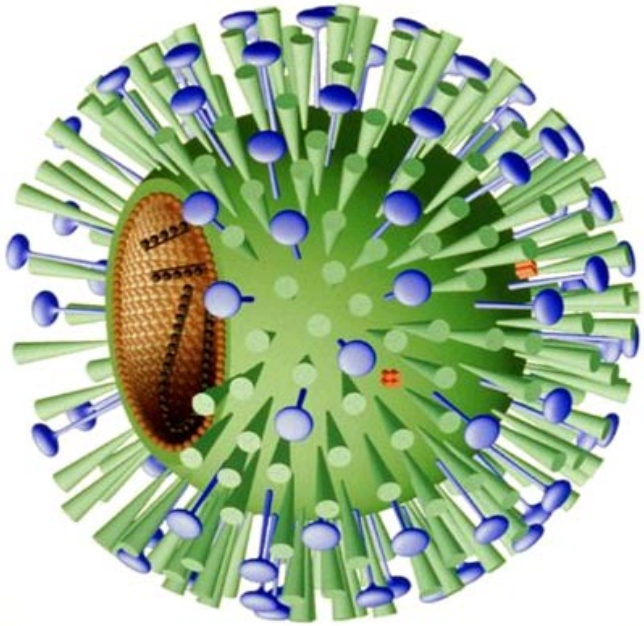
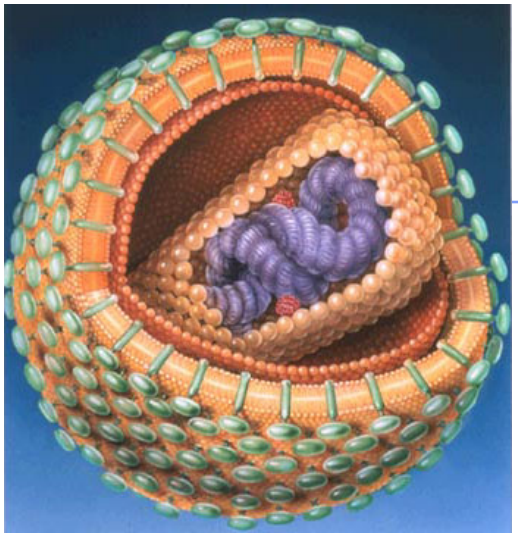


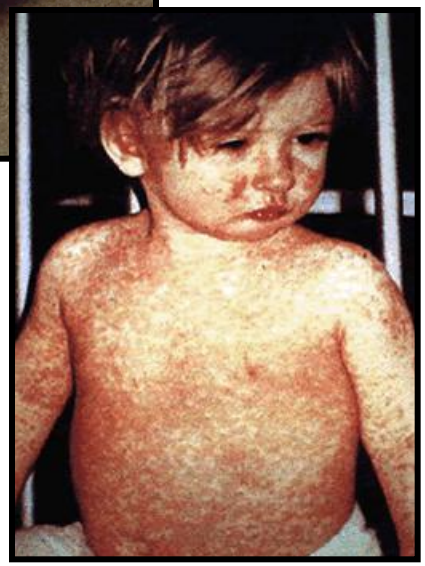
Chapter 19.

Viral Genetics

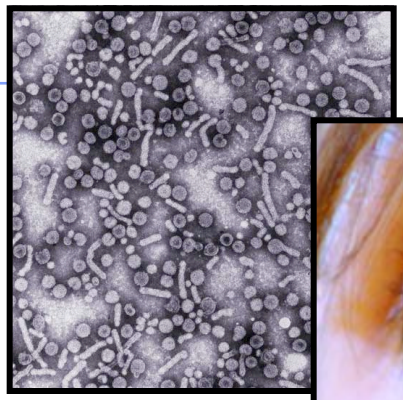


Viral diseases

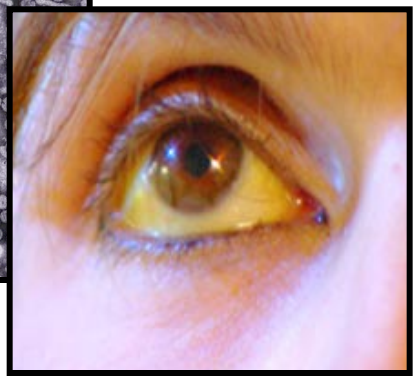
Polio



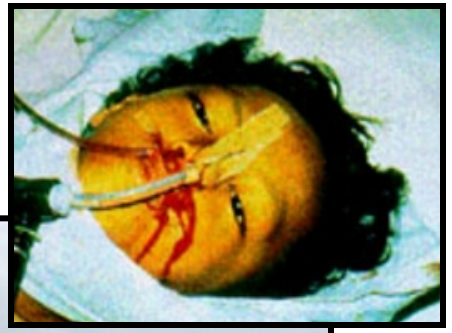
Measles

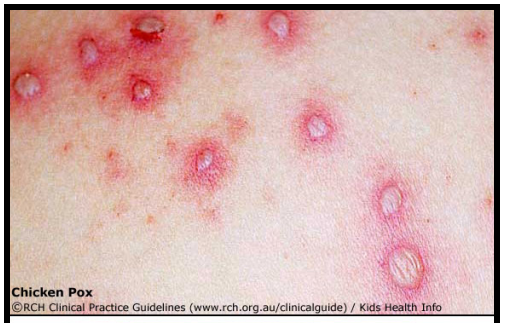


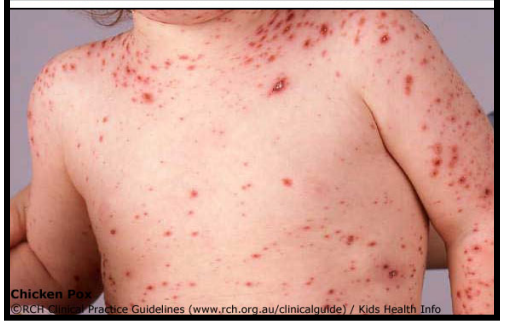
Hepatitis



Ebola







Chicken pox

Outbreaks, Epidemics, & Pandemics

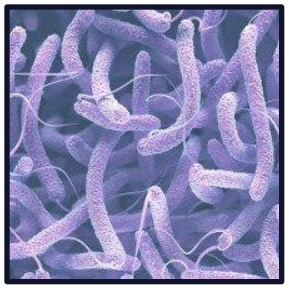
- **Endemic diseases** are present in communities at all times but in low or expected frequencies.
  - Ex: Chicken Pox that occurs at a predictable rate among young school children in the United States.
- **Outbreak**
  - A disease outbreak happens when a disease occurs suddenly in greater number than expected in a region or community or during a season.
    - It can last from days to years.
      - Sometimes a single case of a contagious disease is considered an outbreak if it is new to a community or was absent for a long time.

- **Epidemic**
  - An epidemic occurs when an infectious disease actively spreads rapidly to many more people than expected in an area - it's an infectious disease that has "grown out of control."
    - For example, in 2003, the severe acute respiratory syndrome (SARS) epidemic took the lives of nearly 800 people worldwide.

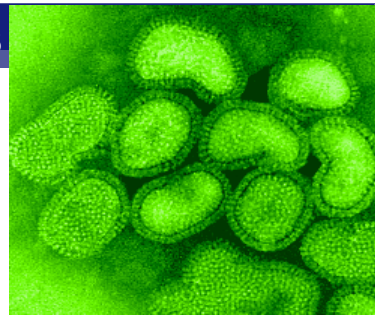
Outbreaks, Epidemics, & Pandemics

Pandemic

- A pandemic is a larger epidemic or a global disease outbreak that covers several countries or spreads from one continent to another.
  - It can last for months or years.



- HIV/AIDS is one of the most destructive ongoing global pandemics in history with with 75 million people having been infected with the HIV virus and over 32 million people having died since the beginning of the pandemic in 1982.
  - An estimated 0.8% [0.6-0.9%] of adults aged 15–49 years worldwide are living with HIV, nearly 1 in every 25 adults in Africa (3.9%) living with HIV though infection is worldwide.
- The cholera pandemic that lasted from 1816 up until 1824, affecting people from all over Asia and Europe and taking over 40 million lives in these eight years.
- There have been three world pandemics of plague recorded, in 541(Africa, Egypt, Mediterranean), 1347 (Asia, Crimea, Europe, Russia), and 1894 (China, Hong Kong, India and beyond)



Influenza: 1918 pandemic

- Influenza pandemics have occurred more than once.
  - Spanish influenza killed 40-50 million people in 1918.
  - Asian influenza killed 2 million people in 1957.
  - Hong Kong influenza killed 1 million people in 1968.

Over 40 million deaths world-wide in one year

In 1918 this was caused by a new strain of the flu virus different enough from earlier strains emerging that people had little immunity to.

How do we fight viral infection?

- Wash your hands often with soap and water.
  - If not available, use an alcohol-based hand cleaner or gel sanitizer.
- Some antiviral drugs have been developed to stop viral replication in an infected host.
- Avoid touching your mouth, nose, or eyes with your hands unless you've just washed them.
- Cover your mouth and nose with a tissue when you cough or sneeze.
  - If you don't have a tissue, cough or sneeze into your elbow crease.
    - Wash your hands and arms afterwards
- If you feel sick, avoid crowds to which you can spread your infection to and avoid contact with many others.
  - If possible, have just one person care for you.

- Depending on the severity of the outbreak or pathogen, consider wearing a face mask when in a crowded area or when within 6 feet of others to prevent becoming infected or infecting others.

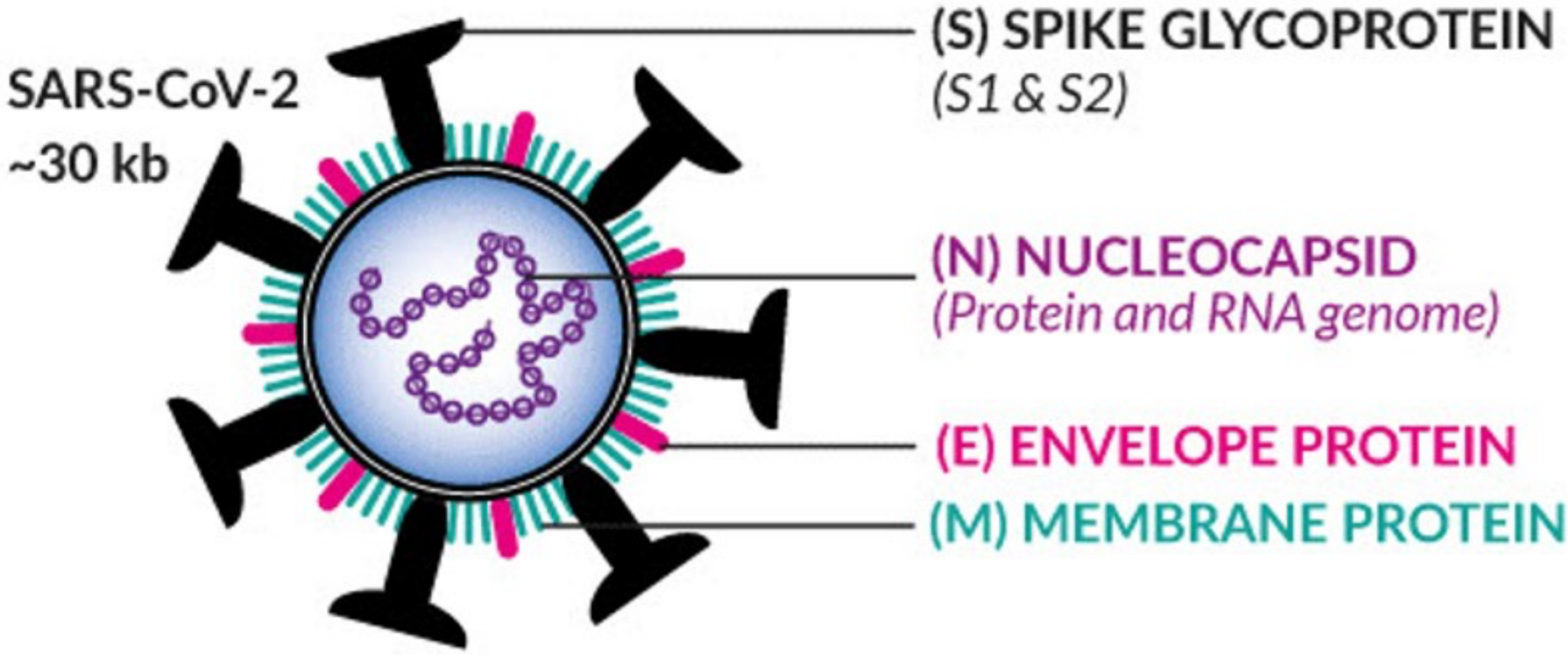
How do we fight viral infection?

- **Vaccines**
  - A vaccine is a biological substance that helps protect vertebrate animals, like humans, from infections caused by bacteria or viruses by training the animal's natural immune systems to better fight a pathogen (disease-causing organism) before they enter the animal's body.

- **How does the Vertebrate Animal's Immune System work?**
  - Molecules on the external surfaces of pathogens (such as outermost proteins of a virus) can be recognized by animal B and T cells, types of white blood cells that are part of vertebrate animal's immune system.
    - Molecules that trigger an immune response (that activate B and T cells) are called anitgens.
  - After the T and B white blood cells of the vertebrate animal recognize an antigen, they fight the antigen (and anything it is attached to like the rest of the pathogen) and try to destroy it.
    - In the process, the vertebrate immune cells maintains a long-term memory of the foreign antigen (on the pathogen) they encountered.
      - If you encounter the same pathogen again (with the same antigens) in the future, your B and T immune system white blood cells will be able to recognize and fight it faster, before it can multiply a lot in the body, cause damage, and do harm

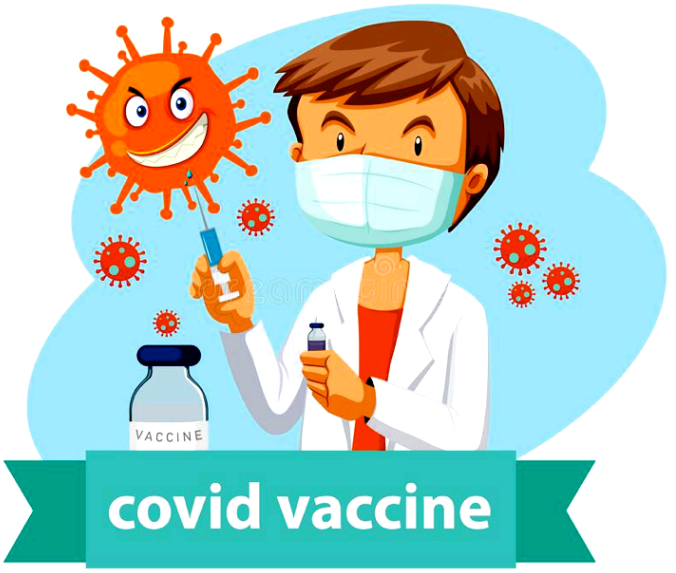
Covid-19 Virus

- The spike protein on the SARS-CoV-2 (virus that causes Covid-19 disease) can trigger a response in vertebrate animal T and B white blood cells of the animal immune system
  - The spike protein is thus considered a possible antigen that the animal immune system can respond to and remember after having encountered it once before.



How does a vaccine work?

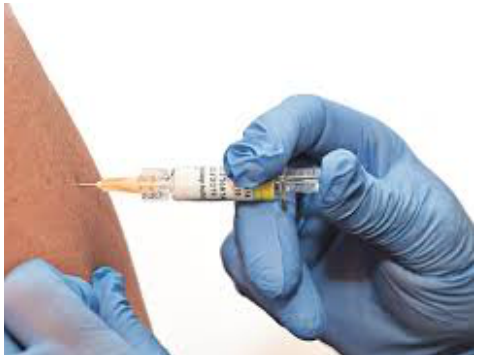
- Vaccines contain antigens from pathogens (even if they don't always contain the entire intact pathogen so as to not cause exposure to the harmful pathogen).
  - The injected antigen triggers an immune response and the building of immune system memory in B and T cells of the animal immune system.
    - Upon any encounter with the same antigen on the real, harmful pathogen (which can be bacteria or viruses), the B and T cells will recognize the danger and fight it off faster by destroying the pathogen and/or pathogen-infected body cells.



AP

How does a vaccine work?

- When someone is injected with a vaccine, their body produces an immune response in the same way it would following exposure to an actual disease-causing pathogen (but without being exposed to the actual harmful pathogen that would cause illness, injury, or death).
  - The person's immune system, their white blood cells, retain a memory of the pathogen's antigen. The organism thus acquired immunity.
    - After the vaccine, IF the person comes in contact with the actual disease-causing pathogen, their body will be able to start an immune response faster than before the vaccine, hopefully preventing the foreign pathogen from being able to reproduce successfully in the host's body, thus helping prevent sickness, injury, or death.

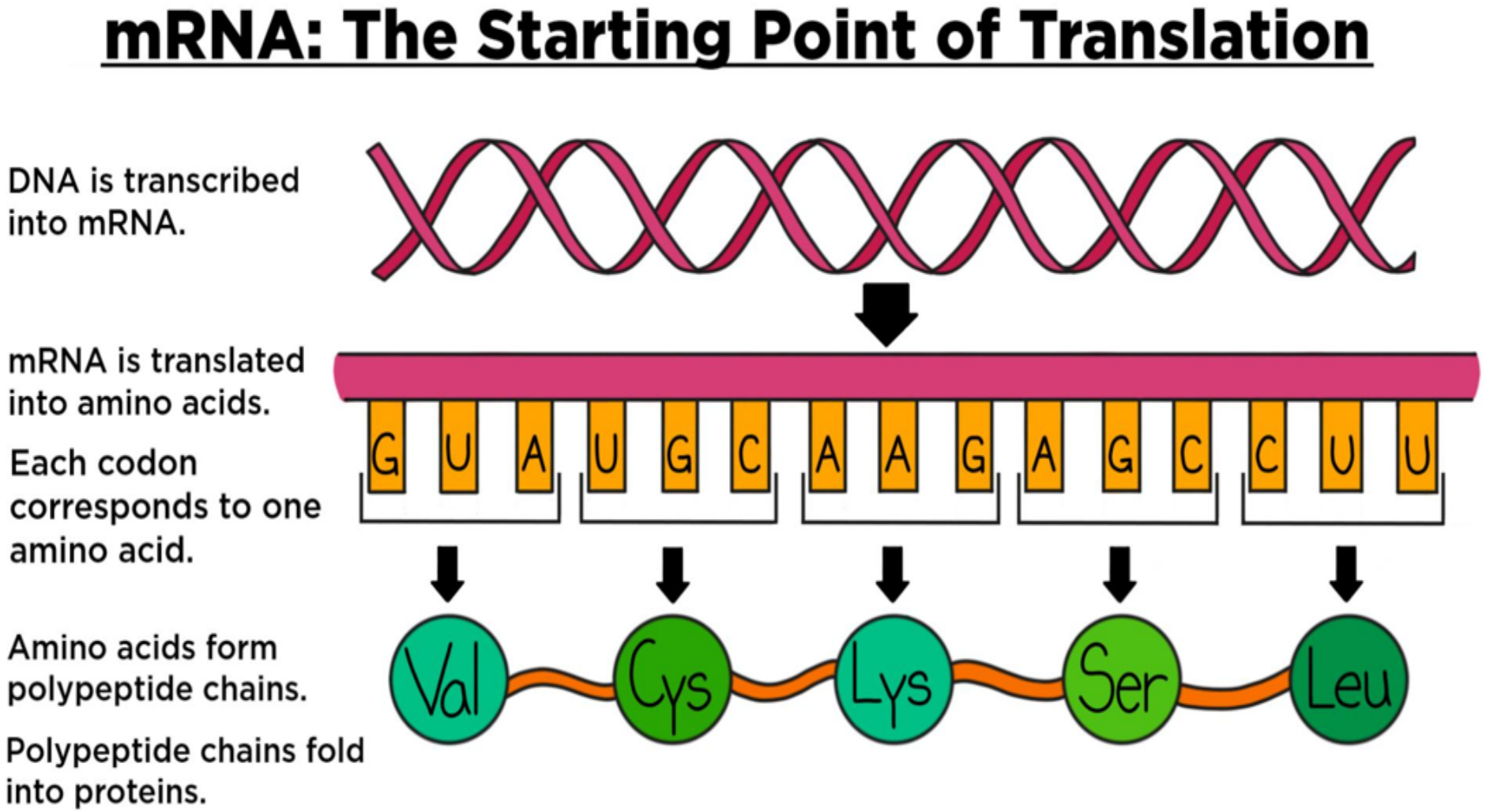


Vaccines contain antigens of the harmful pathogen

- Some vaccines contain a small dose of a **live, but weakened** (attenuated) form of a virus or bacteria, which can't cause disease but look like the virulent (harmful) version of the pathogen you may encounter in nature.
- Some vaccines contain a small dose of **killed** bacteria or **inactive** viruses
- Some vaccines contain only some of the **molecular parts**, like some of the outer most proteins, of a bacteria or viruses
- Some vaccines contain **modified bacterial toxins**, normally released by certain harmful bacteria

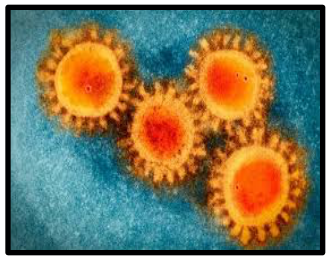
- **New Approach to Vaccines - mRNA vaccines**
  - **mRNA vaccines have been studied before for flu, Zika, rabies, and cytomegalovirus (CMV).**

Recall what cells do with mRNA: Make proteins.



