Continuation of Pathogenesis

Outline and objectives:

This lecture is a brief continuation of pathogenesis, aka, how a virus causes a disease. After the sheet, there is a brief review of lecture 4 the doctor made.

1-Localized and generalized infection (how they happen and where)

2-Some target organs (examples)

3-Pattern of disease (Acute non-persistent, persistent with acute onset, chronic)

Types of infections:

1-Localized:

From its name, they are infections on the same site of entry.

Examples include: Skin, mucous membrane, and epithelial cells found in the skin and mucous membranes of the respiratory tract, genital area and conjunctiva.

1-Skin

For example, Warts.

Warts are caused by the Pox and Papilloma viruses. They might cause proliferative lesions leading to warts.

2-Mucous membrane of the respiratory tract, GI tract, and the urogenital tract. Here, the virus spreads quickly.

3-Conjunctiva

For example, the adenovirus can infect the conjunctiva, causing conjunctivitis.

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2-Generalized

The mechanism is quite vague (not clear), because:
1- we have no animal models
2- some viruses are very dangerous to handle and experiment on
3- it is difficult to grow a lot of viruses in the lab.
An example of a lab virus is the Pox virus in mice, which causes an infection called Ectromeila (not too important), can help in research.
* We must know the stages of generalized infection (see book for clear outline)

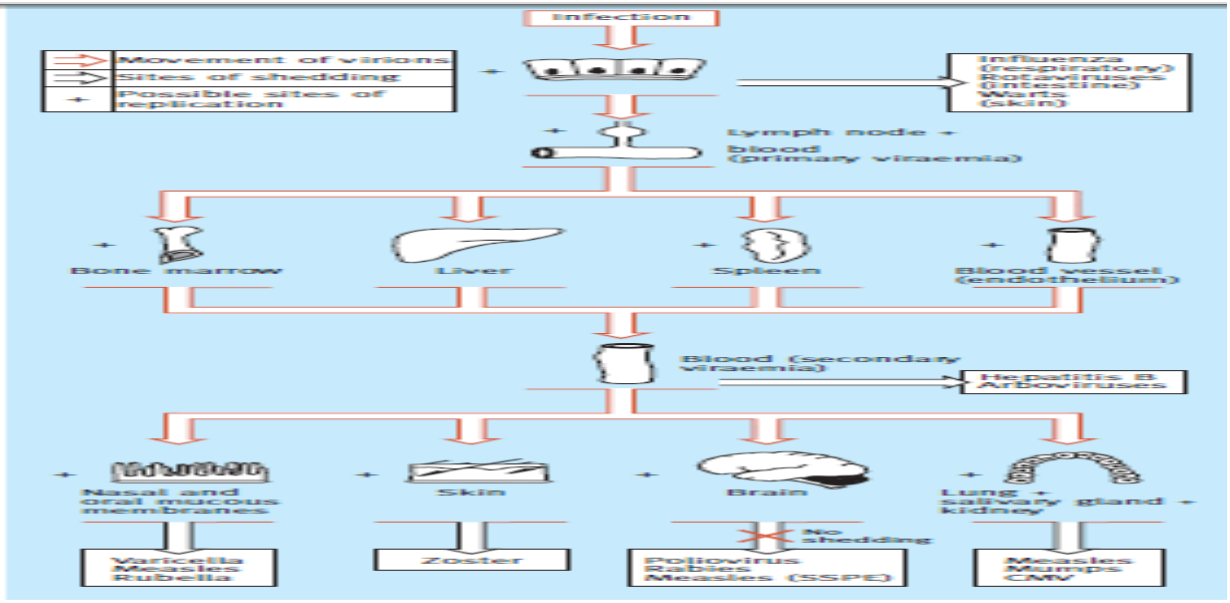


Fig. 4.5 Spread and replication of virus in a typical generalized virus infection. Modified from White D.O. and Fenner F.J. (1986). *Medical Virology*, p. 135. Academic Press, London.

