

VPM 402: VETERINARY VIROLOGY

LECTURE NOTES

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VPM 402: VETERINARY VIROLOGY COURSE OUTLINE

Topic	Lecturer
Herpesviridae:	M. A. Oyekunle
Infectious bovine rhinotracheitis	
Malignant catarrhal fever	
Equine rhinotracheitis	
Equine herpesvirus abortion	
Canine herpesvirus infection	
Feline viral rhinotracheitis	
Infectious laryngotracheitis	
Marek's disease.	
Poxviridae:	M. A. Oyekunle
Orthopoxvirus	
Parapoxvirus	
Capripoxvirus	
Avipoxvirus	
Suispoxvirus	
Leporipoxvirus	
Asfarviridae:	M. A. Oyekunle
African swine fever	
Parvoviridae:	M. A. Oyekunle
Canine parvovirus infection	
Feline panleukopaenia	
Porcine parvovirus infection	
Arteriviridae:	M. A. Oyekunle
Equine viral arteritis	
Bunyaviridae:	M. A. Oyekunle
Rift valley fever	
Orthmyxoviridae:	M. A. Oyekunle
Avian influenza	
Swine influenza	
Equine influenza	
Paramyxoviridae:	O. E. Ojo
Rinderpest	
Peste des petits ruminants	
Canine distemper	
Newcastle disease	
Bovine respiratory syncytial virus	
Retroviridae:	O. E. Ojo
Avian leucosis	
Feline leukaemia	
Feline immunodeficiency virus infection	
Equine infectious anaemia	
Rhabdoviridae:	O. E. Ojo

Rabies and other lyssaviruses infection
Vesicular stomatitis
Bovine ephemeral fever

Caliciviridae:

Swine vesicular exanthema
Rabbit haemorrhagic disease

Togaviridae:

Equine encephalitides

Reoviridae:

Bluetongue
African horse sickness
Rota virus infections

Birnaviridae:

Infectious bursal disease

Circoviridae:

Chicken anaemia infection

Picornaviridae:

Foot-and-mouth disease
Swine vesicular disease
Porcine enterovirus infection
Avian encephalomyelitis

Coronaviridae:

Feline infectious peritonitis
Canine coronavirus infection
Transmissible gastroenteritis
Porcine epidemic diarrhoea
Infectious bronchitis
Bovine coronavirus infection

Flaviviridae:

Classical swine fever (Hog Cholera)
Bovine viral diarrhoea
West Nile virus infection
Wesselsbron virus infection
Louping ill Japanese encephalitis

Papillomaviridae:

Bovine cutaneous papillomatosis

Non-virus Agents:

Chlamydia,
Bovine spongiform encephalopathy
Scrapies

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VETERINARY VIROLOGY
DR. M. A. OYEKUNLE

FAMILY Herpesviridae

- Introduction
- A large diverse family of DNA virus
- It infects Humans and a wide variety of animal host
- Are large in size and noted for their ability to cause latent infection
- Are divergent with regard to genome sequence and protein biological properties
- But are similar in overall virion structure
- And genome organization
- Viral characteristics
- They are enveloped, double stranded DNA Viruses (100 -200nm in diameter with an icosahedral capsid
- The virions consist of four structural units:

The virions consist of four structural units:

1. The core of DNA around that Wrapped a protein fibrillar spool;
 2. A capsid composed of 12 pentameric and 150 hexameric capsomeres
 3. An amorphous protein layer between the capsid and the envelope
 4. The envelope
- Viral characteristics (Contd)
 - The envelope has projections (spikes) evenly distributed over its surface
 - The dsDNA is used as a template for the production of progeny genomes and mRNAs,
 - Following fusion of the viral envelope with the cell membrane, the nucleocapsid migrates to the cell nucleus, where replication takes place.
 - Viral characteristics (Contd)
 - Viral transcription is divided into immediate early, early, and late early transcription. The structural proteins and the genome (DNA and RNA) re assembled into icosahedral or helical virions, then released.
 - Certain host cells can prevent the transcription of genes and thus the viral genome persist, does not replicate, and the host cell doesn't die. This constitutes a form of viral latency.
 - All herpesviruses thus far examined have the capacity for latency in host cells
 - There is no common antigen
 - Classification of the family Herpesviridae
 - Divided into three sub-families

These are

1. Alphaherpesvirinae
2. Betaherpesvirinae
3. Gammaherpesvirinae

Alphaherpesvirinae

- Have relatively short replication cycle (24 hrs)
- A variable host range
- Causes rapid destruction of cultured cells
- Members of this sub-family establish latent infections in neural cells
- Most herpesviruses of vet importance are found in the genus varicelloviruses

Betaherpesvirinae

- Are of little vet. importance
- Contains three genera
 - (i) Cytomegalovirus
 - (ii) Muromegalovirus
 - (iii) Roseolovirus

Gammaherpesvirinae

- Contains two genera
 - (i) Lymphocryptovirus (Marine & Fresh Water Fish)
 - (ii) Rhadinovirus (Disease in marmosets and monkeys)

Unassigned Genera

- Porcine Herpesvirus 2 e.g. inclusion body rhinitis
- Anatid herpesvirus 1 e.g. Duck viral enteritis
- **Herpesvirus Infection: General**
- All herpesviruses are thought to be capable of establishing latent infection
- The classic example is Human Herpesvirus 1 (HSV-1) which infects the dorsal root ganglia
- The virus is latent between episodes of coldsores
- During latency, only a small region of viral genome is expressed
- Although no protein has been identified as a product of this transcription
- The mechanism of this reactivation of the infection is not understood
- Some virus species infecting eukaryotic hosts are cell-associated and a small number are uncogenetic
- Many infections are silent or mild in natural hosts but serious in other hosts

For example, pseudorabies virus has broad range host and causes fatal encephalitis in variety of animal species but not in natural host-the adult pig

- They are widespread and are frequently recovered in diagnostic laboratory as they can be readily cultivated in cell cultures
- Some produce pox on the **CAM**

- A general rule is that every animal species harbors at least one Herpesvirus
- Herpes Virus of Veterinary Importance
- Family-Herpesviridae

A-subfamily-Aphaerpesvirinae

Genus: Varicellavirus

- (i) Bovine Herpesvirus 1
 - * Causes infections bovine rhinotracheitis (IBR) Pustular vulvovaginitis/balanoposthitis
 - (ii) Bovine Herpesvirus 5
 - * Causes Meningo-encephalitis of cattle
 - (iii) Porcine Herpesvirus 1
 - Causes pseudorabies or Aujeszky's Disease
 - Clinical specimen – brain, lungs, tonsils, spleen, kidney, liver & serum in other animals other than pig a portion of the subcutaneous tissues is taken from site of pustule.
 - Herpes virus of Veterinary Importance (Contd.)
 - (iv) Canine Herpesvirus 1
 - Clinical specimen, lung, kidney
 - (v) Equine Herpesvirus abortion
 - Clinical specimen- Foetal liver, spleen & thymus Natal swabs, wholeblood cerebrospinal fluid, acute and convalescent sera, brain from horses with CNS disease.
 - (vi) Equine herpesvirus 1
 - Causes equine coital exanthema
 - Clinical specimen-scraping from lesions
 - (vii) Feline Herpes 1
 - Causes feline viral rhinotracheitis
 - Clinical specimen- conjunctival scraping & swabs, nasal swabs, lung & trachea of necropsied cat.
 - Herpes Viruses of Veterinary Importance (Contd.)
2. Marek's Disease like Virus
 - (i) Gallid herpes virus
 - Causes Marek's Disease
 - Specimen-whole bird
 3. Infectious Laryngo-tracheitis like virus
 - Gallid herpes virus 1
 - Causes infection laryngotracheitis
 - Clinical specimen-trachea and lung

4. Simplexvirus

- Bovine herpesvirus
- Causes ulcerative mammitis, Pseudolumpy skin disease

(ii) Cercopithecine herpes 1 (B virus of monkey)

- Infects Asian malagne monkeys naturally, has created rare fatal encephalitis in monkey handlers
- Herpes Viruses of Veterinary Importance (Contd.)

B. Subfamily-Gammaherpesvirinae

Genus: Rhadinovirus

(i) Alcelaphine herpes Virus 1

- * Causes malignant catarrhal fever in cattle, deer and other ruminants in Africa-natural host is the wildbeast.
Clinical specimen-Fresh leucocyte (buffy coat), fresh thyroid and adrenal tissue, serum.

(ii) Ovine Herpes Virus 2

- * Causes malignant catarrhal fever in cattle and some wild ruminant; sheep are the natural host-occurs worldwide.
- * Herpes Viruses of Veterinary Importance (Contd.)

C. Unassigned Genera

(i) Porcine herpesvirus 2

- * Causes inclusion body rhinitis

(ii) Anatid Herpes virus 1

- Causes Duck viral enteritis
- Family Poxviridae

Introduction

- These are double stranded DNA virus
- Are the largest and the most complex of known animal viruses
- The infect many vertebrates and insect species
- Unlike the other viruses, some pox viruses are large enough to be seen with a leajet microscope

Viral Characteristics

- Large, enveloped (some virions contain double envelope), double stranded DNA virus

- The capsid/nucleocapsid is brick shaped to avoid containing the genome and lateral bodies (function unknown)
- The large complex genome consist of single, linear molecule of double stranded SNA that codes for approximately 200 proteins. The ends are ligated to each other so the DNA molecule is continuous, without free ends.
- There are the only DNA viruses known to complete their replication cycle in the cytoplasm
- **VIRAL CHARACTERISTICS (CONTD.)**
- Virus of this family posses at least 10 major antigen with a common nucleonprotein antigen, which accounts for cross-reactivity among species.
- There are at least 10 viral enzymes contained within the virus particle, many of which function in nucleic acid metabolism and genome replication.
- Poxviruses remain viable in scabs for long periods
- Some (mainly orthoxvirus) produce hemagglutinins that agglutinate red blood cells
- Eosinophilic inclusions called Gaurnieri bodies may be produced in infected cells/tissues

Classification of Pox Viruses

The Poxviridae consists of two subfamilies

- i. Chordopoxirinae (Pox virus of the vertebrates)
- ii. Entomopoxivirinae (Pos virus of insects)

- There are 8 Genera in the Subfamily Chordopoxivinae.
- Each genus of the Subfamily Chordopoxivirinae contains related virus which generally infect related host
- They are with significant diseases as follows:
- Orthopoxvirus
- Vaccinia
- Variola
- Cowpox
- Feline cowpox
- Horsepox
- Camelpox
- Buffalopox
- Monkeypox

- Parapoxvirus
- Bovine Papular
- Contagious Ecthyma/orf
- Pseudocowpox/milker nodules
- Ectromella/mousepox: An important disease of laboratory and wild mice.
- Capripoxvirus
- Sheeppox
- Goatpox
- Lumpy Skin Disease
- Avipoxvirus
- Fowlpox
- Leporipoxvirus
- Myxomatosis
- Rabbit and Squirrel fibroma: Benign tumors, natural host the cottontail rabbit
- Molluscipoxvirus
- Molluscum contagiosum: A common Disease of children
- Suipoxvirus
- Swinepox
- Yatapoxvirus
- Yaba monkey tumor virus and related viruses

Pox Infections: General

- Poxviruses infect epidermis and produce local lesions that frequently become proliferative and later necrotic
- Rare generalized infections can be fatal
- Poxvirus occur naturally in most Veterinary species except Dog
- Many Poxvirus produce an infection resulting in changes conveniently summarized in order of development as:
 1. Papule
 2. Vesicle
 3. Pustule and
 4. Finally, Scabs or Crusts
- Secondary bacterial infections are not uncommon
- Recovery from poxvirus infection usually is followed by long term immunity
- Many poxvirus can be cultivated on the chorioallantoic membrane of chicken embryo
- Because of their large size Poxviruses can be seen with light microscope in stained smears.
- Virus elementary bodies stained by various procedures including Gutstein's and Giemsa can be readily seen either as aggregates (acidophilic cytoplasmic inclusion) or singly
- Poxvirus may survive for years in dust
- Some mammalian poxvirus are considered oncogenic and have been associated with epidermal and fibromatous hyperplasia

- By far the most studied pox virus is vaccinia virus, the Jennerian small pox virus and some virus which infect cattle and mice.
- Clinical specimen: Vesicular fluid swab, scapping from lesions

Family Asfarviridae

Introduction

This is the family for a category that was referred to previously as African swine fever-like virus it consists of one genus and one specie that causes African swine fever.

