**Lecture : VIRAL PATHOGENESIS**

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**OBJECTIVES**

**By the end of this lecture, the student is expected to be able to:**

1. Know the definition and levels of viral pathogenesis.
2. Types of viral infections at cellular level Which include:

 1. Abortive infection (no effect)

 2. Productive infections

 a - Cytolytic (cytopathic effect (CPE))

 b - Noncytolytic (No, or Mild CPE)

 3. Non productive infection

 a- latent

 b- Transformation

1. Know example of viruses causing different CPE e.g. Owl's eye inclusion bodies caused by CMV**.**
2. Know the different route of entry and mode of transmissions.
3. Know the mechanism of virus spread through the body.
4. Differentiate between localized and systemic infections and giving examples.
5. Understand the immune response to viral infection which include innate (nonspecific) immunity and specific immunity (humoral and cellular immunity)
6. Know the stages of viral infection.
7. Know the different types of viral infections with the example of viruses.

**BACK GROUND:-**

Viral pathogenesis refers to the complex interaction between viral and host factors that lead to the disease production.

The ability of viruses to cause disease can be discussed on two distinct level:

 1. The changes that occur within individual cells and

 2. The process that takes place in the infected patient.

Host defense against viruses fall in to two major categories:

 1. Nonspecific, of which the most important are interferon and natural killer cells.

 2. Specific, including both humoral and cell-mediated immunity.

**KEY PRINCIPLES TO BE DISCUSSED**

* Viral pathogenesis means how virus can produce the diseases, which can be discussed in two levels; cellular level and host level.
* The interactions between the virus and the cells within which it replicates, are of importance in determining whether infection takes place at all and the type of infection.

It is possible to divide these in to three categories.

1. Viruses that infect cells but which do not complete the replication cycle. Thus infection is called abortive.

2. Viruses the infect and replicate within cells causing the cells to lyse, when the progeny virions are released. This is called a cytolytic cycle. The infection is productive and host cell and cell culture demonstrate cytopathic effects such as inclusion bodies and syncytium.

 In some instances, viruses are produced from infected cells but the cells are not killed by the process. and the infection is productive but non-cytolytic.

3. Viruses that enter cells but are not produced by the infected cell. The virus is maintained within the cell in the form of its genome. The infection is non-productive. Occasionally this type of interaction induces cell transformation. In other cases a latent infection may result.

**Pathogenesis** in the infected patient involves transmission of the virus and its entry in to the host, replication of the virus and damage to the cells, overcome the local defense. The viruses may remain localized to the primary site of entry, or may spread to one or more organs remote from that area to cause systemic infection. Viruses may be shed from the primary site of multiplication or from the target organs to infect other susceptible host.

* Viruses are transmitted to the individual by many different routes. Including
* Person to Person transmission (vertical & horizontal transmission)
* Animal to human transmission (Zoonotic disease)
* The main portals of entry are the respiratory, gastrointestinal and genital tracts, but through the skin, across the placenta and via blood are important as well.
* Most serious viral infections are systemic, i.e the virus travels from the portal of entry via the blood to targets organs, however, some are localized to the portal of entry, such as the common cold, which involves only the upper respiratory tract.

**Immune response to viral infection:**

 The 1 st line of defense against microorganisms (viruses) is the intact skin and mucous membranes. In addition, basic protection such as tears, ciliated epithelium, gastric acid and bile are a part of the natural barriers of the body. If viruses breach this line and enter the body, then the innate arm of immune system (2°line of defense) is available to destroy the invader, including macrophages, natural killer cells and cytokines such as Interferons.

 Highly specific protection is provided by the acquired (specific) arm of the immune system (3 rd line of defense). They are cell-mediated immunity (CMI) and antibody- mediated (humoral) immunity. They act in a complimentary manner; antibodies reduce or neutralize the infectivity of free virus in fluid phase. So reducing the numbers of viruses infect cells that T cell must deal with. T cells kill virus- infected cells before virus maturation occurred. Therefore, minimizing the release of infectious viruses, thus decreasing the load on antibodies.

**Types of viral infections at host level:-**

* The majority of viral infections are subclinical causing **asymptomatic** infection. The **acute viral infection** in the person typically has fourstage namely, incubation period, prodromal period, specific-illness period and recovery period.
* The signs and symptoms of most viral diseases are usually caused by death of the infected cells by virus and a consequent loss of function. For example, Poliovirus kills neurons, resulting in paralysis .There are other diseases in which the symptoms are caused by immune system rather than by the killing of cells directly by the virus. This process is called immunopathogenesis . Both cytotoxic T cells and antibodies play a role in immunopathogenesis.
* Most acute viral infections resolve spontaneously however, in certain situations the virus may persist for long periods, In these situation, the infection is called **Persistent infection**(PI)
* There are several types of PI such as

1.Late complication of acute disease. The best example is sub acute sclerosing panencephalitis.

2. Chronic infections:

 It is defined by the presence of viral genome in the blood for more than 6 months such as chronic hepatitis caused by HBV or HCV.

3. Latent infections (LI):-

 Herpes viruses have ability to cause LI.

 These infections are not producing virus at the present time (during latency) but can be reactivated at a subsequent time and the virus can be detected at that time.

**TAKE HOME MESSAGES:**

1. The two levels of viral pathogenesis
2. The interaction of viruses with cells can result in:
3. Abortive infection
4. Procedure of new particles with or with out lysis of the host cells
5. Latency
6. Transformation

 3. Cytopathic effect (CPE) such as inclusion bodies is useful for laboratory diagnosis. Two important examples are Negri bodies and Owl's eye inclusions

 4. The symptoms of viral disease are usually caused by death of infected cells, but some are caused by immunologic attack (immunopathology)

 5. Interferons provide a key innate defense to viral infection. Their overall effect is to inhibit viral replication.

 6. Antibodies act on extracellular virus to prevent establishment of infection. In view of their intracellular replication. Viruses are particularly targeted by CMI.

 7. The viruses can cause asymptomatic, acute, chronic and latent infections.

**ADDITIONAL READING**

 1- Medical Microbiology and Immunology.

 By: Warren Levinson.

10th Edition, 2008.

 Published By: McGraw-Hill Co.

 2- Medical Microbiology.

 By: David Greenwood

 Richard C.B. Slack

 John F Peutherer and Mike Barer.

 17th Edition, 2007.

Published By: Elsevier Limited.