A Closer Look at How COVID-19 mRNA Vaccines Work

- COVID-19 mRNA vaccines give instructions for our cells to make a harmless piece of what is called the "spike protein."
  - The spike protein is found on the surface of the virus that causes COVID-19.
    - COVID-19 mRNA vaccines are given in the upper arm muscle.
    - Once the instructions (mRNA) are inside the human cells, the cells use them to make the protein piece.
    - After the protein piece is made, the cell breaks down the instructions and gets rid of them.
    - Next, the cell displays the protein piece on its surface.



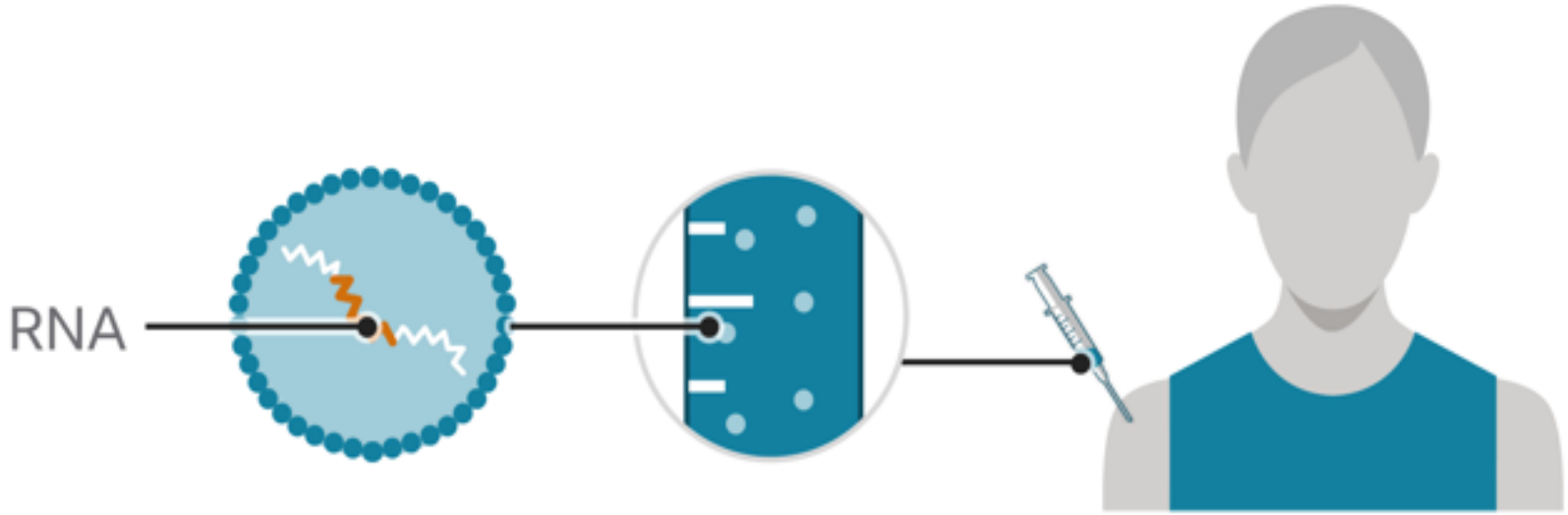
Our immune systems's T cells recognize that the protein doesn't belong there and begin building an immune response and memory like what happens in natural infection against COVID-19.

- Those vaccinated gain this protection without ever having to risk the serious consequences of getting sick with COVID-19.

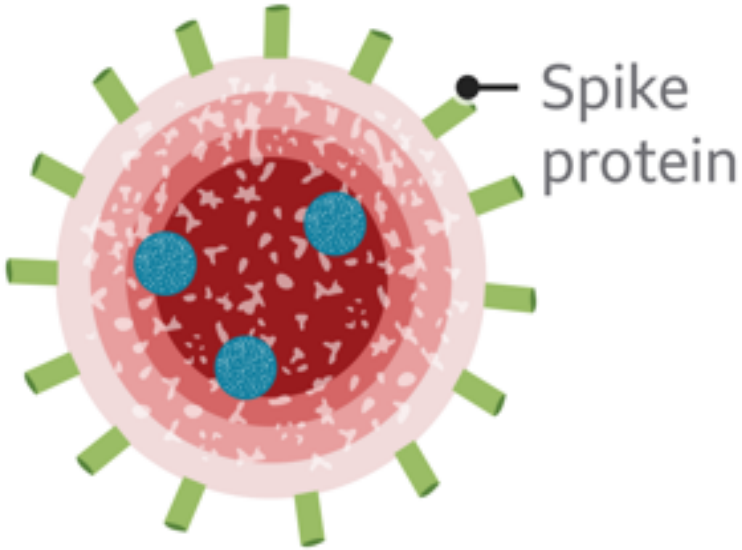
- P.S. Beyond vaccines, cancer research has used mRNA to trigger the immune system to target specific cancer cells.
  - A local injection into a tumor can also deliver some mRNA-based therapies that harness the immune system to fight cancer like mRNA that encodes for tumor proteins or immune signaling molecules to help ramp up the body's attack on cancer cells.

How an RNA vaccine works

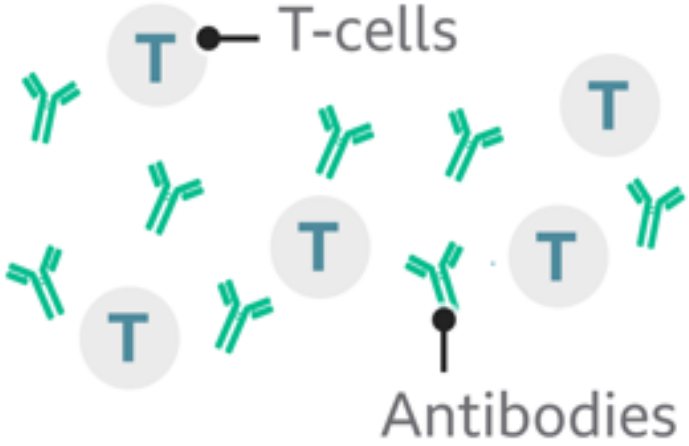
1 Scientists take part of the virus's genetic code and turn it into a vaccine that is injected into the patient



2 The vaccine enters the cells and tells them to produce the coronavirus spike protein

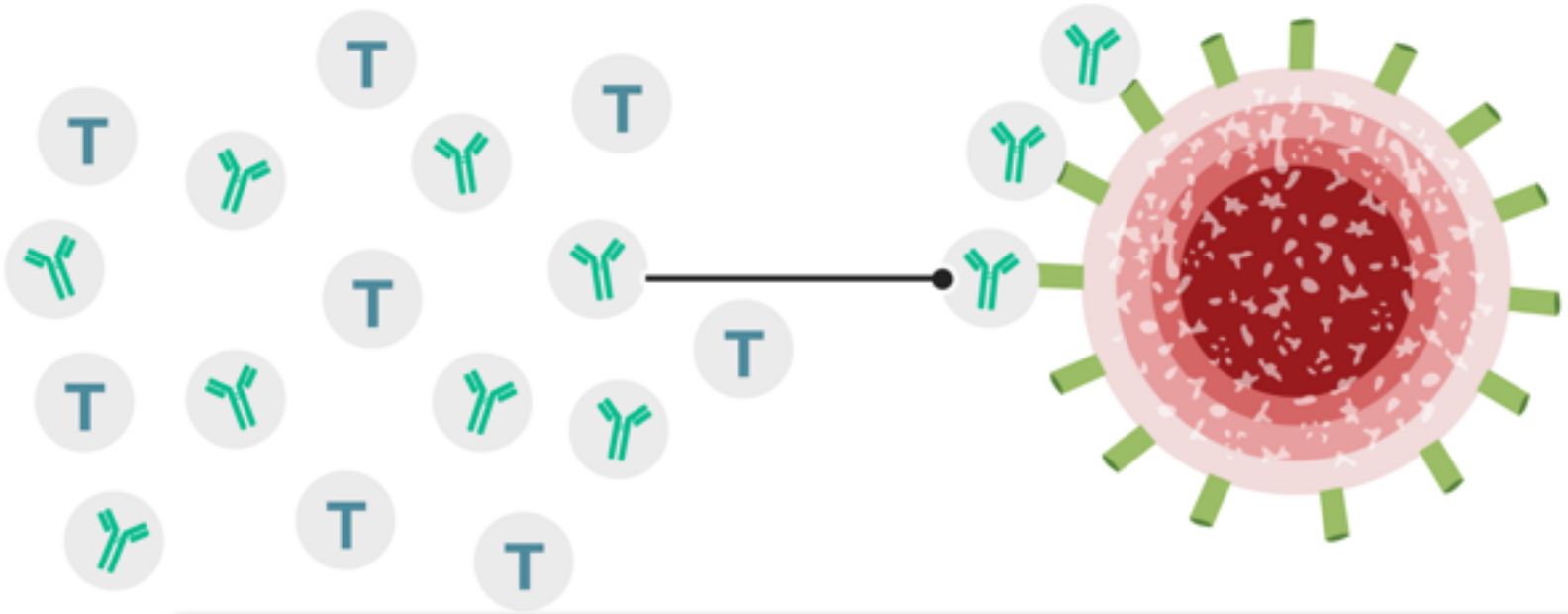


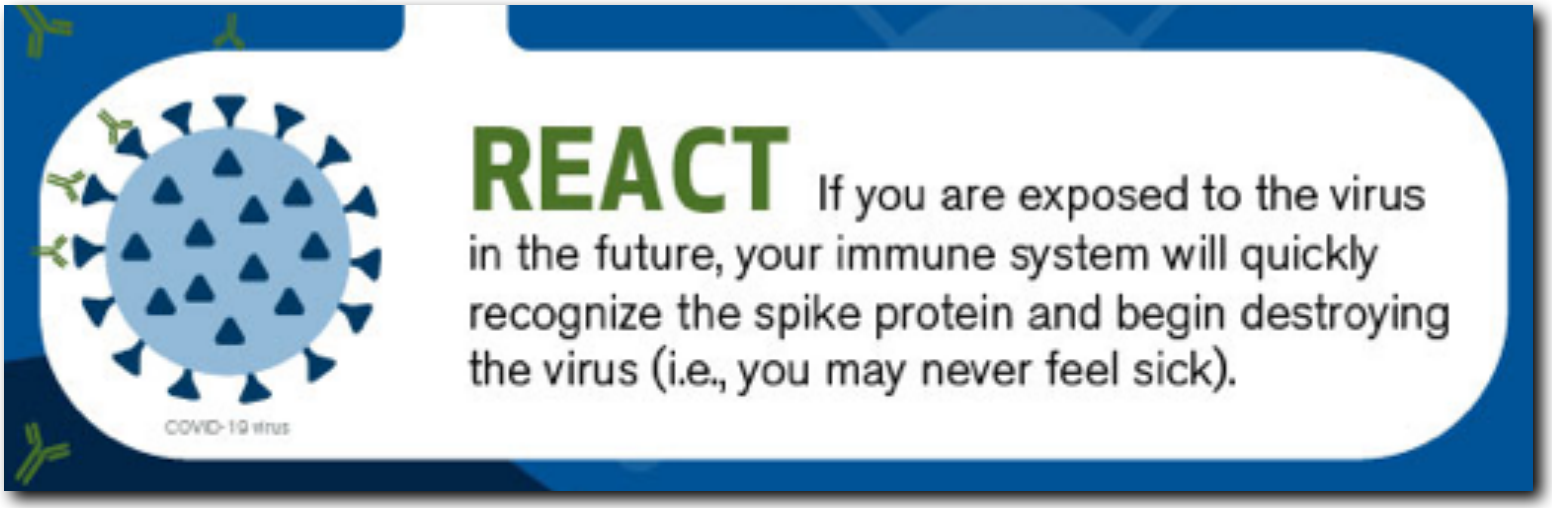
The body's immune system reacts, produces antibodies and activates T-cells to destroy cells with the spike protein



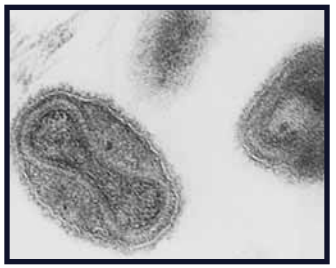
B cells secrete antibodies, proteins that circulates in the blood and body fluids, recognizing foreign antigens like on the surface of bacteria and viruses, and neutralizing the pathogen and tagging them for destruction by other white blood cells known as macrophages.

3 If the patient later catches coronavirus, the antibodies and T-cells are triggered to fight the virus

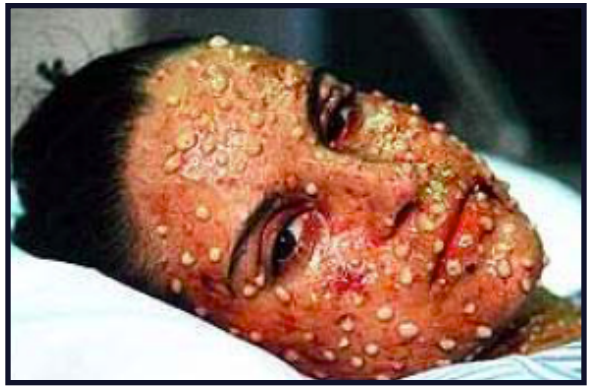




Smallpox (30-35% FATAL) - leads to respiratory illness such as bronchitis, pneumonia, brain swelling, encephalitis, damage to eyes etc..

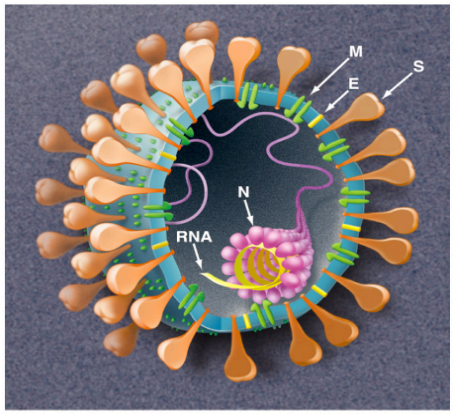


- **Eradicated in 1976**
  - vaccinations ceased in 1980
- **Vaccine:**
  - a biological preparation that improves immunity to a particular disease.
    - A vaccine typically contains an agent that resembles a disease-causing microorganism,
      - a weakened or killed forms of the microbe or a protein component of the pathogen
    - The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.
  - Current efforts are underway to eradicate polio and measles.

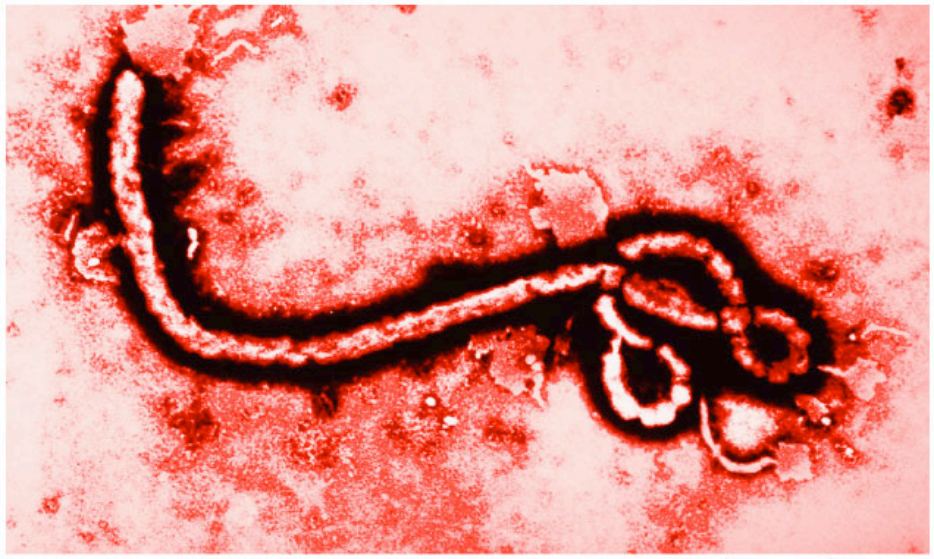


Emerging viruses

SARS



- **Viruses that appear suddenly or are new to medical scientists.**
  - **Viruses that "jump" host**
    - **Switch to infecting a new species as viral nucleic acids mutates over time, changing the shape of the proteins the virus makes and uses to infect host cells**
      - **Ex: HIV, Ebola, SARS, Avian flu, hantavirus**