Viral Characteristics

- The virions of African swine fever are large, complex and in some structural respects resembles poxviruses.
- This DNA virus consist of a nucleoprotein (70-100nm in diameter) surrounded by an icosahedral capsid and externally by a lipid layer.
- The genome is linear, double stranded (170-190kb in length), and encodes 150-200 proteins

- **VIRAL CHARACTERISTIC (CONTD)**

- The virus replication takes place in the cytoplasm of the host cells (swine macrophages in vivo and in vitro) and soft ticks of the genus Ornithodoros.
- The dsDNA is used as a template for both mRNA and Progeny genomes
- The virus particles are stable in the environment being considerably resistant to heat and pH changes. E.g. the virus is stable for 70 days in blood on boards and 140days in salted dried hams

- **Classification**

- The family has only one genus-Asfivirus
- The genus has on specie-African Swine fever virus which cause African Swine fever
- African Swine fever infection
- After infection by the oronasal route, the virus replicates in the pharynx, tonsils and dependent on lymph nodes
- Viraemia follows by infection of bone marrow, lymph nodes, lungs, kidney and liver where further replication takes place in cells of the lymphoreticular systems

- Clinical specimen: Blood, spleen, tonsil and lymph nodes

FAMILY PARVOVIRIDAE

Introduction

- Are the simplest DNA Animal Virus
- Viral replication is dependent on functions supplied by replicating host cells or by co-infecting helper virus because of the small coding capacity of their genome

VIRAL CHARACTERISTIC

- The genome is single stranded DNA , linear 5, 6kb, MW 1-5—2.0 million
- The virion is icosahedral, 18-26nm diameter and 32 capsomeres
- Has one major and minor protein
- There is no envelope
- Replication is in the nucleus and is dependent on functions of dividing host cells.

Outstanding Characteristic

- Very simple virus
- One genus is replicating defective and requires a helper virus

Classification

- The family Parvoviridae is divided into 2 subfamilies

1. Parvovirinae
2. Dependovirinae – which infects only invertebrates

Parvovirinae has 3 genera

1. **Parvovirus**-contains the autonomous parvoviruses which has widespread and capable of autonomous replication e.g Canine Paro virus infection, Feline panteukopamia, Porcinne Pano virus infections
2. **Dependovirus** –requires helper virus function for replication
3. **Erythrovirus** e.g. 819 Parvovirus of human bind to erythrocytes pantigens for replication

Parvovirus Infection: General

- The Parvovirinae is the subfamily that contains parvovirus that are pathogenic to vertebrates.

Genus	Virus	Host	Disease
Parvovirus	Minute Virus	Mice	Subclinical of Mice (MVM)
	Feline Parvovirus (FPV)	Cat	Enteritis, leucopenis Cerebral ataxia
	Canine Parvovirus (CPV)	Dog	Enteritis, myocarditis
	Porcine Parvovirus (PPV)	Pigs	Reproductive failure
Dependovirus	Adeno-associated Virus(AAV)	Human & Others	Unknown
Erythrovirus B19		Man	Respiratory tract illness Aplastic crisis, Hydrops foetalis, Erythema infectiosum, firth Disease
	Simian Parvovirus	Monkey	Anaemia

Orthomyxoridae

Introduction

This is a family of negative-sense, single-stranded RNA viruses. They are smaller than the paramyxoviruses and their genome is segmented (7 to 8 segments) rather than consisting of a single piece RNA. Influenza viruses are the only members of Orthomyxoridae.

Viruses of this family have a predilection for the respiratory tract, but usually do not cause a serious disease on uncomplicated cases. Exceptions are human infections with viruses of avian origin. Principal viruses of veterinary importance are type A influenza viruses, which causes equine, swine, and avian influenza.

Viral characteristics

- i. Viruses have a segmented single-stranded RNA genome, helical nucleocapsids (each RNA segment + proteins nucleocapsid) and an outer lipoprotein envelop.
- ii. The segmented genome facilitates genetic reassortment, which accounts for antigenic shifts. Point mutations in the RNA genome accounts for antigenic drifts that are often associated with epidemics. In either case, the changes are frequently associated with the HA (hemagglutinin) and NA (neuraminidase) antigens.

The envelop is covered with two different kinds of spikes, a hemagglutinin (HA antigen) and a neuraminidase (NA antigen). In contrast, the hemagglutinin and neuraminidase activities of paramyxoviruses are in the same protein spike

In the laboratory, the viruses replicate best in the epithelial cells lining the allantoic cavity of chicken embryos.

The viruses agglutinate red blood cells of a variety of species.

Replication takes place in the nucleus.

The viral RNA-dependent RNA polymerase transcribes the negative-sense genome into mRNA.

Immune Response

The host immune response to influenza viruses includes:

- Non-specific immune response: the release of interferons by the infected cells aids in preventing viral spread to neighboring cells.
- Humoral immune response: IgA in the upper respiratory tract and IgA in the lower respiratory tract.
These antibodies are typically directed against the HA and NA antigens.
- cell-mediated immune response: cytotoxic T lymphocytes are important in recovery

Classification

The family consists of four genera:

Influenza virus A; Viruses cause avian, equine and swine influenza: associated with both epidemics and pandemic; both antigen drift noted. High antigenic variability in the surface glycoproteins HA and NA

Influenza virus B; Members infect only humans; associated with epidemics; antigen drift noted.

Influenza virus C; viruses cause mild, sporadic respiratory infections in humans. May also infect swine.

Thogoto-like viruses: the two species Thogoto and Dhori viruses are tick-borne viruses recovered from cattle, camels, and humans in the regions of Asia, Africa and Europe. They are not considered to be of pathogenic significance for animal.

Antigenic Composition

Knowledge of the antigen nature of influenza viruses is necessary for an understanding of the epidemiology of influenza.

The internal proteins consist mainly of nucleocapsid proteins (NC), some matrix proteins (M1) and three polymerase (PA, PB1 and PB2). The proteins NC and M1 determine type specificity. Even being internal, these proteins (or peptides derived from them) may elicit cytotoxic T cells that are important in recovery from infection.

The nucleoprotein antigen (A,B,C) determine the virus type. The HA and NA antigens determine subtypes.

The hemagglutinin (HA) is an envelope antigen (spike) that can attach to erythrocytes and cause agglutination. It is responsible for the attachment of the virion to cell surface receptors (neuraminic acid, sialic acid) if blocked by antibody, attachment of the virus to a susceptible cell is prevented; thus it is very important in protective immunity mediated by neutralizing antibody. A hemagglutinin-inhibition titer of 1/40 is considered to be protective.

Neuraminidase is an envelope protein whose enzymatic activity results in the liquefaction of mucus thus contributing to viral spread. Specific antibody slows down the spread of virus. Neuraminidase also cleaves neuraminic acid to release progeny virus from the infected cell.

Influenza viruses are designated as follows: type/place/time of isolation/H and N content. In birds, there are approximately 15 H antigens (H1 – H 15) and 9N antigen (N1 – N9), which can be found in all possible combinations. An example would be H7 N3. therefore, the type A virus: A/Bangkok/3/79 (H3N2)₃, first isolated in 1979, and envelope antigen H3N2.

Antigenic Variation

In brief there are two kinds of antigenic change:

Antigenic shift: These are major changes based on reassortment of segments of the genome. In reassortment, entire segments of RNA are exchanged between two viruses

infecting the same host, each of which codes for a single protein, e.g. hemagglutinin. As a result of co-infection by two viruses, a third one may arise.

Antigenic drift: These are minor changes caused by point mutations in the genes encoding the HA and NA glycoproteins.

Genetic Basis for Antigenic Variation

The genes of the type A viral hemagglutinin and neuraminidase are polymorphic, subject to extensive variation. This not the case for types B or C.

The HA and NA genes of types A and B viruses undergo point mutations. When developing a vaccine, the effect of change can be determined by the reciprocal inhibition test. As a result of the change, the immune response generated against vaccine HA or NA is now less effective against mutated (variant progeny) HA or NA.

Influenza A

Equine Influenza

Cause

Equine influenza virus A. The immunologically distinct subtypes involved are usually A/equine/Prague/1/56(H7N7) or A/equine/Miami/2/63 (H3N8). These are also referred to as influenza A/equine 1 and influenza A/equine2. they are also referred to as Type 1 or Equi-1 (Prague) and Type 2 or Equi-2 (Miami). New variants resulting from antigenic drift appear to be infrequent. All recent and current outbreaks have been attributed to A Equi-2.

Clinical specimen: Nasal and ocular swab during a acute phase, Acute and convalescent sera.

Avian Influenza

(Fowl plaque)

Cause

Influenza A virus (avian). There are 15 antigenic groups based on hemagglutinin inhibition and nine based on neuraminidase. The many strains of virus infecting waterfowl provide sources for new mammalian strains, e.g. strain H5N1 a highly pathogenic avian caused influenza with high mortality in humans in Hong Kong. Subtypes H5 and H7 have caused serious outbreaks of avian influenza in commercial flocks of chickens and turkeys. When these pathogenic stains are identified, premises are quarantined and infected flock slaughtered.

Clinical specimen: whole bird or lug, trachea, airsac, spleen, faeces and serum.

Swine Influenza
(Swine flu, Hog flu)
Cause

Influenza virus A. Subtypes H1NA and H3N2 have been frequent causes of swine influenza. More virulent variants H1N1 have appeared in recent years. The H1N2 subtype has also been implicated as a cause of acute swine influenza. It has been suggested that all porcine influenza viruses were derived originally from birds. Secondly infection with *Haemophilus parvisuis* and other bacteria may contribute to a more severe disease.

Clinical specimen: Nasal swabs and lugs, acute phase, Acute and convalescent sera.

Canine Influenza
(Dog flu)
Cause

Influenza A virus, closely related to subtype H3N8 and presumed to have been acquired from horse(s). Subtype H3N8 virus is a frequent cause of equine influenza.

Specimen: Nasopharyngeal swab taken within 72 hours of the appearance of signs, paired serum samples with a 3 weeks interval.

Family – Bunyaviridae

This is one of the arboviruses. Arboviruses are defined (WHO Scientific Wasp) as viruses that are maintained in nature principally or to an important extent, through biological transmission between susceptible vertebrate hosts by haematophagous arthropods or through transovarian and possible venereal transmission in arthropods, the viruses multiply and produce viraemia in the vertebrates, multiply in the tissue of the arthropods, and are passed on to new vertebrates by the bites of arthropods after a period of extrinsic incubation.

There are six families containing the arboviruses. Certain viruses within the 6 families are not transmitted by arthropods but maintained in nature within rodents as reservoirs that may transmit the infection directly to human of Hantavirus genus e.g the family Bunyaviridae.

Characteristics of the family Bunyaviridae

Are single stranded negative sense RNA virus they are enveloped. The capsid is helical virus size is 100 – 120nm. The RNA genome has 11 – 12,000 nucleotides the site of capsid assembly is the cytoplasm by budding through Golgi vesicles. Bunyaviruses have

tripartite genome where the genetic material of the virus is divided between 3 pieces of the single stranded RNA termed large (L), medium (M) small (S) segments.