First stage: Action of virus at the site of infection
Second Stage: The virus then moves to the lymph nodes (regional lymph nodes) Here, the macrophages are supposed to destroy the infected cells. BUT some viruses escape from the lymph to the 3rd stage, into the blood.
Third stage: Aka, **Primary Viremia**. In this stage here we have prodromal symptoms (non-specific, ordinary symptoms) like malaise (general discomfort and uneasiness), fever, tiredness, headaches, and loss of appetite.
Fourth Stage: the virus moves from the blood to a reticular endothelial organ (RES) like the spleen, liver, and bone marrow.
Fifth Stage: The virus goes back into the blood. This is called **secondary Viremia** (because it happened before). Some viruses are found freely

moving in the blood (like hepatitis), and some are found bound to the macrophages of the blood (like measles and cytomegalovirus which is a member of the herpes family).
From the blood, the virus heads towards the target organ

Target Organs:

For example, the skin is the target organ of the zoster virus (a member of the herpes family). It causes zoster shingles (الحزام الناري). Therefore, its tropism is to the skin.
Some viruses go to the brain, like polio.
In all of these target organs, the virus sheds itself from the organs, EXCEPT from brain. It can't be shed from the brain because the brain is a closed system.

What does shedding mean?

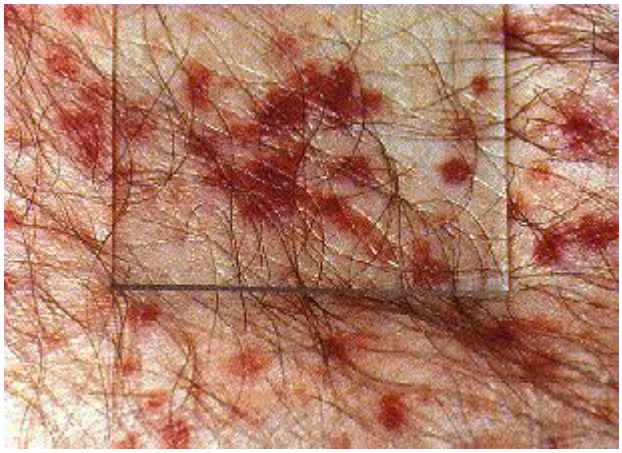
"**Viral shedding** refers to the expulsion and release of **virus** progeny following successful reproduction during a host-cell infection. Once replication has been completed and the host cell is exhausted of all resources in making **viral** progeny, the **viruses** may begin to leave the cell by several methods."

Shedding can occur in the respiratory tract, where the virus can be shed in droplets. It can also occur in the urinary tract, where they can be shed in urine.

We have two rashes caused by viruses, one outside and one inside.
1- Exanthem (ex for OUTSIDE) they're basically cases of rashes on the skin.
2- Enanthem occur on the mucous membrane, like in the throat and tongue.
Macules, papules, vesicles and pustule *What are they?* Skin lesions (abnormality)
But firstly, we should know that primary lesions are physical changes in the skin that are considered to be caused directly by viruses and disease processes.
1-Macule: They are mere flat discolorations of the skin. If you close your eyes and rub your hand over it, you won't be able to feel it. (not elevated)

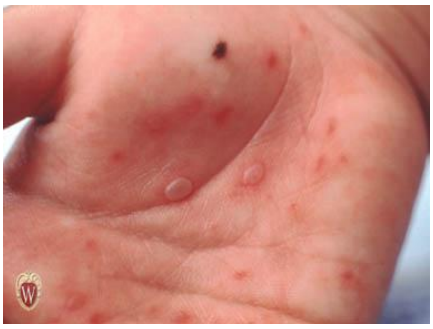
2-Papule: Raised solid lesions of the skin
3-Vesicle: Raised lesion filled with fluid. If you squeeze it, fluid comes out.
4- Pustule: Basically a vesicle (raised lesion of the skin), but filled with pus.

5-Purpuric rash: (purpura means purple, which is the rash's color). They are one of the most dangerous lesions. They are rashes caused by low levels of platelets in the body and bleeding. While pressing on it with a slide, it will not make it disappear.

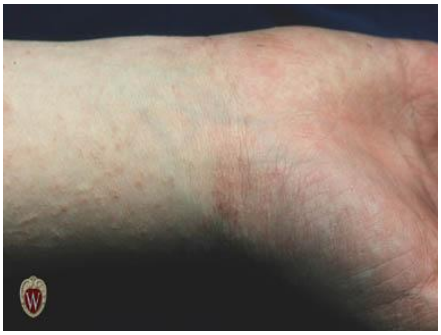


In the slides:

"What is this? Vesicle"



"What is this? Papule. "



"If it has pus → Pustule"

Other target organs:

-Lungs: they can be directly affected by viruses or indirectly as part of general infection (like in measles and cytomegalo)

-Liver: The target of hepatitis, or it might be a part of generalized infections.

