



AIDS

- first emerged in early 1980s
- HIV-1 & HIV-2 are not closely related
- HIV-1 may have originated from a chimpanzee virus
- 1959 first documented case of AIDS
- HIV is found in blood, semen, & vaginal secretions.
- HIV is transmitted by sex, sharing needles, and mother to child.
- HIV does not survive long outside of the body.



HIV

- attacks the T helper cells & macrophages
- first signs of AIDS are opportunistic infections such as *Pneumocystis carinii* pneumonia (PCP) and cancers such as **Kaposi sarcoma**

[Video](#)

TABLE 25.4**Classification System for HIV Infection and Expanded AIDS Case Definition for Adolescents and Adults***

CD4⁺ T-cell Category	Clinical Category		
	(A) Asymptomatic, Acute (Primary) HIV Infection or PGL***	(B) Symptomatic, Not (A) or (C) Conditions	(C) Symptomatic AIDS-Indicator Conditions**
(1) $\geq 500/\mu\text{l}$	A1	B1	C1
(2) 200–499/ μl	A2	B2	C2
(3) $< 200/\mu\text{l}$ AIDS-indicator T-cell count	A3	B3	C3

*Persons with AIDS-indicator conditions (category C) as well as those with CD4⁺ T-lymphocyte counts $< 200/\mu\text{l}$ (category A3 or B3) became reportable as AIDS cases in the United States and territories, effective January 1, 1993.

**Includes opportunistic infections, cancers, wasting, dementia (see figure 25.18).

***PGL = persistent generalized lymphadenopathy.

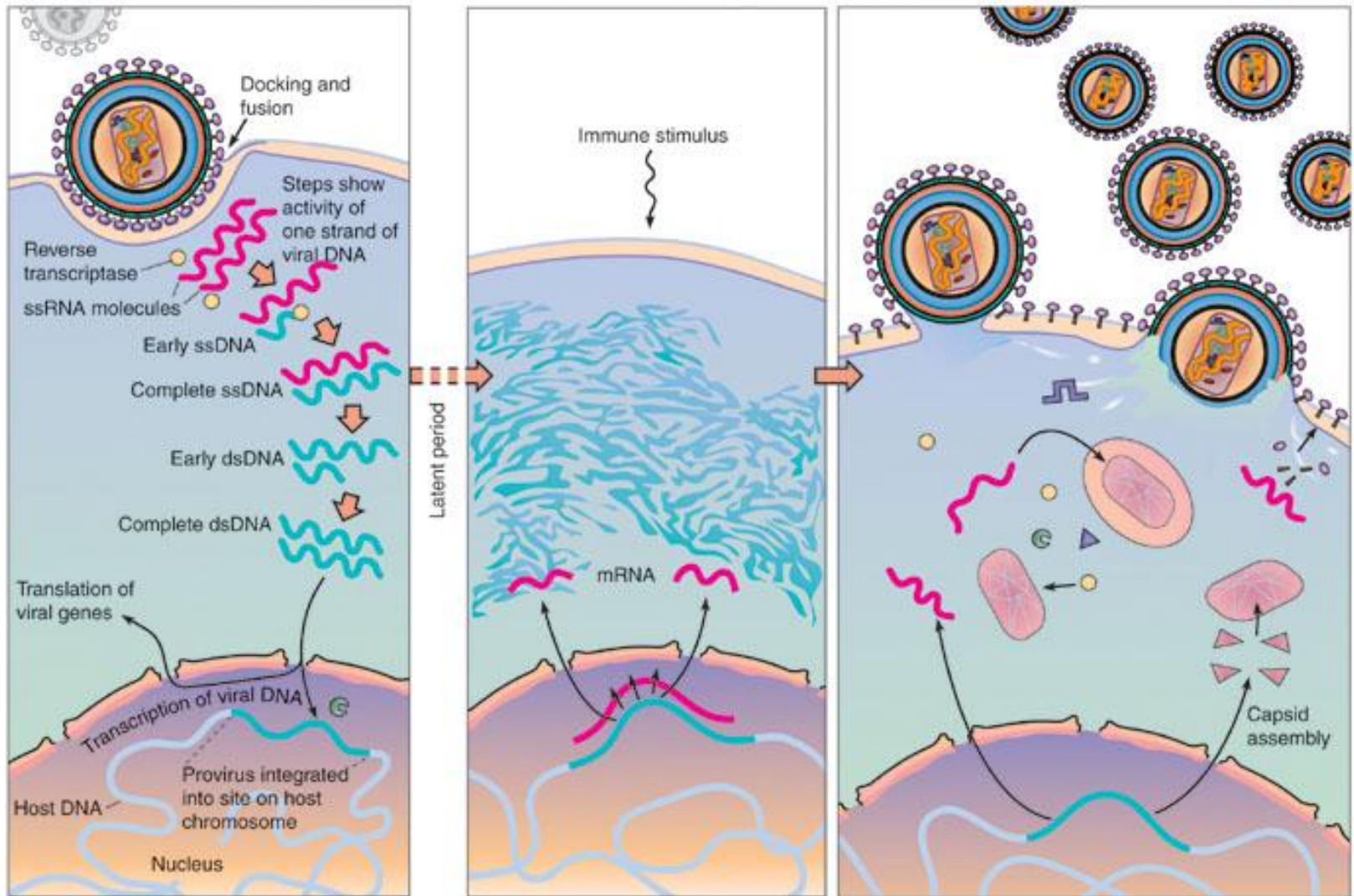
Source: Data from Morbidity and Mortality Weekly Report, vol. 41. December 18, 1992. The Centers for Disease Control and Prevention, Atlanta, GA.

Risk categories

- homosexual or bisexual males – 45%
- intravenous drug users – 30%
- heterosexual partners of HIV carriers – 11%
- blood transfusions & blood products – since testing, no longer a serious risk
- inapparent or unknown risk – 9% - (due to denial, death, unavailability)
- congenital or neonatal – can be reduced with antiviral drugs
- medical & dental personnel – 1/500 needlestick

HIV replication

1. HIV attaches to CD4 & a coreceptor, CXCR4
2. HIV fuses with cell membrane, reverse transcriptase makes a DNA copy of RNA
3. viral DNA is integrated into host chromosome (provirus)
4. can produce a lytic infection or remain latent



(a)

The virus is adsorbed and endocytosed, and the twin RNAs are uncoated. Reverse transcriptase catalyzes the synthesis of a single complementary strand of DNA (ssDNA). This single strand serves as a template for synthesis of a double strand (ds) of DNA. In latency, dsDNA is inserted into the host chromosome as a provirus.

