Genetics and Pathogenesis
2nd Year Medical Students

By

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DipFRCPath

- Viral Genetics and Pathogenesis

  - Genetics & genome based classification

  - Pathogenesis

- Viruses can cause a variety of diseases from common cold and the flu to serious illnesses such as Ebola, AIDS, dengue fever, measles, small pox and avian flu.

- All viruses infect cells and redirect the host cellular machinery for their own benefit.

- Learning about the biology and genetics of viruses can help us better understand the diseases that they cause, their prevention and treatment.

Genomes

- **The genome may be DNA or RNA, SS or ds, in a linear, circular or segmented configuration.**

- **Single – stranded virus genomes may be either (+) sense, (-) sense or ambience.**

- **The Physical nature of nucleic acid dictates the strategy of replication and forms a basis for classification.**

Genomic size

- RNA usually smaller and more fragile than DNA viruses
- Each 1000 bp = kilobases
- For **single-stranded genomes, the** notation **kb is used.**
- **For double-stranded genomes, numbers are** expressed as kilobase pairs (**kbp).**

Classification

- The following are the main criteria used for the classification of viruses:

1. the type of nucleic acid (DNA or RNA);
2. the number of strands of nucleic acid and their physical construction (single- or double-stranded, linear, circular, circular with breaks, segmented);
3. polarity of the viral genome-RNA viruses: ‘positive-stranded’ ‘negative-stranded’;
4. the symmetry of the nucleocapsid;
5. the presence or absence of a lipid envelope.

DNA viruses

Family	Genome	Capsid	Envelop	Enzyme
Poxviridae	ds linear	Complex	yes	DNA dependent RNA polymerase
Herpesviridae	ds linear	Icosahedral	yes	DNA polymerase
Hepadnaviridae	ds (partial) circular	Icosahedral	yes	DNA polymerase (RT activity)
Adenoviridae	ds linear	Icosahedral	No	X
Polyomaviridae	ds circular	Icosahedral	No	X
Papillomaviridae	ds circular	Icosahedral	No	X
Parvoviridae	ss linear	Icosahedral	No	X

Abbreviations: ss: single stranded, ds: double stranded, RT: reverse transcriptase

Negative RNA viruses

Family	Genome	Capsid	Envelop	Enzyme
Bunyaviridae	ss circular /segmented*	helical	yes	yes
Arenaviridae	ss circular/segmented*	helical	yes	yes
Orthomyxoviridae	ss linear/segmented	helical	yes	yes
Paramyxoviridae	ss linear	helical	yes	yes
Rhabdoviridae	ss linear	helical	yes	yes
Filoviridae	ss linear	helical	yes	yes
Reoviridae	ds linear/segmented	Icosahedral	No	yes
Deltaviridae	ss circular	Icosahedral	yes	unknown

The enzyme is RNA dependent RNA polymerase, * ambisense

Positive RNA viruses

Family	Genome	Capsid	Envelop	Enzyme
Retroviridae	ss linear	Icosa	yes	reverse transcriptase
Coronaviridae	ss linear	helical	yes	No
Togaviridae	ss linear	Icosa	yes	No
Flaviviridae	ss linear	Icosa	yes	No
Caliciviridae	ss linear	Icosa	No	No
Picornaviridae	ss linear	Icosa	No	No
Hepeviridae	ss linear	Icosa	No	No
Astroviridae	ss linear	Icosa	No	No

Viral Pathogenesis

- Viral pathogenesis is the process by which a viral infection leads to disease.
- The majority of viral infections are subclinical. It is not in the interest of the virus to severely harm or kill the host.
- The consequences of viral infections depend on the interplay between a number of viral (viral load, route of transmission) and host factors (Age, malnutrition, pregnancy, immune diseases…).

- Viral pathogenesis concerns itself with the mechanisms by which viruses cause injury to cells in different tissues and organs to produce the signs and symptoms of disease.

