MICROBIOLOGY (Virology)

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Routes of entry

- Skin — For example: Human papillomavirus
- Respiratory tract — For example: Influenza virus
- Gastrointestinal tract — For example: viruses that cause gastroenteritis, norovirus, some hepatitis viruses (Hepatitis A&E)
- Genitourinary tract — For example: the viruses that causes STDs, some types of the HPV
- Conjunctiva — For example: adenovirus or herpes simplex virus

Skin

- May be penetrated by viruses as a result of
  - mechanical trauma (HPV,HIV, HSV, HBV, poxvirus)
  - by injection (HBV, HIV)
  - by the bite of an infected mosquito (arboviruses)
  - by the bite of an infected animal (rabies)

- The trauma may not be seen by the naked eye-

– for example a health worker dealing with a Hep B or HIV patient, and after taking a blood sample, unintentionally, injuring themselves by the needle, that's why recapping the needle is unacceptable -

- Generally, viruses do not multiply locally but are carried away from site of infection:
  - by bloodstream (HBV, arboviruses)
  - or migration along nerves (rabies)

– until it meets its target cell-

-retrograde axonal transport-

- **Respiratory Tract**
- **Major route of invasion:**
- For viruses causing local respiratory infections
  - influenza, RSV, rhinoviruses

- Others causing asymptomatic initial infection then generalized spread
  - measles, mumps, chickenpox, enteroviruses

(or enter through the respiratory tract (portal) but their manifestations (and target cells) aren't in the respiratory system, ya3ni affects other parts/systems)

- Transmission usually by droplet infection in aerosols

(large and travel short distances)

(small and travel longer distances).

- ***Gastrointestinal Tract***
- Entry via GI tract may involve
  - local infection (rotavirus, coronavirus, adenovirus) or
  - invasion of the host to produce systemic illness (enteroviruses, hepatitis A)

Local infection : causing gastroenteritis
(the coronavirus might infect the GI tract of animals)

Enter via the GI tract until it reaches its target cells
e.g. Poliooviruses target nerve cells
Hepatitis A infect hepatocytes

- Virus survival depends on:
  - acid stability
  - resistance to bile salts
  - inactivation by proteolytic enzymes, in some cases a requirement!

For example we have rhinoviruse, same family as hep A but it can't reach its target cells because it can't survive the acidity of some parts of the GI tract

- Mostly non-enveloped

Generally speaking , non-enveloped viruses are more resistant and can tolerate the harsh environment of the GI tract

- ***Genitourinary Tract***
- Tears or abrasions of mucosa allow viral entry

- Sexually transmitted viruses
  - HIV
  - herpes simplex (mostly HSV II)

Even though HSV I can infect the genitals

  - papillomaviruses (genital warts)
  - hepatitis B virus

And sometimes hepatitis A, among homosexuals

- Nature of cervical mucus, the pH of vaginal secretions and the chemical composition of urine all play a role in host defense.

*Explanation of the last point in the previous slide

We don’t onky talk about the female genital tract, it includes males, for example, HIV can be transmitted through the anal mucosa. Not that only ! The probability of HUV being transmitted via the anal mucosa is much higher since its tighter and more susceptible to tears.

Localization versus systemic spread

In all the following, the infection is localised (no systematic spread)

Initial replication

- Many viruses multiply in epithelial cells at site of entry, produce a spreading infection then are shed directly to the exterior

- Respiratory infections – influenza, rhinoviruses and RSV
- Gastrointestinal infections caused by rotaviruses
- Dermatologic infections of the papillomaviruses

- Targeting of viral budding to apical or basal surfaces of polarized cells may define subsequent spread

- Baso-lateral budding(Rhabdo and Retroviruses)

- Apical budding (Orthomyxo and paramyxoviruses

Viruses that do apical budding go into the cavities of the organ they replicated in (causing a local infection) but for those that do a basolateral budding, they end up in the blood stream and infect other organs/tissues

Spread

- **Cell-to-cell**.

- **Blood stream**:- free or cell associated viremia.
  Primary Vs secondary viremia.

For example, chickenpox virus infect the respiratory tract then go into the blood stream (primary) then go to the secondary lymphoid tissue causing an infection then AGAIN into the blood (secondary)

- **Neural spread**: - usually preceded by primary viremia but may be direct (rabies).

Cell and tissues tropism is a major determinant of spread.