(b)

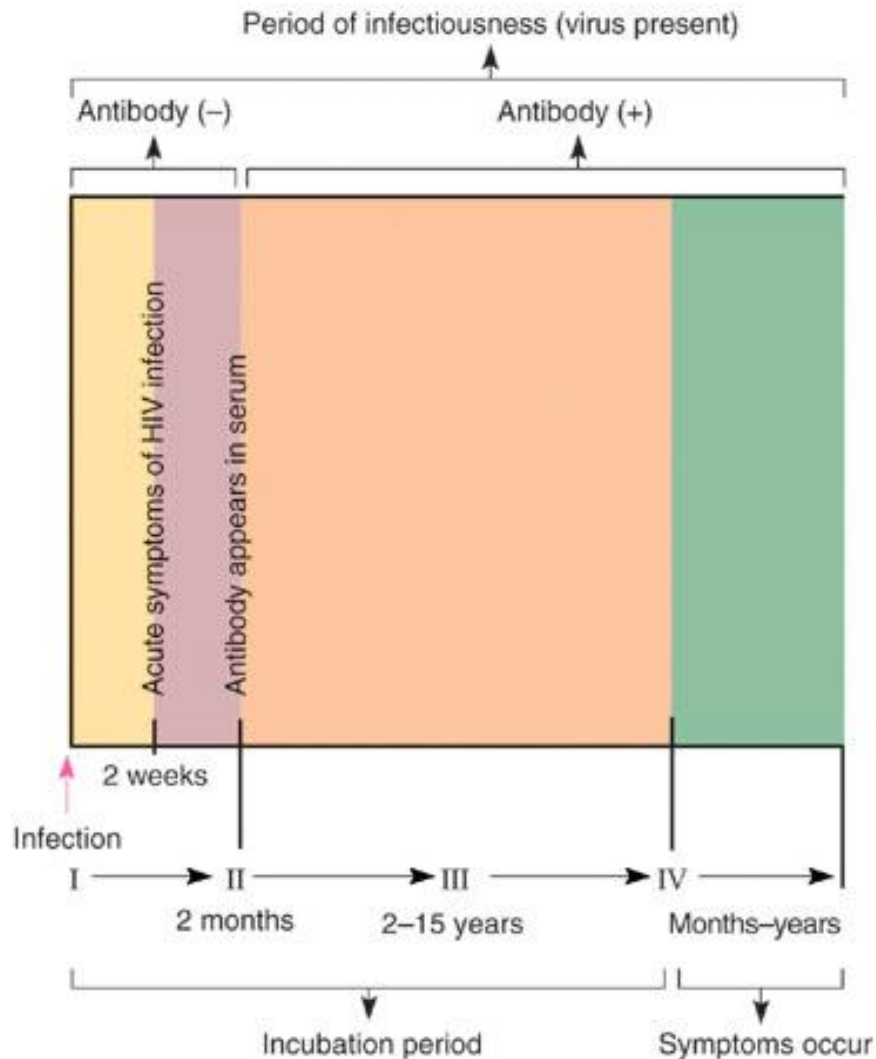
After a latent period, various immune activators stimulate the infected cell, causing reactivation of the provirus genes and production of viral mRNA.

(c)

HIV mRNA is translated by the cell's synthetic machinery into virus components (capsid, reverse transcriptase, spikes), and the viruses are assembled. Budding of mature viruses lyses the infected cell.

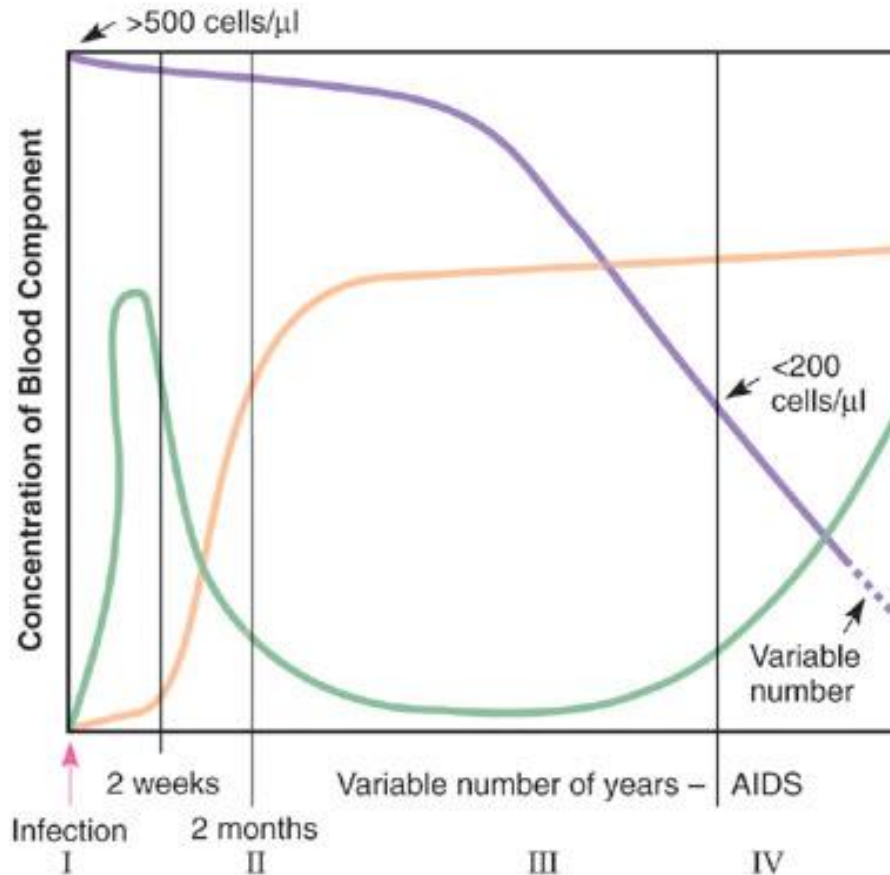
Progression of HIV disease

- initial infection – mononucleosis-like symptoms that soon disappear
- asymptomatic phase 2-15 years (ave. 10)
- antibodies are detectable 8-16 weeks after infection
- HIV destroys the immune system
- when T4 cell levels fall below 200/ μ L symptoms appear including fever, swollen lymph nodes, diarrhea, weight loss, neurological symptoms, opportunistic infections & cancers