- Considering viral diseases, there are two components involved, the direct effect of virus replication and the effects of bodily responses to the infection.

- The vast majority of virus infections are silent and do not result in outward signs of disease.
- Inflammation, fever, headache and skin rashes are usually caused by the cells of the immune system due to the release of potent chemicals such as interferon and interleukins.

Infection Vs Disease

- INFECTION:–Entry of virus into the body, produces no symptoms or transient symptoms due to local irritation

- DISEASE:–Virus at Target organ, produces signs and symptoms associated with disease

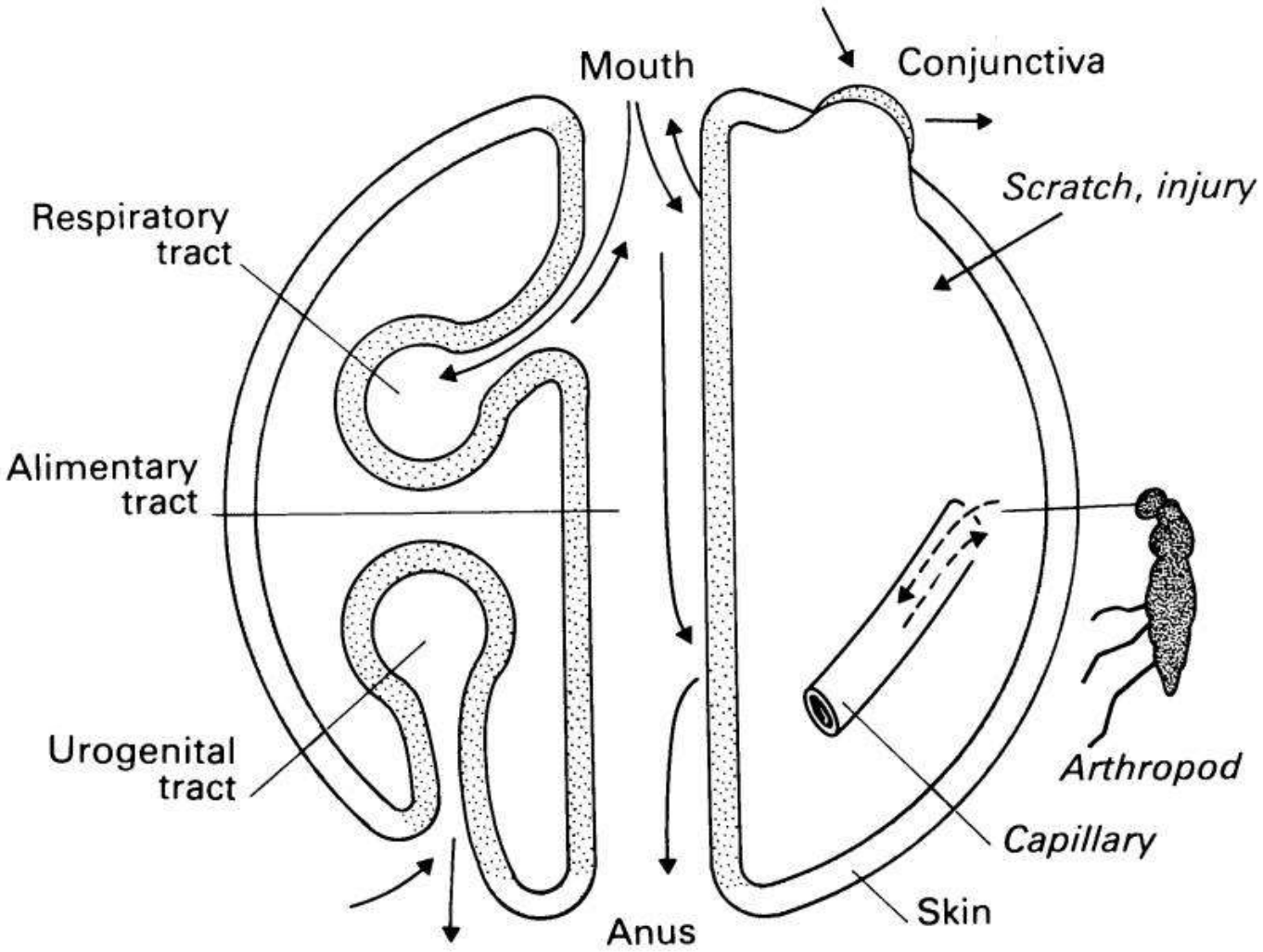
Viral pathogenesis

- Main Stages of pathogenesis:

1. Transmission and portal of entry.
2. Course of Infection (Primary site replication, Systemic spread/not all viruses, Secondary site replication/not all viruses).
