Chapter 6 - Virology

- **Topics**
  - **Structure**
  - **Classification**
  - **Multiplication**
  - **Cultivation and replication**
  - **Nonviral infectious agent**
  - **Teratogenic/Oncogenic**

- Viruses have a **host range**. That is, viruses infect specific cells or tissues of specific hosts, or specific bacteria, or specific plants.

- Viral specificity refers to the specific kinds of cells a virus can infect. It is regulated by the specificities of attachment, penetration and replication of the virus (**Receptors**)

Properties of viruses

- Viruses are not cells, do not have nuclei or mitochondria or ribosomes or other cellular components.

- Viruses replicate or multiply. Viruses do not grow.

- Viruses replicate or multiply only within living cells.

- Viruses are obligate intracellular parasites.

- The term virus was coined by Pasteur, and is from the Latin word for **poison**.

Components of viruses -

A virion is an infectious virus particle - not all virus particles are infectious

Viruses are composed of a nucleic acid, RNA or DNA - never both.

- All viruses have a **protein coat** (capside) or shell that surrounds and protects the nucleic acid core.

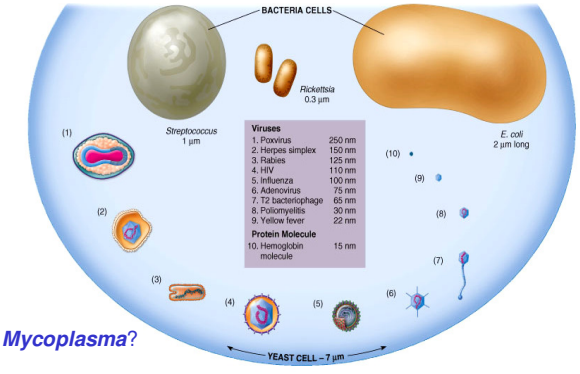
- Some viruses have a lipid envelope or membrane surrounding a nucleocapsid core. The source of the envelope is from the membranes of the host cell.

- Some viruses package enzymes - e.g. RNA-dependent-RNA polymerase or other enzymes - some do not package enzymes

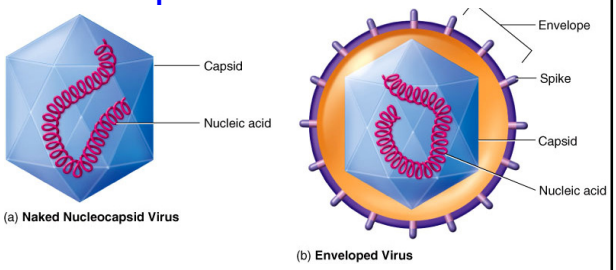
Structure

- **Size and morphology**
- **Capsid**
- **Envelope**
- **Complex**
- **Nucleic acid**

Size comparison of viruses - how big are they?



There are two major structures of viruses called the naked nucleocapsid virus and the enveloped virus



NAKED Enveloped

Capsid

- Protective outer shell that surrounds viral nucleic acid
- Composed of capsomer subunits - collectively protect the nucleic acid from the environment
- Capsid spikes - used for binding to cell surface proteins

Envelope

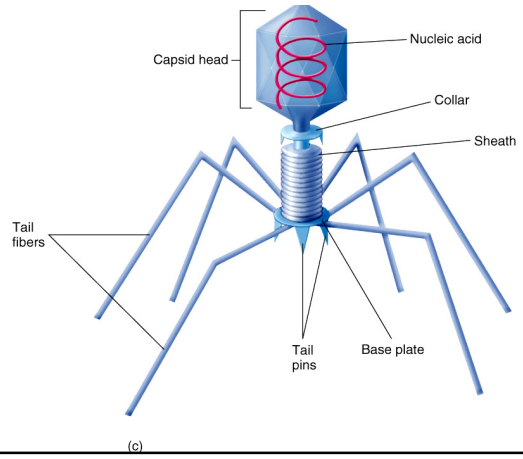
- Lipid and proteins - basically a modified version of our membranes
- Envelope spikes - bind to cell surface proteins
- During release of animal viruses, a part of the host membrane is taken