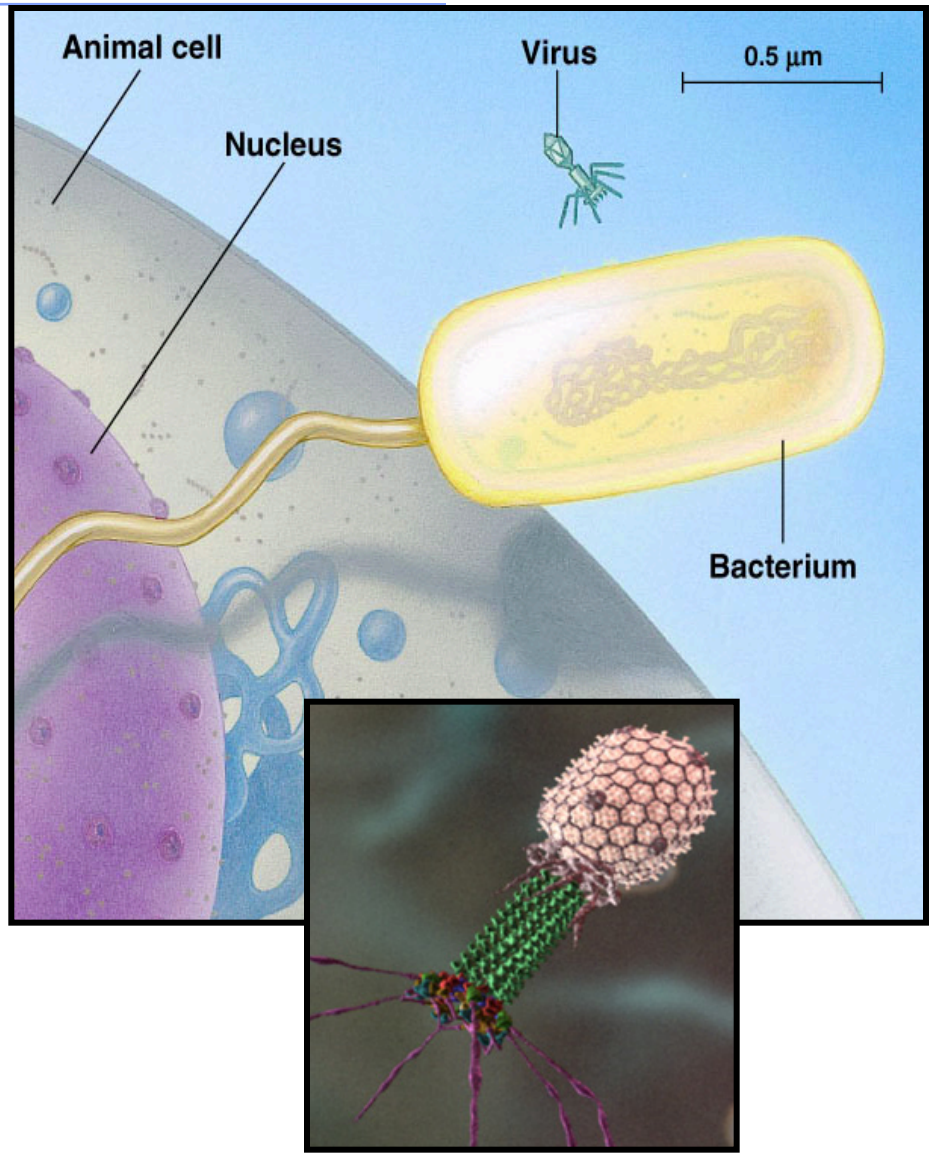


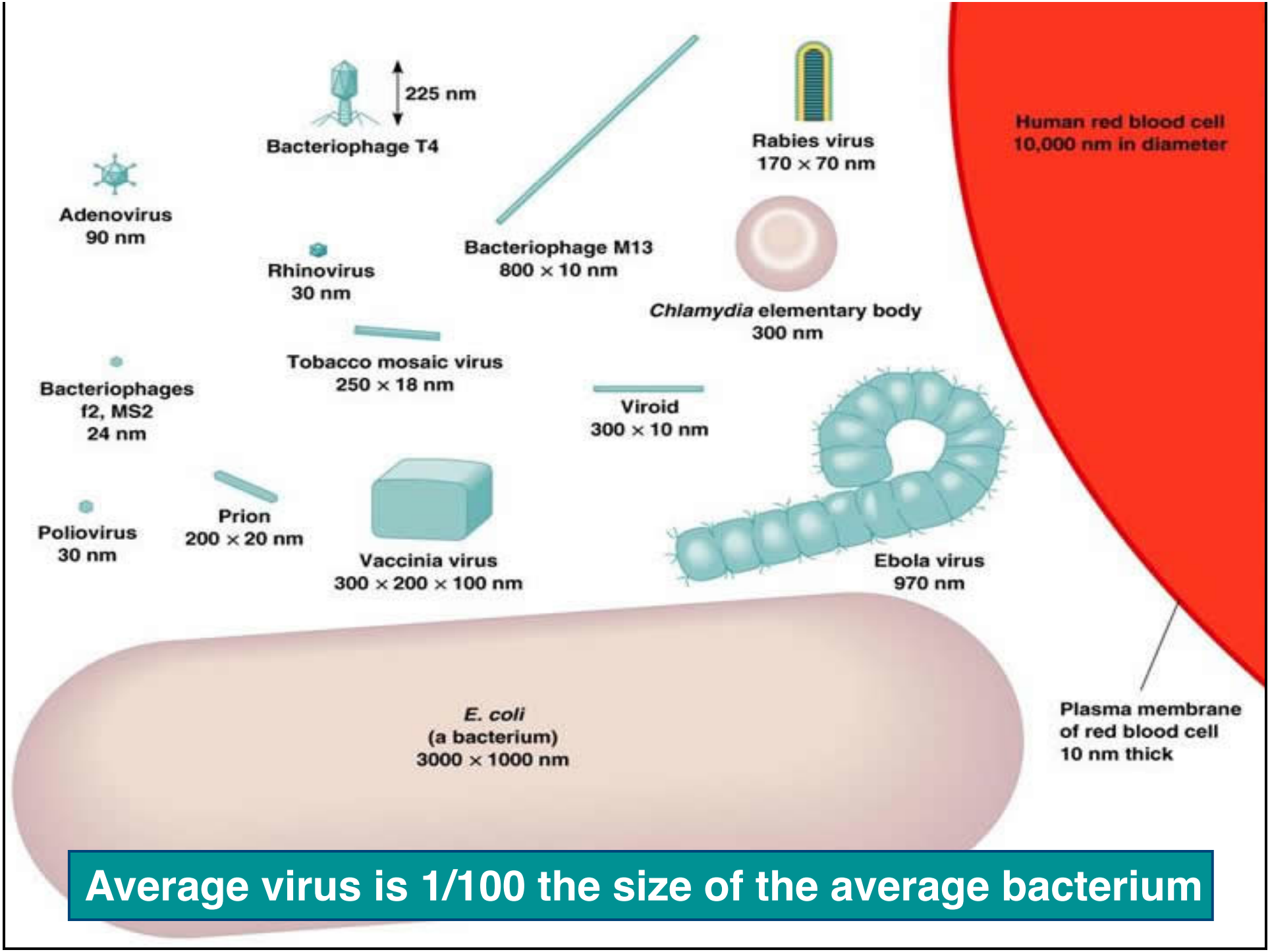
Ebola

Hantavirus

Let's take a closer look at a virus (a virion)

- **Comparing size**
  - eukaryotic cell
  - bacterium
  - virus
    - The tiniest viruses are only 20nm in diameter, smaller than a ribosome electron microscope size
      - ~20–50 nm
  - Composition of Virion:
    - Protein coat filled with nucleic acid
      - Some may contain accessory enzymes
      - Some may have a viral envelope (outer layer of lipids) covering the protein coat





Average virus is 1/100 the size of the average bacterium

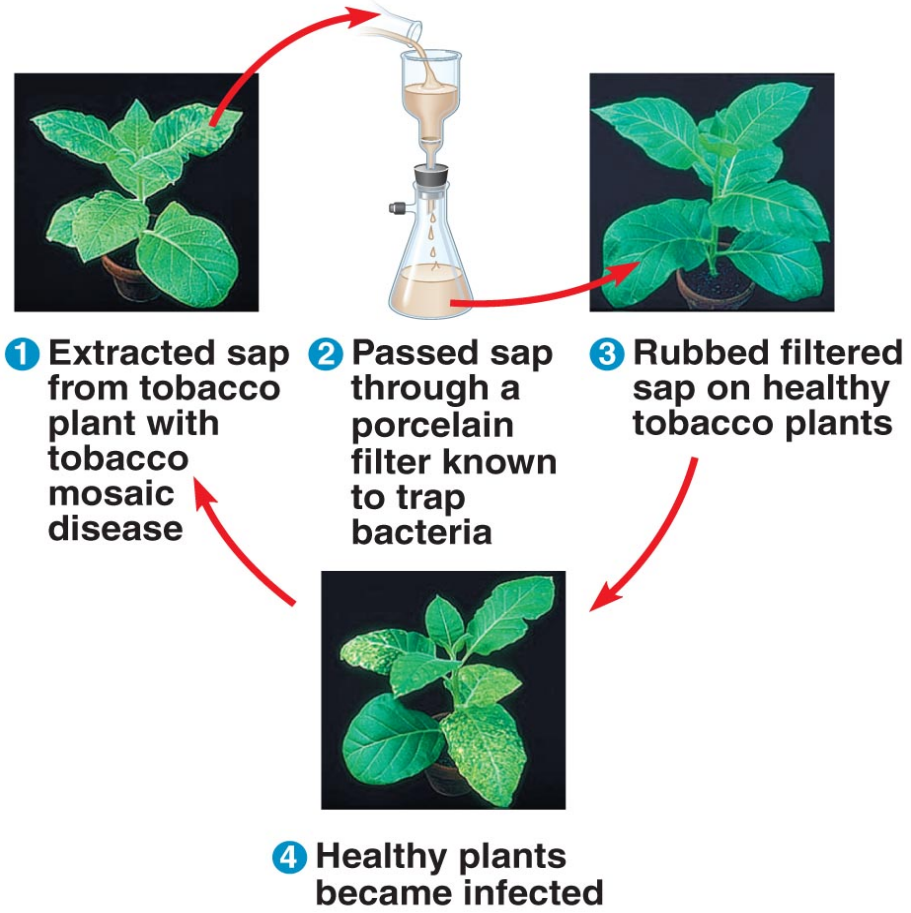
What causes disease?

- In 1882 Adolf Mayer investigated a disease that caused stunted growth and brown spots on tobacco plants, aka Tobacco Mosaic Disease or Spot Disease
  - Could not find the cause and hypothesized that it was an unusually small bacteria

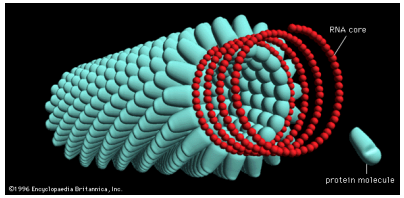
- Dimitri Ivanowsky tried filtering the sap of these plants to remove bacteria but the sap still caused disease when, post-filtering, it was spread on healthy plants.
  - His conclusions:
    - The bacteria was either very small or
    - The bacteria released a toxin that was still present in the plant sap.

Discovery of a new pathogenic agent.

- After experimentation, Martinus Beijerinck concluded that the pathogen must have been reproducing in the plants because sap was able to cause disease after being collected and then transferred, and then collected from the next plant and then transferred to a new plant again, several times over and over.
  - If the disease was caused by a toxin secreted from a bacteria in the first plan, the toxin would have diluted over several transfers eventually not causing illness.
  - But it could not reproduce on media like bacteria can so it was not a bacterium



- Wendell Stanley crystallized the 1st virus, TMV, in 1935.



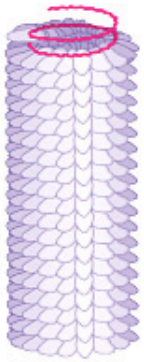
Is a virus alive or dead?

> *"A piece of bad news wrapped in protein"*
>
> – Peter Medawar

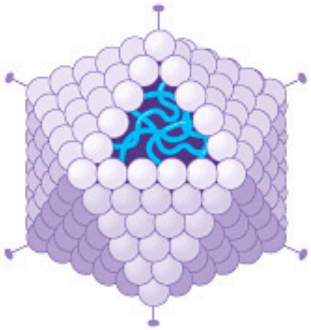
A virus is nucleic acid enclosed in a protein coat

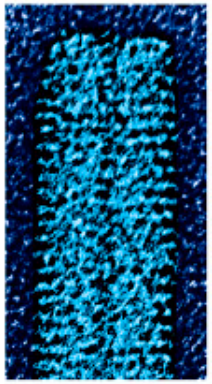
- Viruses are NOT living cells!!!
  - Viruses are "OBLIGATE INTRACELLLAR PARASITES"
    1. lack enzymes for metabolism
    2. lack ribosomes for protein synthesis
    3. lack building materials like nucleotides and amino acids
    4. NEEDS host living cell's "machinery" to reproduce
- Viruses are packages of genes in transit from 1 host cell to another
  - Plant, fungal, animal, bacterial, archaeal cells all can be infected

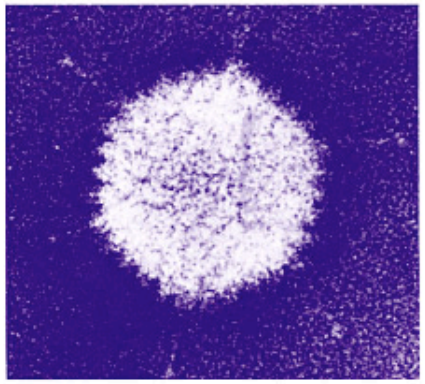
a plant virus



pink eye virus







Viral genomes

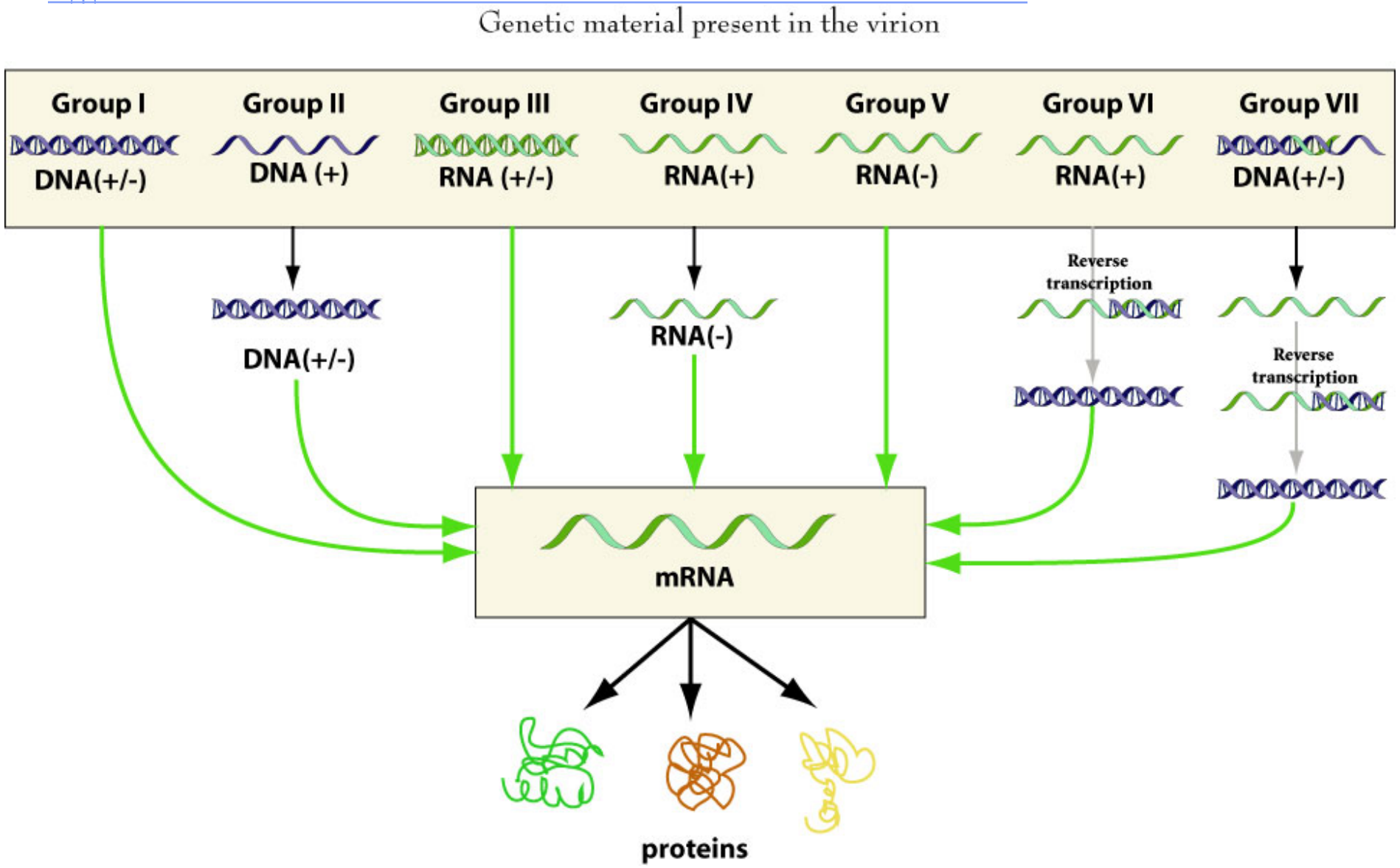
- Their genomes defy convention. They can contain:
  - DNA
    - double-stranded
    - single-stranded
  - RNA
    - double-stranded
    - single-stranded
  - Linear or circular
    - smallest viruses have only 4 genes, while largest have several hundred to a thousand
      - Bacteria for instances have 200 to a few thousand genes.
    - Some do have multiple nucleic acid molecules

Table 18.1 Classes of Animal Viruses, Grouped by Type of Nucleic Acid

Class*	Examples/Diseases
I. dsDNA**	
Papovavirus	Papilloma (human warts, cervical cancer); polyoma (tumors in certain animals)
Adenovirus	Respiratory diseases; some cause tumors in certain animals
Herpesvirus	Herpes simplex I (cold sores), herpes simplex II (genital sores); varicella zoster (chicken pox, shingles); Epstein-Barr virus (mononucleosis, Burkitt's lymphoma)
Poxvirus	Smallpox; vaccinia, cowpox
II. ssDNA	
Parvovirus	Roseola; most parvoviruses depend on co-infection with adenoviruses for growth
III. dsRNA	
Reovirus	Diarrhea; mild respiratory diseases
IV. ssRNA that can serve as mRNA	
Picornavirus	Poliovirus; rhinovirus (common cold); enteric (intestinal) viruses
Togavirus	Rubella virus; yellow fever virus; encephalitis viruses
V. ssRNA that is a template for mRNA	
Rhabdovirus	Rabies
Paramyxovirus	Measles; mumps
Orthomyxovirus	Influenza viruses
VI. ssRNA that is a template for DNA synthesis	
Retrovirus	RNA tumor viruses (e.g., leukemia viruses); HIV (AIDS virus)

Baltimore classification System

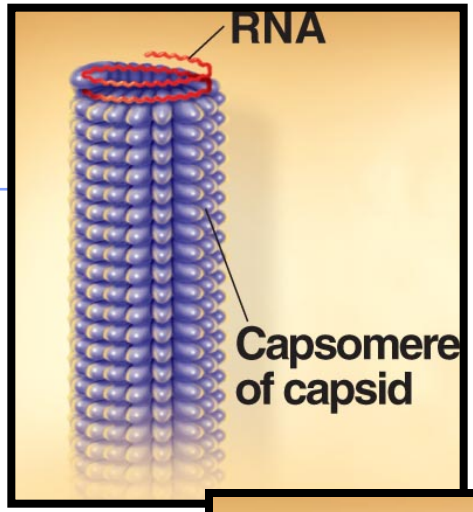
- **Classified viruses based on the way they make mRNA from the nucleic acid the virions contain.**