3. Viral virulence factors and human Immune response.

- Virus Clearance or Persistence.
- Virus shedding and transmission.

Portal of entry and shedding



Transmission

The virus enters the body via different portals of entry, but where did it come from:

1. Person (directly or indirectly) to person
2. Animal to person (Zoonotic infections)
3. Reactivation of a latent infection within the same person
4. Arthropods borne

5- vertical (placenta, milk, perinatally)

Infection of host, viral replication and cellular effect

Infection of the host:

1. Localised infection at entry site e.g respiratory tract (common cold) > asymptomatic – severe symptoms.

2. Systematic infection:

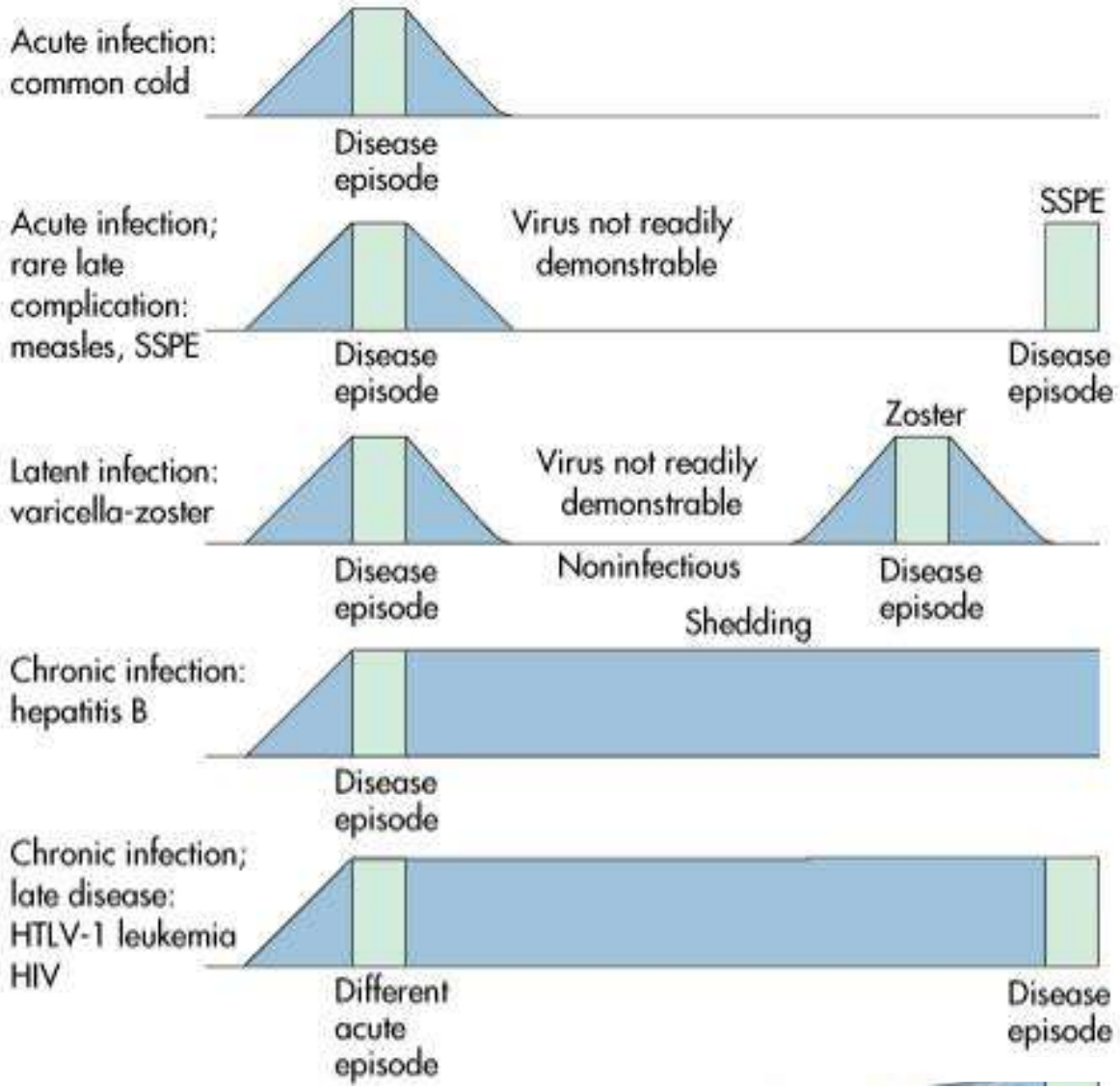
From portal of entry to blood stream/lymph nodes then to specific organs (tissue tropism<> cell receptors)