The L RNA segment encodes the RNA – dependent RNA polymerase also termed L protein. The MRNA segment encodes two glycoproteins termed G1 and G2 that are found on the surfaces of the various and the Bunyaviruses, Tospovirus and Phlebovirus genera have a non-structural protein NSM whose function is unknown. The SRNA segment encodes a nucleocapsid (N) protein. The Bunyavirus a genus also contains a non-structural protein termed NSS in an overlapping reading frame while Phlebovirus and Tospovirus genera also contain NSS gene.

The tripartite genome structure enables the bunyaviruses to undergo genetic reassortment whereby a cell infected by two or more bunyaviruses can result in a progeny viruses containing segments from different viruses. Reassortment has been shown to take place in nature between closely related bunyaviruses and is considered to be a process that contributes to genetic variation and evolution.

A virus that has a negative sense RNA genome must contain virus RNA dependent RNA. Polymerase so that its genome can be transcribed in cells to generate m-RNA of different viral genes. In addition the NSm gene of the Tospovirus genus and the NSs gene of this Phlebovirus and Tospovirus genera are encoded as in genes in the positive sense orientation. Thus, the S and M RNA segments of Tospoviruses and the S RNS segment of the Phleboviruses are termed ambience RNAs to denote that the open reading frames of the genes are in opposite orientation

Classification of Bunyaviridae family

The family has 138 members in 5 genera.

1. Genus Bunyaviruse (172) e.g La Gross
2. Nairovirus (34) e.g Crimea Congo haemirhagic fever Nairobi sheep disease
3. Phlebovirus (51) e.g. Rift valley fever (Zoonolic disease of ruminants)
4. Hantavirus (15) Sin-Nombre (Not arthropod borne)
5. Tospovirus plant viruses

Pathogenesis of the Bunyaviruses

The individual viruses of the family Bunyavividae are named after the disease or the geographical are where the virus is first isolated. Diseases produced by arbovirus generally may be divided into 3 clinical syndromes.

1. Fever with oar without maculopapular rash and is usually benign.
2. Encephalitis – is often with high fatality rate.
3. Haemorrhagic fevers – also frequently severe and fatal .

Specimen for diagnosis: Acute and convalescent sera

Family – Arteriviridae

Characteristics

Single stranded, positive sense RNA virus

Capsid symmetry – Icosahedral

Virion size (nm) - 40 – 60

Genus – Arterivirus

Representative species – Equine arteritis virus.

There is genomic and antigenic variation among the geographically disparate isolates.

The virus strains also vary in their ability to produce disease.

The disease produced by the virus is equine viral arteritis (EVA) which is an acute contagious viral disease of equid.

It is characterised by fever, depression, dependent oedema, conjunctivitis, nasal discharge and sometimes death in young foals.

Specimen for diagnosis. Blood, swab from nasal and conjunctival discharges.

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RHABDOVIRIDAE (*RHABDO* = *ROD*)

Order: Mononegavirale

Family: Rhabdoviridae

Genera:

- Cytorhabdovirus
- Ephemerovirus
- Lyssavirus
- Nucleorhabdovirus
- Vesiculovirus
- Novirhabdovirus: example include Infectious haematopoietic necrosis virus of fish

General properties:

- Members have characteristic rod shapes
- Rhadoviruses of vertebrates are 'bullet-shaped' or cone-shaped
- Enveloped viruses
- Helical symmetry
- About 100 to 430nm x 45 to 100nm
- Possess a linear, non-segmented RNA genome of negative polarity/sense and about 10 – 12 kilobase in size
- Genome encased in a ribonucleoprotein complex
- Contain five major proteins:
 - large RNA-dependent RNA polymerase (L)
 - surface glycoprotein (G): forms the surface spikes for interaction with host cell receptor. Also induces virus-neutralising antibodies and cell mediated immunity
 - nucleoprotein (N)
 - protein component of the viral polymerase (P)
 - matrix protein (M)
- Replication takes place within the cytoplasm with the exception of nucleorhabdovirus

- Virion released by budding from host cell plasma membrane
- Stable at pH 5 to 10
- Inactivated by heating at 56°C, treatment with lipid solvents and exposure to UV light

Genera of Veterinary importance: Lyssavirus, Vesiculovirus and Ephemerovirus

LYSSAVIRUS (*Lyssa = rage/fury*)

Viruses:

- Rabies virus (Lyssavirus genotype 1)
- Lagos bat virus (Lyssavirus genotype 2)
- Mokola virus
- Duvenhage virus
- European bat lyssavirus 1
- European bat lyssavirus 2
- Australian bat lyssavirus

RABIES:

- caused by Rabies virus (Lyssavirus genotype 1).
- Viral infection of the central nervous system of most mammals and man.
- Carnivores (Dogs, foxes, wolves, coyotes, jackal) highly susceptible
- Urban rabies: maintained in dogs
- Sylvatic rabies: maintained in wildlife
- Important reservoirs: skunks, racoon, foxes, bats

Transmission: bite of infected animals. Transmission through scratching, licking, open wound and conjunctiva is also possible. Saliva is rich in the virus. Infected animals may excrete the virus in saliva before clinical manifestation

Clinical sign: Prodromal, furious (excitative) and dumb (paralytic) phases.

Prodromal: Confusion and disorientation

Furious/Excitative: increased aggressiveness, hyperexcitability, bite of inanimate objects

Dumb/paralytic: muscle weakness, difficult swallowing, profuse salivation, dropping of jaw. Difficulty in swallowing water (hydrophobia) due to pharyngeal paralysis

Other lyssaviruses: similar to rabies.

DIAGNOSIS:

- Clinical signs
- Samples for isolation: brain tissue, saliva, CSF, urine
- Histology: non-suppurative encephalitis characterised by perivascular lymphocytic cuffing and intracytoplasmic inclusion bodies (Negri bodies)
- Direct fluorescent antibody test (FAT) with fluorescein labelled specific antiserum
- Virus isolation in neuroblastoma cells or in baby hamster kidney cells. Rabies virus is non-cytopathic and can be detected by FAT
- Virus can also be isolated in newborn mice inoculated intracerebrally with suspected brain tissue. The animal is observed for signs of disease. Rabies virus is detected by FAT
- Reverse transcriptase polymerase chain reaction (RT-PCR) distinguishes rabies from other lyssaviruses.

CONTROL:

- Quarantine
- Isolation of suspected dog for 10 days
- Movement restriction
- Elimination of stray dogs and cat
- Vaccination of susceptible animals (High egg passage and Low egg passage live attenuated rabies vaccine)
- Vaccination of wildlife reservoirs (live oral vaccines, vaccinia-rabies virus glycoprotein, recombinant rabies vaccine)

- Hyperimmune serum

VESICULOVIRUS



Viruses:

- Vesicular stomatitis Indiana virus (type species, most common): three subtypes, Indiana-1, Indiana-2, and Indiana-3
- Vesicular stomatitis New Jersey virus (most severe)
- Vesicular stomatitis Alagoas virus
- Cocal virus

Vesicular stomatitis

- Caused by members of the genus Vesiculovirus
- Clinical similar to Foot-and-Mouth-Disease
- A reportable zoonotic disease
- Affects horses, swine, cattle, llamas, sheep, goats, deer, bobcats, raccoons, monkeys and humans.

Transmission: by contact and insect vectors

- Virus is shed in saliva
- Virus has been isolated from blackflies, mosquitoes, sandflies and houseflies
- Virus can be acquired through skin abrasions and mucous membranes

Clinical signs:

- Subclinical infection is common
- Occur more in animals over one year old
- Fever
- Vesicular lesions typically develop on the tongue and oral mucosa
- Vesicles ruptures and may progress to ulcers and erosions

- There may be secondary bacterial infections.
- Swine usually exhibit lameness
- Vesicular lesions in swine are generally located on the coronary band and snout.
- Cattle may additionally develop lesions around the coronary band, interdigital spaces, and teats (mastitis)
- Humans commonly develop flu-like symptoms including fever, chills, headache, muscle pain and runny nose.
- Humans occasionally develop oral vesicles
- Rarely causes death, but may be fatal due to secondary bacterial infections

DIAGNOSIS

- Differential diagnosis: foot-and-mouth disease, swine vesicular disease, vesicular exanthema of swine, infectious bovine rhinotracheitis, and bluetongue.
- Vesicular lesions in horses
- Suitable samples: Vesicular fluid, epithelium of lesions
- Detection of viral antigen by Enzyme Linked Immunosorbent Assay and Complement Fixation Test
- Virus isolation in suitable cell lines, embryonated eggs or in suckling mice by intracerebral inoculation. Virus produces cytopathic effects.
- ELISA, CFT or virus neutralisation can be used for identification of growing virus
- Electron microscopy of vesicular fluids or fresh lesions

CONTROL:

- Notifiable disease
- Movement restriction
- Control of insect vectors
- Vaccines not commercially available
- Zoonotic

EPHEMEROVIRUS

Virus: Bovine ephemeral fever virus

Disease: Bovine ephemeral fever

Host: Cattle, water buffalo

Transmission: Arthropod-borne (*Culicoides spp*)

Clinical signs:

- More severe in well-fed animals
- Diphasic fever
- Lethargy, anorexia, lameness, constipation
- Muscle stiffness, ruminal stasis
- Abortion
- Recumbency, salivation, nasal and ocular discharges
- Hypocalcaemia
- Short duration and recovery within few days

DIAGNOSIS

- Based on clinical signs
- Demonstration of rising virus specific antibody by virus neutralisation test or ELISA on paired serum sample

CONTROL:

- Attenuated and inactivated vaccines
- Subunit vaccine based on envelope glycoprotein
- Vector control

PARAMYXOVIRIDAE

The paramyxoviruses were formerly grouped together with orthomyxoviruses as myxoviruses because of their affinity for the mucous membranes. Members of the family are pleomorphic viruses of about 150nm or more in diameter, they are enveloped and the genome is a single molecule of single-stranded of RNA. Generally, two types of glycoprotein spikes, which can induce the production of virus neutralizing antibodies in infected host, project from the envelope. The glycoprotein spikes are:

- i. Attachment protein (F). The attachment protein may either be a haemagglutinin-neuraminidase protein (HN) or a protein without neuraminidase activity (G). the attachment proteins allow the virus to bind to cell surface receptors
- ii. Fusion protein: This causes the virus envelope to fuse with the host cell membrane

Paramyxoviruses also possess a non-glycosylated envelope-associated membrane protein (G). they may exhibit haemagglutinating, haemolytic and neuraminidase activities. The nucleocapsid is about 13 to 18nm in diameter and possesses a helical symmetry with characteristic herring-bone appearance. Replication takes place in the cytoplasm of the host cell and mature virions are released by budding from the plasma membrane at the sites containing virus envelope proteins. Virions are very labile and sensitive to heat, desiccation, lipid solvents, non-ionic detergents and disinfectants.

Classification:

Order: Mononegavirale

Family: Paramyxoviridae

Subfamilies:

1) Subfamilies: 2)	3) Genera	4) Viruses
5) a. Paramyxovirinae	6) i. Respirivirus	7) Bovine parainfluenza virus
	8) ii. Morbillivirus	i. Rinderpest virus ii. Peste des petits ruminants virus iii. Phocine distemper virus iv. Canine distemper virus v. Cetacean morbillivirus vi. Equine morbillivirus
	9) iii. Rubulavirus	i. Newcastle disease virus ii. Avian paramyxoviruses 2 – 9 iii. Canine parainfluenza virus 2 iv. Porcine rubulavirus
b. Pneumovirinae	10) i. Pneumovirus	11) Bovine respiratory syncytial virus 12)
	13) ii. Metapneumovirus	14) Turkey rhinotracheitis virus

Clinical infections caused by paramyxoviruses:

Generally, paramyxoviruses have narrow host range. They infect mainly mammalian and avian species. Transmission is by close contact and by aerosol. They have high affinity for the respiratory tract where replication usually takes place. Infection is generally cytolitic. Formation of syncytia and intracytoplasmic, acidophilic inclusion bodies are prominent features of paramyxovirus infections.

