

Virology Lectures

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Virology

References:

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3. Veterinary microbiology, Volume 2, M, I, Sawa, 1991.

Introduction to virology

Definitions:

- **Virology:** the science which deals with study of viruses as causative agents of very important diseases that occurs in human, animals, plants and other living organisms (insects, bacteria,...).
- **Viruses:** They are the smallest and simplest form of life on earth, which can replicate only in living susceptible cells. Viruses consist of:
 1. A nucleic acid genome either DNA or RNA.
 2. A protein coat (capsid) that enclosed the genome.
 3. In some cases a lipid membrane (envelope).
- **Virion:** A complete infectious virus particle.

General characters of viruses:

1. Virus particles are very small in size; they are between 20-500 nm (nanometer) in diameter. $1 \text{ nm} = 1/1000 \mu\text{m}$, $1 \mu\text{m} = 1/1000 \text{ mm}$.
2. Viruses are obligatory intra cellular microorganisms.
3. Multiply inside the cells by replicating their genomes which either DNA or RNA, but not both.
4. The virus does not contain any organelles (ribosomes, t RNA, metabolic enzymes, etc), but they depend on infected cells to provide all their needed organelles.
5. Virus does not affect with antibiotics.
6. Most viruses sensitive to interferon.
7. Viruses can not grow on artificial media, but only in living cells (specific host, Lab. Animals, chicken embryonated eggs & tissue culture).
8. Some viruses cause latent infection.
9. Viruses can not be seen by ordinary microscope, but only by Electron microscope (EM).

N.B;

According to size, viruses can classify beginning from the largest and more complex microorganisms as following **protozoa, yeast, bacteria, mycoplasma, rickettsiae, chlamydia & virus.**

The chemical composition of viruses

Schlesinger in 1933 who firstly showed that bacterial viruses (bacteriophage) consisted essentially of protein and DNA, Stanley in 1935 report that Tobacco mosaic virus (TMV) consisted of protein and RNA, then other biochemists have studied the chemistry of other viruses which infect plants, animals, insects, bacteria. All they found that all viruses contain only one type of nucleic acid (NA) either DNA or RNA but not both, plus a protective coat of protein in addition to that some viruses may contain lipids & carbohydrates .

TMV contains about 95% protein plus 5% NA. So the importance of NA is limited until it was discovered in 1952 that it was DNA which infect bacterial cell during phage replication and initiated the synthesis of progeny virus, where as most of the protein component of the virus particle remained outside the host cell and played no further part in the infection, then NA was responsible for carrying the genetic information of the virus.

The importance of viral NA was increased when they found that TMV RNA was infectious and capable of carrying all the genetic information required for manufacture new virus in the absence of its protein covering.

Also animal viruses like picorna (FMD V) considered as infectious NA that it acts directly as mRNA, it does not need RNA polymerase, in adeno and parvo viruses (DNA) they have also infectious NA.

Structure of viral nucleic acids:

Genetic information are stored as the following:

1. Double stranded DNA cells (animal, plants, bacteria and some viruses).
2. Single-stranded DNA in other viruses (phage Θ x 174).
3. Single stranded RNA (myxovirus).
4. Double-stranded RNA (reoviruses).

How we can differentiate between DNA and RNA?

- By DNAase or RNAase
- Between double and single stranded NA; by acridine orange stain, which is yellowish green in double stranded and red orange in single stranded.

Chemical composition of nucleic acid

NA chain is composed of basic units called nucleotides each of which consist of :

1. Nitrogenous base: ring compound containing nitrogen and carbon.
2. Molecule of a 5-carbon pentose sugar which is either ribose RNA ribose (RNA) or deoxyribose (DNA).
3. Molecule of phosphoric acid which links the base to the pentose sugar.

There are four kinds of nucleotides (bases) in DNA:

Guanine	}	Purines
Adenine,		
Cytocine	}	Pyrimidines
Thymine		

In the RNA molecules the bases are guanine, adenine, cytocine and uracil.

