GENERAL VIROLOGY 3

Viral Pathogenesis - Host Defenses & Viral Genetics

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Viral Pathogenesis

- The process of disease production following infection.
- It may lead to clinical or subclinical (asymptomatic) disease.

Asymptomatic viral disease (subclinical infection):
stimulate humoral and cellular immunity.

Clinical viral disease:
- **Direct** or **indirect viral effects** (e.g. cytolysis, immunologic attack)
- Size of the **viral inoculum**.

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Viral aspects of pathogenesis:

1. Viral entry into a host (Transmission):

- Touch, saliva, air.
- Blood (insect, needle)
- sharing contaminated needles.
- Contaminated food and water
- sexual contact
- Insect bite.

2. Viral attachment proteins (VAPs):

- Interact with cellular receptor.
- Neutralizing antibodies.

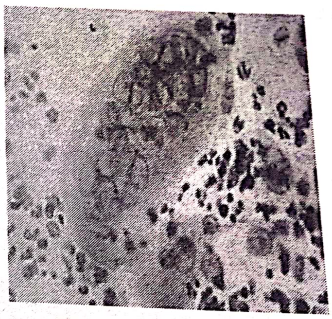
3. Viral virulence: * Genetically determined- ↓ with attenuated strains of virus. (weekend virus)

↳ influenza is so virulent

↳ as in vaccines

Cellular aspects of pathogenesis:

1. **Cellular receptor sites.**
2. **Target organ.**
3. **Cell tropism.** (specific cell for virus that can produce what the virus needs & enzymes so it can replicate)
4. **Cellular responses to viral infection**: may be **inapparent** or **may include:**
   - **Cytopathic effects:** virus-induced damage to the cell e.g. multinucleated giant cells as in herpes simplex.
   - **Cytolysis:** **Non-enveloped** viruses.

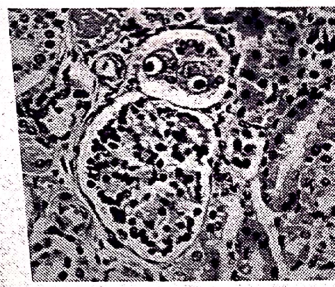


* remember & → enveloped viruses can exit without dangerous effect on cell & may produce persistant infection

* remember → Herpes simplex infects the cell by latent infection which needs ~~at~~ stress or immune problem to elicit it for progeny.
* EM is used to know which type of virus by identifying it's size & morphology but LM is used only to see multinucleated giant cells when staining (we can't identify type of virus cuz more than 1 type does cytopathic effects!)

- **Inclusion body formation:** **Intracytoplasmic eosinophilic**: rabies Negri bodies. **Intranuclear basophilic:** owl eyes in cytomegalovirus.

- **Transformation:** From normal cells into abnormal ones with properties of **cancerous** cells, **here the cell is not dead.**
  ↳ oncogenic viruses



- **Immune complex diseases:** Antigen-Antibody complex is produced that deposit in different places of body. as Joints
- **Interferon (IFN) synthesis.**
  ↳ resist viral infection

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Types of infections

1. Inapparent infections (subclinical disease):

- can cause immunity from further infections.
- virus inoculum is small. ➢ very small destruction → no symptoms!

2. Acute infections :

- **Short IP** (Ds/Ws). days - weeks
- **localized** or **disseminated.**
- **Recovery →elimination** of the virus.
- **Persistent** or **latent** infections may follow.

* localized : Respiratory system in Rhinovirus which causes Flu
* disseminated : more than 1 system
  ↳ viremia

• virus inoculum is large
↳ as in Hepatitis (persistent)
• ~~can be~~

3. Persistent infections: → virus replicate at low level
→ Hepatitis B & C
→ chronic infection

- Clinical symptoms ??. ↳ if virus replication ↑
- Carriers. → u can infect others although no symptoms appear
- High antibody titers for some antigens.

* liver enzymes increase cuz viruses are destroying cells!
* immune responce in blood

4. Latent infections: → as Herpis viruses
→ express antigens just to survive but immune system won't recognize it (no immune responce)

- Periodically reactivate → **recurrent disease.** ↳ when stress or immune deficiency

5. Slow infections: → as HIV (AIDS)
→ prion (Creutzfeld-Jacob disease)

- **Prolonged IP** (Ms/Ys).
- **No clinical symptoms** during **incubation** but can **produce some infectious agents**. until a limit of destroying cells

I can see it in blood & infect others ←

- **Chronic, progressive, fatal viral diseases**.