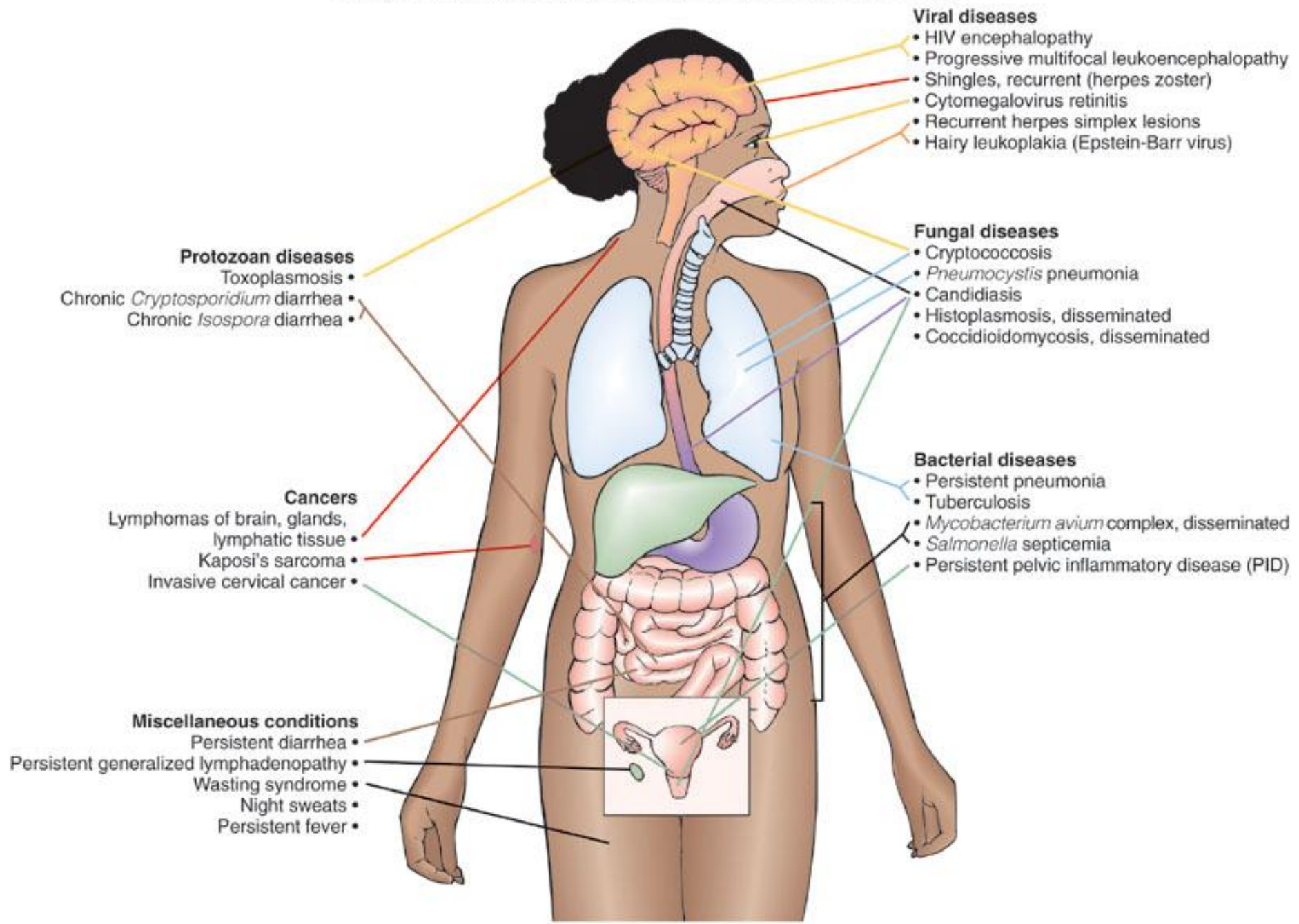


- (I) Infection with virus.
- (II) Appearance of antibodies in standard HIV tests.
- (III) Asymptomatic HIV disease, which can encompass an extensive time period.
- (IV) Overt symptoms of AIDS include some combination of opportunistic infections, cancers, and general loss of immune function.

- Level of virus antigen
- Level of antibodies to one or more antigens
- Level of CD4 T cells



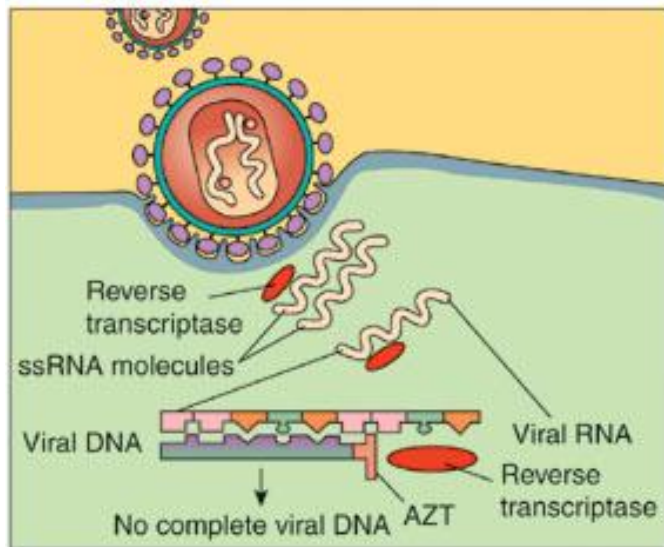
A comparison of blood levels of viruses, antibodies, and T cells covering the same time frame depicted in figure 25.16. Virus levels are high during the initial acute infection and decrease until the later phases of HIV disease and AIDS. Antibody levels gradually rise and remain relatively high throughout phases III and IV. T-cell numbers remain relatively normal until the later phases of HIV disease and full-blown AIDS.