Viral proteins:

Protein coat which encloses the viral genome called **capsid** which consists of **protomers** that accumulated to give pentan or hexan forms producing the **capsomers** which protect the viral NA and have surface characters acts to attach the virus on host cells then penetration, also it contains antigenic determinants.

Viral envelope:

Most viruses contain envelope or membrane surrounding the virus so they called **enveloped** viruses, others have no envelope and they called **naked** viruses. Enveloped viruses contain lipids like orthomyxo and paramyxo viruses, these viruses will become sensitive to organic solvents (ether, alcohol, chloroform), these characters used in newly isolated virus classification.

Also viral membrane contains glycolipids or glycoprotein which appears as projections from the envelope called spikes or peplomers.

Viral shape structure

Nucleocapsid is the arrangement between the viral nucleic acid genome with the capsid, this connection controlled by specific NA genetic information leading to different types of symmetry. Accordingly viruses can be classified into four symmetry structures.

1. Helical symmetry.
2. Cubical symmetry.
3. Binal symmetry.
4. complex symmetry.

1. Helical symmetry

This form can be seen in RNA viruses, that the capsomers surrounded the N.A in spiral or helical manner to give helical symmetry which may be seen naked (TMV) or enveloped in ND & Rinderpest viruses. When the tubular nucleocapsid presented in coil form and surrounded by lipoprotein envelope containing peplomers which is glycoprotein projections (also called spikes) which represent haemagglutinins and neuraminidases but in rabies virus the capsid is straight and surrounded by lipoprotein membrane to give the bullet shape.

2. Cubical symmetry

Many RNA and DNA animal viruses when studied with a method of metal shadowing from two angles by EM, in this method the virus particles have hexagonal outlines with 20 equilateral triangular faces, i.e. icosahedrons, but when these viruses studied by negative stain using phosphotungstic acid which can penetrate even through the finest contours of the viral surface. Many viruses appear to be faceted and each face forms an equilateral triangle consisting of angular arrangement of protein subunits as capsomers. There are generally 20 equilateral triangular faces.

In adeno viruses each side of the equilateral face consists of 6 capsomers linked to each other by divalent bounds. By using special equation to calculate capsomers number which are fixed in number and genetically controlled as the following:

$$\begin{aligned}\text{Capsomers NO.} &= 10 (\text{edge capsomers NO.} - 1)^2 + 2 \\ &= 10 (6 - 1)^2 + 2 \\ &= 10 \times 25 + 2 = 252\end{aligned}$$

In herpes viruses where edge capsomers NO. are 5

$$\begin{aligned}&= 10 (5 - 1)^2 + 2 \\ &= 10 \times 16 + 2 = 162\end{aligned}$$

But in less capsomers number, other equation used.

$$\begin{aligned}\text{Capsomers NO.} &= 30 (\text{edge capsomers NO.} - 1)^2 + 2 \\ &= 30 (2 - 1)^2 + 2 \\ &= 30 \times 1 + 2 = 32\end{aligned}$$

e.g. for cubical symmetry viruses: adeno and picorna which are naked, herpes and toga which are enveloped.

3. Binal symmetry

This type of symmetry show both icosahedral (cubical) and helical symmetry, but with in the same virion like bacteriophage, when the head is cubical and the tail is helical.

4. complex symmetry

Most animal viruses show either helical or cubical symmetry but pox viruses have exceptional and their ultra structure appears to be complex. Some pox viruses are brick- shaped, while others are ovoid and the DNA is contained in nucleoid, shaped like a biconcave disc and surrounded by one or more membranes.

Negative staining shows that the virion contains a surface layer of hallow tube like fibrils which may give the particles a striated appearance.

In some species of pox viruses e.g. orf virus, the thread appears to be continuous and is arranged in a cross or figure-eight pattern across the surface of the virion giving it the characteristic ball of wool appearance.