Also JC virus → multifocal leukoencephalopathy

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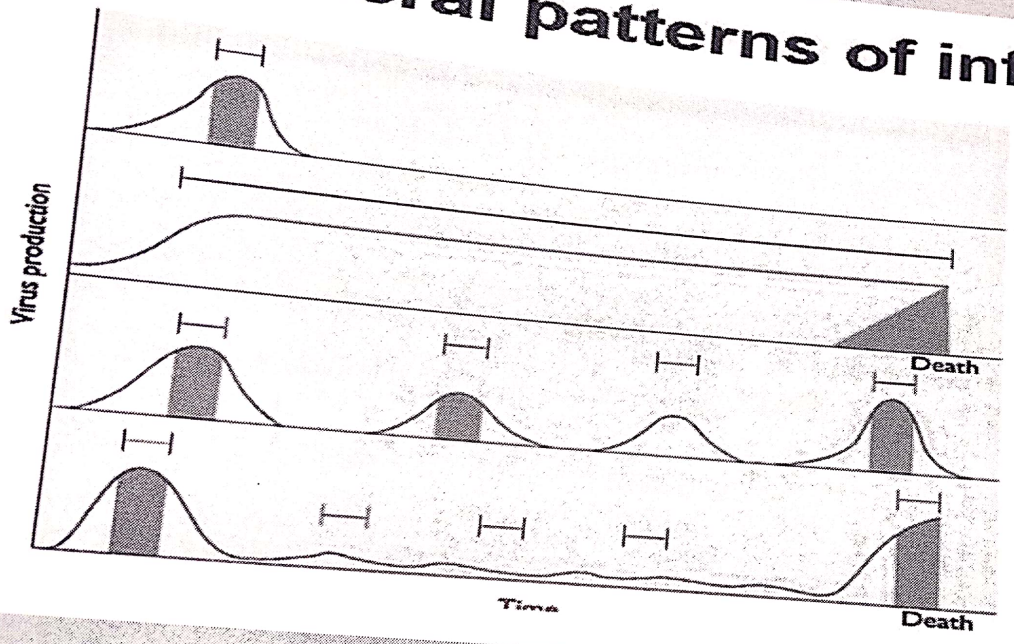
General patterns of infection



Acute infection
- Rhinovirus → cold
- Rotavirus → diarrhea
- Influenza virus

Persistent infection
- Lymphocytic choriomeningitis virus
- Hepatitis B, C

Latent, reactivating infection
- Herpes simplex virus

Slow virus infection
- Measles SSPE → Brain
- Human immunodeficiency virus (HIV)

From Flint et al Principles of Virology

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Host defense mechanisms

Nonimmune defenses:

1. **Innate immunity: anatomic** and **chemical barriers.** ↳ skin
2. **Cellular resistance: non-permissive cells.**
3. **Inflammation.** → ↑fever (Anti virals) → not suitable for virus (low pH)
4. ***IFN: inhibits viral replication.***

Mutations

Types of mutation:

Point mutation ---- **Deletion** ----- **Frame shift** mutation.

* Examples phenotypic changes seen in virus mutants:

- Attenuated mutants. → weakend, used in vaccines
- Antigenic variants. → influenza
- Drug resistant mutants. to certain treatment
- Conditional lethal mutants. → temperare sensitive mutants → done in influenza vaccines
- Defective interfering particles.
  ↳ needs a helper!!

ما بياجع أغلبه

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INTERACTIONS BETWEEN VIRUSES

- **Recombination/ Re-assortment.**
  - ↓ DNA viruse
  - ↓ sigmented RNA viruses
- **Complementation.**
- **Phenotypic mixing.**

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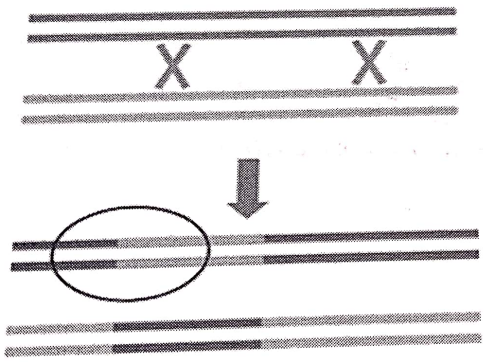
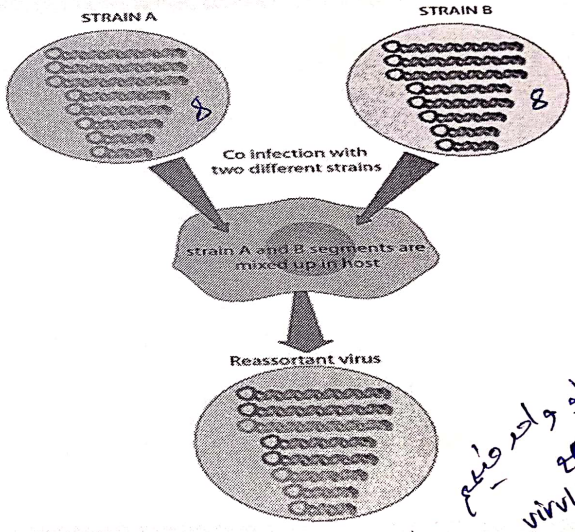
Classic recombination

Common in DNA viruses



Reassortment



2 influenza

لو واحد فيهم virulent معين

Complementation: defective virus + helper

- **Interaction at a functional level NOT at the nucleic acid level.**
- It can occur when either **one or both of the two viruses** that infect the cell have a **mutation** that results in a **non-functional protein**.

Phenotypic mixing:

- If two different viruses infect a cell, progeny viruses may contain **coat components** derived from both parents and so they will have coat properties of both parents.
- **It involves no alteration in genetic material.**

reassortment عكس

بدلوا antigenic determinant,

فصار ممكن يعيب اشتد اكتر بعد أصلا ما دام جيناته ما تغيرت ~~ما تمكنت توزع~~ بعد ما يعمل uncoating ما يدخل الخلية الجديدة ٥ يرجع يعيب نوع واحد لو كان صار طيور وانسان برجع طيور بس

phenotypic masking ٥ تغيير وتبديل كامل بين الفيروسين بالـ coat