Nucleic acid

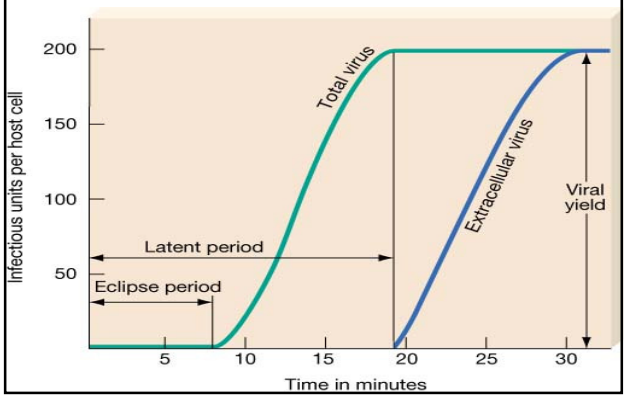
- Viruses contain either DNA or RNA
- Possess only the genes to invade and regulate the metabolic activity of host cells
- Ex. Hepatitis B (4 genes) and herpesviruses (100 genes)
- No viral metabolic genes, as the virus uses the host's metabolic resources

Bacteriophages

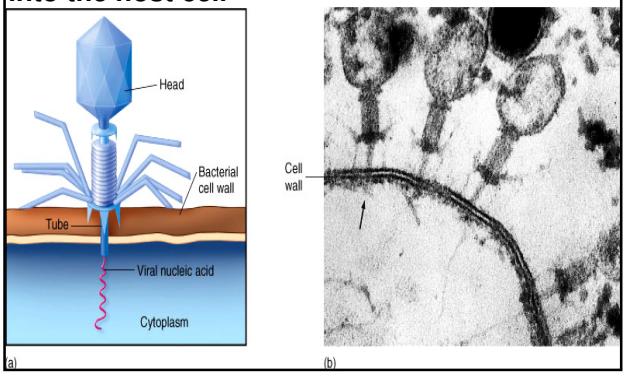
- Bacteriophage
  - Polyhedral head
  - Helical tail
  - Fibers for attachment
- Are considered either LYTIC or TEMPERATE
- Are often associated with virulence genes in bacteria
  - EX. - diphtheria toxin in *Clostridium diphtheriae* - also Botulinum toxin from *C. botulinum*