-Brain: It is affected directly from blood. The virus in the blood can migrate to the brain by crossing the blood brain barrier (like polio) OR, it can migrate towards the brain via the peripheral nerves (like bites from dogs, i.e rabies, might migrate retrospectively from nerve to brain)

Pattern of Disease:

There are 3 patterns mentioned in the textbook:

Acute infection: rapid onset of disease, brief period of symptoms, recovery within a short period of time (a few days)

1-Acute Non-Persistent (Non-Continuous)

For example, getting influenza (acute) and being recovered (non persistent). These viruses are usually not fatal, but some viruses might cause complications.

For example Encephalitis (inflammation of the brain)

**DYK* Meningitis is inflammation of meninges, it differs from encephalitis.*

Encephalitis might be a part of the initial picture of some viral infections, like polio, which gives symptoms (in acute status) of encephalitis. Some develop it lately even after virus disappears (post infectious encephalitis, like in measles, mumps, and rabies)

2- Persistent Infection With Acute Onset

It is a continuous acute infection in the body. It goes in a straight line BUT every now and then we have cases of exacerbation (making bad things even worse-الطين بلة ing,زيد)
So it is acute AND persistent. Acute On Top of Persistent.
These infections can be latent (latency is when the virus hides)
Some viruses, once they infect you, they will directly (within course of infection), go and hide in your body (like in the nerves and the ganglions of nerves).
They will hide there and stay latent. They usually integrate themselves into the host DNA, so they must be DNA viruses (or they won't integrate). They can also be the RNA Retro viruses (ex HIV), because they have the special reverse transcriptase (RT). The RT makes them DNA so it ultimately does the same thing as DNA viruses.
They can stay episomal (as closed circular DNA molecules, separated from the host **chromosome*,** but it can be then integrated or replicated). or integrated with the host DNA.

* It has been written: "separated from the host **nucleus**" but the correction see that it's more accurate to say: "separated from host **chromosome**", and here is the

* Correction Note: Episomal latency refers to the use of genetic episomes during latency. In this type, viral genes are stabilized floating in the **cytoplasm or nucleus** as distinct objects.

During latency, there are no symptoms. The virus hides until it is reactivated. **Reactivation** can occur due to the immune system becoming weak as a result of stress, malnutrition, trauma, or another infection. (البس بحارته أسد)
For example, the cold sores of herpes come. The virus then hides in the trigeminal ganglion. At this point you are cured from the cold sores. However, later on, it can come back when we are stressed. Like before taking a test, we don't eat or drink well. The immune system is weakened, and it is here that the virus will replicate and return once again to result in vesicular lesions in the same area.

So that was latency reactivation. Latency is **asymptomatic**; however in reactivation it will be **symptomatic**.

*Latency might increase the rest of malignancy of malignant changes and the development of malignancies.

3-Chronic, persistent infectiousness:
These infections are due to defects in the immune system, where the virus is continuously produced (Unlike persistent acute onset where it is hidden and then replicates only when suitable for the virus.) So here we have continuous reproduction of virus. This means the virus doesn't have to be a DNA virus. It can be DNA or RNA. Examples include chronic active hepatitis and SSpe. Chronic active hepatitis is caused by chronic hepatitis virus. The virus is there and replicates, but there might be some activation.
* Papilloma virus which causes warts might integrate into host genome and cause some malignancies.

Lastly, **4-insidious infection with fatal outcomes**,
Insidious (*slow, cunning, and lethal*) but the outcome is fatal.
For example, Prions causes Crutzfeld-Jakob disease CJD and in animals.
These infections will take years and end with death.

The rest was a recap and student questions for lecture 4, since this lecture was the last lecture before the midterm. Read it before the final if you want to review.