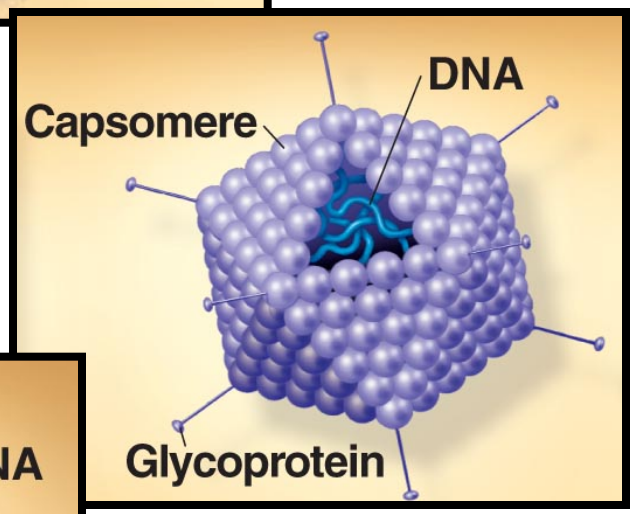


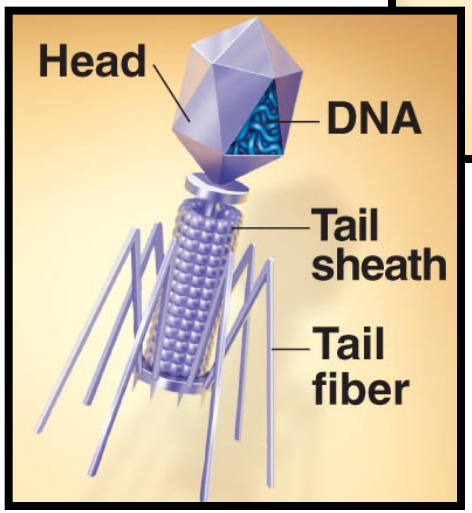
Viral protein coat

Capsid:

- protein shell enclosing the genome of nucleic acid
  - Usually made up MANY COPIES of only 1-2 types of proteins known as CAPSOMERES.
- Different viruses have capsids that vary in 3-D shape
  - Rod-shaped
  - Polyhedral
  - Complex like icosahedral (20 faces)

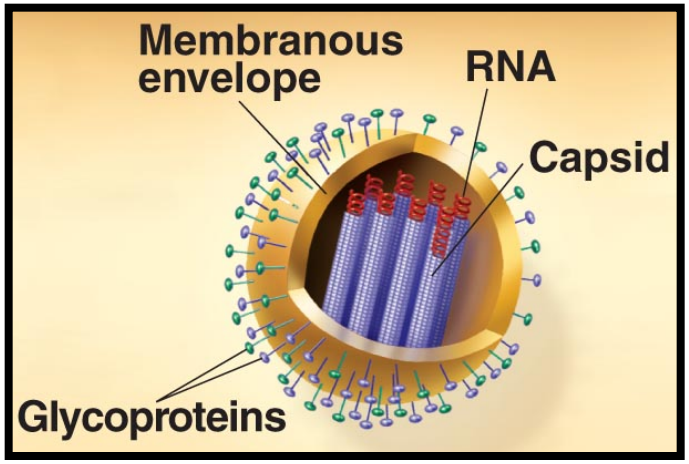


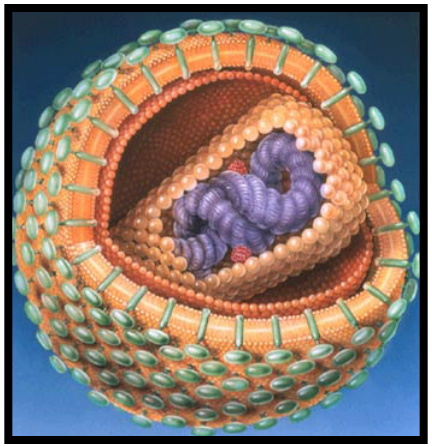




Eukaryotic Viruses often contain Viral Envelopes on the outside of the capsid

- Viral envelopes are phospholipid bilayers (membranes) surrounding the viral capsid
  - envelopes are derived from host cell membrane
    - Contain host AND viral derived proteins and glycoproteins





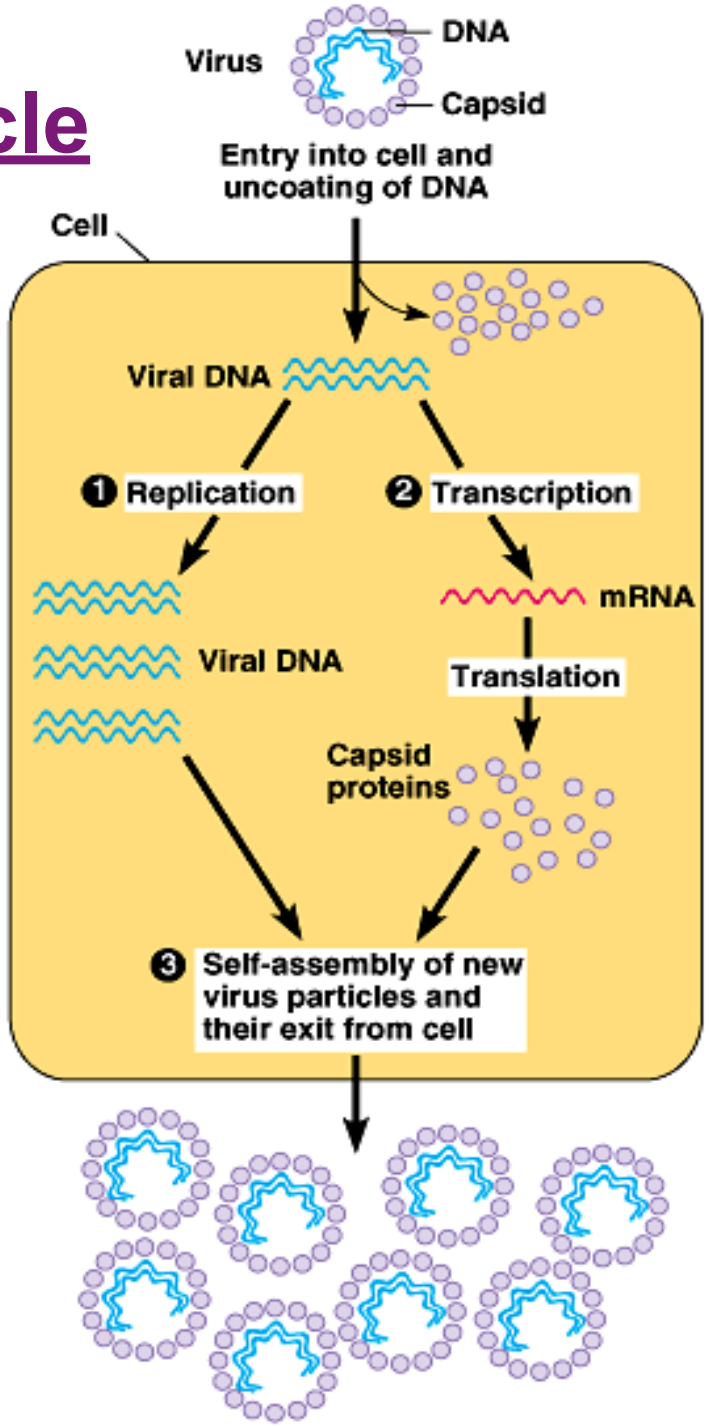
HIV

- The Viral Envelope helps the virus infect host cell.
  - These viruses either are taken into host cell through endocytosis or fusion with host membrane

(c) Influenza viruses

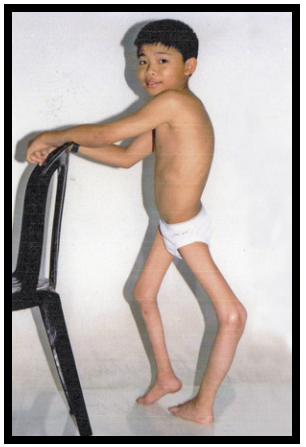
General stages of viral lifecycle

- **Every virus can infect only certain cells = Host Range**
  - **Viruses identify a host cell by a 'lock-&-key' fit between viral surface proteins and receptor molecules on the outside of the host cell**
    - **Narrow = HIV targets only certain immune cell in humans** *(T-helper cells)*
    - **Broad = rabies targets all mammals' neurons**
- **Reproduce Cycle of Virus:**
  1. **Attachment**
     - **Virus 'recognizes' proteins on the surface of the host cell**
  2. **Entry**
     - **virus DNA/RNA enters host cell**
  3. **Assimilation**
     - **viral DNA/RNA takes over host**
     - **reprograms host cell to copy viral nucleic acid & build viral proteins**
  4. **Self-assembly**
     - **nucleic acid molecules & capsomeres then self-assemble into viral particles**
     - **exit cell**



Symptoms of viral infection

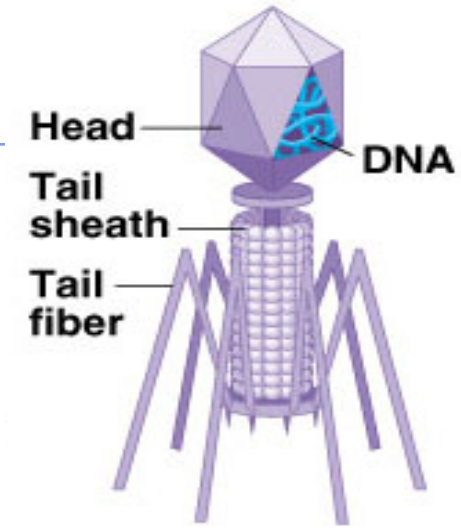
- Link between infection & symptoms varies
  - Exit of hundreds or thousands of viruses form the infected host
    - Damages or kills cells
  - Symptoms (fever, aches, bleeding…) result from
    - Cell death/damage
    - Immune system trying to fight infection
  - Viral components may be toxic
    - Ex: envelope proteins

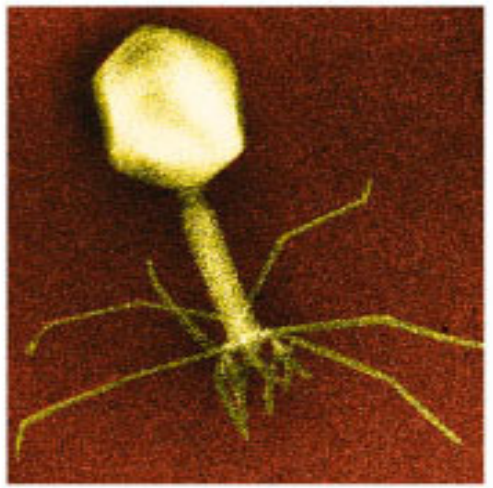


- Do viruses cause permanent damage?
  - It depends…
    - lung epithelium after infection by the flu (influenza virus) is repaired because these cell types divide rapidly
    - nerve cell damage from polio is permanent

Bacteriophages

- **Viruses that infect bacteria**
  - ex. phages that infect *E. coli* include T-even, T-odd, and lambda phages
    - Icosahedral, 20-sided capsid head encloses DNA
      - Bacterial viruses are all <u>double stranded DNA viruses</u> (ds DNA) unlike Eukaryotic viruses which can be ds or ss DNA and ds or ss RNA)
    - Protein tail fibers help phage attach to host ***(host proteins in bacterial cell plasma membranes)***
    - Protein tail sheath injects phage DNA into bacteria

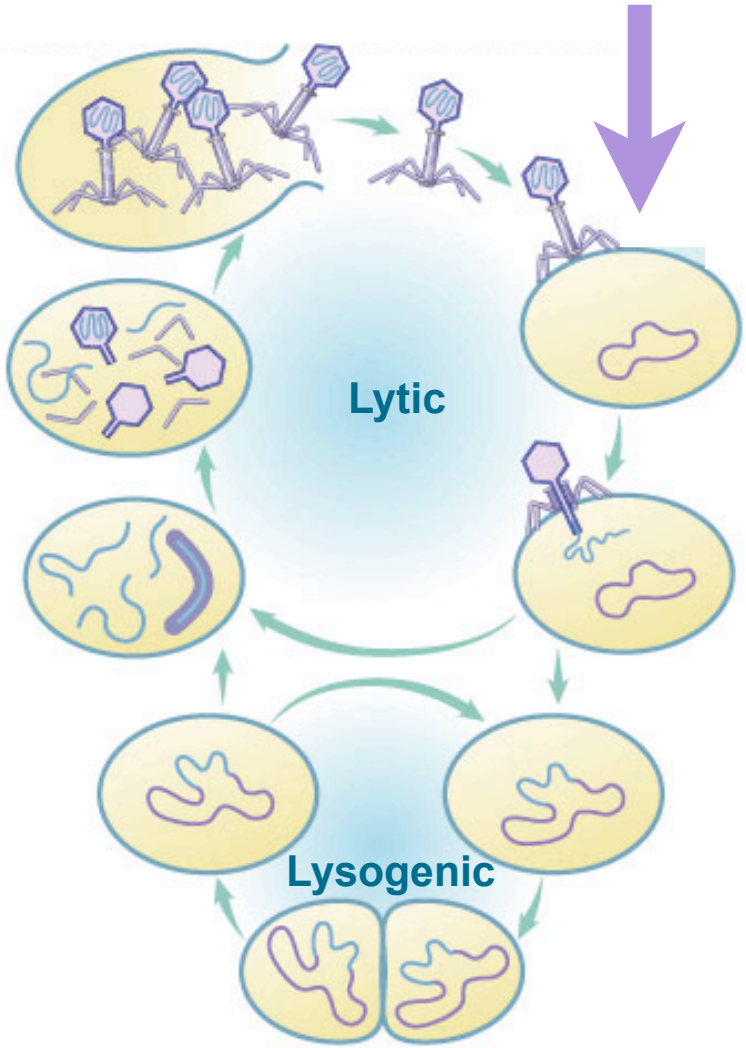




(d) Bacteriophage T4

Two Bacteriophage Life Cycles Exists

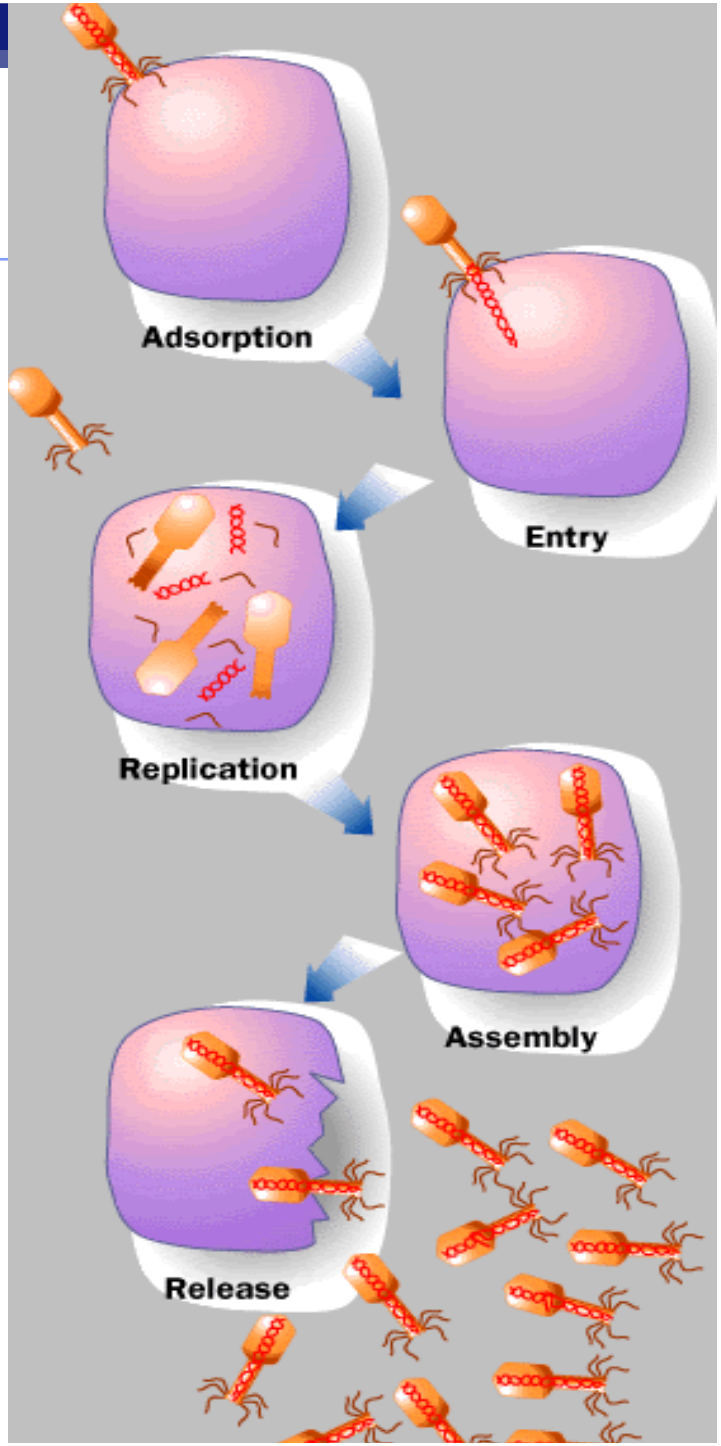
- During the Lytic Cycle
  - viruses are reproduced inside the bacteria *(new virions built)*
  - new virus copies are released by rupturing of bacterial host cell *(killing it)*
- During the Lysogenic Cycle
  - viral DNA is integrated *(inserted)* into bacterial DNA chromosome
  - viral genome copied along with bacteria's genome as bacteria reproduce through binary fission
  - viral DNA is passed down - along with bacterial DNA - to daughter bacterial cells *(no actual virions are made)*
    - Lifecycle may switch to lytic cycle, if conditions demand, it so the bacterial host cell start producing and releasing new intact infectious viruses (virions).