RINDERPEST

Rinderpest has for centuries been recognized as a major cause of morbidity and mortality in cattle and domestic buffalo. It is also called ‘Cattle Plague’. The disease is endemic in parts of Africa, the Middle East and Asia. It is said to have been eradicated in Nigeria. It is caused by Rinderpest virus. Only one serotype of Rinderpest virus is recognized.

Strains of the virus differ in both host range and virulence. Susceptible animals include cattle, buffalo, giraffe, cape buffalo, eland, and warthog. Gazelle and small domestic ruminants (sheep and goats) are less susceptible.

Transmission occurs through close contact and aerosol. The virus is labile and survives for short period outside of the host. Epidemic is associated with movement of susceptible animals to endemic area or the introduction of infected animals into susceptible populations. All ages of animal are susceptible. Morbidity may reach 90% and mortality close to 100%.

Clinical signs: include fever, anorexia, depression, erosion of the oral and respiratory tract mucosae, profuse salivation, oculonasal discharge, profuse diarrhea (dark watery faeces containing mucuc, necrotic debris and blood), dehydration, wasting, collapse and death within 12 days of the onset of clinical signs.

Diagnosis:

- Clinical signs and pathological findings may be suggestive.
- Differential diagnoses include bovine viral diarrhea, infectious bovine rhinotracheitis, malignant catarrhal fever, foot and mouth disease.
- Postmortem enteric lesion: congestion of the folds of the colonic mucosa often produces a Zebra-stripe pattern
- Syncytia formation in stratified squamous epithelium of the upper alimentary tract and in crypts of the small intestine
- During an outbreak, samples for laboratory diagnosis should be collected from febrile animals which have not developed diarrhea. Suitable specimens include white cells from the buffy coat of heparinized blood samples, lymph nodes and spleen
- Rinderpest virus is detectable in tissue by immunofluorescence tests
- Agar gel immunodiffusion or a counter immunoelectrophoresis test can be used for rapid antigen detection. Ocular discharges and mesenteric lymph nodes are suitable specimens for these procedures
- Reverse transcription polymerase chain reaction method can detect rinderpest virus and differentiate it from PPR virus
- Competitive ELISA for detection serum antibodies to rinderpest virus

Prevention and Control:

- Restriction of movement
- Quarantine of imported animals
- Slaughter of infected animals
- Vaccination: modified live tissue culture rinderpest vaccine confers immunity lasting at least five years. The vaccine is easily destroyed by heat after reconstitution
- Recombinant vaccinia and capripox virus vaccines expressing either haemagglutinin protein or fusion protein of rinderpest virus have high heat stability

PESTES DES PETITS RUMINANTS

This disease is also called goat plague. It is an acute contagious disease of ruminants especially goats. It is caused by the virus pestes des petits ruminant virus; a morbillivirus. Members of the morbillivirus are closely related and induce similar clinical manifestation in affected host. The disease occurs in sub-saharan Africa, Middle East, India and Pakistan.

Transmission: close contact is required for aerosol transmission. The virus is very labile.

Clinical signs: In Nigeria, Epizootic of the disease occurs during the rainy season when goats are gathered together for sale. Similar but less severe clinical infection also occurs in sheep. The disease is more severe in young animals. There is fever, dry muzzle, serous nasal discharge that become mucopurulent with secondary bacterial infection. There is erosion of the mucous membrane of the buccal cavity and marked salivation. Signs are similar to those seen in rinderpest.

Diagnosis:

Samples should be collected at the acute phase of infection. Samples to be collected include nasal and ocular swabs, unclotted blood, scrapings of buccal and rectal mucosae in live animals as well as lung, spleen and lymph nodes from animals slaughtered at the acute phase of infection. Laboratory confirmation is based on virus isolation in tissue culture and on antigen detection. Rapid antigen detection is by ELISA, counter immunoelectrophoresis and agar gel immunodiffusion. Antibody detection in serum sample is by virus neutralization and competitive ELISA. Primers are available for the detection of PPR virus nucleic acid.

BLUE EYE DISEASE IN PIGS

This disease is caused by porcine rubulavirus. It is characterized by neurological signs, corneal opacity and reproductive failure. Morbidity and mortality are highest in young pigs.

Diagnosis: Presumptive diagnosis is based on clinical signs and confirmation is by laboratory investigations. Serological testing of paired sera sample to demonstrate fourfold rise in antibody level signifying on-going infection is carried out. Antibody detection is by haemagglutination inhibition test, ELISA and virus neutralization test.

BOVINE RESPIRATORY SYNCYTIAL VIRUS

This virus causes pulmonary disease in cattle, sheep and goat. It induces characteristic syncytial in infected cells *in-vivo* and *in-vitro*. The disease is seen most commonly in animals between three and nine months old. In adults, the disease is mild and usually subclinical. Severe disease rarely occurs in adults.

Diagnosis:

- Specimens include nasal swabs, bronchoalveolar lavage fluid, lung tissue and paired serum samples.
- Since the virus is thermolabile, specimens must be transferred to the laboratory in suitable transport medium
- Commercial ELISA kits are available for the detection of viral antigen
- Immunofluorescence is a rapid and useful technique for antigen detection
- Viral antigen can be detected more rapidly in specimens from the lower respiratory tract than in nasal swabs
- Suitable serological test for demonstrating rising antibody titre include virus neutralization and ELISA. Serum samples should be taken early in the course of the disease as the antibody levels tend to rise rapidly.
- Polymerase chain reaction can be used to detect viral RNA

Control:

- Reducing stress factors within cattle herd
- Maintenance of good hygiene
- Separating calves from among older age groups

- Vaccination with modified live and inactivated vaccine: duration of protection is short therefore frequent booster dose is required

CANINE DISTEMPER

This is a highly contagious disease of dogs and other carnivores caused by Canine distemper virus, a morbillivirus in the family Paramyxoviridae. Canine distemper virus is a pantropic virus that produces generalized infection involving many organs of the body. Only one serotype of the virus is presently recognized. However, a variety of biotypes exist that vary greatly in pathogenicity and tissue tropism within the CNS. Antigenic differences have not been detected among CDV strains using such tests virus neutralization, complement fixation, antigenic precipitation and immunofluorescence. There is evidence of cross-reactivity of CDV with measles virus, rinderpest virus and Peste des petits ruminants virus.

Clinical Signs: incubation period is about one week but may be up to four weeks or more with sudden appearance of nervous signs without prior evidence of infection. Infection spreads among young dogs aged between three weeks and six months about the time of decline of maternally derived passive immunity. Affected animals may manifest biphasic fever, oculonasal discharge, pharyngitis, tonsillar enlargement, coughing, vomiting, diarrhea, skin rashes and pustules, hyperkeratosis of nose and footpad (hard pad), neurological signs such as paresis, myoclonus, epileptiform seizures and death. Manifestation of neurological signs is of grave prognosis. Recovered animals may show residual neurological abnormalities.

Diagnosis:

- Clinical signs may be suggestive.
- Viral antigen may be demonstrated by immunofluorescence in conjunctival or vaginal impression smears or in smears of cells from the buffy coat
- Cryostat section of lymph nodes, urinary bladder and cerebellum are also suitable for the demonstration of viral antigen
- Eosinophilic inclusions can be demonstrated in nervous and epithelial tissues

- Serological demonstration either of IgM antibodies or of a fourfold rise in antibody titre between acute and convalescence sera may be determined by virus neutralization test, ELISA, or indirect immunofluorescence. Antibody may be detected in cerebrospinal fluid
- Virus isolation may be attempted from urinary bladder, cells from the buffy coat and brain tissue. Virus isolation may prove difficult

Control: modified live vaccines are available commercially and it provides adequate protection when administered to puppies after the decline of maternally derived antibody. In endemic areas, pregnant bitches may be vaccinated to offer passive protection to their puppies for the first few weeks of life.

NEWCASTLE DISEASE

Newcastle disease occurs in poultry birds worldwide. It is caused by Newcastle disease virus designated avian paramyxovirus 1 (APMV-1). Avian paramyxovirus 1 is antigenically related to the virus of Mumps. A large number of avian paramyxovirus (APMV) isolates has been recovered from a range of domestic and wild birds worldwide. Nine species of antigenically distinct APMV are currently recognized in the genus Rubulavirus within the family Paramyxoviridae. Avian paramyxovirus 2 and 3 are associated with respiratory disease in turkeys. Newcastle disease manifests either in the respiratory or nervous form. Because of the clinical manifestations, the disease is also called Avian pneumoencephalitis.

A wide range of avian species including chicken, turkey, pigeon, pheasants, ducks and geese are susceptible to NDV. Infection is endemic in wild birds especially waterfowls. The virus is shed in all secretions and excretions of the affected host. Transmission occurs through aerosol or by ingestion of contaminated feed and water. The virus is relatively stable in the environment thereby permitting mechanical transfer of the virus through fomites. Virus is present in all organs of acutely affected birds and in eggs.

Clinical signs: the incubation period is usually about five days. Respiratory, gastrointestinal and nervous signs occur in chickens. The particular clinical presentation relates to the virulence of the virus strain, its tissue tropism and the age and immune status of the host.

Pathotypes of NDV based on virulence and tissue tropism:

1. Viscerotropic velogenic isolates causing severe fatal disease characterized by haemorrhagic intestinal lesions (Doyle's form).
2. Neurotropic velogenic isolates causing acute disease characterized by nervous and respiratory signs with high mortality (Beach's form).
3. Mesogenic isolates causing mild disease with mortality confined to young birds (Beaudette's form). This presents with respiratory signs, occasionally nervous signs but low mortality.
4. Lentogenic isolates causing mild or subclinical respiratory infection (Hitchner's form).
5. Asymptomatic enteric isolates: a form that usually consists of a subclinical enteric infection.

Immunology: Newcastle disease virus induces haemagglutination inhibiting and serum neutralizing antibodies. Antibody production is rapid. It can be detected within 4 to 6 days of infection and persists for at least two years. The level of haemagglutination inhibiting antibody is a measure of immunity. Maternal antibody protects chicks for three to four weeks after hatching. Immunoglobulin G is confined to the circulation and does not protect respiratory infection but blocks viraemia. Locally produced IgA antibodies play an important role in protection in both respiratory and intestinal tracts.