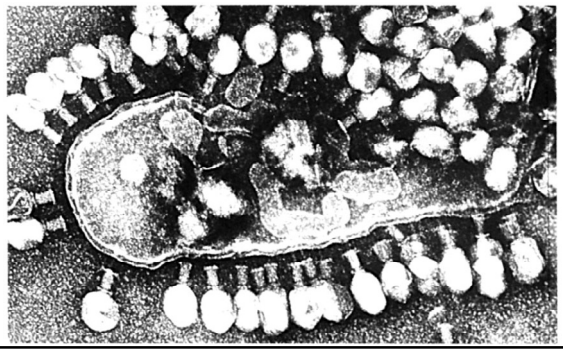
Growth curve for a bacteriophage

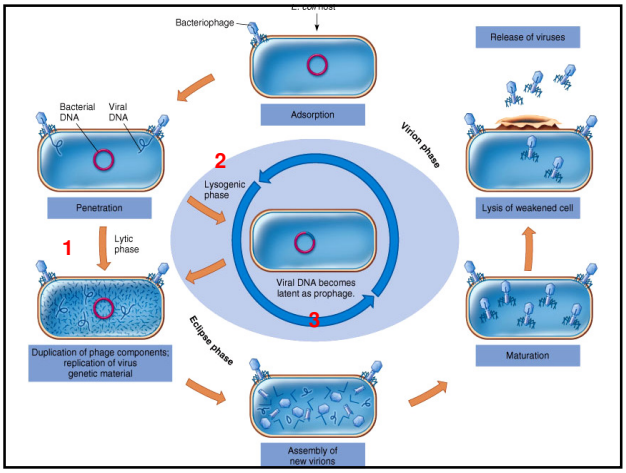


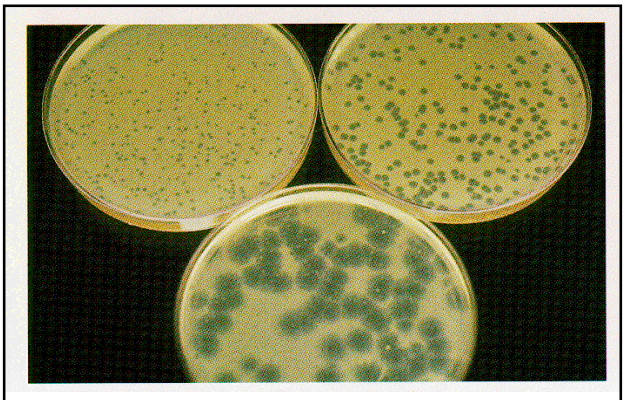
T-even bacteriophage penetrate the host cell by specifically binding and injecting their DNA into the host cell



After replication, bacteriophage release lysozyme, weaken/destroy/rupture cell and release numerous virions







Plaque Assay

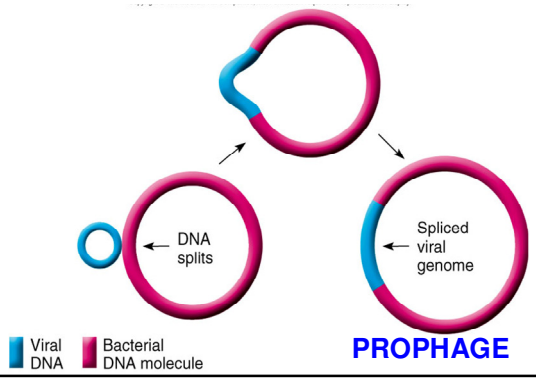
Temperate phages can cause disease

For example, *Corynebacterium diphtheriae* and *Clostridium botulinum* contain **prophages** that have genes which encode for toxins

Without these prophages, they **DO NOT** produce the toxin – without toxin, no disease

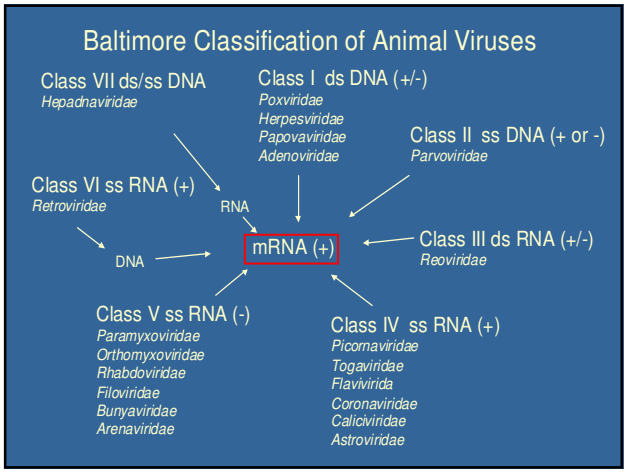
Thus, they are examples of bacteria and viruses interacting to cause medically relevant disease