Classification of Animal Viruses

Animal viruses can be classified into several families according to the following characters:

A- Characters of viral nucleic acid (N.A):

1. Type of N.A if it is DNA or RNA.
2. Shape of N.A strand if it is ring or straight, single or double strand, segmented or not....
3. Molecular weight (size & diameter of N.A).
4. Replication site of N.A if it is in the cytoplasm or nucleus of infected cells.
5. Presence of transcriptase enzyme.

B- Characters of viral capsid:

1. Shape & size of capsid.
2. Symmetry of capsid with N.A (Helical, Cubical, Binal, Complex).
3. Site of capsid assembly in side the infected cells.
4. Lipid solvent sensitivity.
5. Number of capsomeres which consisting the capsid.

According to all above characters recently animal viruses classified into two major groups which are RNA group & DNA group as following:

RNA Viruses families:

1. Picornaviridae
2. Orthomyxoviridae
3. Paramyxoviridae
4. Coronaviridae
5. Reoviridae
6. Retroviridae
7. Rhabdoviridae
8. Birnaviridae
9. Bornaviridae
10. Bunyaviridae
11. Togaviridae
12. Astroviridae
13. Arteriviridae
14. Caliciviridae
15. Flaviviridae

DNA Viruses families:

1. Herpesviridae
2. Poxviridae
3. Adenoviridae
4. Parvoviridae
5. Papillomaviridae
6. Asfaviridae
7. Circoviridae

RNA Viruses

1- Picornaviridae

Pico = small in size.

General characters:

- a. virions are 18-30 nm in size.
- b. replicate in cytoplasm.
- c. resistant to many organic solvents (ether, chloroform).
- d. Non enveloped, positive-sense, single-stranded RNA viruses with icosahedral symmetry.
- e. Individual members differ in their susceptibility to pH change.

Genera of Picornaviridae:

Viruses of veterinary importance in five genera of the family Picornaviridae:

1. Aphthovirus: Foot and mouth disease which have seven serotypes & more than 260 subtypes, unstable at PH values below 6.5.
2. Enterovirus:
 - Avian enterovirus cause avian encephalomyelitis, nephritis in chickens & hepatitis in ducks & turkeys.
 - Bovine enteroviruses cause respiratory & reproductive disease.
 - Swine vesicular disease virus.
3. Cardiovirus: Encephalomyocarditis in Rodents.
4. Hepatovirus: Avian encephalomyelitis-like virus.
5. Teschovirus: Porcine enterovirus (Talfan disease)

2- Orthomyxoviridae

Orthomyxo = Classical mucous

General characters:

- a. Spherical or pleomorphic, enveloped viruses, nucleocapsid helical symmetry.
- b. 80-120 nm in diameter .
- c. Linear, negative-sense, single-stranded RNA.
- d. Replication occurs in the nucleus.
- e. Genome is segmented facilitating genetic reassortment.
- f. Surface projections of glycoproteins from spike or peplomers which is 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.
4. Thogoto virus
Tick born ARBO virus.

Type A viruses are grouped into subtypes on the basis of their H & N antigens. [16] 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: amore 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.

