**Virology**

**Pathogenesis and control of viral diseases**

-**Viral disease**: is some harmful abnormality that results from viral infection of the host organisms.

**-Viral pathogenesis**: is the process that occurs when a virus infect a cell and causes cellular changes.

**-Diseases pathogenesis;** is a subset of events during an infection that results in disease

manifestation in the host

-A virus is pathogenic for a particular host if it can infect and cause signs of disease in the host.

**Host Immune Response**

The outcome of viral infection reflects the interplay between viral and host factors.Ex: innate immune response is the introduction of cytokines

 (**Cytokines** are a large group of proteins, peptides or glycoproteins that are secreted by specific cells of immune system. **Cytokines** are a category of **signaling molecules** that mediate and regulate immunity, inflammation and hematopoiesis.)

1. **Innate immune Response**
2. -The innate immune response is a largely mediated by **Interferon (IFNs) which is host-coded proteins that are members of the large cytokine family that inhibit viral replication.**

-They are **quickly (within hours) in response to viral infection** or other inducers and are one of the body’s first responders in the defense against viral infection. **IFNs** also modulate humoral and cellular immunity and have broad cell growth regulatory activities**.(IFN-α, INF-β, INF-γ)**

-infection with viruses is potent inducer of INFα and INFβ production, **RNA viruses are stronger inducers of INF than DNA viruses.** INFs also can be induced by double-stranded RNA and bacterial endotoxin**. INF-γ is not produced** in response to most viruses but is induced by mitogen stimulation.INF is secreted and binds to cell receptors, where it induces an antiviral state by prompting the synthesis of inhibit viral replication.

-Viruses display different mechanisms that **block the inhibitory activities of INFs on virus replication** .examples includes specific viral proteins that:

1. Block induction of expression of INF (herpesviruses,papillomaviruses,hepatitis C virus ,rotavirus).

 2. Block the activation of the key protein kinase (adenoviruses ,herpesviruses). activate cellular inhibitor of PKR (infuenze ,poliovirus)

3.Block INF-induced signal transduction (adenoviruses ,hepatitis B virus).

**Adaptive Immune Response**

-Both humoral and cellular components of the adaptive immune response are involved in control of viral replication. Viruses elicit a tissue response different from the response to pathogenic bacteria. Whereas polymorphonuclear leukocytes from the principle cellular response to the acute inflammation caused by pyogenic bacteria.

-Virus-encoded proteins serve as **targets** for the immune response. Virus-infected cell may be lysed by cytotoxic T-lymphocytes as a result of recognition of viral polypeptides on the cell surface.

-**Humoral immunity** protects the host against reinfection by the same virus (Memory cells).Neutralizing antibody directed against capsid proteins blocks the inhibition of viral infection.

- **Secretory IgA antibody is important** in protecting against infection by viruses through respiratory or gastrointestinal tracts.

**EX: HIV infection may be cause: (Adaptive immune response)**

1. They may infect neurons that express little or no MHC **(Herpes virus)**
2. They may encode immunomodulatory proteins that inhibit MHC-Major histocompatibility complex function **(adenovirses )**
3. Inhibit cytokines activity **(poxvirus)**

**Family: Orthomyxoviruses (influenza viruses)**

-Respiratory illnesses are responsible for more than half of all acute illnesses each year in the United States. The orthomyxoviridae (influenza viruses) are a major determinant of morbidity and mortality caused by a respiratory disease.

-Influenza type A is antigentically highly variable and is responsible for most cases of epidemic influenza. Influenza type B may exhibit antigenic changes and sometimes cause epidemics. Influenza type C is antigentically stable and cause only mild illness.

**Antigenic Drift and Antigenic Shift**

The two surface proteins of influenza undergo antigenic variation. Minor antigenic changes are termed **antigenic drift** ; major antigenic changes in HA or NA are termed **antigenic shift** ,result in the appearance of a new subtype.