HIV

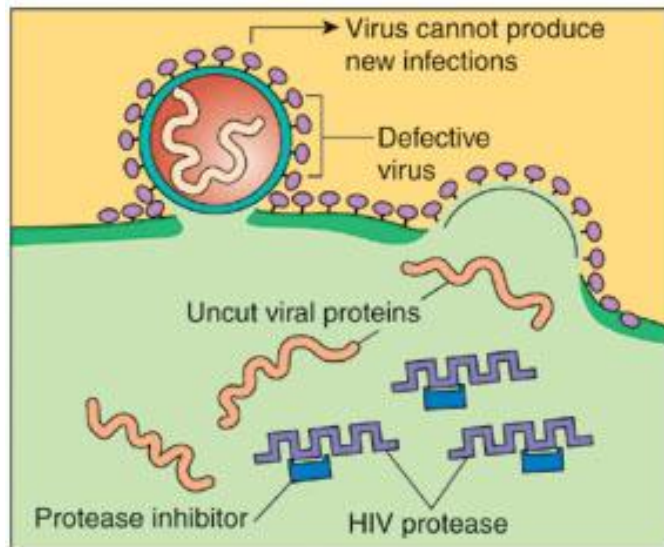
- treatments
 - inhibit viral enzymes: reverse transcriptase, protease, integrase
 - inhibit fusion
 - inhibit viral translation
- no vaccine
- prevention
 - monogamous sexual relationships
 - condoms
 - universal precautions



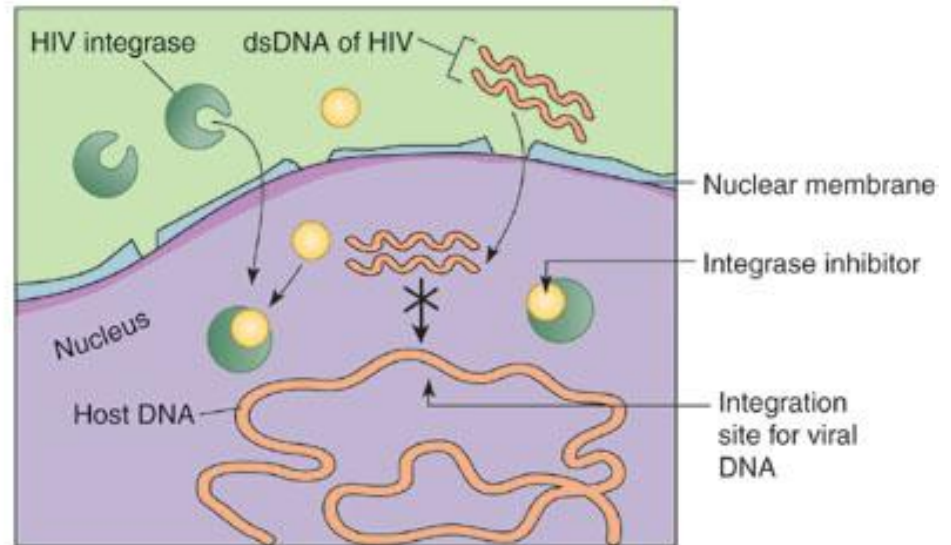
Location of reaction

- External to cell
- Cytoplasm
- Nucleus

(a) A prominent group of drugs (AZT, ddi, 3TC) are nucleoside analogs that inhibit reverse transcriptase. They are inserted in place of the natural nucleotide by reverse transcriptase but block further action of the enzyme and synthesis of viral DNA.



(b) Protease inhibitors plug into the active sites on HIV protease. This enzyme is necessary to cut elongate HIV protein strands and produce functioning smaller protein units. Because the enzyme is blocked, the proteins remain uncut, and abnormal defective viruses are formed.



(c) Integrase inhibitors are a new class of experimental drugs that attach to the enzyme required to splice the dsDNA from HIV into the host genome. This will prevent formation of the provirus and block future virus multiplication in that cell.

Nonenveloped ssRNA viruses

- **Picornaviruses**

- *Enterovirus* – poliovirus, HAV
- *Rhinovirus* - rhinovirus
- *Cardiovirus* -

- **Caliciviruses**

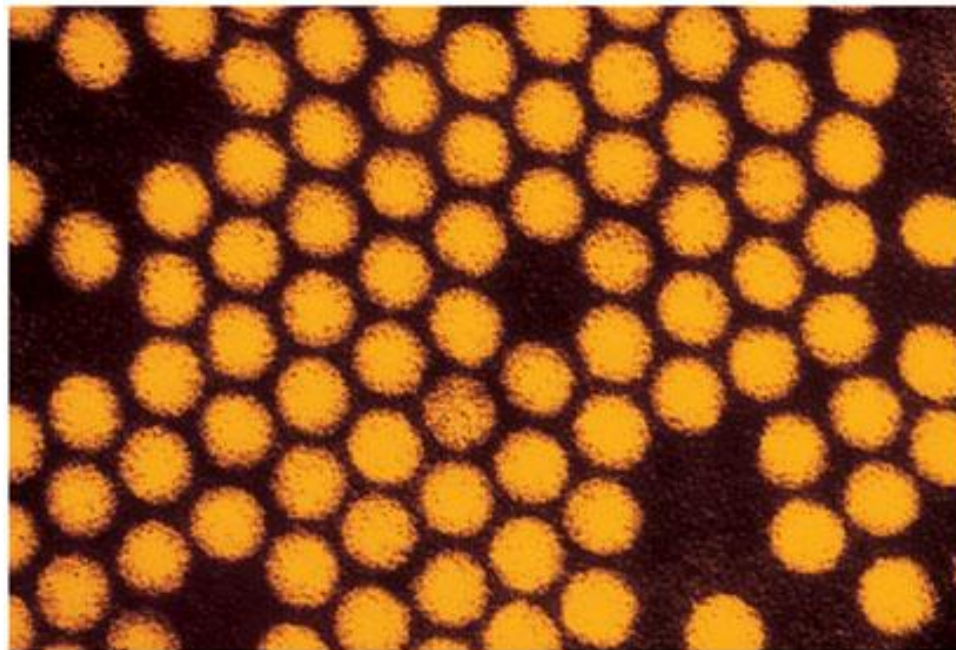
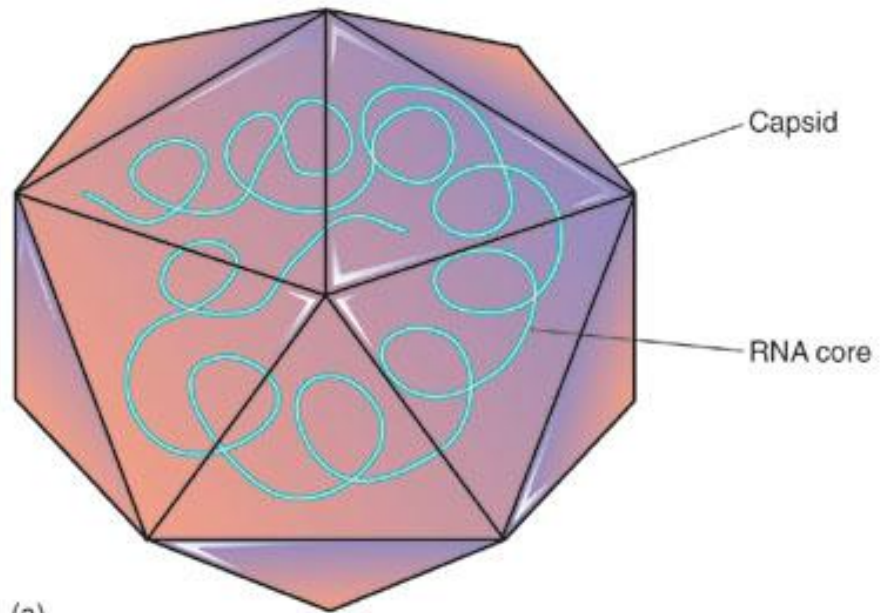
- Norwalk agent (Norovirus) – common cause of viral gastroenteritis (cruise ships)