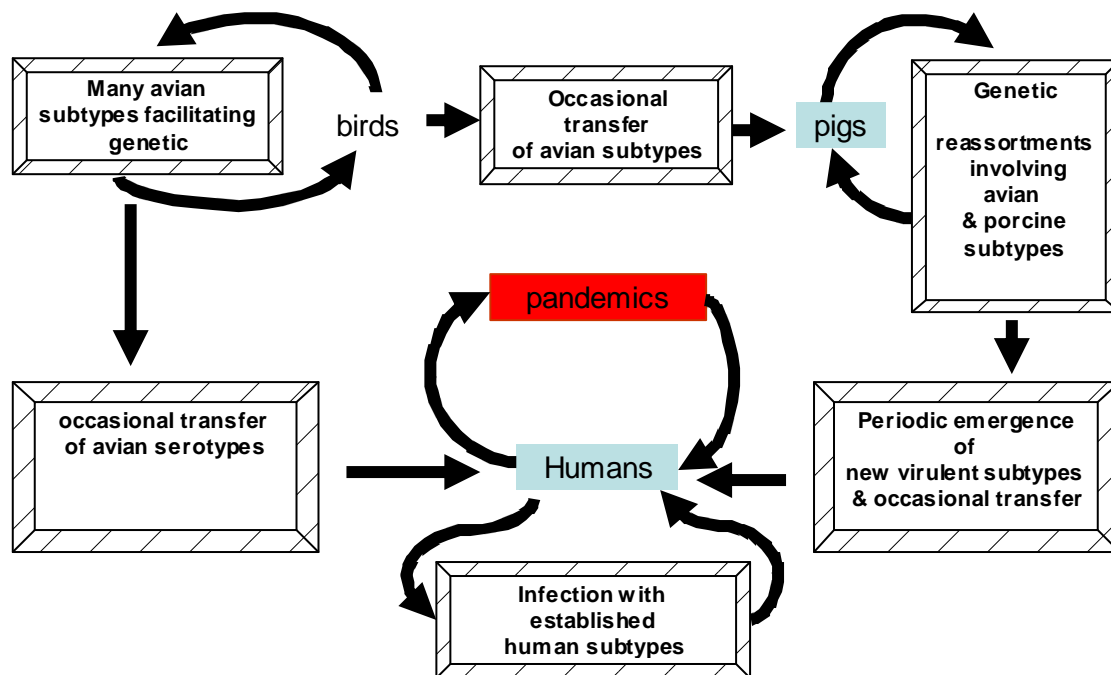


Figure 1 Flue Pandemic

3- Paramyxoviridae

Paramyxo= Along - side mucous

General characters:

- a. Large pleomorphic enveloped viruses (150 nm or more).
- 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. Respiro virus: Bovine parainfluenza virus 3.
2. Morbillivirus : - Rinderpest virus.
 - Peste des petits ruminants virus.
 - Canine distemper virus.
3. Rubella virus : - Newcastle disease virus.
 - Avian parainfluenza virus.
4. Pneumovirus : Bovine respiratory syncytial virus.
5. Meta pneumovirus: Turkey rhinotracheitis virus.

4- Coronaviridae

Corona = crown

General characters:

- a. Large (120-160 nm) pleomorphic, enveloped virus.
- b. Single – stranded, positive – sense RNA.
- c. Replicate in cytoplasm.
- d. Club- shaped glycoprotein peplomers projecting from the envelope as crown – like appearance.
- e. Sensitive to heat, lipid solvents, some are stable at PH= 3.

Genera of coronaviridae:

1. Corona virus: spherical, helical nucleocapsid causing respiratory disease in poultry (infectious bronchitis disease).
2. 2. Toro virus: Tubular nucleocapsid, kidney- shaped or rod shaped 120-140 nm in diameter.

5- Reoviridae

Respiratory enteric orphan

General characters:

- a. Non-enveloped with double or triple layered capsid & icosahedral structure 60-80 nm in diameter.
- b. Segmented (10-12 segments) double- stranded RNA.
- c. Replicate in cytoplasm with intracytoplasmic inclusion bodies.
- d. Genetic reassortment readily takes place.
- e. Resistant to heat, organic solvents.

Genera of Reoviridae :

1. Orthoreovirus: cause arthritis & tenosynovitis in poultry.
2. Rotavirus : cause enteritis in neonatal farm animals.
3. Orbivirus: Arthropods- borne infections (Arbo), cause:
African horse sickness in horses, Bluetongue disease in sheep , and in other domestic & wild ruminants.