Temperate phage - formation of a prophage and LYSOGENY



Classification

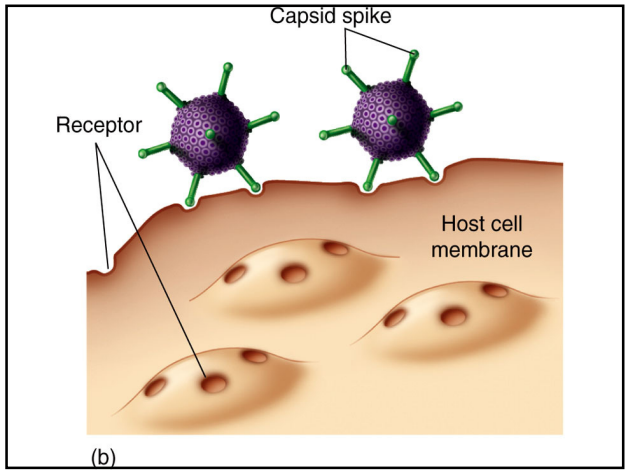
- Host Range
- Envelope or Naked virus
- Type of disease
- **Baltimore Classification of Viruses (4 major groups)**
  - **+ vs - sense**

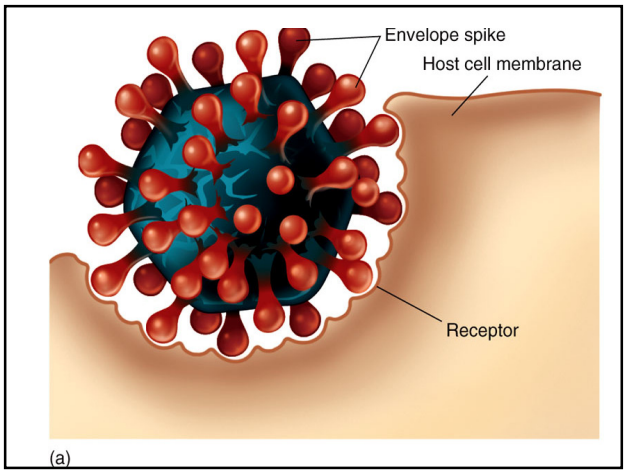


General Steps in Viral Multiplication

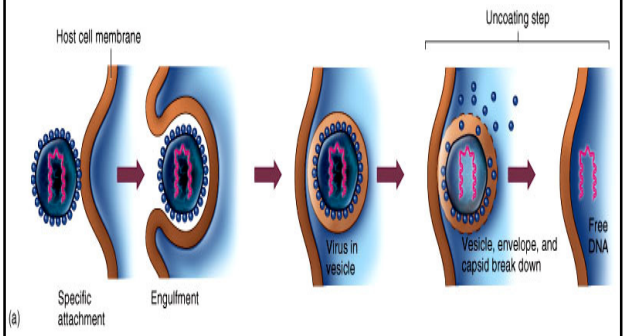
- **Adsorption**
- **Penetration**
- **Uncoating**
- **Synthesis**
- **Assembly**
- **Release**

Viruses recognize specific receptors Figure 6.12 and then the virus penetrates the cell Figure 6.13

