Interferon
Soluble substance produced by living cells of many different types in cell cultures, embryonated eggs, in lab. animals when infected by some animal viruses either DNA or RNA and can inhibit multiplication of active virus e.g. influenza virus.

Characteristics of interferon molecules:
1. It is small protein without nucleic acid.
2. Low molecular weight of about 25- 45000 Dalton.
3. Thermo stable at 4 C° and resist heating at 50 C° for I hour.
4. Interferon is active through a wide range of pH values (2-12).
5. It is relatively non-toxic, weakly antigenic and cannot neutralized by the specific antiserum.
6. Inactivated by protolytic enzymes such as trypsin.
7. Not affected with RNase & DNase.
8. Interferon specific to animal species but not to virus's species i.e.: it act against wide variety of viruses.

Disinfection and inactivation of viruses:

**Heat**
Most are inactivated at 56 °C for 30 minutes or at 100 °C for a few seconds

**Drying**
Variable; enveloped viruses are rapidly inactivated.

**Ultra-violet irradiation**
Inactivates viruses

**Organic solvents**
(Chloroform, Ether, Alcohol)
Enveloped viruses are inactivated; those without are resistant.
Lecture 5: Introduction to virology

By Dr. Maha Adel
(2016-2017)

Oxidizing and reducing agents

Viruses are inactivated by formaldehyde, chlorine, iodine and hydrogen peroxide.

Phenols

Most viruses are resistant.

Viral Control

1. Interferon are proteins made by cells to fight viruses.

2. Two types of viral vaccines exist — inactivated & attenuated.

   - Inactivated virus vaccines: don't replicate in the host's system.
   - Attenuated viral vaccines: have been genetically altered so they can't cause disease.

3. Antiviral drugs: (AZT, acyclovir, & azidothymidine) interfere with viral DNA synthesis.

4. Protease Inhibitors: interfere with viral capsid production.

ANTI-VIRAL DRUGS

In principle, a molecule can act as an anti-viral drug if it inhibits some stage of the virus replication cycle, without being too toxic to the body's cells. The possible modes of action of anti-viral agents would include:

1. Inactivate extracellular virus particles.
2. Prevent viral attachment and/or entry.
3. Prevent replication of the viral genome.
4. Prevent synthesis of specific viral protein(s).
5. Prevent assembly or release of new infectious virions.

As we investigate how some of these drugs work at the molecular level, we must keep in mind that the potential problem of the
emergence of mutant virus strains resistant to a drug is always a concern.

**Genetics & Evolution of Viruses**

**Mutation:** - spontaneous and random errors in the copying of viral N.A. which can occur during the replication of viruses, leading to change in nucleic acid sequence to produce mutant when differ somewhat than original organism. Mutant rate in RNA viruses are higher than DNA viruses although some RNA viruses such as those of mumps in man and Newcastle disease in poultry are remarkably stable over many years, but others like influenza A are labile and show tendency to variation in some their properties, leading to producing new pandemics. Some times virus mutation may lead to loss of virulence still immunogenic which called attenuated viruses like vaccinia which is mutant of variola, then it can be used is vaccine against small pox in human.

**There are some viruses properties may change through mutation:**-
1. Loss of virulence.
2. Increase rate of reproduction.
3. Extension of natural host range.
4. Altered haemagglutination activity and changes of antigenic structure, plaque size, morphology or resistance to heat.

**Viral recombination:**- the transfer of genetic material between closely related viruses infecting the same cell, e.g. Sheep pox and Goat pox virus, then new recombinant virus will produced with genome contain new genetic information. The alteration of genetic information in recombinant may result from:-

1. **Intramolecular recombination:** usually occurs in DNA viruses and involved dissociation and re-establishment of covalent bonds within the nucleic acid.
2. Copy-choice recombination: usually occurs between positive sense single stranded RNA viruses. e.g. Picorna, Corona, and Toga viruses.

3. Reassortment: occurs randomly in RNA viruses with segmented genome e.g. Orthomyxo viruses (influenza), Reoviruses and Bunyaviruses.

Oncogenic Viruses:
Oncogenes can be activated to function abnormally by many mutagens and by viruses. Viruses that are capable of inducing tumors are oncogenic viruses. Examples: Human Papilloma Virus (HPV), Hepatitis B, and Epstein-Barr.

Bacteriophages or T-Phages:
- Among the most complex viruses
- Attack bacterial cells
- Composed of a icosohedral head, tail with helical symmetry, base plate, & tail fibers
- Long DNA molecule is inside the head
- Tail helps inject the viral DNA into host cell
- Tail fibers used to attach to host

Viroids:
- ss RNA genome and the smallest known pathogens.
- Affects plants

Prions:
- Infectious particles that are entirely protein.
- No nucleic acid
- Highly heat resistant
Animal disease that affects nervous tissue
Affects nervous tissue and results in:

- Bovine spongiform encephalitis (BSE) “mad cow disease”,
- scrapie in sheep
- kuru & Creutzfeld-Jakob Disease (CJD) in humans

**Laboratory diagnosis**

There are four approaches to confirming a viral infection in the laboratory. Namely:

- **serology:** demonstrating an antibody response in a patient's serum
- **direct detection** of viral antigens in a clinical sample
- viral culture
- viral **nucleic acid detection**

