University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Introduction to

Microbiology

Title :

Virology

Professor:

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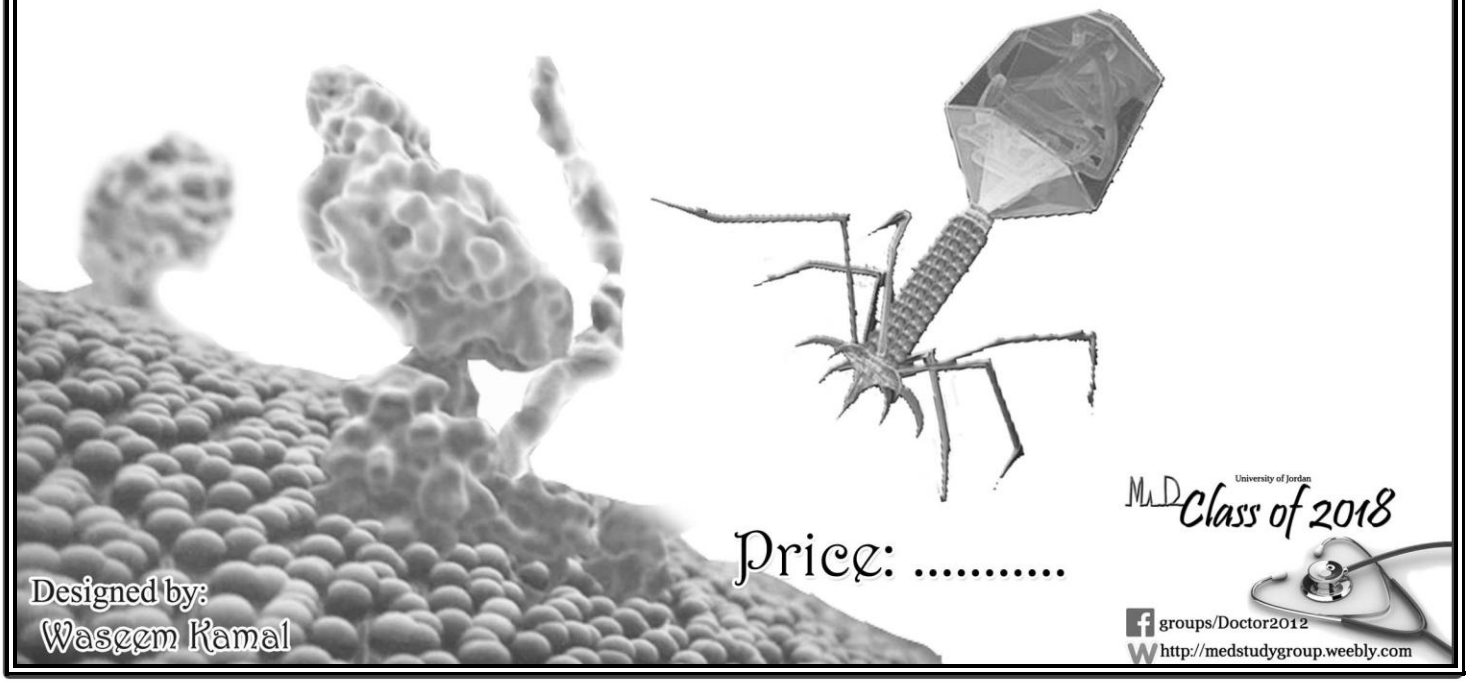
: 6

- ○ Slides
- ○ Handout
- ● Sheet

Done by: **Alaa Abu Dayeh**



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Last time we gave an introduction about viruses, we talked about; definition of viruses, characters of viruses, structures of viruses and classification of viruses.

One of the classifications was if the virus is enveloped or naked.

For the enveloped viruses:

• The envelope is obtained by **budding** through a cellular membrane, as a general rule when we talked about envelope, it's gained during the exit of the virus through the cell and it's taken from the cellular membrane.

But there is an **exception**:
some viruses acquire it's envelope from **Golgi apparatus** -not from the endoplasmic reticulum- or from **the nuclear membrane**. (It's our duty to find which viruses acquire their envelope from Golgi apparatus and which acquire it from the nuclear membrane. This might be a quiz for us next time or the time after, as the doctor said).

*__Possibility of exiting the cell without killing it:__
Q: What is the fate of the cell that the virus takes this small bit (the envelope) of its membrane?
Ans: At the beginning most of the cells tolerate that to a certain extent, and after that the final fate of the cell, depending on the type of the virus and the production of many viruses, is **death**.

• Contains at least one **virally coded protein**.

Q: If the virus acquires it's envelope from the cellular membrane, then why doesn't that help the virus to evade the immune system by pretending it's one of the body cells?