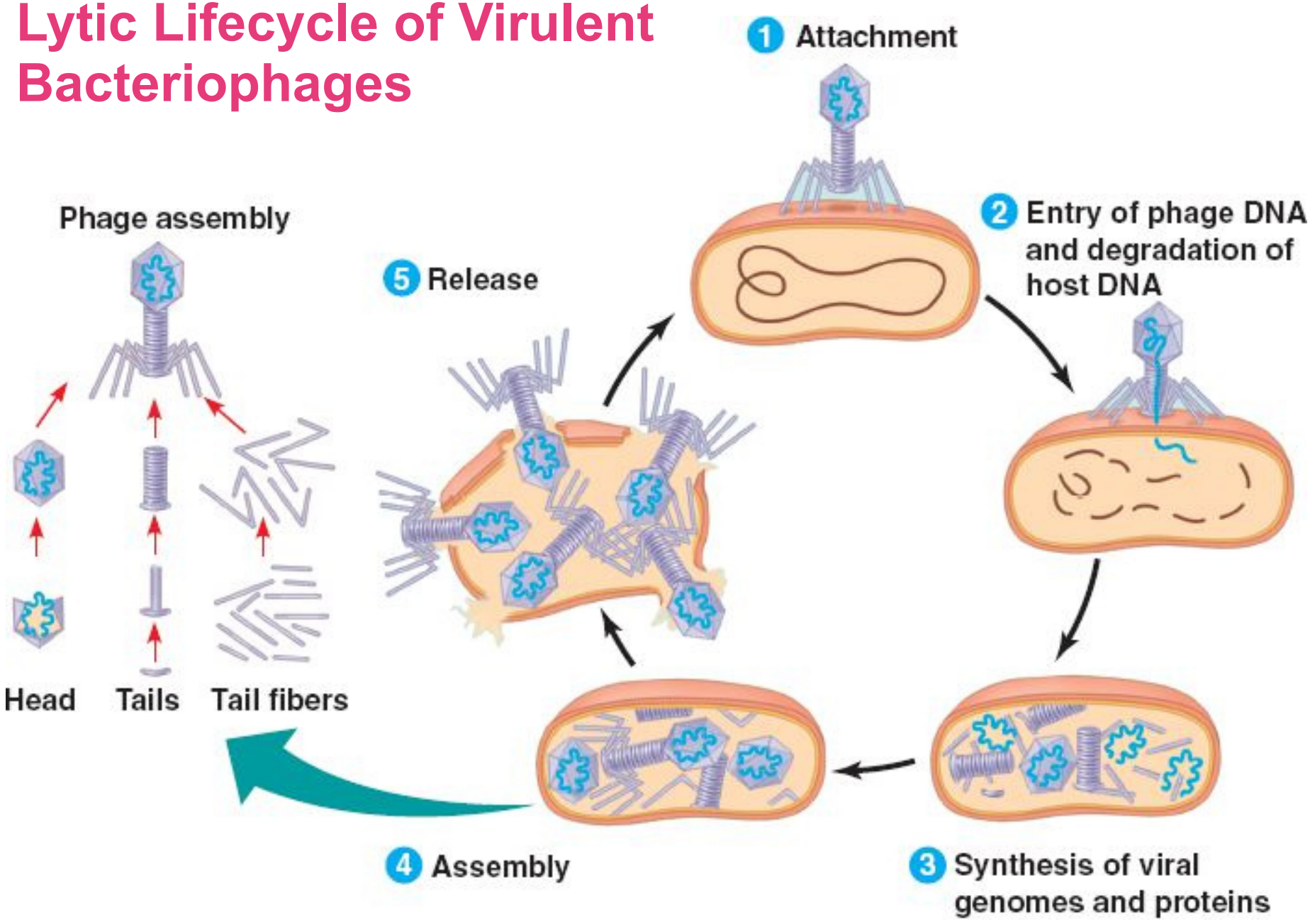
Stages of Lytic Phage Infection

(Seen in Prokaryotic cells)

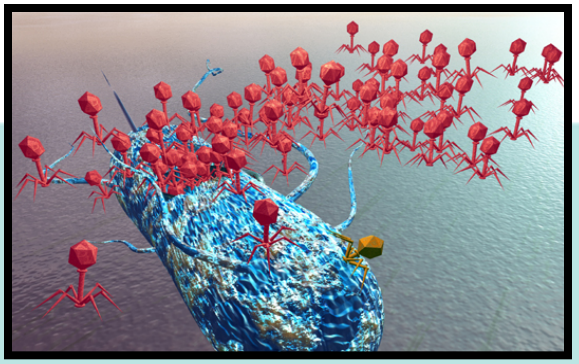
1. Absorption
2. Entry
3. Replication
4. Assembly
5. Release



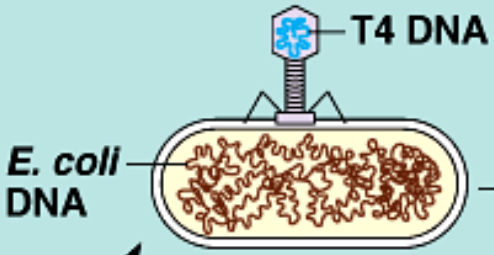
Lytic Lifecycle of Virulent Bacteriophages



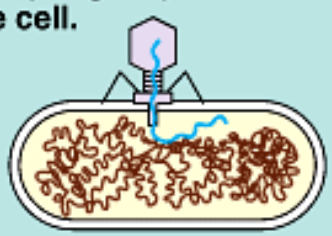
Lytic Lifecycle of Virulent Phages



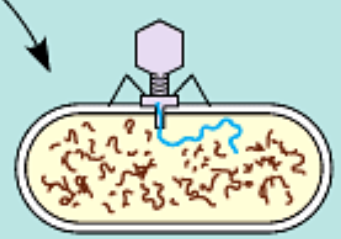
1. The T4 phage uses its tail fibers to stick to specific receptor sites on the outer surface of an *E. coli* cell.



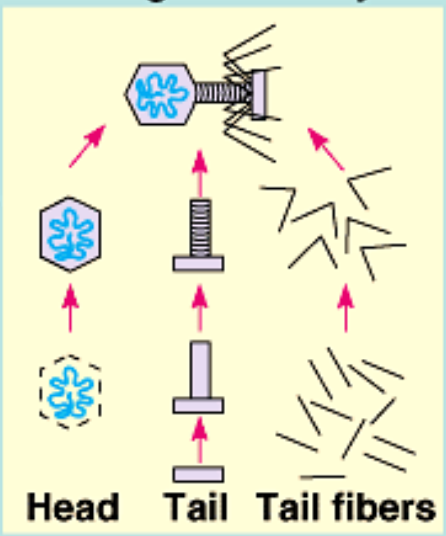
2. The sheath of the tail contracts, thrusting a hollow core through the wall and membrane of the cell. The phage injects its DNA into the cell.



3. The empty capsid of the phage is left as a "ghost" outside the cell. The cell's DNA is hydrolyzed.

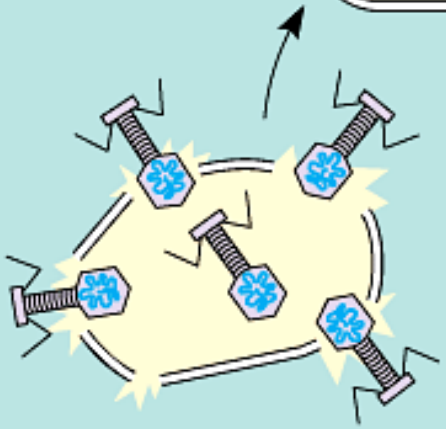


Phage assembly

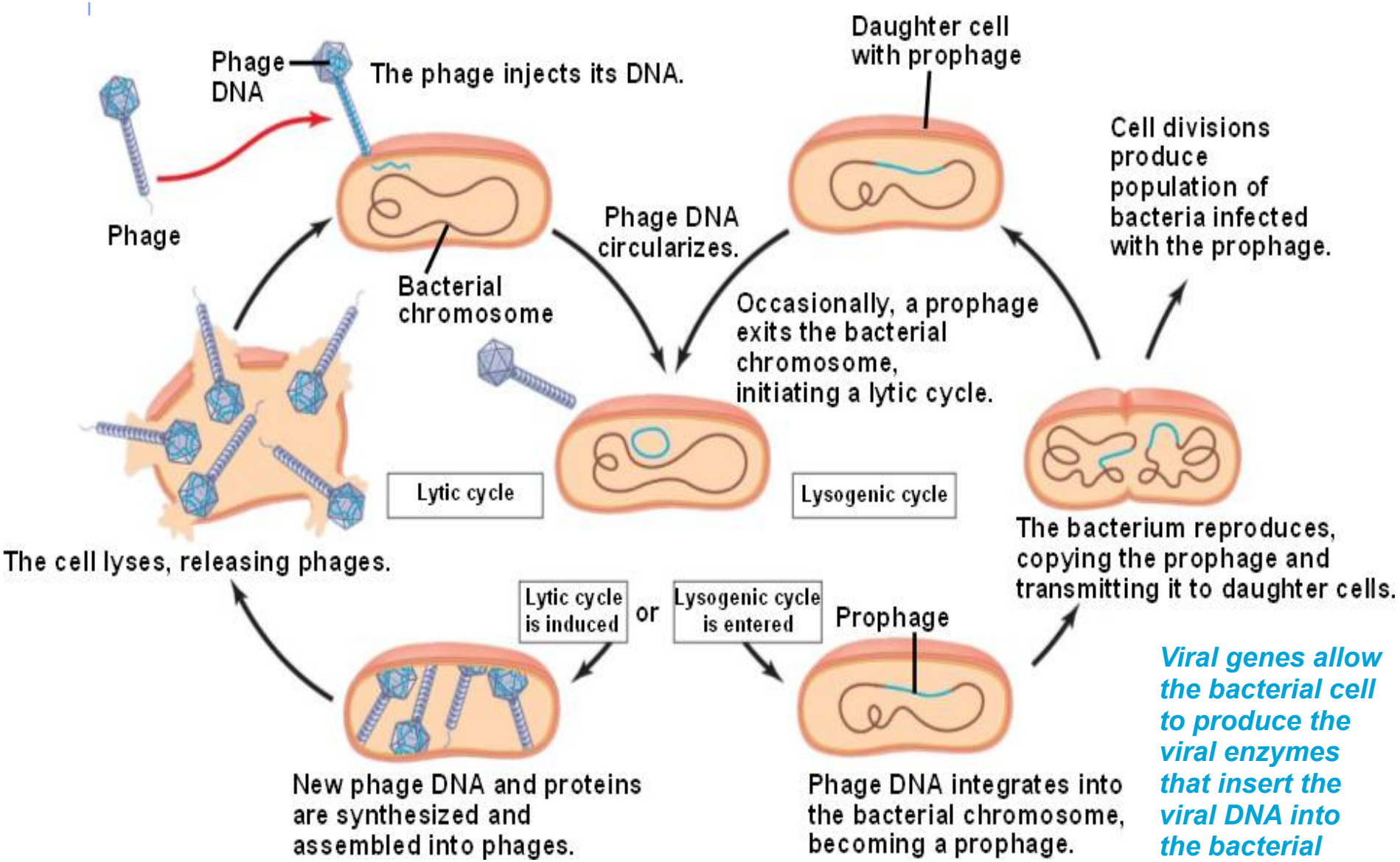


4. The cell's metabolic machinery, directed by phage DNA, produces phage proteins, and nucleotides from the cell's degraded DNA are used to make copies of the phage genome. The phage parts come together. Three separate sets of proteins assemble to form phage heads, tails, and tail fibers.

5. The phage then directs production of lysozyme, an enzyme that digests the bacterial cell wall. With a damaged wall, osmosis causes the cell to swell and finally to burst, releasing 100 to 200 phage particles.

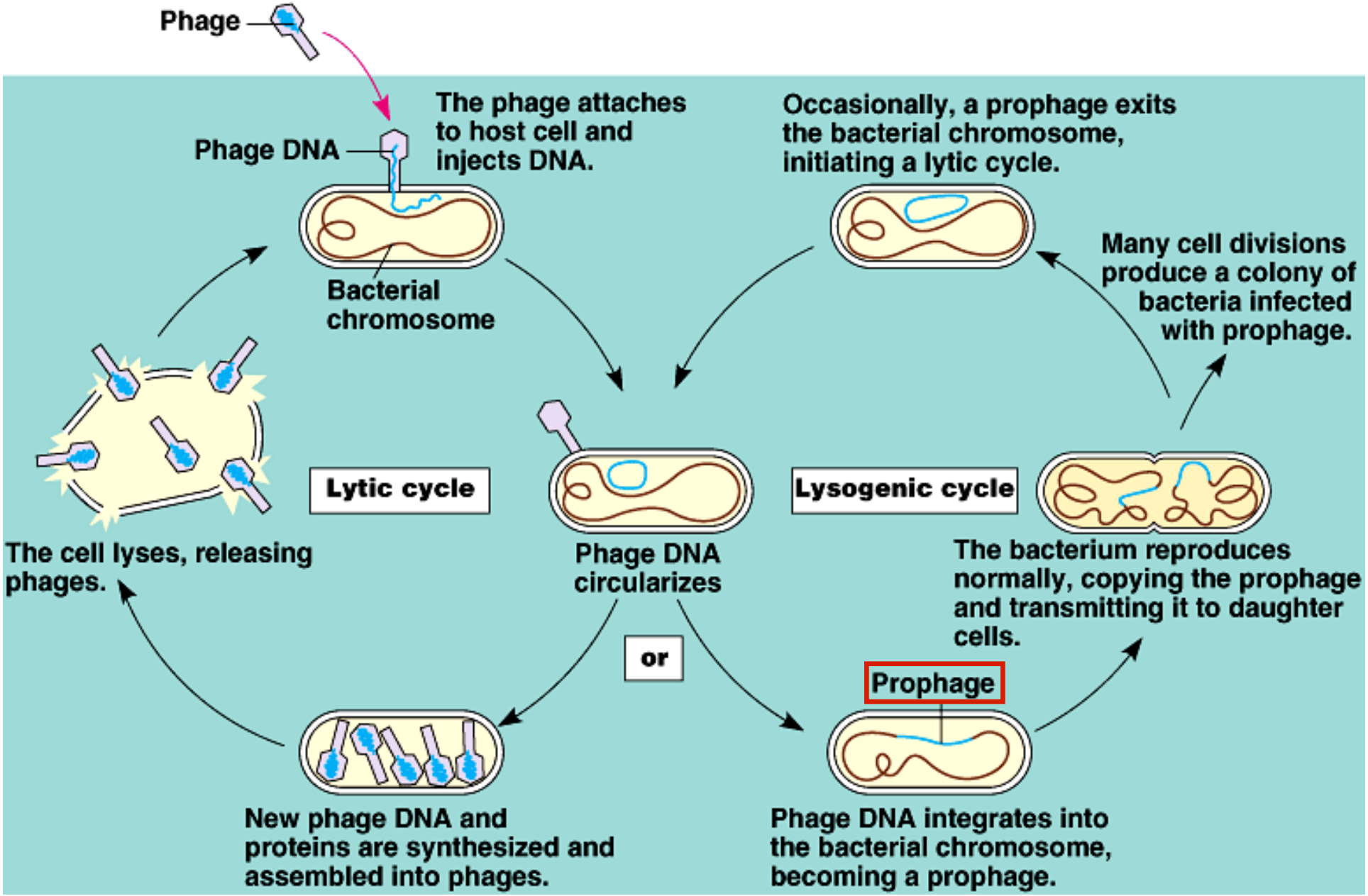


Lysogenic Reproductive cycle of Temperate Phages



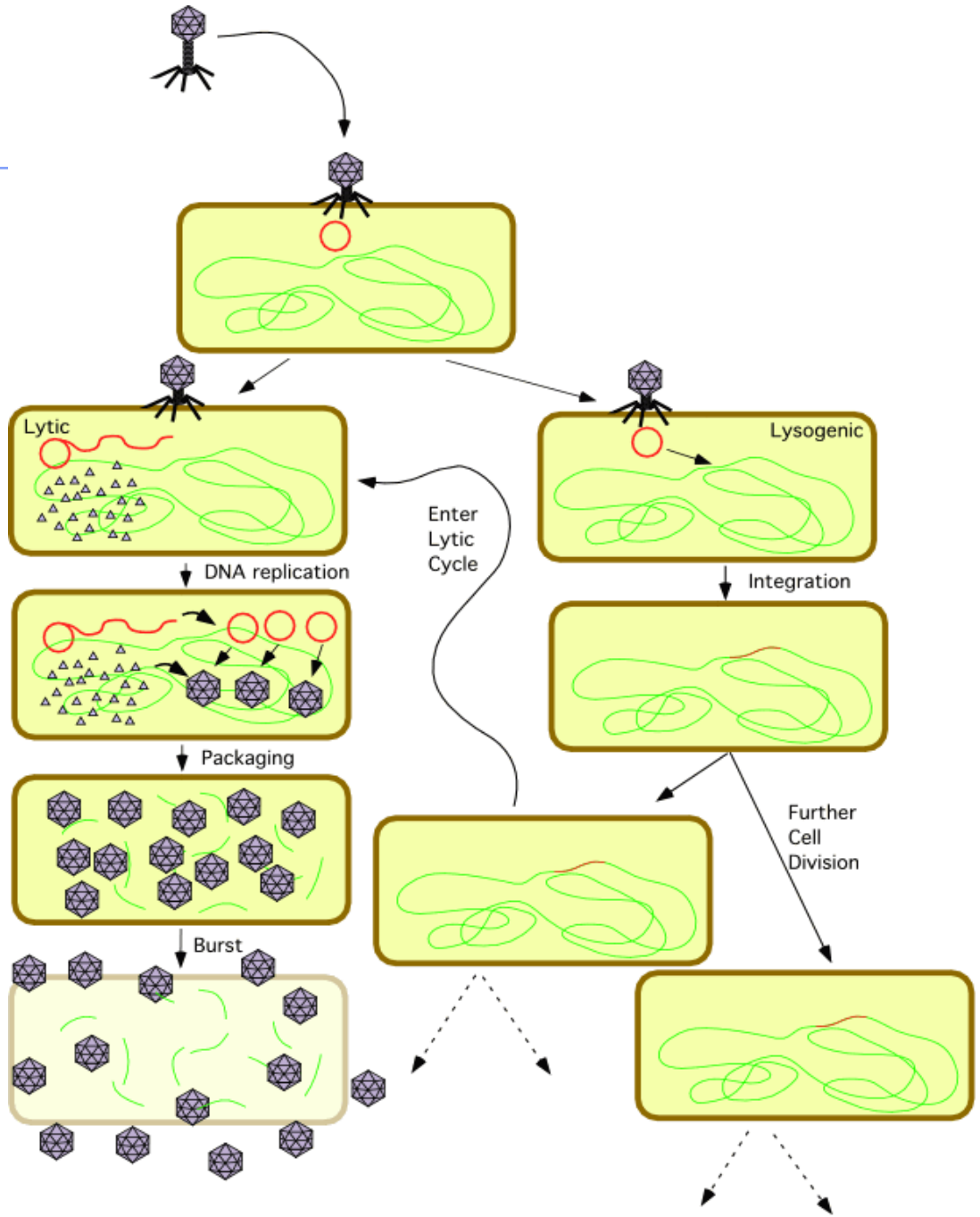
Viral genes allow the bacterial cell to produce the viral enzymes that insert the viral DNA into the bacterial chromosome.