Diagnosis:

- Presumptive clinical diagnosis is based on clinical signs and post mortem findings
- Suitable samples for laboratory confirmation include tracheal and cloacal swabs from live birds for virus isolation
- Postmortem samples for laboratory investigations include faeces, intestinal content and tissues from trachea, intestine, spleen, brain and lung.
- Samples may be stored at 4°C for up to four days
- Virus isolation is carried out in embryonated egg from specific pathogen free flocks. Sample is inoculated into the allantoic cavity of the embryonated egg. After incubation, allantoic fluid is tested for haemagglutination activity
- Haemagglutination inhibition test using specific antiserum confirms the presence of NDV

- Demonstration of antibody to NDV is of diagnostic value only in unvaccinated flocks. The haemagglutination inhibition test is the most widely used assay. Commercial ELISA kits are also available
- Demonstration of viral antigen in tracheal section or impression smear using immunofluorescence test is a less sensitive technique than virus isolation

Control:

- Locating poultry farms far apart
- Preventing wild birds from having access to pens and feed-stores
- Restricted human access to farm
- Movement restriction between farms
- Thorough cleaning and disinfection of vehicles and equipment
- Some countries practice test and slaughter policy
- Vaccination: lentogenic or mesogenic strains of NDV propagated in egg or tissue culture are used in live vaccines. They are administered as sprays, in drinking water or by intranasal or intraconjunctival instillation
- The presence of maternally derived antibodies may interfere with the efficacy of live vaccines
- Practice in Nigeria:
 - Day 1 – 10: intraocular vaccination with Hitchner B-1 strain
 - 3 weeks: oral vaccination in drinking water with LaSota strain
 - 6 weeks: intramuscular vaccination with Komarov strain
 - Quarterly intramuscular vaccination with Komarov strain in laying birds or bimonthly oral vaccination with LaSota strain

BIRNAVIRIDAE

Members of the virus family Birnaviridae possess two segments of linear double stranded RNA genome, an icosahedral capsid symmetry and are about 60nm in diameter. Five polypeptides designated VP1, VP2, VP3, VP4 and VP5 have been identified. The VP2 is the major capsid protein and contains epitopes which induce neutralizing antibodies. Birnaviruses replicate in the cytoplasm of the host cells and the process involves a virion-associated RNA-dependent RNA polymerase.

Classification

Family: Birnaviridae

- Genera:
1. Avibirnavirus (infect chicken)
Virus: Infectious bursal disease virus
 - 2: Aquabirnavirus (infect fish)
 3. Entomobirnavirus (infect insects)

Birnaviruses are stable over a wide pH range and at temperature of 60°C for one hour. They are resistant to ultraviolet irradiation and photodynamic inactivation. They are resistant to treatment with ether and chloroform. Infectious bursal disease virus is inactivated at pH 12.0 and by exposure to 1% phenol for 1 hour or 1% formalin for 1 hour. It is also inactivated by heat at 70°C for 30 minutes. It does not haemagglutinate erythrocytes unlike Newcastle disease virus.

Two economically important diseases associated with birnaviruses are infectious bursal disease of chickens and infectious pancreatic necrosis of salmonids. These diseases occur worldwide and cause considerable losses in poultry units and in farmed salmon.

INFECTIOUS BURSAL DISEASE

Infectious bursal disease has been reported in most major poultry producing areas of the world. The greatest incidence is in chicks 3 to 8 weeks old. However, outbreaks have been reported in 9 days old chicks and in 20 weeks old layers. Infection which is usually acquired by the oral route occurs when maternally-derived antibody levels are waning at two to three weeks of age. Virus is shed in the faeces for up to two weeks after infection and can remain infectious in the environment of a poultry house for several months. Mortality is usually between 20 – 30% but could be as high as 37% while morbidity is usually high approaching 100%. The disease shows a spiking mortality curve. It is a self-

limiting disease. Infection can spread to other poultry units via fomites. Vertical transmission and carrier state have not been demonstrated. Clinical infection occurs majorly in chicken but turkeys, ducks and guinea fowls may be infected.

Antigenic properties of IBDV:

Based on neutralization tests, isolates of IBDV are assigned to two serotypes:

Serotype 1: contains viruses that are pathogenic for chicken. There is considerable variation in the virulence of isolates in serotype 1. Very virulent (VV) strains of serotype 1 can cause disease even when maternally-derived antibody against the classical vaccine is present. These variants are classified as subtypes of serotype 1 because of their antigenic similarity. There are at least about six subtypes of serotype 1.

Serotype 2: these isolates infect chickens and turkey but these infections are of relatively low significance.

The two IBDV serotypes share group antigen detectable by IFT and AGID

Clinical signs of IBDV infection: the severity of clinical signs is influenced by the virulence of the virus, the age of chicks at the time of infection, the breed of the chicks as well as the level of maternally-derived antibody. An acute form of the disease develops following a short incubation period at about three to six weeks of age. Affected birds show signs of depression, loss of appetite, diarrhea and vent pecking due to irritation resulting from inflammation of the bursa of Fabricius. The disease is of very short course with surviving birds recovering within four days of onset of clinical signs.

Diagnosis:

CIRCOVIRIDAE

The virus family Circoviridae is a recently established virus family. Members cause diseases in vertebrate animals and plant. They are about 17 to 22nm in diameter. They are non-enveloped virus with icosahedral symmetry. Circoviruses are stable in the environment at pH 3 to 9 and are resistant to heating at 60 °C for 30 minutes. They possess a circular single stranded DNA genome.

There are three genera in the family circoviridae based on genomic composition:

1. Gyrovirus: chicken anaemia virus, type species of the family belongs to this genus
2. Circovirus: Porcine circovirus and beak and feather disease virus are members of this genus
3. Nanovirus: members of this genus have been removed from the family Circoviridae. They are plant viruses

Clinical Infections

Circoviruses are host specific and infect cells of the haemolymphatic system. Diseases of veterinary importance include:

- i. Chicken anaemia virus infection
- ii. Pig circovirus infection
- iii. Beak and feather disease (a debilitating immunosuppressive disease of young psittacine birds especially cockatoos)

Chicken anaemia virus infection

This disease can be transmitted by vertical and horizontal (faeco-oral) transmission. It causes aplastic anaemia and generalized lymphoid atrophy in young birds. Only chickens are susceptible.

Clinical signs: depression, anorexia, paleness, mortality of about 10% but may reach 50%. Other immunosuppressive diseases especially infectious bursal disease increase susceptibility.

Diagnosis:

- Clinical signs and gross postmortem lesions are suggestive.
- Laboratory confirmation is by viral antigen detection using immunocytochemical technique.

- Viral DNA can be detected in bone marrow and thymus samples using in situ hybridization, dot-blot hybridization or by polymerase chain reaction
- Serological tests include virus neutralization, indirect immunofluorescence and ELISA

Pig circovirus infection

This disease was first described as a picornavirus-like contaminant of the continuous pig kidney cell line (PK115). The virus is of doubtful pathogenicity. Another antigenically and genomically distinct circovirus, porcine circovirus 2 (PCV 2) has been isolated from piglets with wasting disease. Porcine circovirus 2 affects piglets of about six weeks of age causing post-weaning multisystemic wasting syndrome (PMWS), a progressive wasting condition with lesions in several organ systems.

Diagnosis:

- Clinical signs and pathological findings
- Antibodies detection by using indirect immunofluorescence or ELISA
- Virus isolation in pig cell line
- Demonstration of PCV 2 antigen antigen by immunocytochemistry or nucleic acid by molecular techniques

CALCIVIRIDAE

- Latin *calyx* = *cup*
- They have cup shape depression, demonstrated by electron microscopy on the surface of virion
- Virion are 27 – 40nm is diameter
- They have icosahedral symmetry and are non-enveloped
- Genome consist of a single molecule of linear, positive sense single stranded RNA
- Replication takes place in the cytoplasm and virion are released by cell lysis
- Many calciviruses have not yet been cultured
- They are resistant to heat but are sensitive to acid pH values
- Calcivirus are closely related to piconaviruses and were formerly grouped within the picornaviridae
- Genera: (4) two named, two unnamed (human)
 1. Vesivirus: vesicular exanthema of swine virus
Type species of the family
 - San Miguel sea lion virus
 - Feline calcivirus
 2. Lagovirus
 - Rabbit haemorrhagic disease virus
 - European brown hare syndrome virus
 3. Norwalk-like viruses: (referred to as small, round, structural virus group 1 and 2).
They have fuzzy appearance and lack surface detail at electron microscopy.
Cause gastroenteritis in human
 4. Sapporo-like viruses: cause gastroenteritis in human

Vesicular Exanthema of Swine

- First reported in the USA (Southern California) in 1932
- Widely spread in the USA in the 1950s and eradicated in 1959
- A highly contagious, acute disease similar to foot-and-mouth disease

- Caused by VESV
- Reservoir of virus exists in marine animals
- Probably occur due to feeding sea lion and seal meat contaminated with SMSV to pigs
- Strains of SMSV produce VES in pigs experimentally inoculated
- Antigenic heterogeneity: 13 serotypes of VESV and 17 of SMSV

C.S

- Incubation period about 72 hours
- Course of disease is about two weeks
- Vesicles develop on the tongue, lips, snout, interdigital spaces and coronary band
- Fever, lameness
- Weight loss
- Neonatal mortality
- High morbidity, low mortality
- Differentials: FMD, vesicular stomatitis, swine vesicular disease

DX

- Samples: vesicular fluid, epithelial layer/scrapings
- Isolation of virus in pig kidney cell lines
- Identification of isolates by ELISA, CFT and immunoelectronmicroscopy

Feline Calicivirus Infection

- Aetiology Feline calicivirus
- Account for about 40% of upper respiratory tract inflammatory disease in cats worldwide
- All felidae susceptible, natural infection more in domestic cats and captive cheetahs
- Incubation period: up to 5 days
- Clinical signs confined to upper respiratory tract and the conjunctivae
- Fever, oculonasal discharges, conjunctivitis, vesicles on the tongue and oral mucosa

- Lameness and stiff gait at acute phase
- High morbidity and mortality

DX

- C.S, upper respiratory signs, ulcer on the oral mucosa
- Differential: feline herpesvirus 1 infection (most severe infection)
- Sample: oropharyngeal swab, lung tissue
- Isolation of feline cell line
- Isolation may not connote active disease because of wide carrier state in cats
- Demonstration of a rising antibody titre in paired serum samples necessary for laboratory confirmation

CX

- management practices to reduce exposure to virus
- vaccination
 - inactivated vaccine for parenteral administration
 - modified live vaccine for parenteral and intranasal administration
- vaccination does not prevent subclinical infection and carrier state but protects against clinical disease
- live vaccine may cause clinical infection (if given by other routes apart from injection)

Rabbit Haemorrhagic Disease

- highly contagious, acute often fatal disease of European rabbits (*Oryctolagus cuniculus*)
- first reported in china (1984) and has since been encountered in many parts of the world
- occur in rabbits above two months of age
- RHDV is considered a mutant of a non-pathogenic virus, rabbit calicivirus known to be endemic in commercial and wild rabbits in Europe for many years
- RHDV has been used as a biological control for rabbit populations in Australia and New Zealand

- Transmission: faeco-oral, inhalation, through the conjunctiva. Mechanical transmission by mosquitoes and fleas and other insects has been demonstrated. Indirect transmission through fomites and foodstuff. Close contact required

C.S

- Incubation period is up to three days
- Characterised by high morbidity and high mortality
- The course is short, death occurs within 36 hours of infection
- Virus targets cells of the mononuclear, phagocyte lineage
- Rabbits under two months are not susceptible
- There is severe hepatic necrosis and there may be disseminated intravascular coagulation
- Pyrexia
- Depression
- Increased respiratory rate
- Serosanguinous nasal discharge
- Haematuria
- Neurological signs including convulsion
- Some animals may survive for a few weeks with jaundice, weight loss and lethargy

DX

- High mortality and with characteristic gross lesions (hepatic necrosis, congestion of liver, lung, spleen)
- Virus culture is difficult and usually unsuccessful
- Confirmation is by electron microscopy, demonstration of antigen by ELISA, IF or haemagglutination using human erythrocytes
- Demonstration of virus-specific antibodies by ELISA and haemagglutination inhibition test. Reverse transcriptase PCR for detection of RHDV nucleic acid

CX

- Vaccination in endemic regions
- Inactivation and adjuvanted given at 10 weeks of age
- New vaccine based on recombinant eyxoma virus expressing RDHV capsid protein and virus-like particles from capsid protein produced in baculovirus expression system are being developed

TOGAVIRIDAE

Latine Toga=cloak

Togavirus are enveloped RNA viruses approximately 70nm in diameter with icosahedral symmetry. The envelope contains glycoprotein spikes and is closely bound to the capsid.