- **Antigenic drift: is caused by the accumulation of point mutations in the gene,resulting in amino acid changes in the protein. Sequence change can alter antigenic sites on the molecule such as virion can escape recognition by host’s immune system.**

**-Antigenic shift: reflect severe changes in the sequence of a viral surface protein, caused by genetic reassortment between human swine, and avian influenza viruses.**



**Pathogenesis of influenza in humans**

-When influenza virus is introduced into the respiratory tract, by aerosol or by contact with saliva or other respiratory secretions from an infected individual, it attaches to and replicates in epithelial cells. The virus replicates in cells of both the upper and lower respiratory tract.

-Viral replication combined with the immune response to infection lead to destruction and loss of cells lining the respiratory tract. As infection subsides, the epithelium is regenerated, a process that can take up to a month. Cough and weakness may persist for up to 2 weeks after infection.

**influenza-virus-symptoms**

-Influenza complications of the upper and lower respiratory tract are common. These include otitis media, sinusitis, bronchitis, and croup. Pneumonia is among the more severe complications of influenza infection, an event most frequently observed in children or adults. In primary viral pneumonia, the virus replicates in alveolar epithelial cells, leading to rupture of walls of alveoli and bronchioles.

-Influenza H5N1 viruses frequently cause primary viral pneumonia characterized by diffuse alveolar damage and interstitial fibrosis. Primary viral pneumonia occurs mostly in individuals at high risk for influenza complications (e.g. elderly patients) but a quarter of the cases occur in those not at risk, including **pregnant women**.

-Combined viral-bacterial pneumonia is common**. In secondary bacterial pneumonia**, the patient appears to be recovering from uncomplicated influenza but then develops shaking chills, pleuritic chest pain, and coughs up bloody or purulent sputum. Often influenza virus can no longer be isolated from such cases.

-The most common bacteria causing influenza associated pneumonia are **Streptococcus pneumoniae, Staphylococcus aureus, and Hemophilus influenzae**. These cases can be treated with antibiotics but the case fatality rate is still about 7%. Secondary bacterial pneumonia was a major cause of death during the 1918-19 influenza pandemic, during which antibiotics were not available.

**Immunity**

Immunity to influenza is long lived and subtype specific whereas antibodies against HA and NA are important in immunity to influenza**. Resistances** to initiation of infection is related to antibody against the HA, but decrease severity of disease and decrease ability to transmit the virus to contact are related to antibody directed against the NA.

The primary role of cell-mediated immune response in influenza is **believed to be clearance of an established infection, cytotoxic T cell lyse infected cell, the cytotoxic lymphocyte response is cross-reactive (able to lyse cell infected with any subtype of virus).**

**Laboratory diagnosis**

**A-polymerase chain reaction (PCR)**

 Rapid test on detection of influenza RNA in clinical specimen using reverse transcription polymerase chain reaction (RT\_PCR)

**B.Isolation and identification**

The sample to be tested for virus isolation should be held at 4C until inoculation into cell culture because freezing and thawing reduce the ability to recover virus.

-cell culture : by hemadsorption 3-5 days after inoculation or the culture fluid can be examined for virus after 5-7 day by hem agglutination or immunofluorescence.

Cell culture on coverslips in shell virus may be inoculated and stained 1-4 days later with monoclonal antibody to respiratory agents.

**C.Serology**

Antibodies to several viral proteins (HA,NA,NP, and matrix) are produced during infection with influenza virus .

**Prevention and treatments**

-Amantadine hydrochloride and an analog **rimantadine** . classed **as adamentadine drugs,** are M2 ion channel inhibitors for systemic use in treatment and prophylaxis of influenza A

-The NA inhibitors **peramivir** useful in treatment of infl.virus A and B type

-Resistance viruses emerge more frequently during therapy with M2 inhibitors than with NA inhibitors and more frequently therapy in children than adults

**Prevention and control by vaccine**

**A. Preparation of inactivated viral vaccines**

**B. Live-virus vaccine**

**C. Use of influenza vaccines**