TABLE 25.5**Selected Representatives of the Human Picornaviruses**

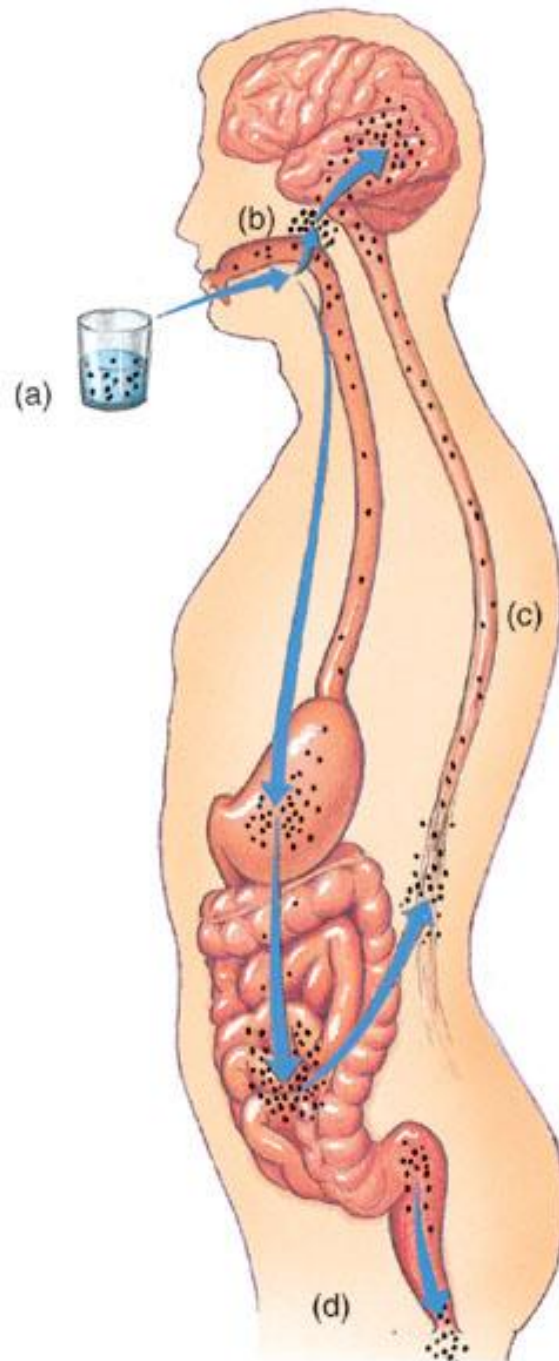
Genus	Representative	Primary Diseases
<i>Enterovirus</i>	Poliovirus	Poliomyelitis
	Coxsackievirus A	Focal necrosis, myositis
	Coxsackievirus B	Myocarditis of newborn
	Echovirus	Aseptic meningitis, enteritis, others
	Enterovirus 72	Hepatitis A
<i>Rhinovirus</i>	Rhinovirus	Common cold
<i>Cardiovirus</i>	Cardiovirus	Encephalomyocarditis
<i>Aphthovirus</i>	Aphthovirus	Foot-and-mouth disease (in cloven-foot animals)

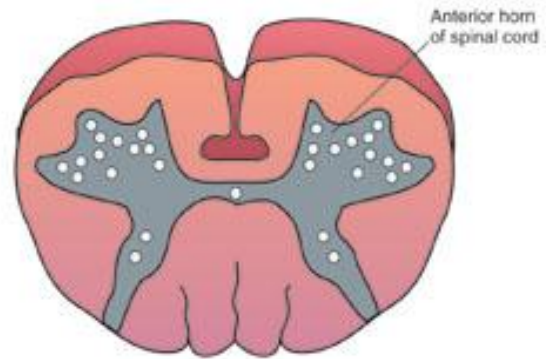
Poliovirus

- resistant to acid, bile, & detergents
- can survive stomach acids
- virus is ingested
- grows in oropharynx & intestine
- most infections are mild
- if viremia persists, virus spreads to spinal cord & brain
- invasion of motor neurons causes flaccid paralysis
- decades later post-polio syndrome (PPS)