They agglutinate goose and chick erythrocytes

There are two genera in the family Togaviridae:

1. Alphavirus: virus of veterinary importance
2. Rubivirus: only one member; rubella virus which causes German measles in children and young adults

Alphavirus are divided into a number of groups based on their genomic composition.

These groups are:

1. Venezuelan equine encephalitis virus (VEEV) complex
2. Eastern equine encephalitis virus (EEEV) complex
3. Semliki forest virus complex
4. western equine encephalitis (WEEV) complex

western equine encephalitis virus has been shown to have originated by a recombination between EEEV and Sindbislike viruses

Alphaviruses have positive sense, single-stranded RNA genome and replicate in the cytoplasm. The nucleocapsids are assembled in the cytosol. They are released from infected host cell by cytolysis. The viral envelope is composed of virus-derived glycoprotein spikes expressed on the host cell plasma membrane.

Viral infection of invertebrate cell is usually non-cytolytic and is persistent. In this case, virus assembly occurs in association with intracellular membranes rather than through the plasma membrane.

Alphavirus are sensitive to pH changes, heat, detergents and disinfectants. They are not stable in the environment.

Alphaviruses and certain members of the flaviviridae, Reoviridae, Rhabdoviridae and Bunyaviridae are arthropod-borne and are thus termed "arboviruses".

Domestic animals and humans are usually considered to be 'dead-end' hosts of alphaviruses because they do not develop a significantly high titre of circulating virus to act as reservoir hosts.

A number of important equine diseases are caused by the alphaviruses. The three equine encephalitis viruses (Venezuelan, Eastern and Western) are confined to the western hemisphere and are transmitted by mosquitoes. Getah virus occurs mainly in south-east Asia and Australia. The three equine encephalitis viruses produce similar clinical signs but infections by Western equine encephalitis virus tend to be milder.

Eastern equine encephalitis virus: mosquito (*Culiseta melanura*) and *Aedes* species

VEEV: mosquito (*Culex* species)

WEEV: mosquito (*Culex tarsalis* and other *Culex* species, *Aedes* species)

Getah virus: mosquito

Clinical signs of Equine Encephalitis

The clinical manifestations of the three equine encephalitis viruses are similar. Incubation period may be up to nine days and clinical signs may last from four to nine days. Clinical signs range from mild fever and depression to fatal febrile encephalomyelitis. Some of the neurological signs commonly observed include photophobia, blindness, head pressing, circling, ataxia and difficult deglutition. Terminally, animals become recumbent and semi-comatose with convulsion prior to death. The case fatality rate is 90% for EEE, 50% - 80% for VEE and 20% - 40% for WEE.

Diagnosis

- clinical signs and history of previous cases of equine encephalitis in the same region may be suggestive
- laboratory confirmation:
 - virus isolation carried out in cell culture or in suckling mice whole blood or serum collected during the pyrexial phase of the disease is suitable for virus isolation. Brain and/or cerebrospinal fluid collected at PM are also suitable for virus isolation. In cases of VEE, isolates should be typed to distinguish virulent from non-virulent subtype

- EEEV antigen in fixed brain section can be detected by an immunohistochemical staining technique
- WEE and EEE are usually diagnosed by serological assays. A rising antibody titre is demonstrated in paired serum samples. ELISA, phage reduction neutralization assay, haemagglutination inhibition and complement fixation tests are usually employed for serology.

An IgM capture ELISA has been used to provide evidence of infection in single serum samples. The vaccination status of an animal must be considered in interpreting the result of serological tests. The interpretation of serological results for VEEV is complicated by the presence of antibodies produced in response to inapparent infection with non-virulent subtypes.

Treatment and Control

- Suppurative palliative treatment may be beneficial but prognosis is poor
- Effort should be made to control mosquito population
- Horses should be housed in netted stables
- Monovalent, bivalent and trivalent vaccines are available. Vaccines for EEE and WEE are inactivated. A live attenuated TC-83 VEEV vaccine provides effective protection and has been used successfully to prevent epizootics of VEE
- It should be noted that the alphaviruses produce zoonotic infections.

RETROVIRIDAE

- Latin: Retro = backward
- Labile enveloped RNA viruses
- About 80 – 100nm in diameter
- Possess a reverse transcriptase encoded in the viral genome
- Envelope acquired from plasma membrane of host
- Envelope surrounds an icosahedral symmetry capsid
- Capsid contains two linear, positive sense single stranded RNA and core proteins including the enzymes reverse transcriptase and integrase
- Reverse transcriptase is an RNA-dependent DNA polymerase which transcribe RNA to DNA
- Four major genes encoded by the viral genome are the gag, pro, pol and env
- Gag (group specific antigen) gene encodes internal structural proteins
- Pro (protease) gene encodes the enzyme protease
- Pol (polymerase) gene encodes the enzymes reverse transcriptase and integrase
- Env (envelope) encodes surface (SU) and transmembrane (TM) envelope glycoproteins

Viral Replication:

- Attachment to cell surface receptors by envelope glycoproteins
- Synthesis of double stranded DNA copies of viral genome in the cytoplasm under the influence of reverse transcriptase
- DNA synthesis are integrated into the chromosomal DNA of host cell as provirus through the action of viral integrase
- Synthesis of mRNA and virion RNA from provirus
- Release of mature virion by budding from cell membrane
- If the provirus of certain retroviruses is inserted close to the host genes which regulates cell division, the proviral long term repeat (LTR) may increase the rate of mitosis resulting in neoplasia (insertional mutagenesis)

- A high mutation rate is a feature of retroviral replication because errors are relatively frequently encountered during reverse transcription
- Recombination between retroviral genomes in doubly infected cells can occur because reverse transcription can transfer from the RNA template of one virus to that of another
- Consequently, antigenically different retroviruses often emerge making classification of species and subtypes difficult

Insert a diagram here

- The family is composed of seven genera:

1. Alpha retrovirus

Viruses: Avian leucosis virus
 Avian sarcoma virus
 Avian myeloblastosis virus
 Raus sarcoma virus

2. Beta retrovirus

- Mouse mammary tumour virus
- Jaagsiekte sheep retrovirus (ovine pulmonary adenocarcinoma virus)

3. Gamma retrovirus

- Feline sarcoma virus
- Feline leukaemia virus
- Avian reticuloendotheliosis virus (Turkey, ducks, chicken, snail, pheasants)

4. Delta retrovirus

- Bovine leukaemia virus
- Human T-lymphotropic virus 1,2

5. Epsilon retrovirus

- Fish tumour virus

6. Lentivirus

- Human immunodeficiency virus 1, 2
- Simian immunodeficiency viruses
- Maedi/Visna virus
- Caprine arthritis encephalitis virus
- Equine infectious anaemia virus
- Feline immunodeficiency virus
- Bovine immunodeficiency virus

7. Spumavirus

- Virus causing vacuolation of cultured cells not associated with clinical diseases
- Retrovirus are sensitive to heat, lipid solvents and detergent
- Relatively resistant to UV light because of their diploid genome

Clinical infection

- Alpha, Beta-, Gamma-, Delta-, and Epsilon- retrovirus are frequently referred to as oncogenic retroviruses because they can induce neoplastic transformation in cells which they infected.

Retrovirus classified as endogenous or exogenous

Endogenous occurs widely among vertebrates. Resulted at some time from injection of germline cells and are transmitted only as provirus in germ cell DNA from parent to offspring. They are regulated by cellular genes and are usually silent

Oncogenic viruses are designated as slowly transforming (cis-activating viruses or as rapidly transforming/transducing viruses).

Slowly transforming retroviruses induce B-cells, T-cells or myeloid tumours after long incubation periods. For malignant transformation to occur, the provirus must be integrated into the host cell DNA close to a cellular oncogene resulting in interference with the regulation of cell division.

- Rapidly transforming retroviruses which can induce tumour transformation after short incubation periods, contain viral oncogenes (virons)

- Epsilon retrovirus (newly establish) contains viruses associated with neoplasia in fish
- Lentiviruses (Latin: lentus=slow), long incubation period, insidious protracted courses
- Spomaretroviruses (spoma = foam) cause vacuolation of altered cells. Not associated with clinical diseases

Avian Leukosis

- Aetiology: avian leucosis virus (ALV) group
- Causes neoplastic conditions including lymphoid, erythroid and myeloid leucosis in chickens. Also associated with fibrosarcoma, haemangiosarcoma, and nephroblastoma
- Lymphoid leucosis, a B-cell lymphoma, is the most common and most economically important of the condition
- Avian leukosis viruses are divided into ten subgroups (A-T) on the basis of differences in viral envelope glycoproteins
- Isolates from chicken belong to subgroup A,B,C,D,E and J
- Most isolates from outbreaks in chicken belong to subgroup A.

Endogenous retroviral genome may contribute env genes to produce recombinant feline leukaemia viruses and avian leucosis viruses occasionally they can be activated by irradiation, mutagens or carcinogens with production of new virion

- There is usually an incubation period of months to years between natural infection with ALV and the development of neoplasia because of the time required for the genetic events to occur that lead to transformation of cells to malignancy
- Neoplastic condition associated with ALV includes lymphoid leucosis, myeloid leucosis, sarcomas and renal tumours. Avian leucosis virus also associated with osteoporosis

- Endogenous ALVs carried by chickens in most flocks do not directly cause tumours

Epidemiology

- Vertically through virus present in egg albumin
- Horizontally by cloth contact
- Chicks hatch from infected eggs are usually immunotolerant and exhibit persistent viraemias
- They are the principal form of virus in flock
- Virus transmitted in saliva and faeces to in-contact birds
- Viral shedding in oviduct results in transmission to chicks/embryo
- Chicks hatched develop transient viraemia before neutralizing antibodies
- Such birds become carriers and shed virus intermittently and produce infected chicks
- Natural exposure of adult birds to infection does not usually result in virus shedding
- Neoplasms develop most often in persistently-viraemic birds
- Virus neutralizing antibodies are passed from antibody-positive hens to the yolk sac to their chicks offering passive immunity to infection for the first few weeks of life

C.S:

- incubation period usually more than four months. Diseases usually sporadic in infected flock but occasional epidemics have been described
- Inappetent
- Weakness
- Emaciation
- Pale shaggy
- Enlarged liver and spleen of fabrisiosis
- Osteoporosis
- Thickened long bones

- Decreased egg production
- Decreased fertility
- Decreased hatchability
- Decreased growth rate
- Increased death rate

Diagnosis

- P.M findings. Histopathology to determine type of tumour
- Differential diagnosis: Marek's disease (based on age of affected birds, presence of burred tumour, absence of thickened peripheral nerves, histology of neoplastic cell types)
- Virus isolation is difficult and not attempted
- Commercial ELISA kit for detection of ALV group-specific antigen
- Detection of antibodies in serum or egg yolk by virus neutralization test, ELISA and indirect immunofluorescence
- PCR for detection of ALV nucleic acid

Control

- High standard of hygiene
- Raising birds from disease free or genetically resistant flock
- All-in-all ovt management system
- Raise younger birds away from older ones
- Vaccination with inactivated or modified live ALV vaccines not very successful
- Recombinant avian leucosis and fowlpox viruses expressing subgroups A envelope glycoproteins have been shown to have potential as effective vaccines

Feline Leukaemia

- Caused by feline leukaemia virus (FeLV)
- A germine retrovirus
- Isolates of FeLV are assigned to three subgroups (A,B and C) on the basis of the gp70 envelope glycoprotein

- Feline leukaemia virus A is the predominantly isolated from cases of feline leukaemia in cats
- Subgroup B is present in about 50% of cases, usually in combination with subgroup A