Lysogenic reproductive cycle of Temperate Phages



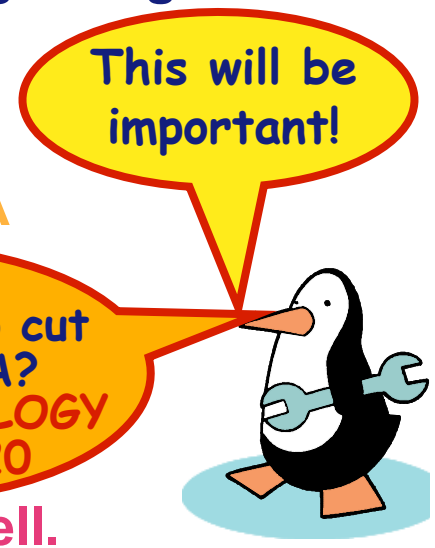
Stages of Lysogenic Phage Infection

1. Absorption
2. Entry
3. Integration
4. Replication
5. Assembly
6. Release



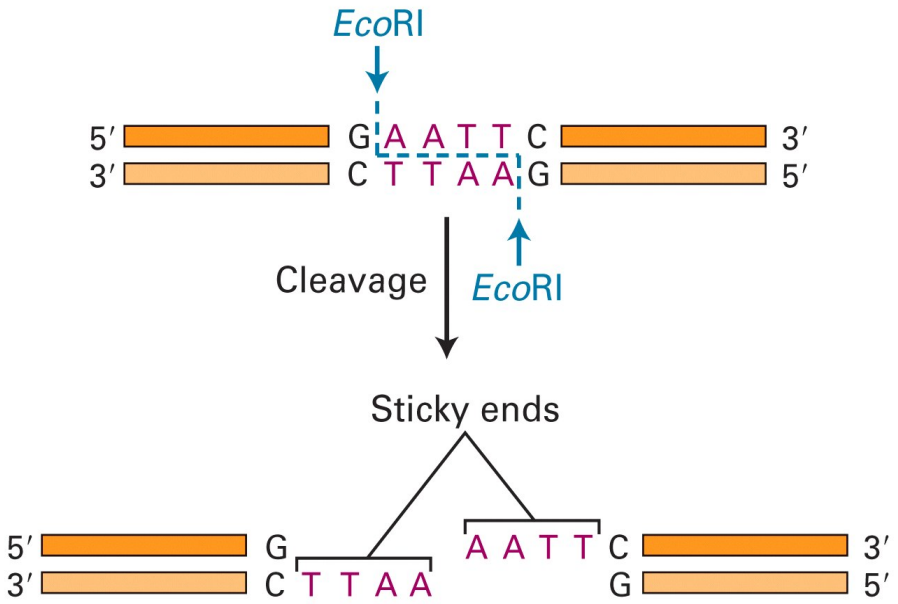
Bacterial Defense Against Viruses

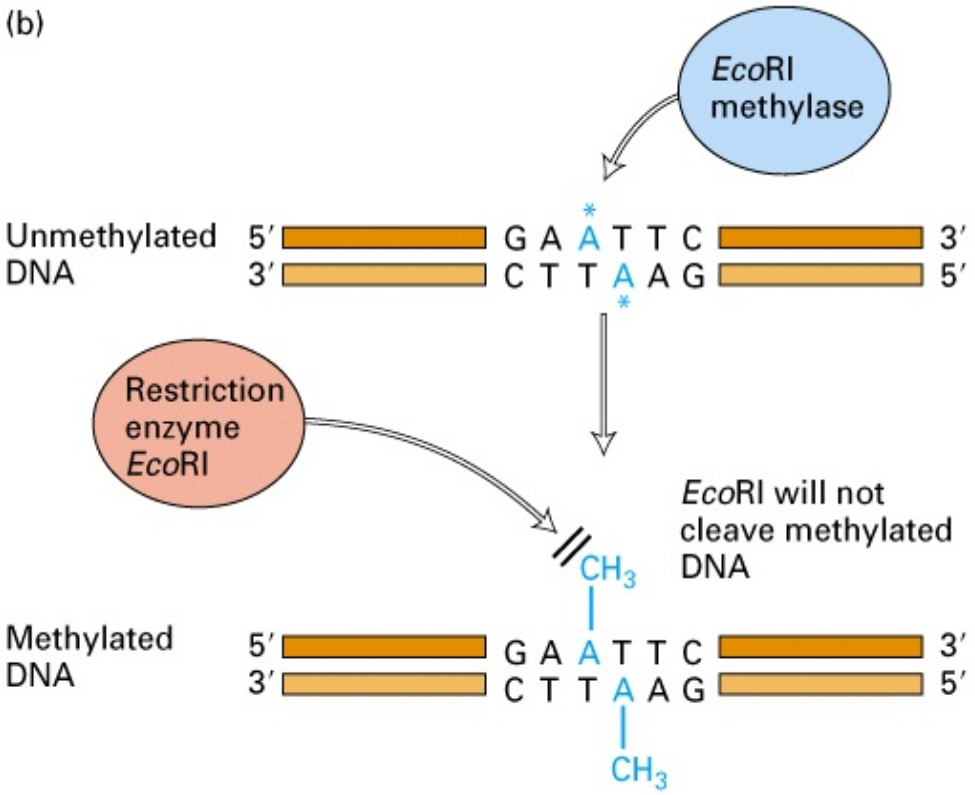
- **Bacteria have evolved defenses against phages:**
  1. **Bacterial mutants with receptors that are no longer recognized by a phage**
     - **natural selection favors these mutants**
  2. **Bacterial CRISPR-Cas provides protection from viruses.**
     - **This complex multi-protein molecular machinery uses RNA molecules as molecular guides to recognize the invading viral nucleic acid in order to destroy it, directly degrading the DNA or RNA of the invading viruses.**
  3. **Bacteria also produce Restriction Enzymes**
     - **Recognize & cut up foreign invading viral DNA**
- **Of course, it's an escalating war due to evolution!**
  - **natural selection favors phage mutants resistant to bacterial defenses as well.**



How does a bacteria protect its own DNA?

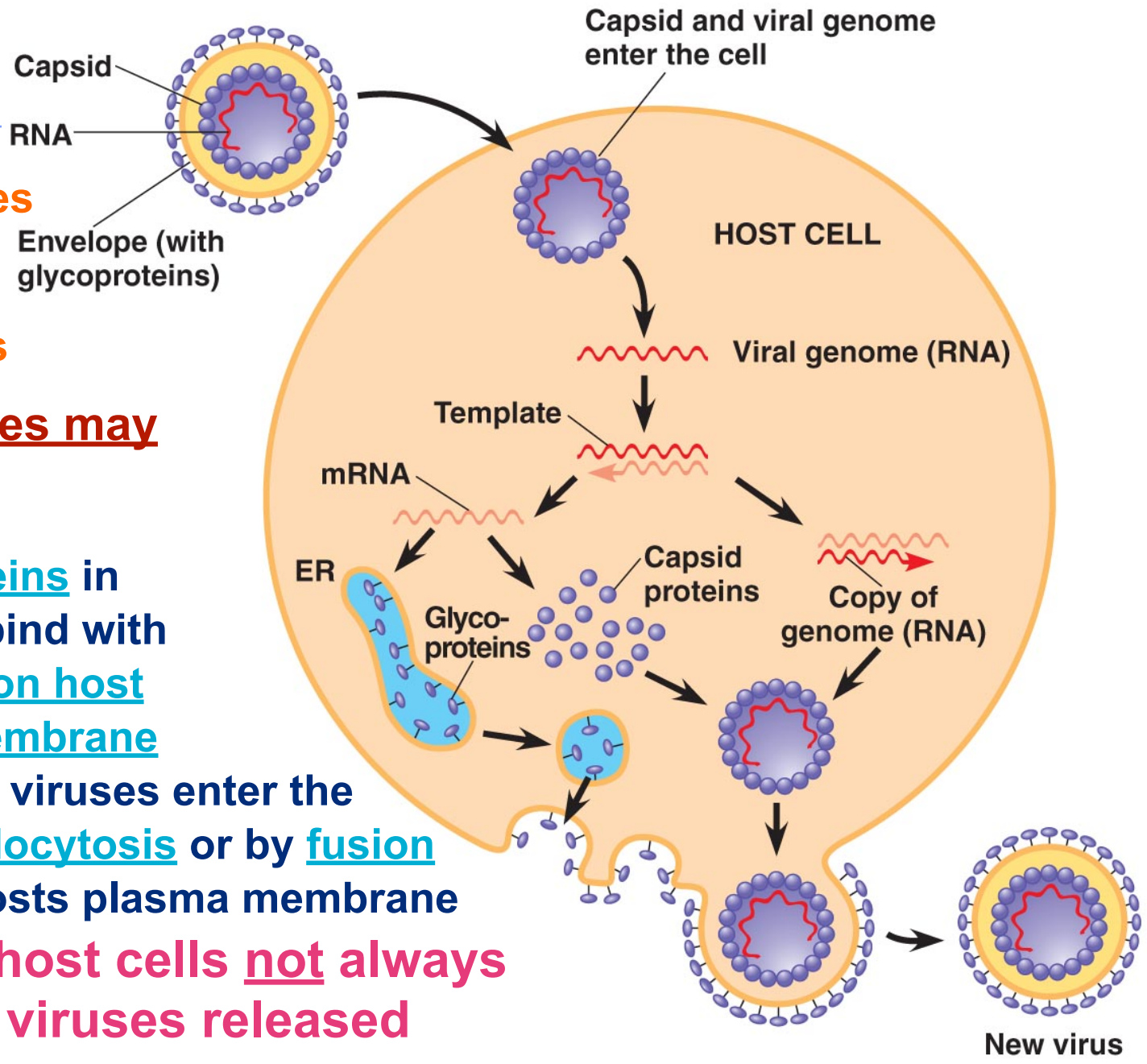
- Bacteria methylate the DNA near the restriction sites, the sites recognized and cut by these restriction enzymes.





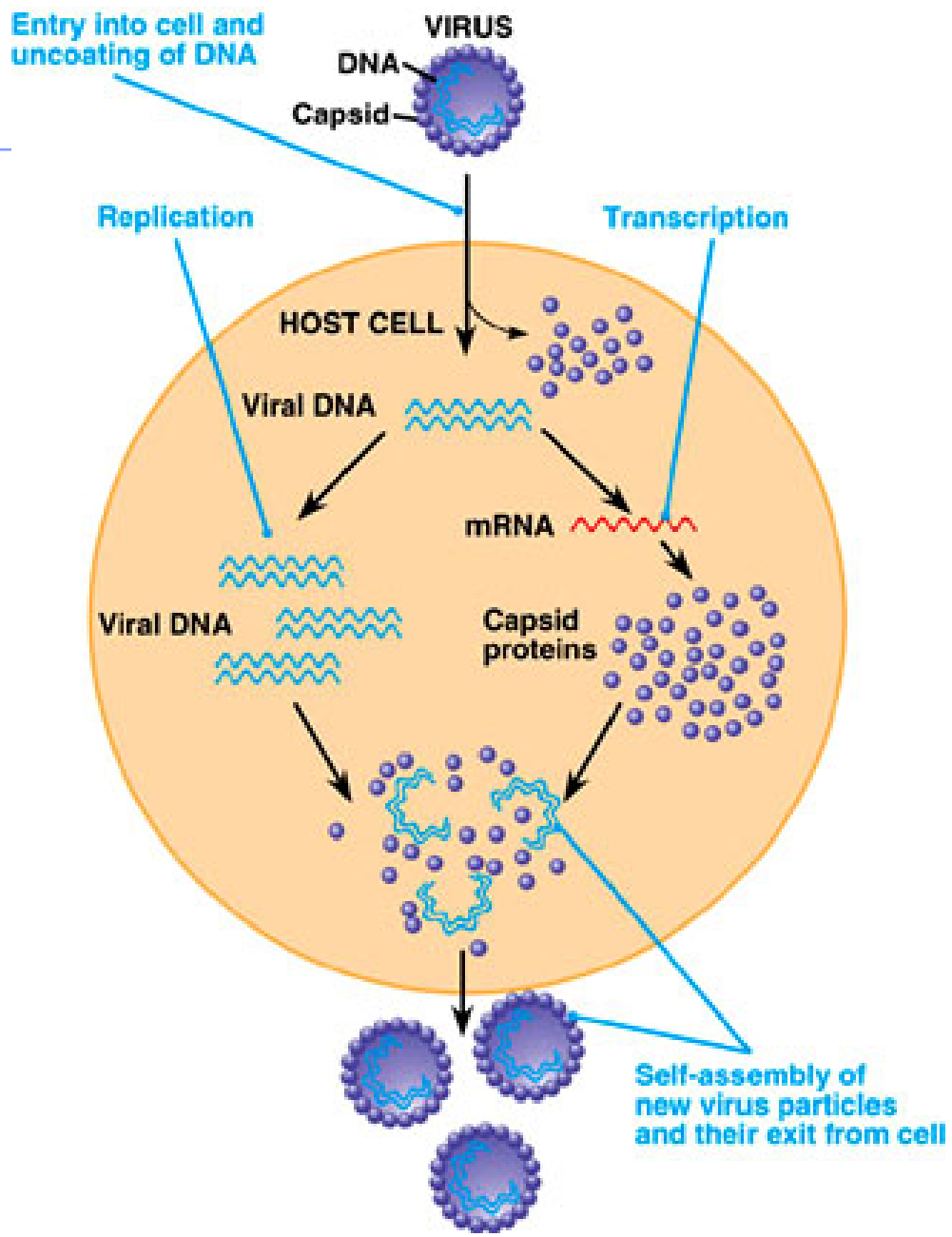
Animal Viruses

- Very few bacteriophages have envelopes or RNA genomes
- **Animal viruses may have both.**
  - Glycoproteins in envelope bind with receptors on host plasma membrane
  - Enveloped viruses enter the cell by endocytosis or by fusion with the hosts plasma membrane
- Eukaryotic host cells not always killed when viruses released



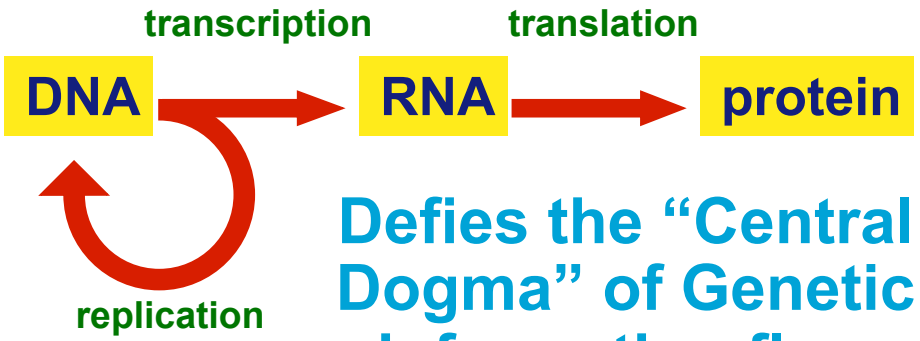
Stages of Eukaryote Viral Replication

1. Attachment
2. Entry
3. Uncoating
4. Replication
5. Maturation/ assembly
6. Release

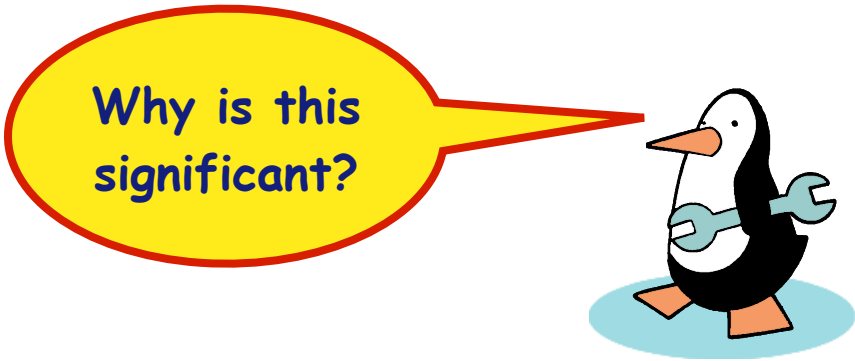


Class VI Viruses

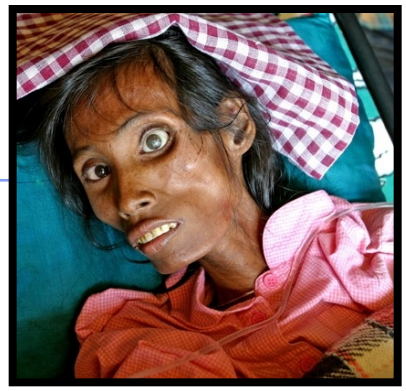
- **Retroviruses**
  - these viruses copy viral RNA into host DNA!!!
    - enzyme = reverse transcriptase
      - RNA → DNA → mRNA
  - Once a DNA copy of the RNA genome is made, the host's RNA polymerase transcribes the viral DNA into viral mRNA
    - mRNA codes for viral components
    - host's ribosomes produce new viral proteins



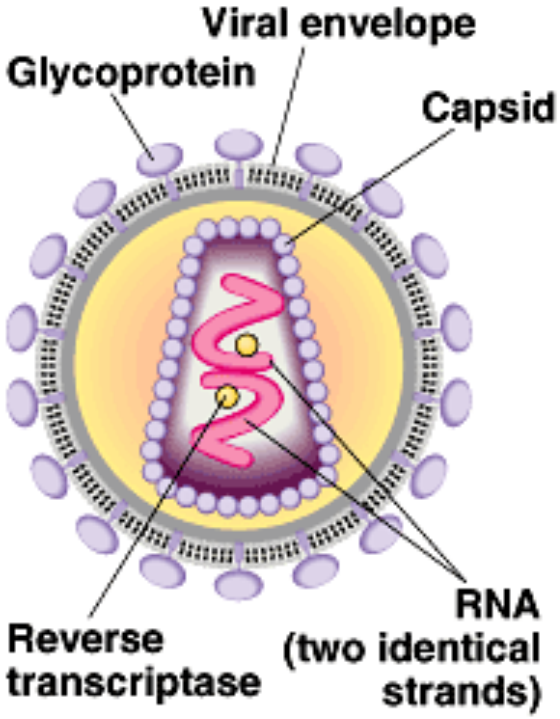
Defies the "Central Dogma" of Genetic information flow



Retroviruses - HIV



- **H**uman **I**mmuno**D**eficiency **V**irus
  - causes AIDS by infecting & damaging the white blood cells known as T lymphocytes and macrophages, parts of the immune system the protects us against invading germs.
    - **AIDS = A**cquired **I**mmuno**D**eficiency **S**yndrome
      - a disease that makes it difficult for the body to fight off infectious diseases
        - You become susceptible to opportunistic diseases and cancers & neural disorders



Transmission

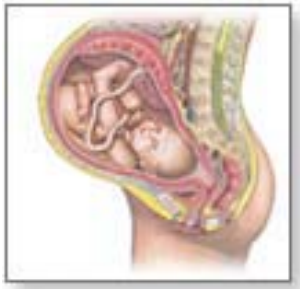
- **HIV can be transmitted through direct contact with the blood or body fluid of someone who is infected with the virus.**

The most common methods of transmission of HIV are:

Unprotected sex with an infected partner

Sharing needles with infected person

Almost eliminated as risk factors for HIV transmission are:



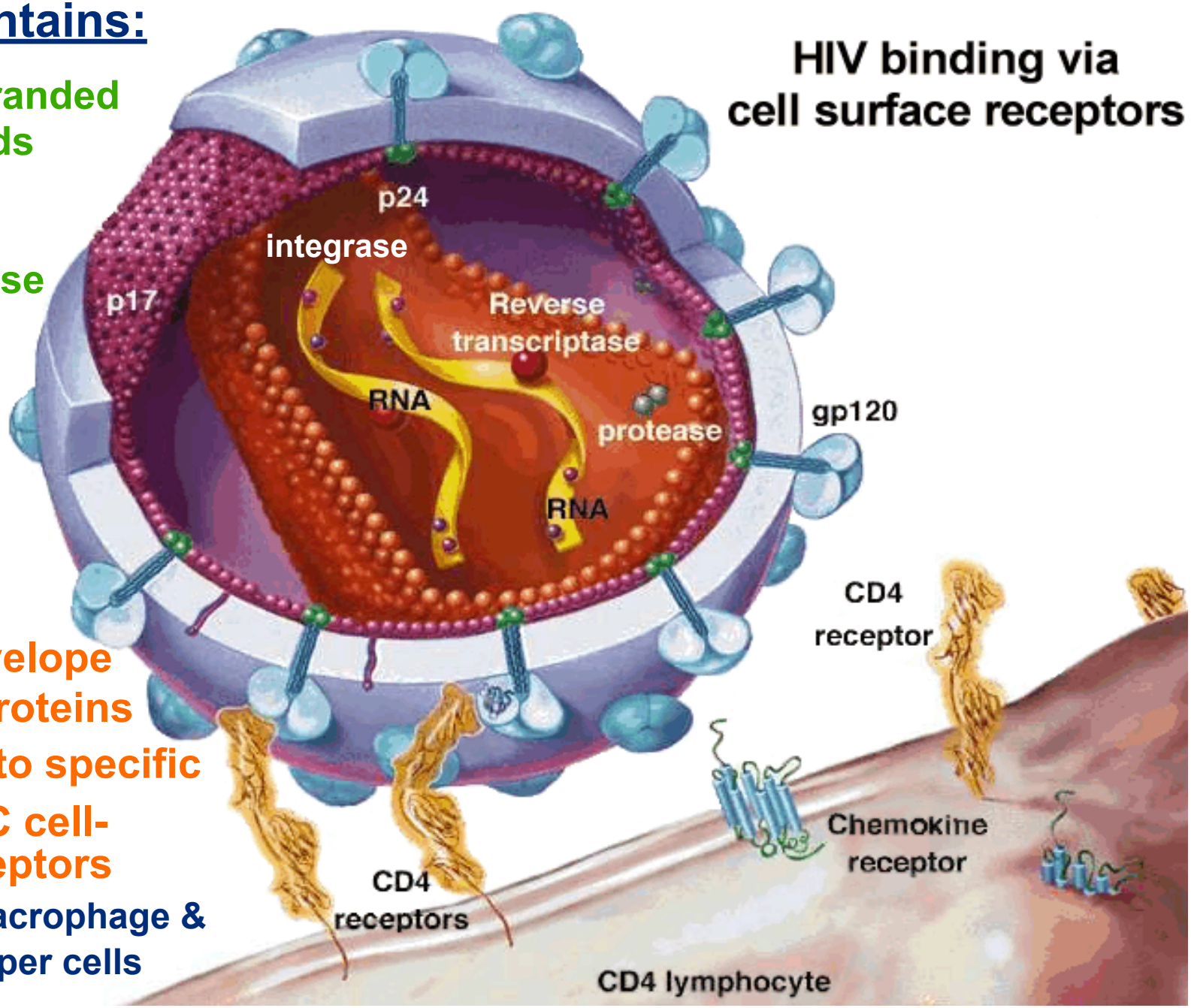
Transmission from infected mother to fetus