Ans: Because the envelop contains virally encoded proteins, so in the virus's gene these virally encoded proteins, which we called **spikes or glycoproteins** , are present on the surface and imbedded within this envelope, and these proteins are the most immunogenic structures in the viruses, so the immune system knows, identifies and targets the viruses through these structures.

- So we can say that these structures are **fingerprints** for the viruses at the level of the immune system.

- These virally encoded proteins help in the **attachment** of the virus with the receptors on the host target cell.

- Loss of the envelope results in **loss of infectivity**. This is true for the enveloped viruses **only**.

How do naked viruses differ from enveloped viruses in their properties?

1. **Stable in hostile environment.**
   In general they tolerate more harsh and difficult situations in the environment than the enveloped viruses.
   Both of them are made of proteins either glycoprotein (envelope protein) or capsid protein, but the capsid protein is stronger and more resistant to the environmental conditions.
   Not damaged by drying, acid, detergent, and heat.
2. **Released by lysis and death of host cells.** While enveloped ones take a part of the cell membrane. Some viruses might exit the cell by **exocytosis**.
3. **Can sustain in dry environment**
4. **Can infect the GI tract and survive the acid and bile**; most viruses that infect the GI tract are naked viruses.
5. **Can spread easily via hands, dust, and fomites** أداة عدوى(Fomites: things that the patient uses in directly contact with, like hand towels, mugs, etc.)
6. **Can stay dry and still retain infectivity**
7. **Neutralizing mucosal and systemic antibodies are needed to control the establishment of infection.** In a way that is similar to the enveloped viruses. In order to control the infection, you need to stabilize the effect of naked viruses.

Refer to slide #46:

These are some types of naked viruses, most of them, the primary root of infection is through the GI tract, because as we said they can tolerate the high acidity of the stomach.
RNA reverse transcribing viruses that start with RNA and reverse transcribe it to DNA.
An example of RNA reverse transcribing viruses are **HIV virus** and **retrovirus**.
DNA reverse transcribing viruses that start with DNA (This is an exception; we will talk about it in details when we talk about hepatitis viruses, this is the hepatitis b virus which has a partial dsDNA genome, then the partial dsDNA becomes complete and it enters the replication stage).

Refer to slide #47:

All viruses must produce mRNA, or (+) sense RNA, then it goes to ribosome and starts translation.
A complementary strand for nuclei acid is (-) sense.
Q: what do we mean by complementary strand?
Complementary strand: has the complementary (المكملة) nucleotides for the basic strand.
Q: AUG is a code on RNA, what is the complementary of it?
UAC.
<u>Just to remember:</u>
A, U, G, C these are **nucleotides**

3 nucleotides give **codon**
Each codon represents **one amino acid**
A number of amino acids give **one polypeptide** which might give us a **protein**, or a number of polypeptides give a protein.

Refer to slide #48:

Parvo virus is one of the smallest viruses known; it's totally dependable of the cellular machinery for replication.
Lenti virus is a subgroup of retro viruses.

Sub-viral agents

Sub-viral agents: small structures that might mimic viruses in behavior, infecting cells.

1)Satellites

- Contain nucleic acid
- Depend on co-infection with a **helper virus** (difference between satellites and viriods).
  So it can't infect any cell except in the presence of another virus.
  Example: hepatitis D virus can't infect any cell except in the presence of hepatitis B virus, so again the cell had to be infected by hepatitis B virus then hepatitis D virus might come and either develop co-infection (both viruses come together) or super infection (infected by hepatitis B after a while - because of a drop in the immune system- hepatitis D comes).
- May be encapsidated (satellite virus)
- Mostly in plants, can be human e.g. hepatitis delta virus
- If it contains only nucleic acid we call it a **virusoid**.
  If it has other structures, proteins and enzymes we call it **satellites**.

2)Viroids

- Unencapsidated, smallest pathogens, **small circular ssRNA** molecules that replicates autonomously.
- Only in plants, e.g. potato spindle tuber viroid.
- Depend on host cell **polymerase II** for replication, no protein or mRNA.
- They are obligate intracellular parasites
- Viroids are very short 200-400 nucleotides, with a rod-like **secondary** structure.
- They do not encode any proteins, they don’t depend on the presence of another virus.

In their replication they utilize cellular RNA polymerase.
Their replication is performed by **“rolling circle mechanism”;** once the cellular RNA polymerase attaches the single strand of the circular RNA, it starts generating new multiple new copies of circular RNA. This mechanism is **continuous**.

3)Prions

•No nucleic acid
• Infectious particles entirely made of proteins ex.BSE (Bovine spongiform encephalitis).

The most widely accepted theory is that Prions are made of proteins only. This fact is still debatable till now. But there are other theories that are being investigated.

These theories are based on the basis that the nucleic acid is in **the central dogma** of a living cell; the explanation is that the nucleic acid is a code, and everything in relation with the living cell is built on the code, so nucleic acid has genes that code for structural and non structural proteins and the idea of replication and generation is built on it.