C.S

- Seen in cats about 2-4 years of age
- Lymphosarcoma
- Long incubation period
- Fever, malaise lymphadenopathy
- Non-specific clinical signs: anaemia, reduced reproductive performance, enteric secondary infections due to immunosuppressive effect
- Myeloid and fibrosarcoma tumour

Diagnosis

- Sample: blood, saliva
- Commercial ELISA for antigen detection (major capsid protein p27)
- Immunofluorescent antibody, last for detection of viral antigen in the cytoplasm of leukocytes in blood smears (IFT is more sensitive and more specific than ELISA) it is a confirmatory test
- Serological testing for antibodies is not used because viraemic tests are immunotolerant and do not have anti FeLV antibodies. Detection of neutralizing antibodies indicates that a cat is immunized and resistant to infection
- An antigen termed feline oncovirus-associated cell membrane antigen (FOCMA) is expressed in all FeLV and feline sarcoma virus (FeSV) transformed cells. The development of antibodies to FOCMA provides protection against FeLV-associated neoplasia

Control

- Test and removal policy
- Retesting after 12 weeks
- Quarantine before introduction

- Vaccination (killed whole virus vaccine), recombinant canarypox virus vaccine, subunit and recombinant subunit vaccines
- Vaccination does not offer complete protection

Feline Immunodeficiency Virus Infection

- First reported in 1987
- World wide disease of cats
- Referred to as feline AIDS
- Similar to acquire immunodeficiency syndrome caused by human immunodeficiency virus
- Five subtypes of FIV identified based on diversity in the envelope gene amino acid sequences
- Diversity may account for varied pathogenicity and clinical progression of the disease
- Occur in domestic cat. Related virus seen in wild felidae (lion, and pomes)
- Animal remains infected for life
- Virus shed in saliva, transmitted through bite
- Transmitted in uterus from queen to kitten during parturition or in milk especially during acute phase of infection

C.S

- Clinical disease prevalent most in cats over 6 years
- Acute phase characterised by pyrexia, generalized lymphopathy and neutropenia
- Asymptomatic phase: marked by immunodeficiency used by recurrent fever, leukopenia, anaemia, weight loss, lymphadenitis, chronic gingivitis, behavioural changes, opportunistic infections predominate, chronic retinopathy, enteric and skin infection. There may be neurological signs
- Concurrent FeLV infection may exacerbate the immunodeficiency and accelerate the appearance of C.S

D.X

- Serology for detection of FIC antibodies is the major method for confirming infection. ELISA, immunoblotting and indirect immunofluorescence
- Some cats fail to produce antibodies for several months following infection
- Antibody levels may become undetectable in terminally ill cats
- Kittens of infected queens may remain seropositive for up to five months due to infection of colostrum antibodies
- Virus may be isolated from saliva and blood but it is not a realistic procedure for routine diagnosis
- Proviral DNA detectable by PCR

R.X and C.X

- Treat secondary infections
- Use of antiviral drugs e.g. azidothymidine direct against viral reverse transcriptase in clinical cases but does not eliminate infection
- No vaccine (multiple virus subtype confound vaccine production)
- Control based on prevention of exposure by depressing infected and non-infected cats, prevent roaming, use seronegative semen for breeding
- Screening and seromonitoring

Equine Infectious Anaemia

- Affect horse, mule, donkeys
- Also called swamp fever
- Caused by equine infectious anaemic virus
- Infected equidae remains viraemic for life
- Transmitted mechanically by haematophagous insects particularly *Tabanus spp* and *Stomoxys spp*
- Introgenic transmission through contaminated needles of surgical instruments
- In-vitro transmission is uncommon

C.S

- Majority of infected animals display nite signs which may go undetected

- Most clinical signs are due to immune response by animals rather than direct viral damage
- Incubation period usually three years
- Fever, depression, petechial haemorrhage on mucous membrane
- Rarely epistaxis, ventral oedema, death
- Recovery and recrudescence of signs
- Normal apparently healthy carrier status

D.X

- Demonstration of antibody to the core virus protein p26
- Serological test recognised for international trade is the AGID test (Coggible test)
- ELISA result should be confirmed by coggins (AGID) test or by immunoblotting
- Antibodies may not be detected early in infection
- False positive result in foals for up to 6months due to colostral antibodies
- Presence of virus in blood demonstrable by inoculation of susceptible horse
- Virus isolation in leukocyte culture prepared from blood of susceptible horse. Isolation is rarely attempted (time consuming, expensive)
- Proviral DNA detectible by PCR

C.X

- Certification of freedom before importation
- Restriction of movement
- Test and removal of seropositive animals
- Insect control
- Disinfection of surgical instrument to destroy EIAV

REOVIRIDAE

Virus in the family reoviridae are icosahedral, 60 to 80nm in diameter, non-enveloped and possess a layered capsid which is composed of concentric protein shells. They are originally isolated from respiratory and enteric sources without any clinical condition and were thus named orphan.

The genome of reoviruses is composed of ten to twelve segments of double-stranded RNA. Genetic reassortment readily occur in cells co-infected with viruses of the same species. Replication takes place with the cytoplasm of the host cell often with the formation of intracytoplasmic inclusions. There are nine genera in the family:

1. Orthoreovirus: causes arthritis and tenosynovitis in poultry
2. Rita virus: causes enteritis in neonatal farm animals
3. Orbivirus: members are arthropod-borne viruses that cause African horse sickness in horses and blue tongue in sheep and in other domestic and wild ruminants
4. Colti virus (Colorado tick fever virus): primarily infect rodents and human but occasionally cause clinical disease in domestic animals
5. Fiji virus
6. Orthoreovirus
7. Oryza virus
8. Cypovirus: virus of arthropods
9. Aqua reovirus: viruses that infect fish

Reoviruses are moderately resistant to heat, organic solvents and non-ionic detergents. Orthoreoviruses and rotaviruses are stable over a wide range of pH values while orbiviruses lose infectivity at low pH values

Genus: Orbivirus

- African horse sickness virus
- Blue tongue virus
- Epizootic haemorrhagic disease virus
- Ibaraki virus

- Equine encephalosis virus
- Palyam virus

Bluetongue

This disease is a non-contagious viral disease of sheep and other domestic and wild ruminants. It is transmitted principally by biting midges (*Culicoides spp*). The disease is caused by serotypes of bluetongue virus (BTV) in the genus orbivirus of the family Reoviridae. Twenty four serotypes of the BTV have been described.

Transmission: the disease is transmitted by *Culicoides imicola* in Africa and Asia. Venereal transmission through the semen of ram and bull has been reported. It can also be transmitted by embryo transfer.

Blue tongue is of great significance in sheep and deer. In endemic areas, infection of cattle is common and usually inapparent. The viraemia in cattle commonly lasts several weeks facilitating transmission of the virus to susceptible host by the insect vector. Cattle are considered to be important reservoir of the virus.

Clinical signs: clinical signs are diverse and varied. There may be fever, depression, vascular congestion of the lips and muzzle, oedema of lips, face eyelids and ear, erosion and ulceration of oral mucosa, excessive salivation and watery nasal discharges which later becomes mucopurulent, swollen and cyanotic tongue, lameness from coronitis and laminitis, tortocillitis, abortion and mortality of up to 30%.

Diagnosis

- Clinical signs and postmortem findings are suggestive
- Laboratory confirmation requires isolation and identification of the virus or demonstration of BTV-specific antibodies
- Samples: unclotted blood from febrile animals or fresh spleen and lymph node collected at post mortem
- Virus isolation in embryonated egg inoculated intravenously
- Antigen detection by ELISA
- Serological test for detecting antibodies to BTV serotypes using Complement fixation test, Agal gel immunodiffusion, indirect immunofluorescence and competitive ELISA

- Demonstration of type-specific antibodies is by neutralization test and haemagglutination inhibition test.
- In animals from endemic regions, a rising antibody titre must be demonstrated in paired serum samples to confirm on-going active infection.
- Polymerase chain reaction for detecting BTV nucleic acid in clinical samples.

Control:

- Vector control
- Live attenuated vaccine for protection against virulent virus of homologous serotype
- Polyvalent vaccine in regions where more than one serotype is prevalent
- Live attenuated vaccine may be teratogenic when used in pregnant animals during the first half of gestation
- Live attenuated vaccine should not be used during the period of high vector activity because of the possibility of transferring the vaccine virus to pregnant animals and the possible genetic reassortment with field virus.
- Live attenuated vaccine virus may revert to virulence
- Killed adjuvanted vaccine can induce protection but requires booster dose. It is more expensive to produce.
- Recombinant virus-like particle capable of inducing protective immunity have been produced in insect cells infected with recombinant baculoviruses expressing BTV protein.

African Horse Sickness

This is a non-contagious disease of horse, mules and donkeys.

Aetiology: African horse sickness virus (AHSV), an orbivirus. The African horse sickness subgroup is made up of nine serotypes of AHSV and they are distinguishable by neutralization tests.

African horse sickness is endemic in subtropical and tropical Africa. Outbreak have also been reported in some parts of Asia (Middle East, India, Pakistan) and Europe (Spain and Portugal)

Transmission: AHS is transmitted by haematophagous insects. The major vector is *Culicoides imicola* (a species of Afro-Asian midge). *Culicoides imicola* once infected

remains infected for life. The warm climate of Africa supports the multiplication of the midge and endemic disease occurs only in regions where *C. imicola* is constantly present. Outbreak occurs in regions outside the warm climate when wind blows the midge for up to 700km to those regions. Outbreaks occur majorly during the warm humid season (summer). The virus may be isolated from clinically normal maintenance hosts such as the zebra and African donkey.

Clinical signs:

Four clinical forms of AHS are recognized:

1. A peracute pulmonary form characterized by depression, nasal discharge with rapid progression to severe respiratory distress. Mortality is close to 100%
2. a subacute cardiac form manifesting as conjunctivitis, abdominal pain and progressive dyspnoea
subacute oedematous swelling of the head and mouth are most obvious in the supraorbital fossae, palpebral conjunctiva and intermandibular space. Mortality rate is up to 70%
3. A combination of pulmonary and cardiac features
4. a mild or subclinical form termed horse sickness fever observed in zebra and donkeys

Diagnosis:

- characteristic clinical signs and postmortem findings
- samples: blood, lymph nodes, spleen
- virus isolation in embryonated eggs or cell culture as well as intracerebral inoculation of newborn mice
- identification of isolated virus by immunofluorescence and typing by virus neutralization with monovalent antiserum or competitive ELISA
- reverse-transcriptase (RT)-PCR can be used for detection of viral RNA
- serological test by CFT, AGID, ELISA and serum neutralization tests

Control:

- vector control, quarantine and vaccination
- attenuated vaccines both monovalent and polyvalent containing up to four serotypes are available, vaccines do not prevent viraemia. Vaccine virus can revert to virulence and be transmitted by vectors. Vaccinated animals can not be differentiated serologically from those with foal infection
- inactivated vaccines based on serotype 4 are effective in preventing both clinical disease and viraemia
- a polyvalent vaccine must be used if there is a risk of exposure to different serotypes
- protective immune response may be generated using recombinant expressed structural proteins as subunit vaccines. Such vaccines should be safe and permit differentiation of vaccinated from infected animals

VETERINARY VIROLOGY (VPM 402) LECTURE NOTES
DEPT. OF VETERINARY MICROBIOLOGY AND PARASITOLOGY
COLLEGE OF VETERINARY MEDICINE
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Poxviridae

The double-stranded DNA virions of this family are the largest and most complex of known animal viruses. They infect many vertebrate and insect species. Unlike other viruses, some poxviruses are large enough to be seen with a light microscope.