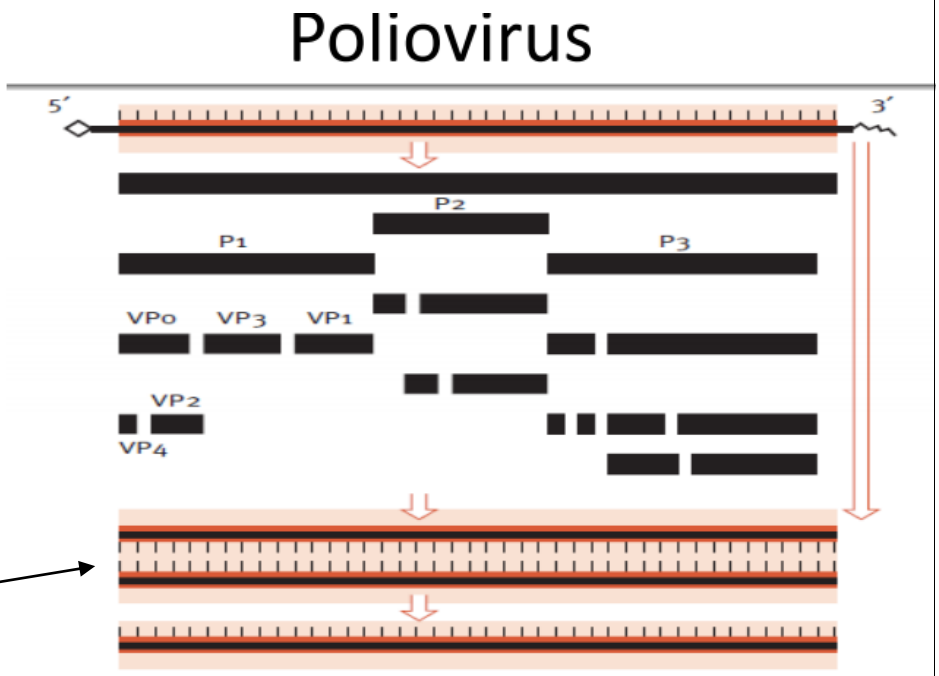
Recap of lecture 4 life cycles and FAQs.

The doctor say that the figures are not enough, you must try and analyze.

Polio belongs to picorna It has a positive RNA, and it is not enveloped. As we know, naked viruses lyse cells (most of cases). It will attach to receptors on cells, and then becomes internalized (if non-enveloped viropexis) Then, it uncoats itself inside the cell in the eclipse phase. The eclipse phase ends at assembly. (So from uncoating to assembly, we are in the eclipse phase; here we cannot see virus under microscope, and it is non infectious.) Then we have replication, which is in between the eclipse and assembly phases. Assembly is when viruses comes together. This can occur at more than one site, some in the cytosol and others on the membrane. As we know, positive should come out positive. The virus comes in with its parts and must leave with them.

Once it comes out, the post maturation modifications take place.

During polio replication we have positive, negative, positive (this is the common theme/pathway). So positive is treated as mRNA because it's positive, doesn't need an enzyme. It translates some proteins, some of which are enzymes. We have early and late proteins. SO it will be translated and then spliced (for example, particle 1 spliced into 3 particles). The positive RNA is copied into negative. They (+ve and –ve) are bound together, because if they weren't the cellular proteases would break it. It is now available as a positive strand and a negative strand, which we call the **intermediate** double stranded RNA



molecule; this is just a transitional status to protect itself. The negative will be made into more positives, then the positive will either be made into protein or go into the offspring. (The original positive strand is used for protein translation while the other produced copies are used for early and late proteins and to go out with the virus).

Rabies.

It is a negative RNA virus, which becomes positive, then binds to negative to achieve intermediate status. Here we have no extensive cleavage of proteins.

Miscellaneous (random) notes

- Influenza is an enveloped virus

-Don't throw away needles in basket. The waste basket is only for non medical waste. Instead, use the sharp bin for medical waste.

-How are capsomeres attached to receptors?

When virus is naked, it has no spikes. But the capsid is not straight; at nano-level some areas are sinuous and overall its conformation is well fit to receptors.

-Influenza is orthomyxo, and parainfluenza is from paramyxo. These are two completely separate families.

So we have two types of influenza, but they have common symptoms.

-Influenza differs from the common cold الرشح (common cold doesn't have fever, etc.)

- Influenza and parainfluenza are both enveloped.

-Not every HIV patient has AIDS, but every AIDS patient has HIV.

-latency only occurs in DNA viruses and RETRO

And that concludes this sheet :)
Dedications to caramel, cause its delicious, and then _____ (just fill in your name)
Midterms came and passed. Some excelled and some didn't. For those of us who didn't, we have a month and half to find out why, and FIX it. Good luck always.

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