Phases of infection:

Incubation period > nonspecific symptoms > specific symptoms

- recovery from acute infection e.g common cold
- Latent (HSV) or chronic (HBV) infection
- A long silent period (persistence) before disease e.g. HIV, SSPE

Different patterns of viral infections



Cellular effects

1. No effect / recovery after production
2. Cellular Death
3. Malignant transformation > oncoviruses lecture
4. Other cytopathogenic effect such as

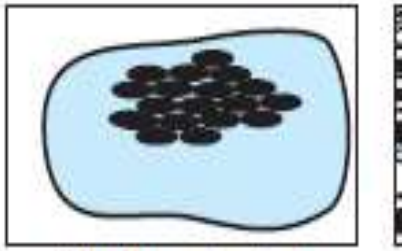
A. Inclusion bodies

- Inclusion bodies are nuclear or cytoplasmic aggregates which are stainable substances, usually proteins, and formed due to viral multiplication or genetic disorders in human cells
- These bodies are either intracellular or extracellular abnormalities and they are specific to certain diseases.

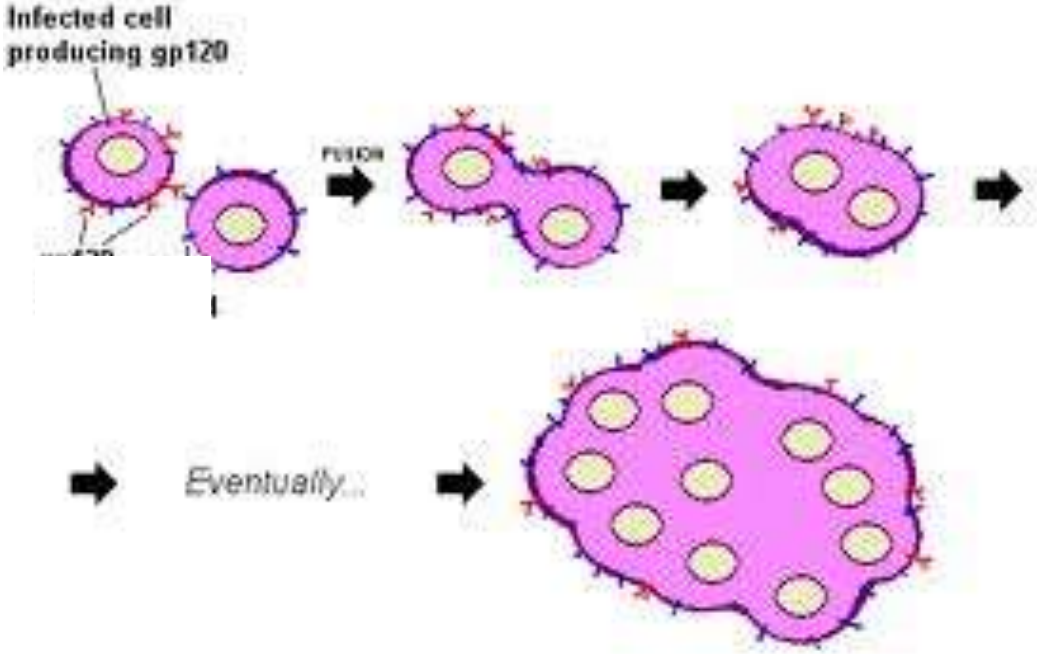
- Intracytoplasmic eosinophilic: rabies Negri bodies
- Intranuclear basophilic: owl eyes in cytomegalovirus