Infection from blood products

- **Though there are treatments for HIV and AIDS, there are no vaccines or cures for them.**
  - **Many infected with HIV may appear perfectly healthy & take years to display symptoms of AIDS.**

Capsid contains:

- 2 single-stranded RNA strands
- 2 copies of reverse transcriptase
- Integrase and protease enzymes

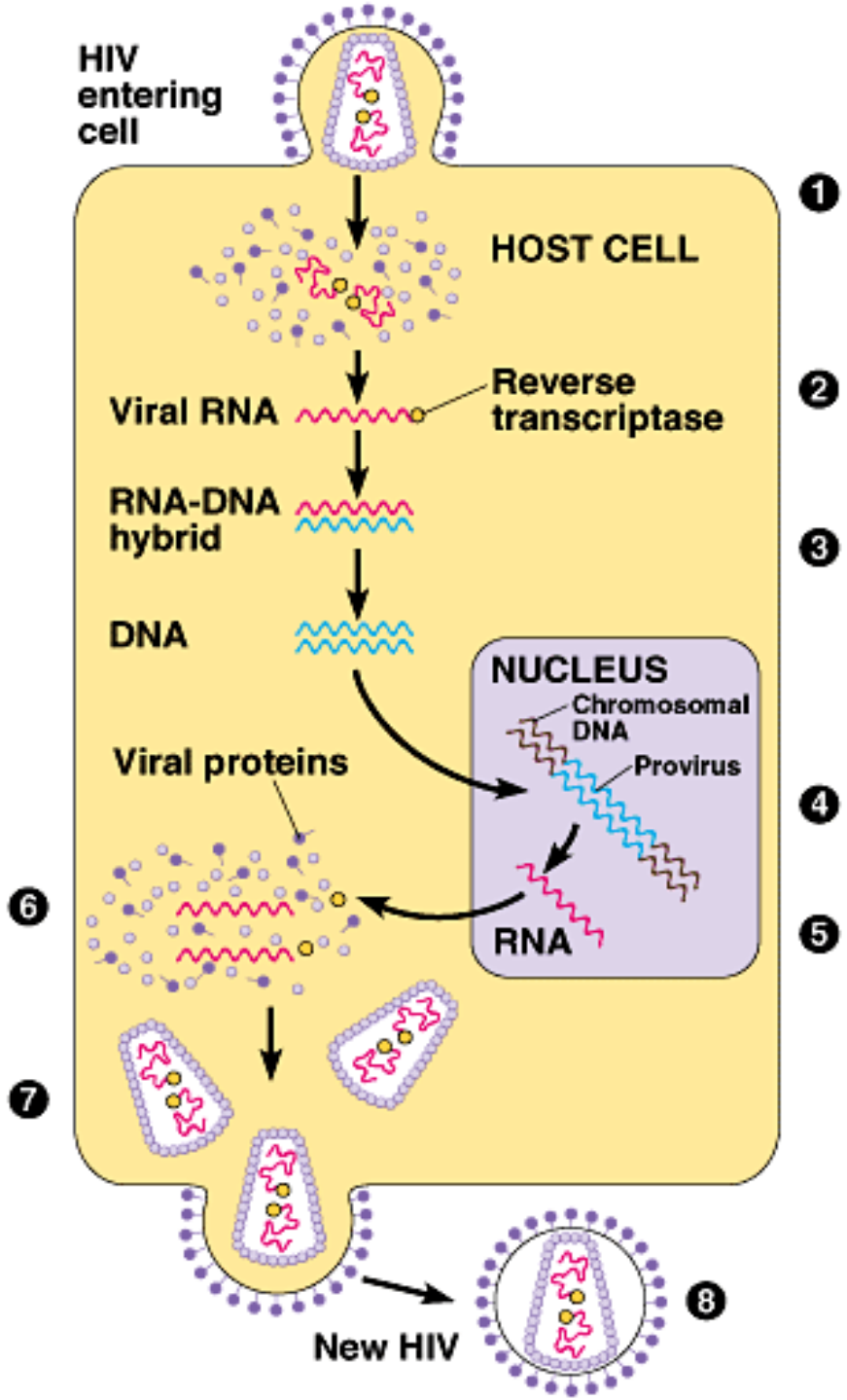


HIV has Envelope with glycoproteins for binding to specific human WBC cell-surface receptors

- Infects Macrophage & CD4/T-Helper cells

HIV infection

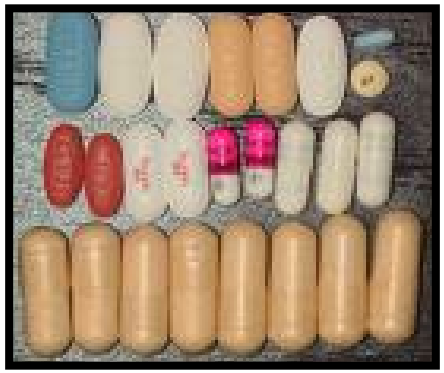
1. HIV fuses with host cell membranes
2. Next the capsid is degraded, releasing its contents
3. Reverse transcriptase synthesizes double-stranded DNA from viral RNA (High mutation rate)
4. Viral DNA integrates into the hosts DNA becoming a PROVIRUS
5. Transcription produces more copies of viral RNA
6. RNA is translated by ribosomes into viral proteins
7. Viral proteins & viral RNA self-assemble into virus particles
8. Viruses released from cell by "budding"
   - In the process capsids acquire an envelope an



HIV treatment: Currently, there are 30 approved antiretroviral drugs treat people infected with HIV.

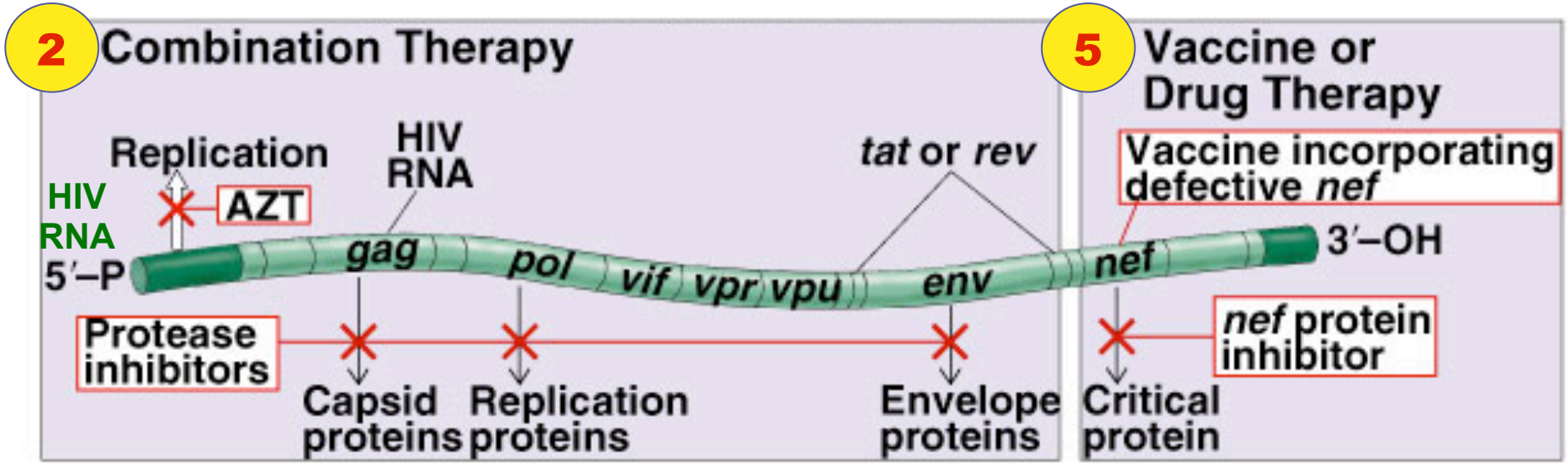
- These drugs fall into different classes.
  - *1. Reverse transcriptase (RT) inhibitors*
    - interfere with the critical step during the HIV life cycle known as reverse transcription.
    - During this step, RT, an HIV enzyme, converts HIV RNA to HIV DNA.
    - There are two main types of RT inhibitors.
      - *Nucleoside/nucleotide RT inhibitors* are faulty DNA building blocks. When these faulty pieces are incorporated into the HIV DNA (during the process when the HIV RNA is converted to HIV DNA), the DNA chain cannot be completed, thereby blocking HIV from replicating in a cell.

        Ex: AZT which mimics Thymine
      - *Non-nucleoside RT inhibitors* bind to RT, interfering with its ability to convert the HIV RNA into HIV DNA.



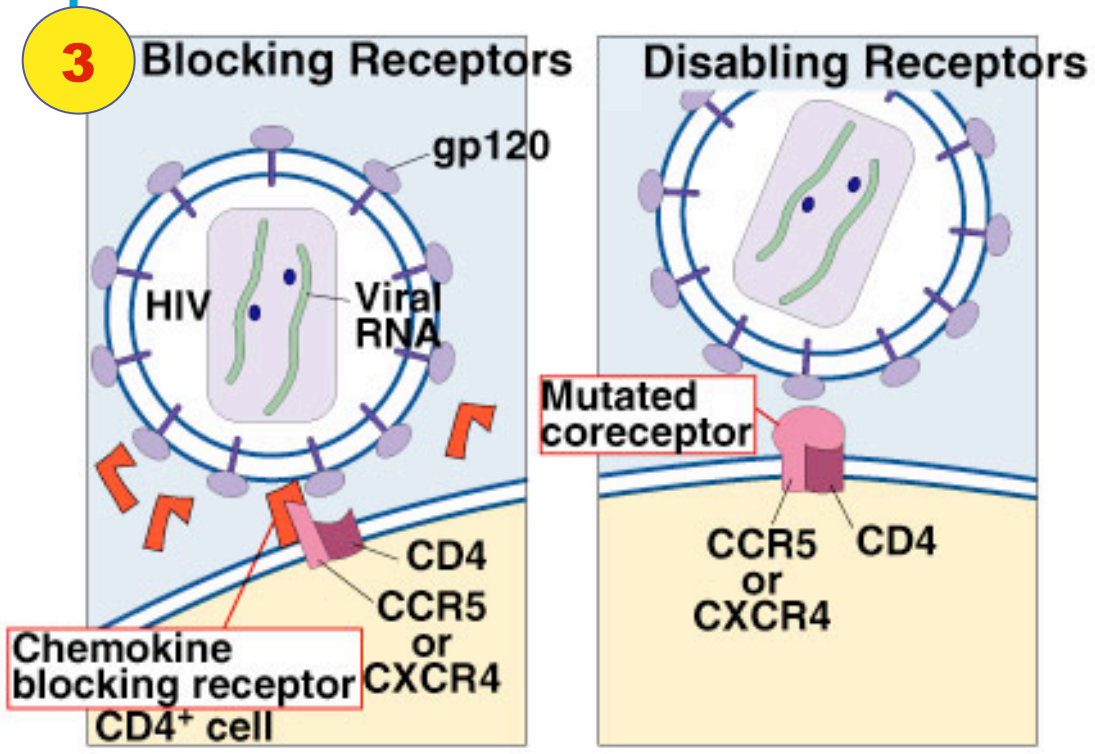
HIV treatment

- ***2. Protease inhibitors*** **interfere with the protease enzyme that HIV uses to produce infectious viral particles.**
  - **The protease cleaves the long polypeptide that is made from translation of the viral (m)RNA, the cut sections of the polypeptide then each folding into individual capsid, envelope, enzyme, and other factor proteins**
    - **If the polypeptide can't be cleaved, all necessary viral proteins for of new virions can't form.**



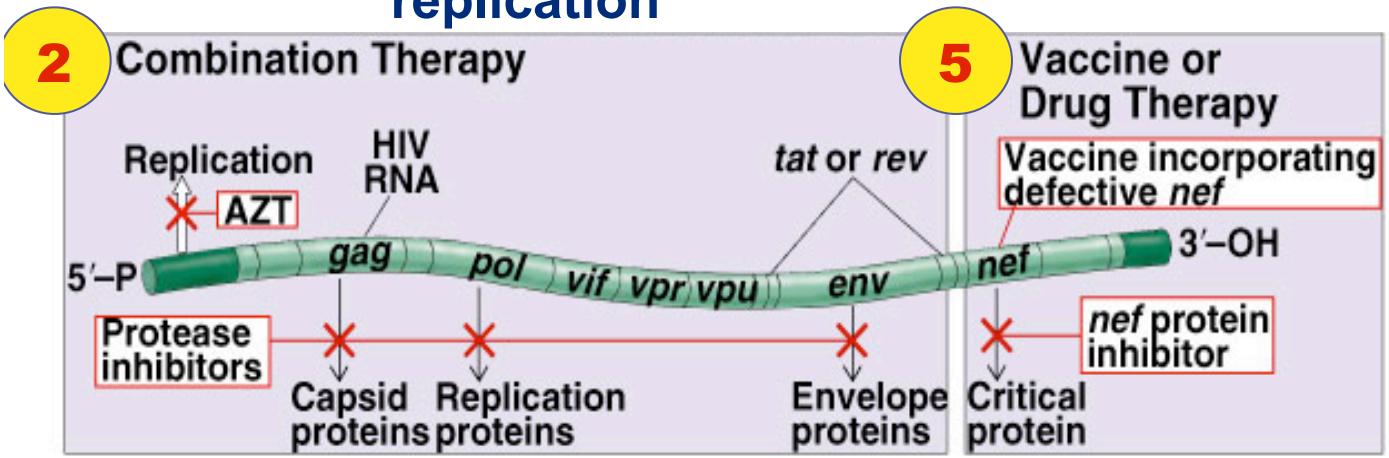
HIV treatment

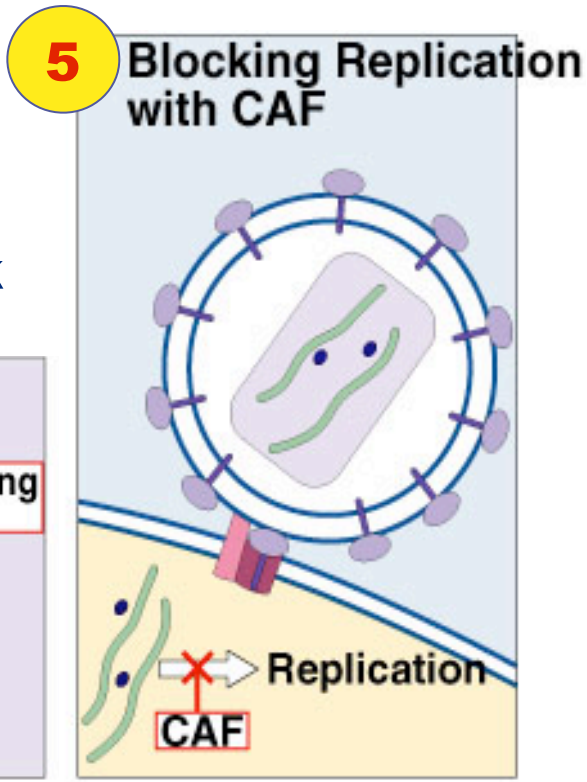
- ***3. Entry and fusion inhibitors*** interfere with the virus' ability to fuse with the cellular membrane, thereby, blocking entry into the host cell.
  - Block Host Cell Receptors
    - 11% of Caucasians have recessive mutant recepto allele, which prevents HIV infection



HIV treatment

- ***4.Integrase inhibitors*** **block integrase, the enzyme HIV uses to integrate genetic material of the virus into its target host cell.**
- ***5.New experimental drugs:***
  - **NEF inhibitors and CAF activators**
    - **Block NEF protein which normally causes a high amount of viral production**
    - **CAF (Cell antiviral Factors) that block replication**



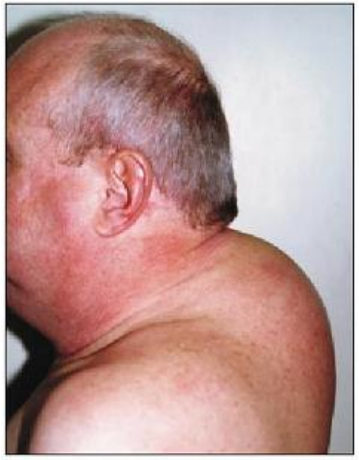


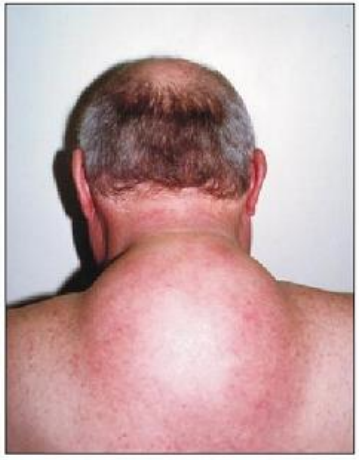
HIV treatment

- ***Multidrug combination products*** combine drugs from more than one class into a single product.
  - **Currently available drugs do not cure HIV infection or AIDS.**
    - **They can suppress the virus, even to undetectable levels, but they cannot eliminate HIV from the body. Hence, people with HIV need to continuously take antiretroviral drugs and can still often infect others.**
  - **HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)**
  - **As HIV reproduces itself, variants of the virus emerge**
    - **reverse transcriptions introduced constant new mutations including some that are resistant to antiretroviral drugs.**
    - **Medications are extremely effective and carry significant amounts of unpleasant and even dangerous side effects.**

AP

Drug Side Effects can include organ damage, nausea, and a host of physical body changes