6-Retroviridae

Reverse transcriptase

General characters:

- a. Labile enveloped RNA viruses 80-100 nm in diameter.
- b. Diploid containing two linear positive- sense strands of RNA.
- c. Most members of this family possessing a reverse transcriptase which transcribes viral RNA to double-stranded DNA.
- d. Mutation and recombination occur with high frequency.

Genera of Retroviridae:

1. Alpha retrovirus causing- avian leucosis, avian sarcoma, avian myeloblastosis, rous sarcoma
2. Beta retrovirus : mouse mammary tumor virus.
3. Gamma retrovirus: feline leukemia feline sarcoma.
4. Delta retrovirus: bovine leukemia.
5. Epsilon retrovirus: fish tumor virus.
6. Lentivirus :
 - Human immunodeficiency virus 1,2 HIV (AIDS)
 - Simian immunodeficiency virus.
 - Maedi/visna virus.
 - Caprine arthritis, encephalitis virus.
 - Equine infectious anemia virus.
 - Feline immunodeficiency virus.
 - Bovine immunodeficiency virus.
7. Spuma virus: viruses causing vacuolation cultured cells not associated with the clinical disease.

7. Rhabdoviridae

Rod

General characters:

- a. Have characteristic rod shapes and bullet-shaped in vertebrates .
- b. enveloped RNA viruses with helical symmetry.
- c. virions size (100-430 nm X 45-100 nm).
- d. Stable in the pH range of 5- 10.
- e. Rapidly inactivated by heating at 56 C°.
- f. Sensitive to lipid solvents and UV light.

Genera of Rhabdoviridae:

1. Lyssavirus: Rabies virus .
2. Ephemero virus: Bovine ephemeral fever virus.
3. Vesiculovirus: vesicular stomatitis virus.

8. Birnaviridae**Bi-RNA****General characters:**

- a. Double stranded RNA icosahedral symmetry.
- b. Virions are 60 nm in diameter.
- c. 3. Virions stable over a wide pH range and 60 C° for 1 hour, resistant to ether and chloroform.

Genera of Birnaviridae:

1. Avibirna virus: - infectious bursal disease (Gumboro).
2. Aquabirna virus: - infectious pancreatic necrosis in salmonids (fish).
3. Entomobirna virus: - infect insects.

9. Bornaviridae**General characters:**

- a. Enveloped virus, spherical 90 nm in diameter.
- b. Single stranded RNA, negative-sense.
- c. Replicates in nuclei of neural cells.
- d. Sensitive to heat, lipid solvents and low pH values.

Only one genus: Borna virus causing Borna disease an infection of the CNS, fatal in many domestic species, particularly horses.

Antibodies reacting with BDV have been found in the sera of human patient with psychiatric disorders and a possible link between infection with the virus and human neurological disorders is being investigated.

10- Bunyaviridae**Bunyamwera (place in Uganda)****General characters:**

- a. Medium sized 80-120 nm, enveloped, single stranded RNA viruses, and spherical shape.
- b. Sensitive to heat, acid pH levels, lipid solvents.
- c. More than 300 viruses in the family most of them Arbo.

Genera of Bunyaviridae:

Family composed of five genera.

1. Bunyavirus: causes congenital defects in cattle and sheep.
2. Phlebovirus: rift valley fever.
3. Nairovirus: Nairobi sheep disease.
4. Hantavirus: haemorrhagic fever in human.
5. Tospovirus: viruses of plants.

11- Togaviridae:

General characters:

- a. Enveloped RNA viruses with icosahedral symmetry.
- b. 70 nm in diameter.
- c. The envelope is closely bound to capsid.
- d. The virus agglutinate goose and chick RBCs.
- e. Positive- sense single-stranded RNA.
- f. Alphavirus, in common with certain members of the Flaviviridae, Reoviridae, Rhabdoviridae, Bunyaviridae are termed Arboviruses indicating that they are arthropod- born.