The presence of the virus receptors on cell surfaces determine its spread

- After traversing the epithelium and its basement membrane at the body surface, invading viruses face multiple tissue and cellular defenses The immune system
  - enter directly into blood stream (arboviruses)
  - initially taken up by the lymphatic system

- Viruses may also enter directly into peripheral nerves (rabies)

- Invasion of mucosal tissue and subsequent spread by the bloodstream results ultimately in the infection of particular target organs

- Incubation period ends with the onset of symptoms

The incubation period: is the period between being infected by the oathogen and the occurrence of the symptoms, for example, for Covid19 it's 2-14 days and in average 5 days[depending on the amount of virus one has been infected with (infectione dose] and the strength of the immune system]

  - from a few days (localized infections – paramyxoviruses

  - to a few weeks (systemic infections - chickenpox, hepatitis A)

  - or years (chronic, persistent and "slow" viruses)

VIRUS SHEDDING AND TRANSMISSION

- **Horizontal:** From host to host of the same generation

  1. **Direct:** host to host by contact
     - skin lesions – papillomavirus
     - saliva – rabies, mumps, CMV, EBV, HIV
     - mechanical trauma – HIV, HSV
     - aerosols - influenza, measles, rhinoviruses

  2. **Indirect:** host to fomites (food, water, needles, vector-mediated) to host - hepatitis A, polio, hepatitis B and yellow fever

Not sure about that

- **Vertical:** From host to progeny

- Congenital transmission (Rubella, Cytomegalovirus, HIV) The agents are TORCH , بنعرفهم بعدين😝

1. **Transplacental:** CMV, parvovirus B19 cross the placenta and can cause fetal infections

2. **Perinatal:** infection with HIV or HSV can occur during birth (during passage of infant through birth canal)

3. **Via breast milk:** breast milk can serve as a vehicle for transmission of HIV1 and HTLV1

The course of virus infection

- **Abortive Infection**

The host cells are un able to complete the replication of the virus or induce infection

- A virus infects a cell but cannot complete the full replication cycle (non- productive).
- May result in transformation
- **Acute infection**
  - The virus is usually eliminated by the immune system.
  - Brief infection but may have a lasting effect (VZV).
  - Recovery with no residual effects
  - Recovery with residual effects e.g. acute viral encephalitis leading to neurological sequelae.
  - Death
  - Proceed to chronic infection

Explanation of the acute infection

1. After the replication of the virus, the immune system defend it so the symptoms occur only during the acute inflammation
2. Brief infection: we'll have symptoms during the acute inflammation, then it will end BUT the virus won't leave the body (latent)
3. Cured
4. Acute inflammation but then it can cause permanent consequences
5. Like covid19, in some cases
6. If the infection by certain viruses happened at a young age

Chronic Infection

- The converse of acute infection (prolonged and stubborn).

- To cause this type of infection, the virus must persist in the host for a significant period.

For example, hep B&C viruses can cause acute and <u>sometimes</u> chronic infections if it persisted in the host for more than 6 months

- In chronic infections, a limited number of cells are infected.

- These infected cells may demonstrate a cytopathic effect, synthesize virus macromolecules, and release infectious virus.

Persistent infection

- Continuous production of virus particles.

The difference between this and the chronic infection is that the body can eliminate the chronic infection eventually but the persistent will remain with the host during its whole life

- This infection results from a delicate balance between the virus and the host organism, in which ongoing virus replication occurs, but the virus adjusts its replication and pathogenicity to avoid killing the host.

- It differs form chronic infection in that in chronic infection the virus is usually eventually cleared by the host (unless infection proves fatal), whereas in persistent infection the virus may continue to be present and to replicate in the host for its entire lifetime.

- May trigger autoimmune injury.

Latent infection

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Very few viruses are expressed just to preserve the virus's existence in the host, until the immune system weakens or the cells get injured, it starts replicating and infecting the cells again

- Existing but not exhibited.
- This is The ultimate infection.
- In a latent infection, the virus is able to down regulate its gene expression and establish an inactive state (strictly limited gene expression without ongoing virus replication).
- They typically persist for the entire life of the host.
- Can be reactivated.

Further explanation of the previous point.

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For example, herpes virus, all of them cause latent infection.
Usually its primary infection is asymptomatic or if it was symptomatic, very few vesicles will be present on the skin and will disappear eventually but the virus remains in its latent state in the dorsal ganglia. Then when the immunity drop or the stress increase, the virus travels to the skin or the oral mucosa and starts replicating