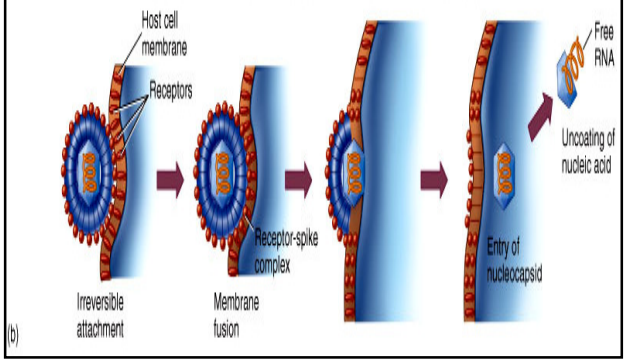




Endocytosis



Membrane Fusion

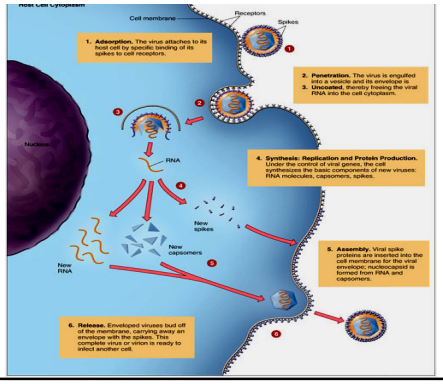


Animal Virus Replication

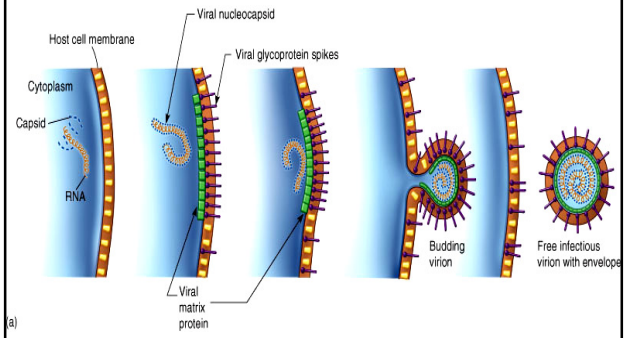
General Steps in Viral Multiplication

- **Adsorption**
- **Penetration**
- **Uncoating**
- **Synthesis**
- **Assembly**
- **Release**

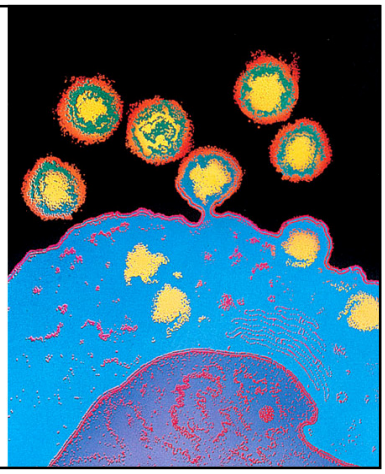
General replication scheme for an animal virus



A Magnified View of Viral Budding - ENVELOPED VIRUSES



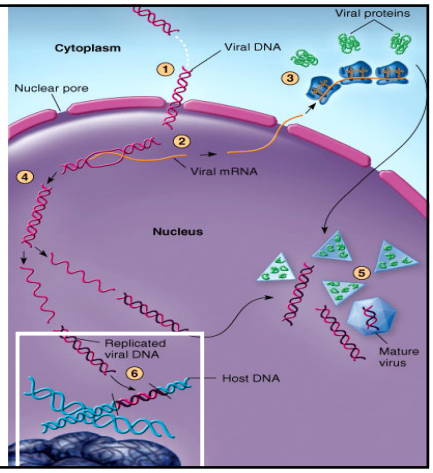
Worst case scenario - HIV virions exiting from a T cell



What happens if it is a dsDNA virus???

Examples: Herpes virus

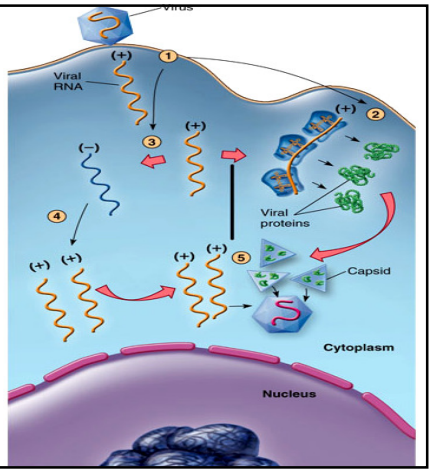
Gift of life!!