NIGHT SWEATS

CRIX BELLY

DIARRHEA

FACIAL WASTING

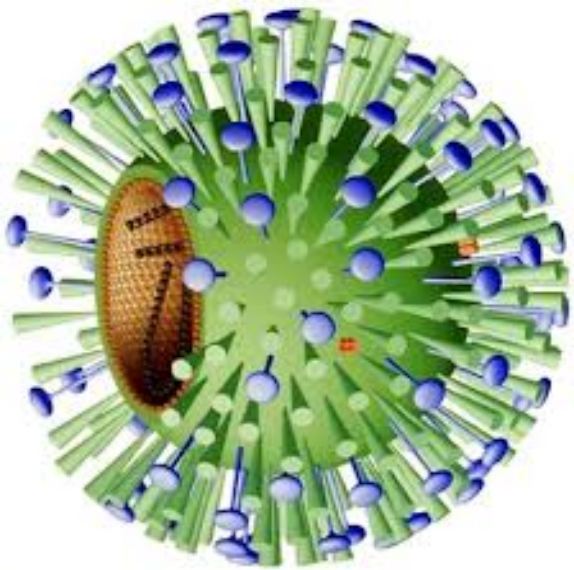
AP

Cancer viruses

- Some viruses cause certain human cancers by, at times, disrupting or damaging tumor suppressor or proto-oncogenes that are needed to control the cell cycle
  - **Hepatitis B virus**
    - linked to liver cancer
  - **Epstein-Barr virus** = causing infectious mononocluosis
    - linked to lymphoma
  - **Papilloma viruses**
    - linked with cervical cancers
  - **HTLV-1 retrovirus**
    - linked to adult leukemia

Cancer viruses

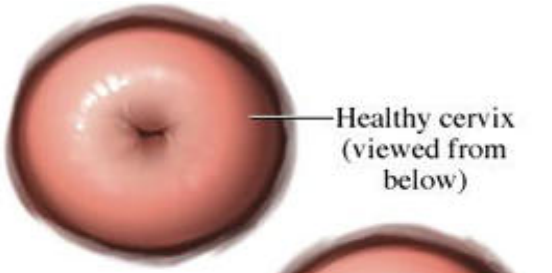
- Transform cells into cancer cells after integration of viral DNA into host DNA
  - Some viruses even carry oncogenes in their genome that trigger cancerous characteristics in cells
- Most tumor viruses probably cause cancer only in combination with other DNA mutagenic events

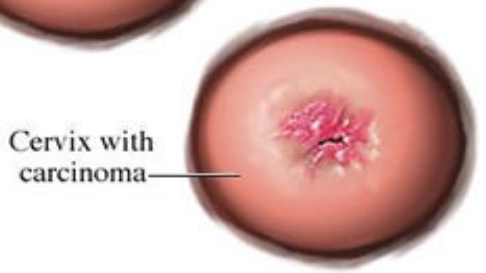


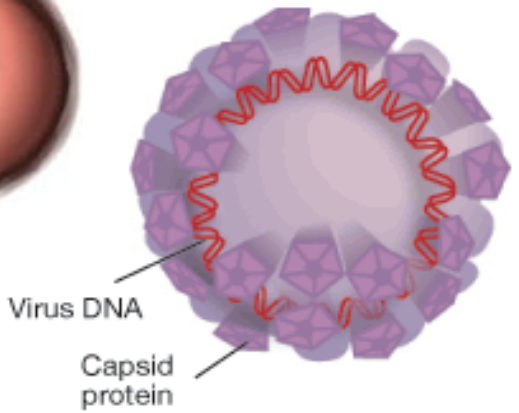
Over 100 types of Human Papilloma viruses (HPV) are known…

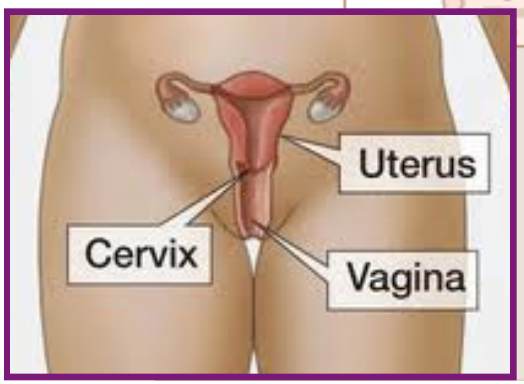
2 strains cause 80% of…

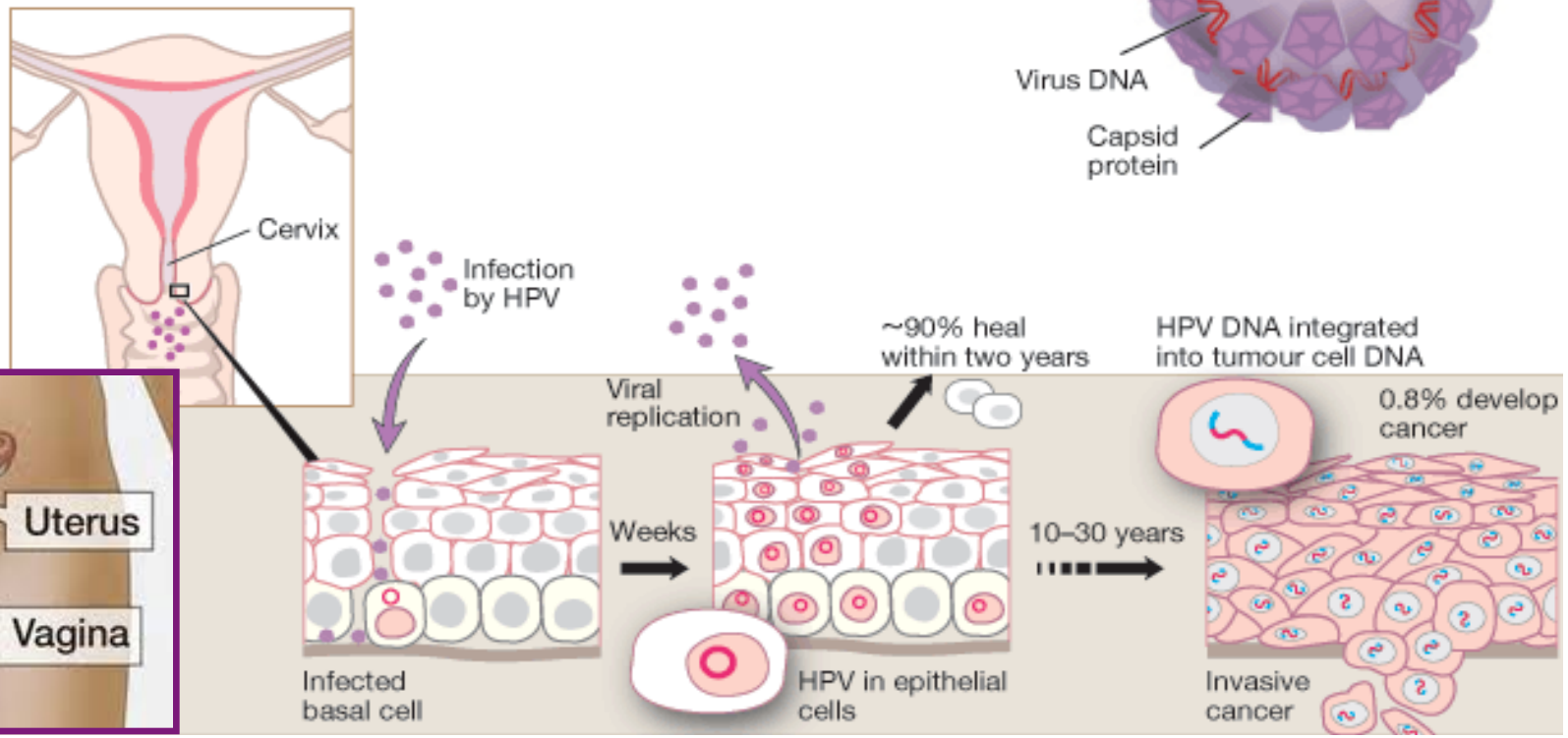
Cervical Cancer









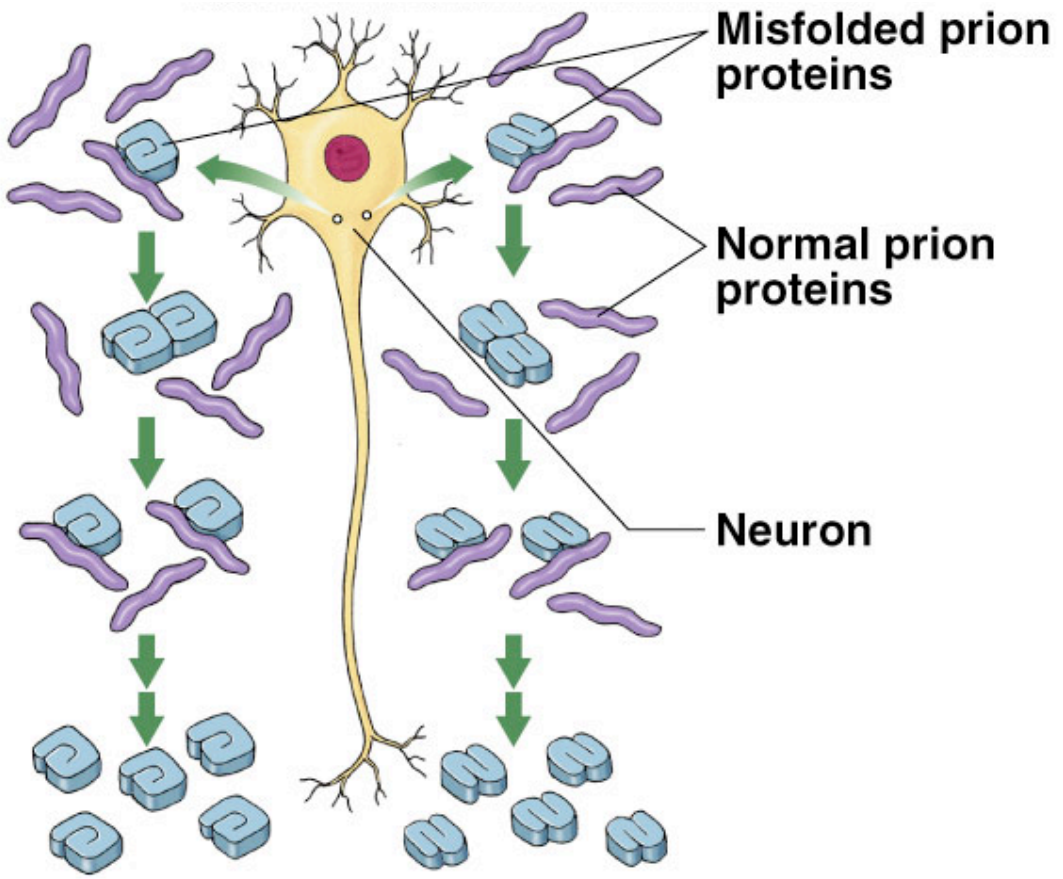


Prions = misfolded infectious proteins

- Cause normally shaped proteins to misfold as well
  - *make plaques (clumps of proteins) in cells & holes in brains as neurons die*

Alarming Characteristics:

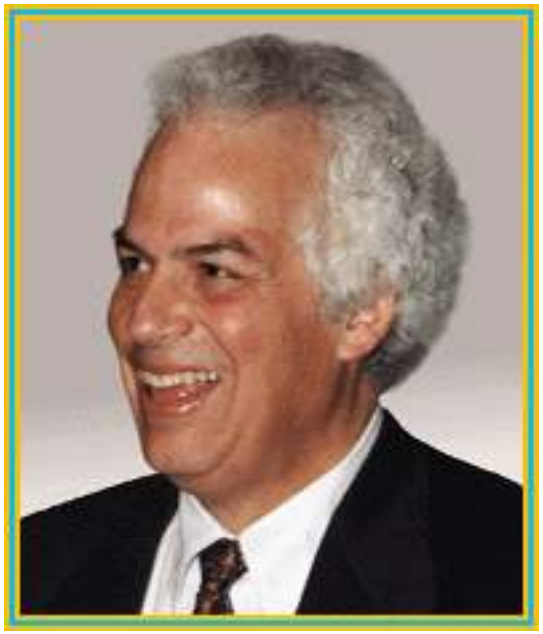
1. Have a very long incubation period before symptoms develop (10 years+).
   - Allows for increased chances of transmission.
2. Indestructible even at normal cooking temperatures



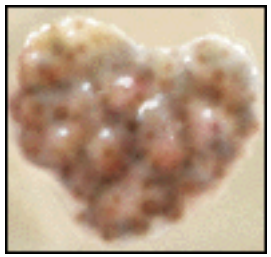
Protein as information molecule?!

1982 | 1997

- Prions challenge Central Dogma
  - A protein that transmits information to other proteins was unheard of before



Stanley Prusiner
UC School of Medicine



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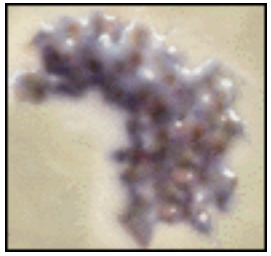

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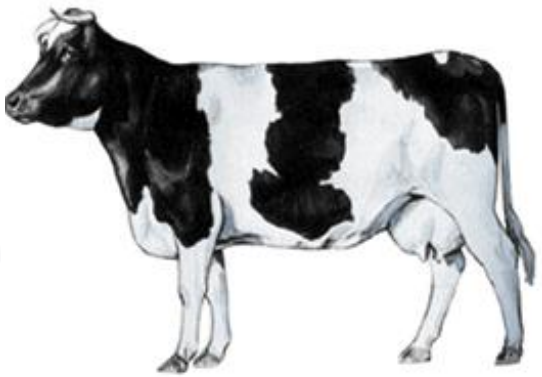
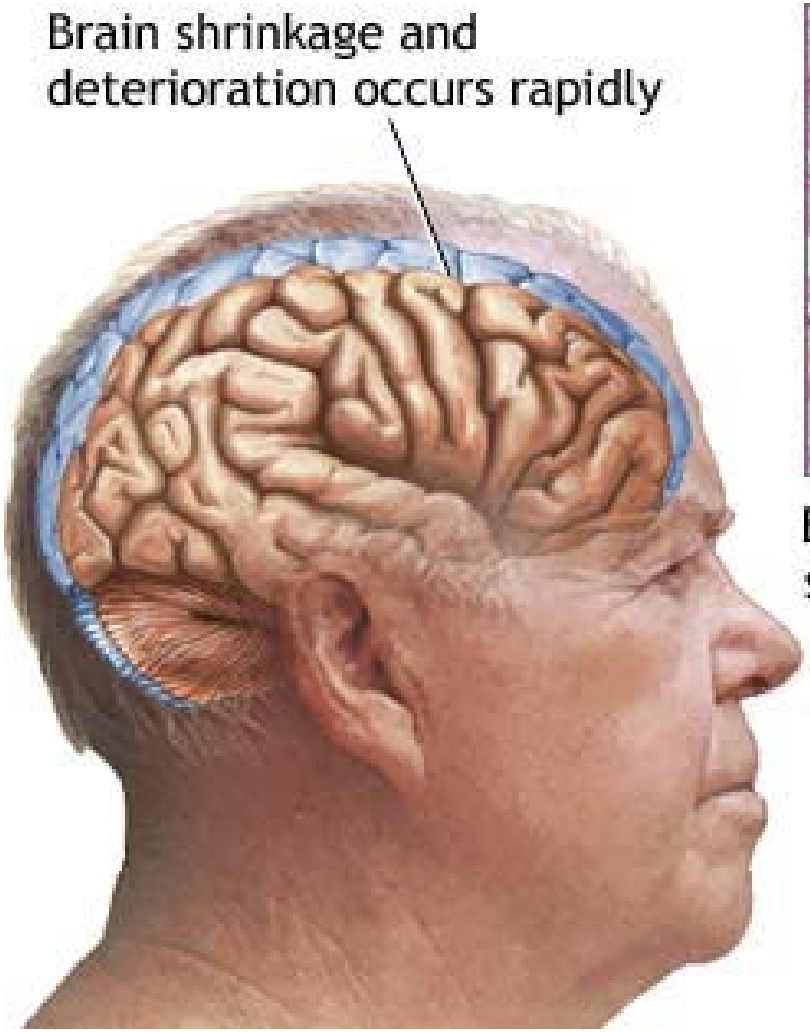
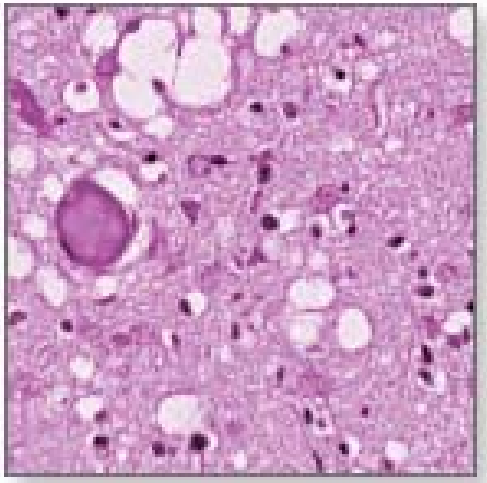


Causes neurological degeneration

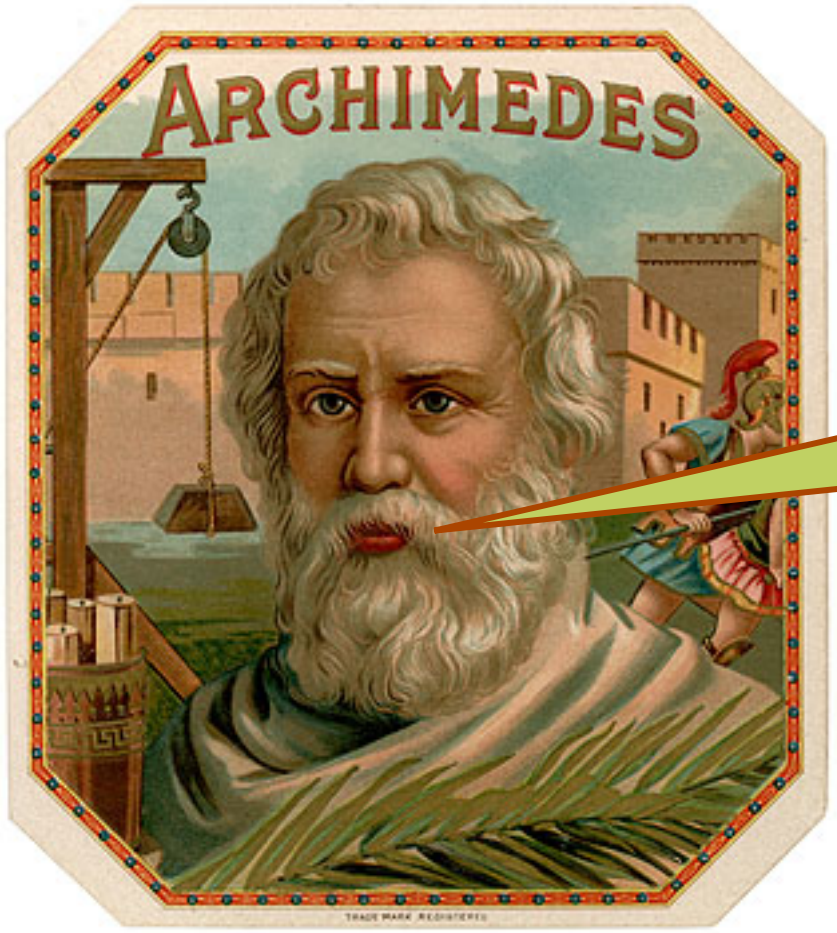




Brain section showing spongiform pathology characteristic of Creutzfeldt-Jakob

Creutzfeldt-Jakob disease is the human form of prion disease

MadCow Disease



"Knowledge is Freedom"