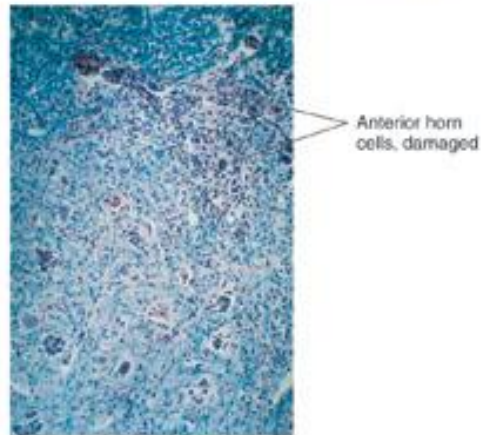
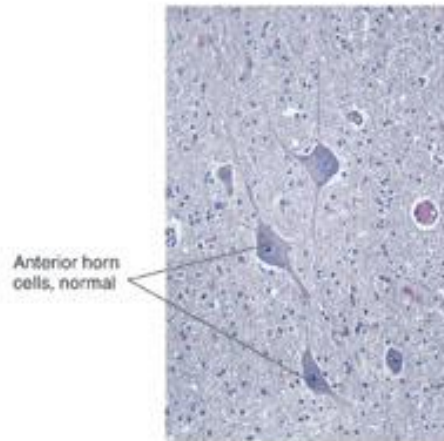


(b)





(a)



(b)

Polio

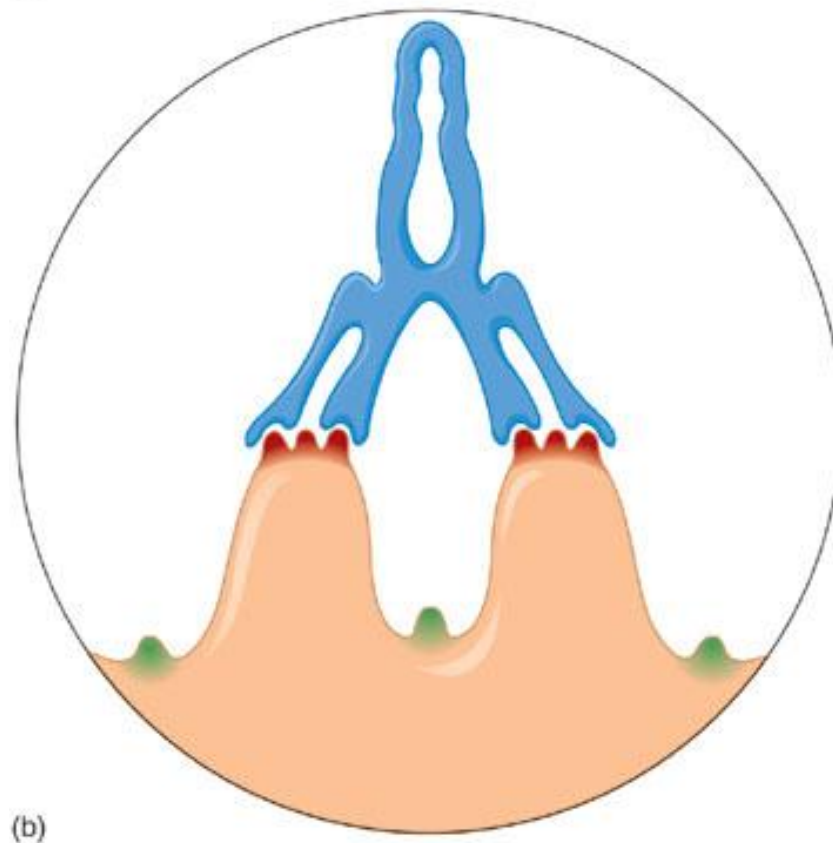
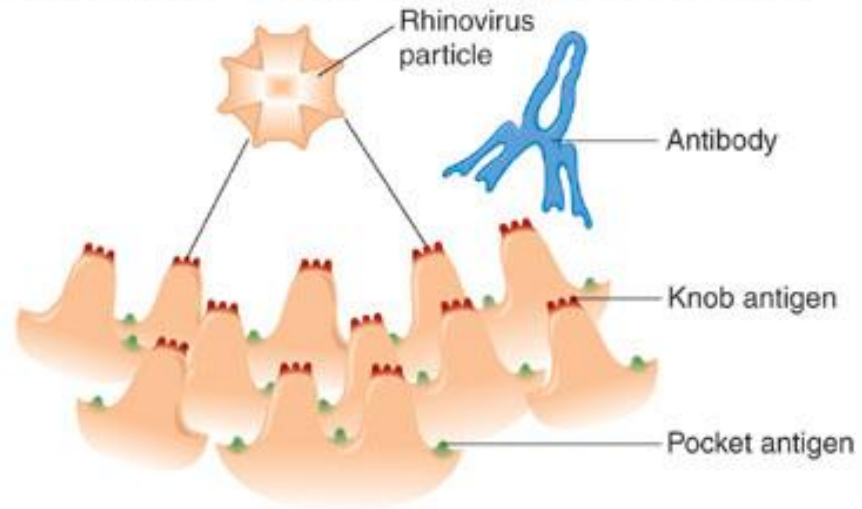
- inactivated polio vaccine (IPV) Salk vaccine
- oral polio vaccine (OPV) Sabin vaccine, attenuated virus
- both are trivalent
- goal of eradicating polio by 2005