**RNA Viruses**

1- **Family Orthomyxoviridae :** *(Orthomyxo = Classical mucous)*

**General characters:**

a. Spherical or pleomorphic, enveloped viruses, nucleocapsid helical symmetry.
b. Linear, negative-sense, single-stranded RNA.
c. Replication occurs in the nucleus.
d. Genome is segmented facilitating genetic reassortment.
e. Surface projections of glycoproteins form spike or peplomers which is in influenza: A & B viruses are of two types: a haemagglutinin (H), responsible for virus attachment and envelope fusion, and a neuraminidase (N) capable of cleaving viral receptors & promoting both entry of virus into cells & release of virions from infected cells.
Genera of orthomyxoviridae:
1. Influenza virus type A: Pathogen for human and animals.
2. Influenza virus type B: Pathogen for human.
3. Influenza virus type C: Pathogen for human.

Type A viruses are grouped into subtypes on the basis of their H & N antigens. H antigens & [nine] N antigens are recognized. New subtypes of influenza A virus emerge periodically by two mechanisms; point mutation & genetic reassortment.

Point mutations: give rise to antigenic drift in which variation occurs within subtype.
Genetic reassortment: a more complex process producing antigenic shift, results in the development of new subtypes. The frequency of genetic reassortment in birds & pigs can lead to the emergence of virulence influenza virus subtypes which are capable of infecting humans & and initiating pandemics.

2- Paramyxoviridae (Paramyx= Along - side mucous)
General characters:
a. Large pleomorphic enveloped viruses.
b. Negative sense single –stranded RNA, (non segmented).
c. Helical symmetrical nucleocapsid.
d. Replicate in the cytoplasm.
e. Genetically stable & not exhibit recombination but some antigenic variation may occurs through mutation.

Genera of Paramyxoviridae:
1. Morbillivirus : e.g. Measles
2. Rubulla virus : e.g. Mumps

**Measles:**

Clinical features:
Incubation period: 7-14 days
Illness begins with a prodrome of fever, conjunctivitis, cough, coryza. 3-5 days into the illness a macular popular rash erupts on the face and spreads to involve the rest of the body. Patients are most ill during the first 2 days of the rash. The virus is highly cytopathic causing widespread damage to respiratory and gut epithelium and transient immunosuppression. These
Virology

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Factors put the patient at risk of secondary bacterial and viral complications such as otitis media, pneumonia, diarrhoeal disease. The virus also invades the brain during the acute phase of the illness. Various neurological complications may occur during and after infection (acute measles encephalitis, post-infectious measles encephalitis, sub-acute measles encephalitis and sub-acute sclerosing pan encephalitis).

Epidemiology:
Measles is one of the most infectious diseases known. Infection is spread by respiratory droplets and the airborne route. Globally, it was a leading infectious cause of death in children under the age of five years.

Vaccine:
The measles vaccine (MMR) is a live attenuated virus. All infants are required by law to be immunized against measles. Two doses of vaccine are given (at 9 and 18 months). The vaccine cannot be given earlier because maternal antibody interferes with vaccine replication and no immune response develops. Individuals in whom vaccine is contra-indicated (infants < 1 year, pregnant women and severely immuno-compromised patients) should be given normal human immunoglobulin.

Mumps:

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Clinical features:
The classic picture is of parotitis, which occurs in 95% of symptomatic infections. The incubation period is 16-18 days. There may be a prodromal stage, with malaise, headache, fever, and myalgia. Swelling of the one parotid gland is usually (75% of cases) followed by the other parotid gland between 1 and 5 days later. Sometimes other glands are involved. The parotid swelling subsides after about 7-8 days.

Mumps is also a common cause of aseptic meningitis. Recovery is usually complete. Some patients also show signs of encephalitis, such as convulsions, abnormal movement. Hearing loss is a less common complication of mumps.

About a quarter of mumps cases in males after puberty are complicated by orchitis, with 20-40% of these being bilateral. Late complications include
infertility. Oophoritis (inflammation of the ovary) is less common in than orchitis is in males, and it is not associated with female infertility.

Other complications: involvement of other glands, such as the pancreas, prostate, lacrimal glands, and other salivary glands; arthritis; myocarditis; transient renal dysfunction; nephritis; thrombocytopenia; abortion (there is, however, no evidence of an increased risk of congenital abnormalities.)

Pathogenesis

Infection is transmitted by respiratory droplets. The primary site for replication is the mucosal epithelium of the upper respiratory tract and the eye. From there the virus spreads to the local lymphoid tissues, and then the primary viraemia occurs, where the virus spreads to other organs - usually the parotid, but also the pancreas, testis, ovary, and central nervous system. A secondary viraemia occurs, with further spread. Virus is excreted in urine and breast milk, but the main source of spread is via droplets from the respiratory system. Interferon appears to play a significant role in the pathogenesis, and stimulates IgG, IgM, and IgA, as well as a cell-mediated response.

Epidemiology: The highest incidence of mumps is in children between the ages of 5 and 9.

Vaccine:

The vaccine is a live attenuated virus, and usually forms part of the MMR vaccine (against measles, mumps, and rubella).