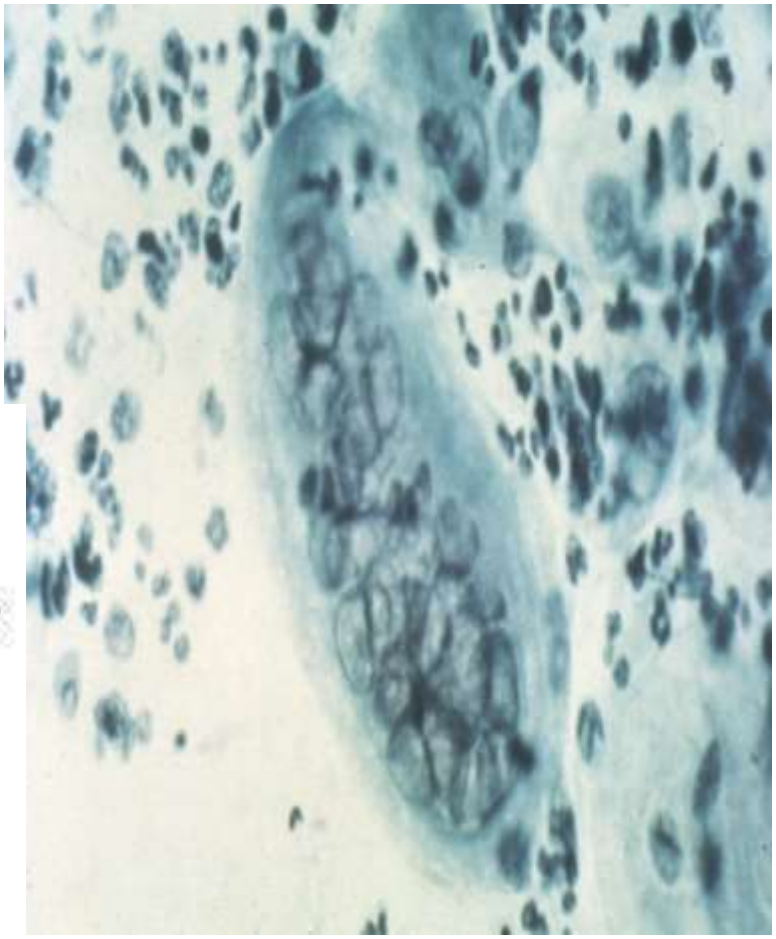
B. Fusion of many cells together:

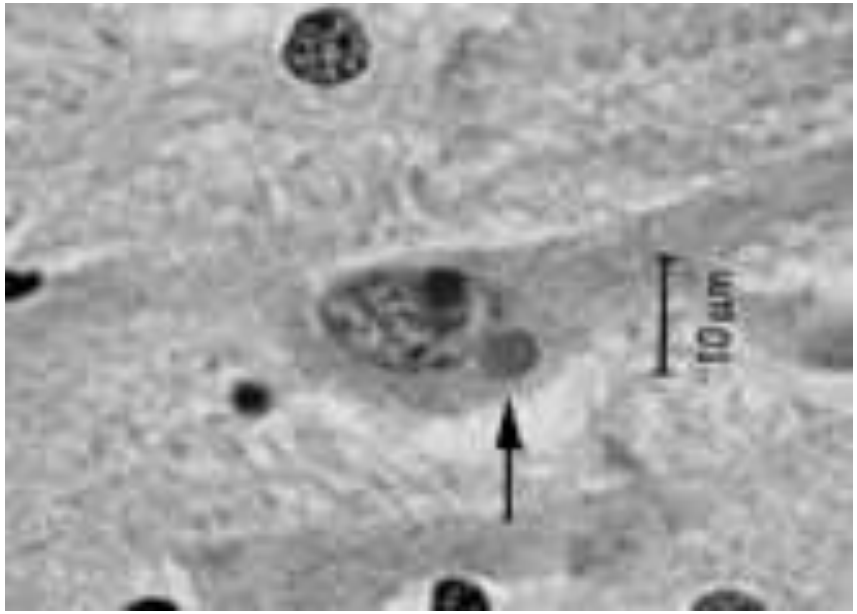
Tzanck cell or multinucleated giant cells as in herpes simplex virus (HSV) infection.



Multinucleated syncytium



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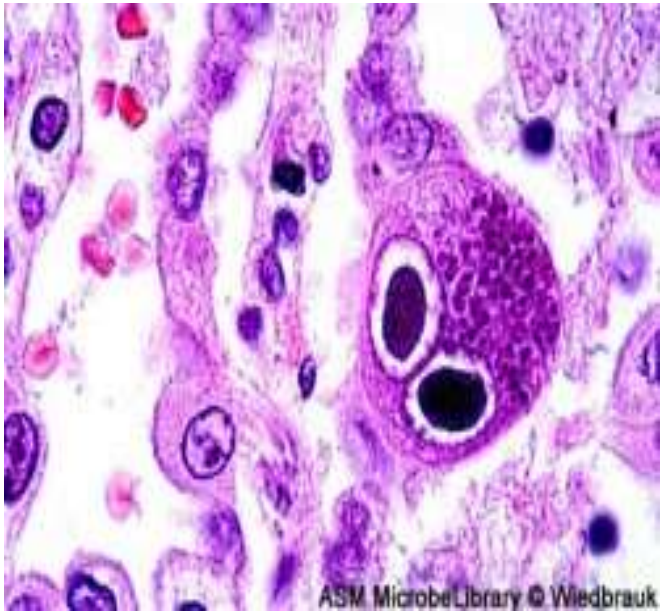
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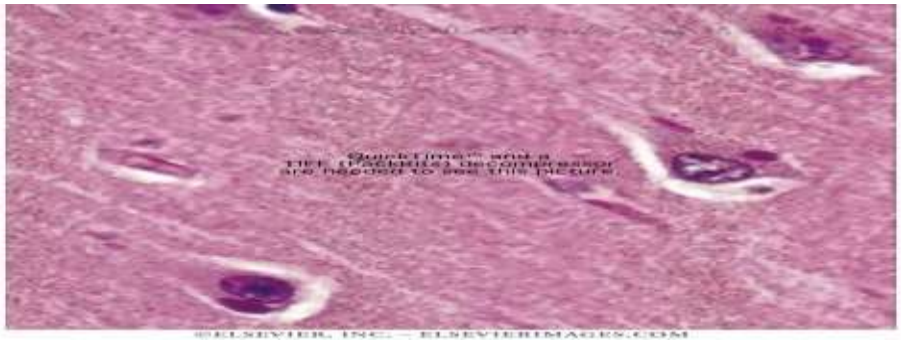

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