Genera of Togaviridae:

There are two genera:

1. Alpha virus: Arboviruses cause eastern equine encephalitis (EEE), Western equine encephalitis (WEE), Venezuelan equine encephalitis (VEE).
2. Rubivirus: rubella virus which causes German measles in children and young adults.

12- Astroviridae

Star

General characters:

- a. small 28- 30 nm in diameter single strand RNA viruses with icosahedral symmetry, non enveloped.
- b. The viruses resistant to low PH values, heating at 60°C for 5 minutes.
- c. Trypsin is required for cultivation on cell cultures.
- d. Only one genus Astrovirus which produce mild gastroenteritis in most domestic species, in ducks serious disease may occurs.

13- Arteriviridae

General characters:

- a. Medium sized (40 – 50), enveloped single stranded RNA.
- b. Icosahedral symmetry spherical shape.
- c. Replicate in cytoplasm of macrophages and endothelial cells.
- d. Sensitive to heat, low PH, lipid solvent, detergent treatment UV irradiation and many disinfectants.
- e. It have only single genus, Arterivirus which cause equine viral arteritis.

14- Caliciviridae

Cup

General characters:

- a. Have cup – shaped depressions on surface of virions
- b. Small (27- 40 nm) non enveloped, positive – sense, single stranded RNA with icosahedral symmetry.
- c. Resistant to ether, chloroform and mild detergents and heat.
- d. Sensitive to acid PH values.

Genera of Caliciviridae:

It has four genera:

1. Vesivirus: cause vesicular exanthema of swine and feline calicivirus infection.
2. Lagovirus : cause rabbit hemorrhagic disease.
3. Two genera contain human caliciviruses which cause gastroenteritis.

15- Flaviviridae

Yellow

General characters:

- a. Enveloped, 40-60 nm in diameter, positive- sense, single stranded RNA, icosahedral capsids & tightly adherent envelopes.
- b. Sensitive to heat, detergents & organic solvents.
- c. Agglutinate goose red cells.

Genera of Flaviviridae

1. Flavivirus: contains 70 members most of them are Arbo viruses which require either mosquitoes or ticks as vectors.
2. Pestivirus: transmitted directly or indirectly cause bovine viral diarrhoea (BVD), border disease and classical swine fever.

DNA Viruses

1- Herpesviridae: creeping

General characters:

1. Enveloped DNA viruses with icosahedral symmetry.
2. Replicate in nucleus, with intranuclear inclusion bodies.
3. 120-200 nm in diameter.
4. Latency is a common outcome of infection with these viruses.
5. This family contains more than 100 viruses which cause different diseases in human, birds, mammals, fish, amphibian & reptiles.

There are three subfamilies of veterinary importance:

Alphaherpesvirinae, Betaherpesvirinae, Gammaherpesvirinae which cause diseases of the respiratory reproductive & nervous systems, in different animal species:

e.g. Herpes infections of ruminants:

- a. Bovine herpes virus cause (infectious bovine rhinotracheitis (IBR).
- b. In poultry: a. infectious laryngo-tracheitis (ILT).
 - Marek's disease.
 - Duck plaque.
- c. Human: Herpes simplex type 1 cause:
 - Fever blisters.
 - Chicken pox or varicella zoster or shingles.

2- Poxviridae:

General characters:

1. Largest viruses (220-450 nm x 140- 260 nm).
2. Complex symmetry, brick shaped viruses.
3. Enveloped DNA viruses replicate in cytoplasm.
4. Virions are stable at room temperature under dry conditions, but sensitive to heat, detergents, formaldehyde and oxidizing agents.
5. Skin lesions prominent feature.
6. Genetic recombination within genera results in extensive serological cross-reaction and cross- protection.

Genera of Poxviridae:

- a. Orthopoxvirus: Vaccinia, cow pox , variola virus .
- b. Parapoxvirus: Orf virus, Bovine papular stomatitis virus, pseudo complex.
- c. Capripox virus : goat pox, sheep pox, lumpy skin disease virus.
- d. Avipoxvirus: Fowl pox virus, pigeon pox, Turkey pox.
- e. Suipox virus: Swinepox virus.
- f. Leporipox virus: Myxoma virus. (Rabbit)
- g. Entomopox virus: infect insects.