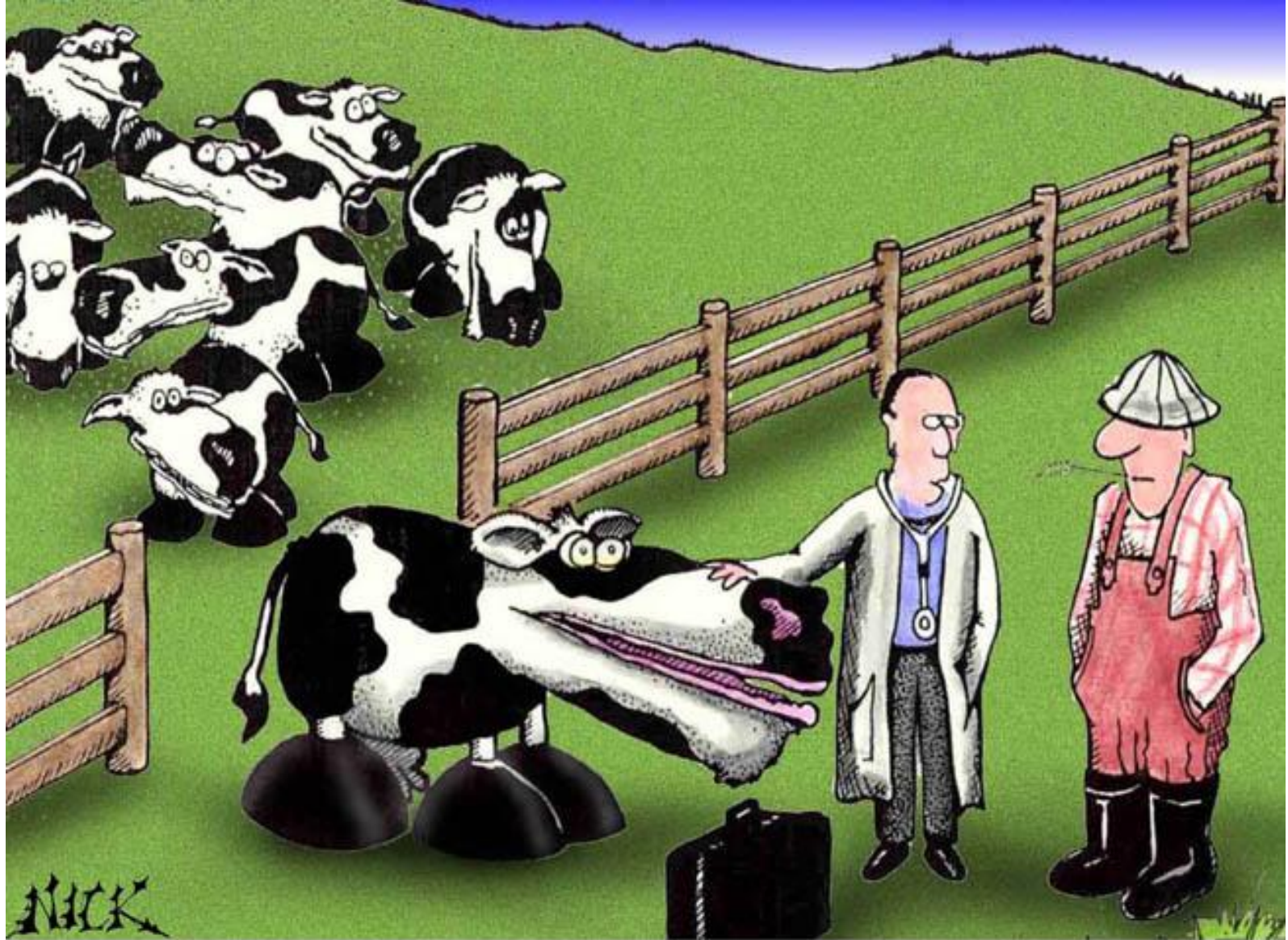
Hepatitis A virus

- causes short-term hepatitis
- **fecal-oral** transmission
- inactivated viral vaccine
- attenuated viral vaccine
- pooled immune serum globulin

Human Rhinovirus

- 110 serotypes
- cause the **common cold**
- sensitive to acidic environments
- optimum temperature is 33°C

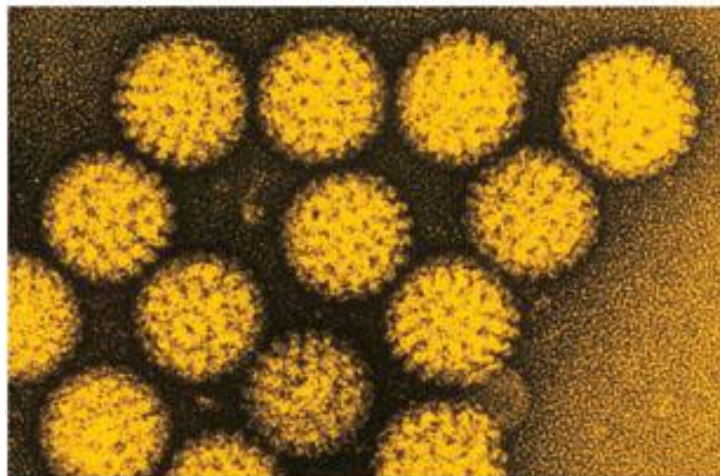




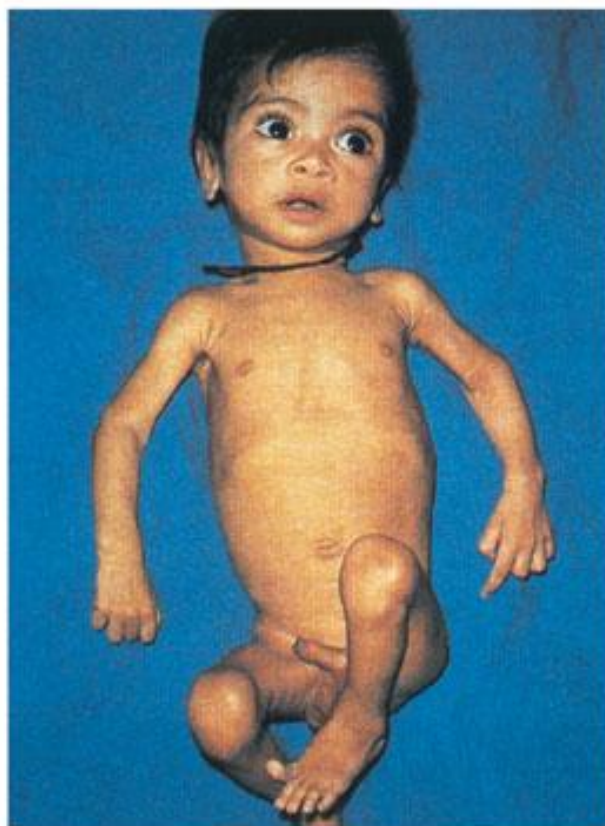
"Well I'll do what I can, but frankly, this is one hell of a breed to come down with foot and mouth..."