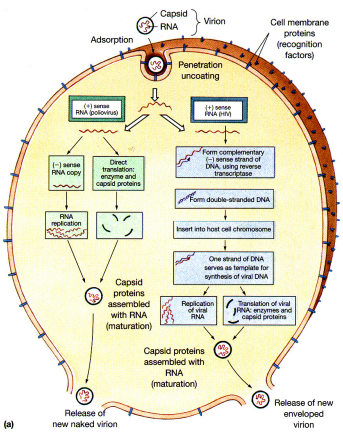


Most simple - and efficient case = ss+ RNA virus

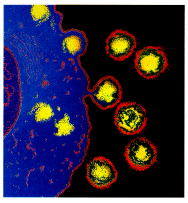
Examples: Coronavirus

RETROVIRUS





➢ Figure 10.13 **Replication of RNA viruses.** (a) Two of the replication mechanisms used by different (+) sense RNA animal viruses. *Left:* In the poliovirus the viral (+) sense RNA serves as mRNA—it is translated immediately to produce proteins needed for reproduction of the virus. A (–) sense RNA copy is then made, which serves as a template for the production of more viral (+) sense RNA molecules. Mature polioviruses lyse the cell during release. *Right:* In HIV each (+) sense RNA, copied with the help of reverse transcriptase, forms an ssDNA, which serves as template for the synthesis of the complementary strand. The dsDNA is then inserted into the host chromosome, where it can remain for some time. When virus replication occurs, one strand of the DNA becomes the template for the synthesis of viral (+) sense RNA molecules. Mature HIV particles usually do not lyse the cell but rather bud off the cell surrounded by an envelope. (b) HIV viruses budding from a T-4 lymphocyte.



Replication of RNA viruses

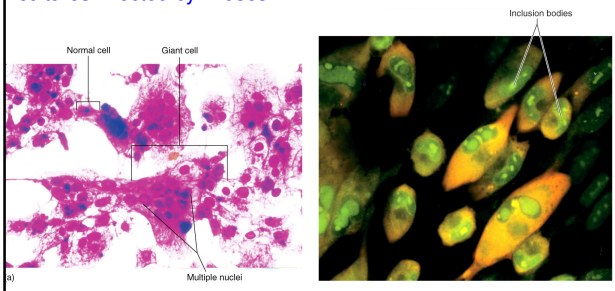
Insight 6.2 - Note differences between + sense, - sense and retrovirus replication

Also, be able to compare -contrast phage and animal virus replication

Cytopathic effects

- **Damage to the host cell due to a viral infection**
  - **Transformation**

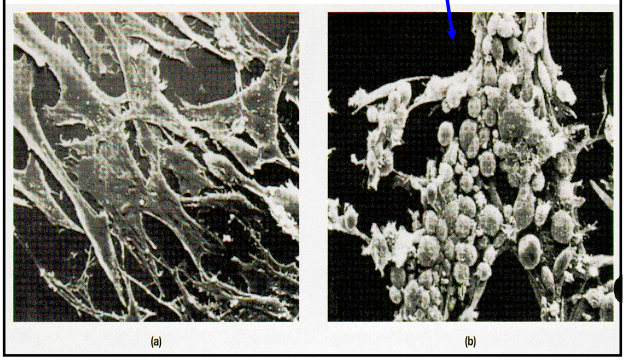
Fig. 6.16 Cytopathic changes in cells and cell cultures infected by viruses



Syncytia – multinucleated cells **Inclusion bodies**

Tight Junction Disruption

Viral **transformation** of cells – Oncogenic viruses dsDNA viruses (Papillomavirus, EBV, Hep B)



Cultivation and Replication

- ***In vivo*** **methods**
  - **Laboratory animals**
  - **Embryonic bird tissues**
- ***In vitro*** **methods**
  - **Cell or tissue culture**