•High heat resistant
•Animal disease that affects nervous tissue
•Affects nervous tissue and results in: 1)Bovine spongiform encephalitis (BSE) “mad cow disease” 2) scrapie in sheep 3) kuru 4) Creutzfeld-Jakob Disease (CJD) in humans

In human there are four diseases that are caused by prions:
1) Kuru **2)** CJD **3)** GSS (Gertmann-Straussler-Scheinker)
4) FFI (Fatal familial insomnia).

*Hepatitis B Virus

It's a chimeric molecule, half viroid and half satellite. It shares some characteristics of satellites and some characteristics of viroids.

- **Viriod like properties**: **1)** Rod like RNA molecule **2)** Rolling circle replication **3)** Self cleaving activity

- **Satellite like properties** : **1)** encodes proteins which is necessary for replication **2)** depends on presence of other viruses **3)**genome larger that viroids

*More details about prions:

* The name "Prion" comes from “Proteinaceous **in**fectious particle, analogy for virion"
But they but the "I" letter before the “O" letter.

They are **proteinaceous transmissible pathogens responsible for a series of fatal Neurodegeneration diseases in human.

***Prion is a type of infection agent that doesn't carry the genetic information on the nucleic acid.

**** Prions are proteins with the pathological conformation that are believed to infect and propagate the conformational changes of the native proteins into the abnormally structured form.

Explanation of this point: prion protein is present in our body (especially in the nervous system). We might get some genetic mutations, some people inherit this ability of genetic mutations, and this changes the prion from normal cellular protein into the infectious and pathologic protein.

How do we get prion's diseases?

1) Sporadic 85%

- In sixth or seventh decade, rapid progress.
- A gene with spontaneous mutation, during replication of normal CNS cells, they might change from normal into abnormal or pathologic form.
- Example of sporadic diseases: CJD.

2) Familial (inherited) 15%

- Mutations in the **PrP gene**.
- The prion protein which present in the body (in the CNS we) called it PrP^{C}, it's the normal form (c from cellular).
- PrP^{Sc} it's the pathologic form (Sc from Scrapie)
- In elder there is a tendency of transformation from c form into sc form.
- Example: fatal familial insomnia.

3) Transmissible (rare)

- Propagation of Kuru disease in Papua New Guinea native (ritualistic cannibalism)
- In New Guinea, at the beginning of the 1900's, if they want to mourn someone, they open his head, take his brain and eat it. After the discovery of prions, it became known as one of the causes of the disease and they stopped this habit. So Kuru disease dropped dramatically in New Guinea native.

Transmissible Spongiform Encephalopathy (TSE)

Also known as **prion diseases** are a group of progressive conditions that affect the nervous system of many animals and humans .They are transmitted by prions.
Pathology » neuronal loss, astrocytosis, spongiform change and amyloid plaque formation.
Clinical signs » loss of motor function, depression, insomnia, confusion and personality changing.

Definitive diagnostic test » biopsy of brain tissue, which shows the presence of PrP^{Sc} in CNS.
There is no cure.
The illness progresses in a short period of time, within months to a year the patient might die.

- The structure of PrP^{C} (The normal prion protein) is mainly composed of α helical structure with two short β sheets .
- The structure of PrP^{Sc} (The abnormal prion protein) is made mainly of β sheet with small amount of α helical structure, this leads to **misfolding** of the protein, changing in its structure making it nonfunctional, so it aggregates in the CNS, and makes vacuoles. So, it loses its biological function and becomes toxic.

Replication cycle in prion

In the presence of Normal protein in the body, once there is a mutation (endogenous source or exogenous source such as eating meat or cannibalism), then when PrP^{C} comes in contact with $PrP^{Sc,}$,PrP^{Sc} transforms it into PrP^{Sc} (It's not an infection , the process of attachment, between normal and abnormal proteins, is responsible of the conversion of the normal protein to the abnormal protein).
This leads to spread of the abnormal protein to the neighboring cells, and becomes biologically nonfunctional and aggregates in the CNS.

This is a comparison between normal and abnormal prion proteins:

Normal(C protein)	Abnormal(Sc protein)
Cellular	Scrapie
Digested by proteases	Resistant to digestion by proteases .
Has dominant secondary structure (αhelix)	Has dominant secondary structure (β sheet)
Soluble	Insoluble (aggregates)
Monomeric	Multimeric

If we add protease to the prion gene, it will be broken. If we add nucleases (which digest the nucleic acid) to it, it doesn't make any difference and that supports the widely accepted theory that prions are made of proteins only.

Important point about prions:
Prions don't induce any immune reaction (the immune system doesn't respond) or any inflammatory reaction.

- Not everything in the slides is written here, so please **check the slides**.

BEST WISHES ☺