Reoviruses

- nonenveloped, segmented dsRNA viruses
- inner & outer capsid
- *Rotavirus* – causes 50% of cases of diarrhea & death of over 600,000 children
 - usually mild in US
 - attenuated oral vaccine discontinued for causing intestinal blockage
- *Reovirus* – not a significant human pathogen



(a)



(b)

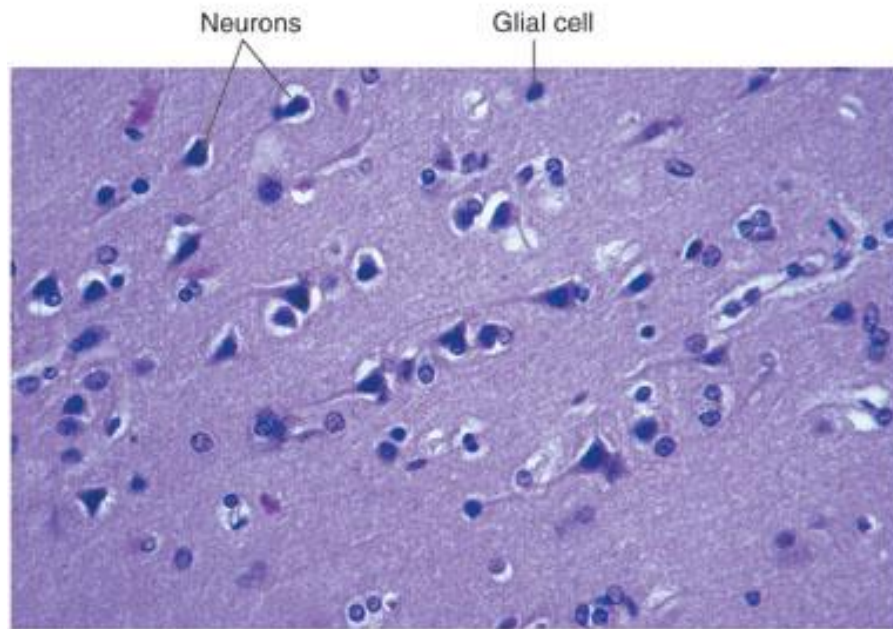
Unconventional viruslike agents

- cause spongiform encephalopathies
- transmissible, fatal, chronic infections of the nervous system
 - Creutzfeldt-Jakob Disease (CJD)
 - New variant CJD
 - kuru
- caused by **prions** – infectious proteins

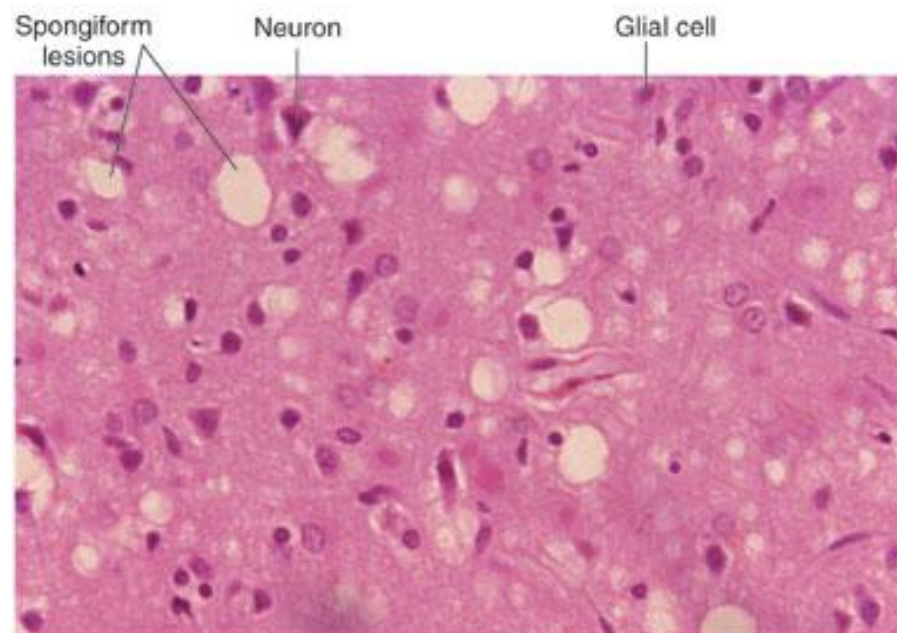
TABLE 25.6

Properties of the Agents of Spongiform Encephalopathies

- Very resistant to chemicals, radiation, and heat (can withstand autoclaving)**
- Do not present virus morphology in electron microscopy of infected brain tissue**
- Not integrated into nucleic acid of infected host cells**
- Proteinaceous, filterable**
- Do not elicit inflammatory reaction or cytopathic effects in host**
- Do not elicit antibody formation in host**
- Responsible for vacuoles and abnormal fibers forming in brain of host**
- Transmitted only by intimate contact with infected tissues and secretions**

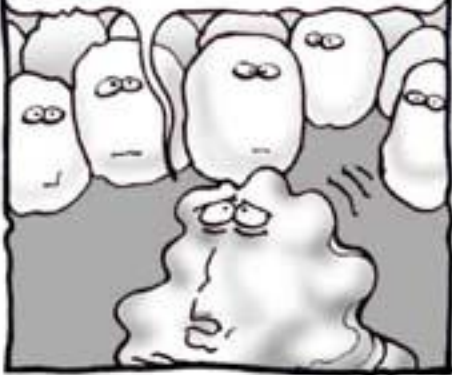


(a)



(b)

I CAN'T HELP IT FELLAS —
SUDDENLY I'M FEELING ALL
BLOATED AND DEPRESSED.
AND I SEEM TO BE
SLOWLY DRIFTING AWAY...



HELP! WHAT'S HAPPENING
TO ME?! WHERE'D ALL
THESE UNSIGHTLY BUMPS
COME FROM...?? AM I
BOILING OR SOMETHING...?



AND WHAT'S UP WITH MY
CHROMATIN? I DON'T LIKE
THE LOOK OF ALL THIS
DNA CONGREGATING IN A
CONDENSED BLOB! DNA
IS A BOSSY ENOUGH
MOLECULE AT THE BEST
OF TIMES!!



HELP ME FELLAS! I'M
FALLING APART!! I
DON'T KNOW HOW MUCH
LONGER I'LL BE ABLE
TO HOLD —



SPLOOCH!
Eeeeeeeewwwww!!!



MUNCH
MUNCH
SLURP
MUNCH
MUNCH
MUNCH



THE TRAGIC
EVERYDAY STORY
OF CELL APOPTOSIS...