3- Adenoviridae

Gland

General characters:

1. Non enveloped, double-stranded DNA viruses.
2. Icosahedral symmetry, 70-90 nm in diameter.
3. Replicate in nuclei, forming intranuclear inclusion bodies.
4. Fibers project from twelve vertices of capsid.
5. Agglutinate rat or monkey RBCs
6. Resist freezing, mild acid & lipid solvents, 56C for 10 min.

Genera of Adenoviridae

1. Aviadenovirus: hydropericardium hepatitis syndrome (HHS), Egg drop syndrome in layers .
2. Mastadenovirus mammalian adenovirus which cause sever infections in dogs (infectious canine hepatitis .pulmonary infections in equine, which fatal in Arabian foals.

4- Parvoviridae

small = picodna

General characters:

1. small (18-26 nm), non enveloped DNA viruses.
2. Icosahedral symmetry, single stranded DNA.
3. Replicate in the nucleus forming intranuclear inclusion bodies.
4. Require rapidly- dividing cells for replication.
5. Resistant to heat 56C for more than 60 minutes also resistant to lipid solvents, pH (3-9).
6. Inactivated by formalin, - Propiolacton, sodium hypochlorite

Genera of Parvoviridae:

Parvovirus: cause of enteric & systemic disease in dogs & cats (Feline panleukopenia or feline infectious enteritis).

5-Papillomaviridae

General characters:

1. Non-enveloped, circular double strand DNA viruses.
2. Icosahedral symmetry, 55 nm in diameter.
3. Replications in nucleus
4. 4-Resistant to lipid- solvents, acids, 60°C for 30 minutes.

Genera of Papillomaviridae:

Contains one genus, Papillomavirus:

- a. Have not been cultured in vitro.
- b. Cause papilloma & fibropapilloma in domestic animals.

6- Circoviridae

General characters:

1. Non enveloped 17- 22 nm in diameter.
2. Circular single stranded DNA, Icosahedral symmetry.
3. Stable at pH 3-9, heating at 60 °C for 30 minutes.

Genera of Circoviridae:

There are two groups of circo viruses:

- a. Chicken anaemia virus (CAV).
- b. Porcine circovirus.

7- Asfaviridae: African Swine Fever

General characters:

1. Enveloped DNA viruses, 175-215 nm in diameter.
2. Icosahedral symmetry.
3. Replicate in cytoplasm of host cells & in soft ticks.
4. Stable at 4-20 °C, persist for months in meat.
5. Only one genus which Asfa virus causing African Swine Fever.

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), Reo viruses and Bunya viruses.

Viral cell interactions

When an intact of infectious virus particles makes contacts with a susceptible host cell may develop a number of reactions at the cell surface lead to release of the genetic material at the virus within the cell. This is immediately followed by a series of biosynthetic processes lead to formation of new virus like e.g.

1. Defective virus:- viruses that have lost ability to perform any one of the essential steps required for successful replication.
2. Incomplete virus:- abnormal viruses produced due to inoculation of high titer virus solution in limited number of host susceptible cells like inoculums containing a high rating of infective units to cells this called Von Magnus phenomena. That the produced viruses without nucleic acid e.g. influenza virus.

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 1 hour.
4. Interferon is active through a wide range of pH values (2-12).
5. It is relatively non-toxic, weakly antigenic and cannot be neutralized by the specific antiserum.
6. Inactivated by proteolytic enzymes such as trypsin.
7. Not affected with RNase & DNase.
8. Interferon specific to animal species but not to viruses species i.e.: it acts against a wide variety of viruses.