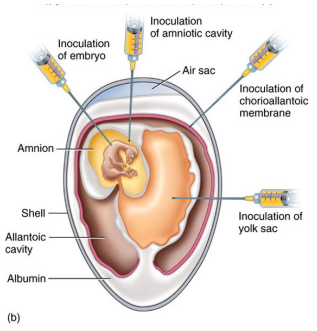
Cultivation of animal viruses –

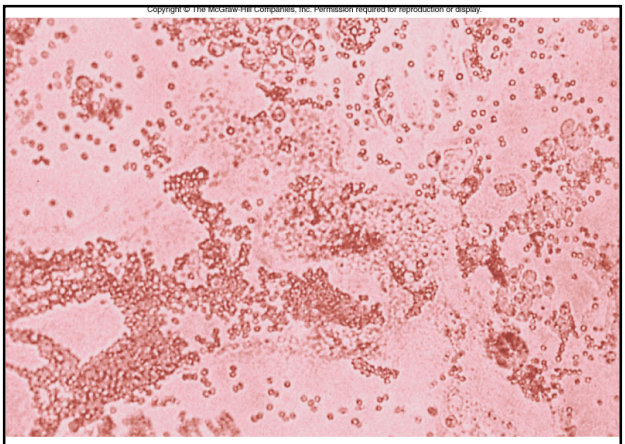
It is possible to study viruses in animals, but due to the complexity of the animal, expense of animals and the political environment relative to the use of animals, alternatives have been developed.

Chick embryos in eggs - influenza

Persistent infection – transformation/cancer

Making the Influenza vaccine





(c) Infected

Noncellular Infectious Agents

- **Prions**

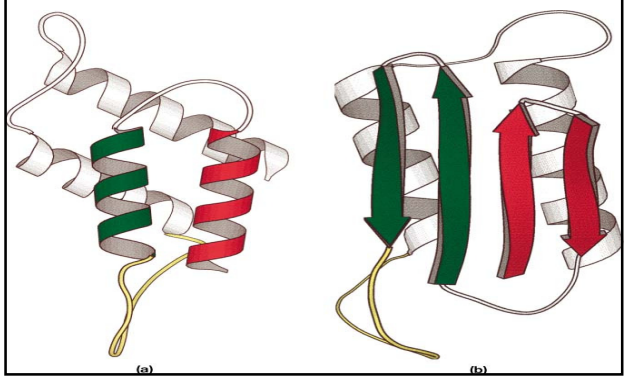
Prions – Stanley Pruisner – Nobel Prize in Medicine: 1978

Prions are proteinaceous infectious agents - Prions do not have nucleic acid.

Prions are considered to be the causative agents of Creutzfeld Jakob disease, scrapie, bovine spongiform encephalopathy (BSE) and kuru.

Protein structure of the two forms of the prion protein

GOOD!!!! BAD!!!



Oncogenic potential of viruses -

Cancer is a set of diseases known to disturb the normal functioning and properties of cells.

Tumors may be malignant or benign - malignant tumors spread by metastasis.

Peyton Rous in 1911 discovered that a filterable agent could transmit a sarcoma (a type of cancer) in chickens - Rous sarcoma virus - the first retrovirus described.

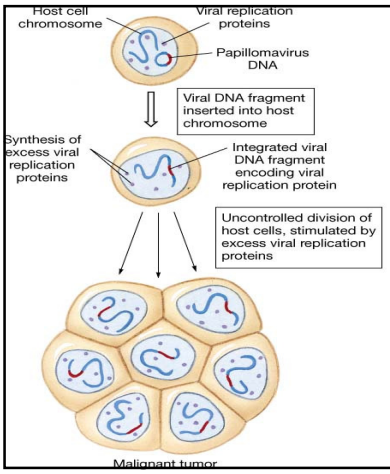
At least six viruses have been found to cause human cancer - Epstein-Barr virus, hepatitis B virus, hepatitis C virus, human papilloma virus (HPV-8, HPV-16), HTLV-I (adult T-cell leukemia and lymphoma), HTLV-II (hairy cell leukemia),

Oncogenes are normal cellular regulatory genes. When modified, these genes code for gene products that disturb the normal regulatory patterns of cells and can result in a loss of the normal properties of cell growth and division resulting in “cancer”.

Viral oncogenes are found usually in retroviruses.

Viral oncogenes are viral homologs of the cellular oncogenes.

Viral oncogenes can disturb normal regulatory properties by certain mechanisms.



Malignant tumor formation