Control on viral infections

Control on viral infections and diseases by the following main methods:

1 - Host defenses.

2 - Viral vaccines.

3 - Antiviral chemotherapy.

4 - Public hygiene (include personal and community).

1 - **Host defenses**:

Host defenses against viruses fall into two major categories:

1 - **Nonspecific defenses (innate immunity)**, of which the most important are **anatomic harriers**, **interferon (IFN)** and **natural killer (NK) cells.**

2 - **Specific defenses (acquired immunity),** including both humoral and cellular immunity.

A-Nonspecific host defenses:

1 - Anatomic barriers:

Anatomic barriers are located at body surface (skin and mucosa) or within the body (endothelial cell). They are partly effective in preventing viral infection.

2 - **Interferon**:

Interferon is glycoprotein produced by any type of cell (all vertebrate species) after viral infection.

Interferon is produce from infected cell with virus to protect other cell from viral infection interferon does not protect the virus-infected cell that is producing it.

Interferon are divided into three types based on the cell of origin:

1 - IFN-**alpha** is produced by **leukocytes.**

2 - IFN-**beta** is produced by **fibroblasts**.

3 - IFN-**gamma** is produced by l**ymphocytes**.

●IFN-alpha and beta are induced by viruses. Whereas IFN-gamma is not

Produced in response to most viruses but is induced by mitogen stimulation. The induction of IFN is not specific to any virus.

●Action of IFN:

IFN inhibits replication of widely viruses range. IFN don't interact directly with virus but move to other cells and bind to receptor on cell surface which induces the cells to activate specific. Signals for synthesis of antiviral proteins (AVP) that are usually result in an inhabit viral replication. IFN inhibit the growth of virus by blocking the translation of viral mRNA into proteins without affecting the translation of cellular mRNA.

3 - **NK cells and phagocytosis:**

NK cell are important parts of the innate defenses against virus-infected cells. They kill virus-infected cells by secreting some enzymes which cause death of the infected cells.

Viruses may be phagocytosis by different PMN leukocytes and macrophages. The effect of phagocytosis may be virus inactivation and result in clearance of virus.

4 - Inflammation and Fever:

Inflammation inhibits viral replication through (i) **elevated local temperature (ii) reduced oxygen tension (iii) metabolic alteration, and (iv) acid production.**

Fever may act in two ways **(1) higher body temperature may inactivate the virus particle, particularly enveloped viruses, which are more heat-sensitive than non-enveloped viruses. (2) Fever may inhibit replication of some viruses**.

B-specific host defense:

Specific defenses, including both **humoral and cell-mediated immunity** (CMI).The most important type of host defense is acquired immunity, either actively acquired by exposure to the virus, or passively acquired by transfer of immune serum (such as: transfer of IgG from mother to fetus across placenta ,or transfer of IgA from mother to newborn in the colostrums).

The first exposure to virus stimulates the production of antibodies and activation of cytotoxic T-cell .The IgM and IgG confer protection against viruses that enter or are spread through the blood. Secretory IgA is important in protecting against infection by virus that enters through mucosa of respiratory and gastrointestinal tracts.

How does Ab inhibit virus? Two main mechanisms for kill virus by antibodies:

First: neutralization of infectivity of virus by Abs binding to viral antigens (proteins on the surface of virus) .This binding lead to prevent the interaction of virus with cellular receptor and inhibit viral replication. The Ab-coated virus is more rapidly phagocytized than normal virus.

Second: is lysis of virus-infected cell in presence of Ab and complement Ab binds to virus antigens and then binds complement, which enzymatically degrades the cell membrane of virus-infected cell.

Because the cell is killed before yield of virus is produced, the spread of virus is significantly reduced.

Action of cellular immunity: Lyses of virus-infected cell by cytotoxic T-cell. The T-cell recognizes viral antigens only when it is presented in association with class I MHC .They kill virus-infected cell by the methods:

(1) **Releasing perforins**, which make holes in cell membrane of infected cell.

(2) **Releasing proteolytic enzymes** into infected cell, which degrade the contents of the cell.

2 - Viral vaccines:

Prevention of viral diseases can be achieved by use vaccines that induce active immunity.

Main types of viral vaccines are:

(i) **attenuated live-virus vaccine**, and (ii) **killed-virus vaccine.**

Attenuated-virus vaccines: The vaccines contain live virus whose pathogenicity has been attenuated (weakened). The pathogenicity of virus is attenuated either by serial passages in animals or by repeated sub culturing in cell cultures.

The live vaccine is preferred to vaccine containing killed virus because the live vaccine has several **advantages**:

1 - The virus in such vaccine can be replicate in the host and tend to:

(i) Stimulate Ab production (IgG) in longer duration, and induce local Ab production (IgA), therefore resistance at portal of entry .

(ii) Induce a good cell-mediated response, and stimulate cytotoxic T-cell.

2 - In vaccination with live vaccines lead to herd immunity because the attenuated viruses can replicate in immunized persons and spread to other members of population, thereby increasing the number of people protected.

Disadvantages of these vaccines;

(1) The attenuated virus has risk reversion, the virus can revert to virulence during vaccine preparation or in immunized person. For this reason, live vaccine should not be given to immunocompromised peoples or pregnant women because the fetus may become infected.

(2) Interference may occur with other viruses result in contamination of vaccine during vaccine preparation.

Killed-virus vaccines: The vaccines contain killed virus (killed by chemicals such as formalin or by UV radiation or by heating).

The killed vaccines have two advantages (1) They **cannot revert to virulent**, and (2) they are **more heat stable** (at room temperature), therefore can be used more easily ,especially in tropical climate.

The vaccines have many disadvantages ;(1) **Cell mediated immunity is poor** and don't stimulate cytotoxic T-cells because the virus in the vaccine does not replicate. (2) **Stimulate IgG and IgM in shorter duration**, but do not induced local resistance (IgA) therefore not resistance at portal of entry. Because they induce shorter duration of Ab production are less protective .The immunity conferred is often brief, and must be boosted.

(3) **Some killed vaccines may induce hypersensitivity to subsequent infection**.

Most viral vaccines are usually given before exposure to viral infection (pre exposure) except two vaccines rabies and hepatitis B vaccines are effective when given post exposure because the incubation period of disease is long enough that the vaccine induced immunity can prevent the disease.

3 - Antiviral Chemotherapy:

The viruses are unaffected by antibiotic agents but affected by antiviral

chemotherapy agents and interferon.

Number of antiviral drugs (AVD) is very few compared with large number for antibacterial drugs. The major reasons for these difference and limitation are due to some problems with viral chemotherapy:

1 - All viruses are obligate intracellular parasites.

2 - Obligatory dependence upon metabolic of host cell , Therefore ,AVD interfere with cellular processes .Antiviral drugs are difficulty in obtaining selective toxicity against viruses without normal cell .

3 - Some viruses become latent within host cell, and no antiviral drug can eradicate them.

4 - Drug-viral mutants may occur in some viruses , and cause drug resistant viruses .

Mode of action:

Antiviral chemotherapy drugs are available to treat only a few viral diseases Antiviral drugs (AVD) specifically inhibit one or more steps of viral replication, which act as target site for AVD.

1- Inhibition of early events of viral infection (attachment, penetration, uncoating).

2 - Inhibition of viral N.A replication.

3 - Inhibition of viral proteins synthesis.

4 - Inhibition of late events (assembly and release)