Replication of Viruses

Viruses can multiply only in active host cells, the replication cycle of viruses can be divided into a number of stages:

1. Attachment to surface receptors on the susceptible host cell.
2. Entry into the cell.
3. Uncoating of viral nucleic acid.
4. Replication of viral nucleic acid and synthesis of virus encoded proteins.
5. Assembly of newly-formed virus particles and release from host cell.

1. Attachment to surface receptors on the susceptible host cell:

Virions must first attach to cell surface receptors in order to produce infection, this attachment depends on the number of the virus particles present and the availability of appropriate receptor molecules, virus-cell interaction determines both the host range and tissue tropism of viral species. Viruses can select a point where they can utilize the wide range of host cell surface proteins as receptors.

Some viruses have more than one type of ligand molecules and they may bind to several surface receptor proteins in sequential order during attachment, in some species of virus, individual virion can attach and adsorb to another cell when infection of particular host cell does not proceed, e.g. in orthomyxo and paramyxo viruses detachment from host cells is mediated by viral neuraminidase, a receptor-destroying enzyme.

2. Entry into the cell:

Virus penetration is an energy-dependent process which can occur in a number of steps:-

- a. receptor-mediated endocytosis occurs after virus attaches to receptors and particular sites on the plasma membrane, this virus-receptor complex is taken into the cell in specialized vesicles, then by acidification within the vesicles leads to degradation of viral structures.

- b. In enveloped viruses (Paramyxovirus, Retrovirus and Herpesvirus), involves fusion of the viral envelop with the plasma membrane, this allows release of the nucleocapsid directly into the host cells cytoplasm.
- c. Direct introduction or translocation of viral genomes into the cytoplasm through channels in the plasma membrane e.g. non-enveloped viruses (Picornavirus).

3. Uncoating of viral nucleic acid:-

Uncoating means:- the process where by the viral genome is released in a form suitable for transcription. e.g.

- a. In enveloped viruses: nucleocapsid is discharged directly into the cytoplasm, transcription can usually proceed without complex uncoating
- b. In non- enveloped virus uncoating may results from lysosomal proteolytic enzymes activity.

4. Replication of viral nucleic acid and synthesis of virus encoded proteins:

- a. replication of DNA virus:-

Double stranded DNA viruses (Herpes, Para, Adenovirus) which replicate in the nucleus of the cell have relatively direct replication strategy, the viral DNA is transcribed by cellular DNA-dependent RNA polymerase (transcriptase) to form messenger RNA.

- b. replication of RNA virus:-

Double stranded RNA virus (Reo, Birnavirus) transcription occur in the cytoplasm by viral transcriptase, which produced by ribosome of infected cells after viral RNA binding. In positive sense single strand RNA viruses it's RNA can act directly as messenger RNA after infection.

- c. according to viral gene code different types of proteins are produced inside infected cells by it's ribosomes membrane proteins and glycol proteins are synthesized on membrane bounded ribosomes while soluble proteins including enzymes and synthesized on ribosomes free in cytoplasm. Short specific amino acid sequences, known as sorting sequences facilitate the incorporation of proteins of various cellular location where they are required for metabolic activity.

5. Assembly of newly-formed virus particles and release from host cell:

Procapsid were formed by incorporation of viral N.A. in structural formed proteins according to the symmetry of original infected virus.

Non-enveloped viruses are usually released following cellular disintegration. The assembly of Picorna and Reovirus occur in the cytoplasm of the cell where as Parvo, Adeno and Papova are assembled in nucleus. Enveloped viruses released by budding form infected cell membrane at that time the viral enveloped was formed by cell membrane modification through the insertion of virus-specified transmembrane glycoproteins but some those enveloped viruses like Toga, Paramyxo and Rhabdo viruses are cytolytic in there releases. Flavi, Corona, Artiri and Bunya virus acquire there envelops inside cell by binding through the membrane of the rough endoplasmic reticulum or Golgi apparatus. Herpes viruses which replicate in the nucleus they bud from nuclear membrane.