Viral Characteristics

- Large, enveloped (some virions contain double envelope), double-stranded DNA viruses (see Fig. 1).
- The capsid / nucleocapsid is brick-shaped to ovoid containing the genome and lateral bodies (function unknown).
- The large complex genome consists of a single, linear molecule of double stranded DNA that codes for approximately 200 proteins. The ends are ligated to each other so the DNA molecule is continuous, without free ends.
- These are the only DNA viruses known to complete their replication cycle in the cytoplasm.
- In the cytoplasm, the dsDNA is used as a template for both mRNA production (for translation of proteins) and copies of the genome for progeny virions; viral enzymes largely mediate both processes. As the virions are large and complex, the mechanism associated with virion assembly is largely unknown. Virions are released from the cell by budding.
- Viruses of this family possess at least 10 major antigens with a common nucleoprotein antigen, which accounts for cross-reactivity among species.
- There are at least 10 viral enzymes contained within the virus particle, many of which function in nucleic acid metabolism and genome replication.
- Poxviruses remain viable in scabs for long periods.
- Some (mainly orthopoxviruses) produce hemagglutinins that agglutinate red blood cells.
- Eosinophilic inclusions called Guarnieri bodies may be produced in infected cells/tissues.



Figure 1. Poxviridae (220 - 450 x 140 - 260 nm). Indicated are the surface tubules, the envelope (present only when virions have budded), the biconcave core that surrounds the nucleoprotein, and the lateral bodies (function unknown).

Classification

The Poxviridae consists of two subfamilies, Chordopoxvirinae (poxviruses of vertebrates) and Entomopoxvirinae (poxviruses of insects).

There are eight genera in the subfamily Chordopoxvirinae. They are, with significant diseases, as follows:

- ***Orthopoxvirus:***
 - Vaccinia
 - Variola
 - Cowpox
 - Feline Cowpox
 - Horsepox
 - Camelpox
 - Buffalopox
 - Monkeypox
- ***Parapoxvirus:***
 - Bovine Papular Stomatitis
 - Contagious Ecthyma / orf
 - Pseudocowpox / milker's nodules
 - Ectromelia / mouse pox: An important disease of laboratory and wild mice

- ***Capripoxvirus:***
 - Sheeppox
 - Goatpox
 - Lumpy Skin Disease
- ***Avipoxvirus:***
 - Fowlpox
- ***Leporipoxvirus:***
 - Myxomatosis
 - Rabbit and squirrel fibroma: Benign tumors; natural host the cottontail rabbit
- ***Molluscipoxvirus:***
 - Molluscum contagiosum: A common disease of children
- ***Suipoxvirus:***
 - Swinepox
- ***Yatapoxvirus:***
 - Yaba monkey tumor virus and related viruses

Poxvirus Infections: General

Poxviruses infect the epidermis and produce focal lesions that frequently become proliferative and later necrotic. Rare generalized infections can be fatal. Poxviruses occur naturally in most veterinary species, except the dog.

Many poxviruses produce an infection resulting in changes conveniently summarized in order of development as papule, vesicle, pustule, and finally scabs or crusts. Secondary bacterial infections are not uncommon. Recovery from poxvirus infection usually is followed by long-term immunity.

Many poxviruses can be cultivated on the chorioallantoic membrane of chicken embryos producing focal lesions or "pocks" and most can be grown in cell cultures.

Because of their large size, poxviruses can be seen with light microscopy in stained smears. Virus elementary bodies stained by various procedures, including Gutstein's and Giemsa, can be readily seen either as aggregates (acidophilic cytoplasmic inclusions) or singly.

Poxviruses may survive for years in dust.

Some mammalian poxviruses are considered

Capripoxvirus

Lumpy Skin Disease

(Neethling virus)

Cause

Lumpy skin disease virus, a *capripoxvirus*.

Occurrence

Lumpy skin disease is endemic on the African continent with higher prevalence in the central and southern regions.

The main hosts are cattle, but also buffalo, giraffe, and impala; all ages are susceptible. An interesting feature of the disease in unvaccinated cattle is that it occurs in epidemic form every 5 - 6 years.

Transmission

The virus is thought to be spread mechanically by biting flies.

Clinical & Pathologic Features

The incubation period is usually 2 to 4 weeks. Some animals may be subclinically infected or only show a mild febrile response with few skin lesions.

Clinical signs include fever, lacrimation, and nasal discharge. The more severely affected may develop numerous nodules over large areas of the skin and on mucous membranes of the eye, nose, mouth, and genitalia. Nodules may become necrotic leading to secondary bacterial infections. Morbidity may be as high as 20% but mortality is generally low.

Diagnosis

- Clinical specimens: Biopsies (fresh and fixed) from lesions.
- Gross and microscopic findings are suggestive.
- The finding of typical poxviruses in lesion material by electron microscopy is supportive, but confirmation requires virus isolation (lamb cells) and identification of the virus by electron microscopy and/or immunological methods.
- An antigen-capture / trapping ELISA can also be used in detection of the virus.
- Antibodies can be assayed by indirect immunofluorescence, virus neutralization and Western blot.

Prevention

- This is a reportable disease. State and federal regulatory officials should be contacted if lumpy skin disease is suspected.
- Modified live virus vaccines are used as well as a live, attenuated strain of sheeppox virus.

Picornaviridae

This family consists of the smallest RNA viruses. They are naked, positive sense and single-stranded. There are six genera, four of which contain pathogens of veterinary importance.

Viral Characteristics

- The picornaviruses are small (22 - 30 nm), naked, icosahedral viruses
- Replication takes place in the cytoplasm and the picornaviral RNA itself is infectious.
- The genome is approximately 8000 bases in length. It possesses a 3' polyA tail. However, the 5' end has a small virus-encoded protein called VPg or 3B.
- Near the 5' end is a region known as the internal ribosomal entry site (IRES), which is unique to the picornaviruses. This site functions to enhance ribosomal recognition of the virus RNA facilitating translation of viral proteins.
- Most picornaviruses can be propagated in cell culture producing a characteristic and rapid cytopathic effect. Exceptions are some rhinoviruses, which require a

lower temperature and can be cultured *in vitro* in very few cell types such as human fetal tracheal cells.

- Most picornaviruses are host specific.
- Picornaviruses are able to survive in the environment for some time. They have been demonstrated to be infectious for several hours to one year, depending upon conditions.
- Picornaviruses are resistant to ether, chloroform and alcohol. They are susceptible to radiation, phenol, and bleach (chlorination). They are highly resistant to most disinfectants. However, 0.2% citric acid, 0.4% sodium carbonate, or acid-containing iodophore disinfectants are effective.

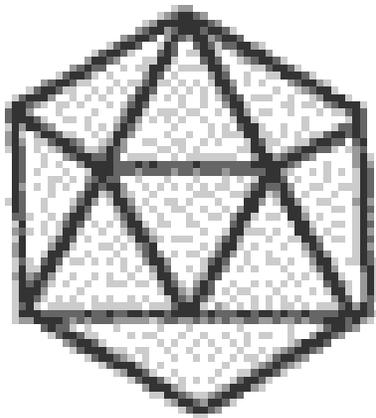


Figure 2. Picornaviridae (22 - 30 nm). Small, naked, icosahedral virions.

Classification

The Picornaviridae contains five genera, *Enterovirus*, *Aphthovirus*, *Teschovirus*, *Cardiovirus*, and *Hepatovirus*. The significant veterinary diseases and viruses in each genus are as follows:

- ***Enterovirus***
 - Teschen and Teschen-like diseases
 - Swine vesicular disease
 - Porcine enteroviruses
 - Bovine enteroviruses
 - Avian enteroviruses
- ***Aphthovirus***
 - Foot-and-mouth disease virus
- ***Cardiovirus***
 - Encephalomyocarditis virus

- ***Hepatovirus***
 - Avian encephalomyelitis-like virus: a tentative species in this genus.
 - Human hepatitis A virus
- ***Parechovirus***: Cause gastrointestinal and respiratory illness in humans.
- ***Rhinovirus***
 - Three species of equine rhinoviruses.
 - Bovine rhinoviruses 1, 2 and 3.
 - More than 100 human rhinoviruses. They are widespread and cause usually mild respiratory infections.

Aphthovirus

Foot-and-Mouth Disease

Cause

Foot-and-mouth disease virus (FMDV). A total of seven different serologic types are recognized. They are FMDV-A, FMDV-O, FMDV-C, FMDV-ASIA1, FMDV-SAT1, FMDV-SAT2 and FMDV-SAT3.

The first serotypes of FMD are often referred to as European types because they were first isolated in France and Germany, although they do occur in other countries. The SAT types were isolated in "Southern African Territories" and are restricted to Africa.

Serotypes C, A and O have been isolated in South America; the recent (less than a decade) outbreaks in Argentina and Brazil were caused by serotypes A and O.

The Asia type has only been reported in various parts of Asia.

No serological/protection cross-reaction occurs between different types.

Occurrence

All cloven-footed animals including swine, sheep, goats, deer and water buffalo are susceptible. Guinea pigs, rabbits, mice and some other species can be infected experimentally. Contact with infected animals rarely results in infection of humans, which is characterized by development of vesicular lesions on the hands, feet, and in the mouth.

Foot-and-mouth disease (FMD) is widespread, occurring in South America, Africa, Europe, the Middle East and Asia. North America, New Zealand, Australia, and the United Kingdom are free at present. The Canadian outbreak of 1952 was traced to an European immigrant. A devastating outbreak occurred in Britain in 2001. A number of outbreaks occurred in Argentina, southern Brazil and Uruguay in 1999 - 2000.

Most South American countries are in the process of eradication with only a few small outbreaks in the last two to three years. Effective continental strategies of control and eradication have been implemented.

Transmission

The disease is spread by contact, fomites, and migratory birds. The mode of infection is by inhalation and ingestion. Airborne transmission has been reported and attributed to a combination of winds and humidity. The virus is considered particularly infectious and transmissible.

Clinical & Pathologic Features

The FMD virus produces a highly contagious disease of cloven-hoofed animals and is characterized by the production of vesicular lesions in the mouth, muzzle, interdigital space, and on the coronary band of the foot after a usual incubation period of 2 to 5 days. Vesicular lesions may also be found on the udder and teats of cows, and the snout of swine. The most common and characteristic sign is excessive salivation; the saliva is sticky, foamy, and stringy. The vesicles, which are pronounced on the buccal mucous membrane and tongue, break, erode, ulcerate, and eventually heal. Myocardial degeneration may be seen in the malignant form in calves but is rare. Pregnant animals may abort.

Morbidity is very high; mortality is low. Lameness and marked loss of condition are frequent sequellae. Affected animals may recover in one to two weeks. Some may become carriers but their role in transmission is controversial.

Diagnosis

- Clinical specimens: vesicular fluid, affected mucous membranes, pharyngeal and esophageal fluid (obtained with a probang), blood, and serum.
- Diagnosis is based upon detection of FMDV in the aforementioned clinical materials. ELISA and complement fixation procedures are used.
- A mouse inoculation test is widely used to demonstrate virus. Suckling mice are inoculated intraperitoneally with liquid from vesicles and macerated tongue/foot lesions. If the material is positive, mice die in a few days. Several passages are made before the material is considered negative. This test is usually performed along with a serological test.
- The FMD virus can be isolated in a variety of cell cultures. Viral growth with accompanying cytopathology occurs best in primary cell cultures. Identification is accomplished by virus neutralization and complement fixation tests.
- A test for virus infection associated antigen detects antibody against the viral polymerase, which is considered present only during infection and not upon vaccination. It is used to distinguish active infection from vaccination with inactivated antigen.
- Real time PCR has been used to rapidly detect virus.

Prevention

- FMD is the most important economic disease of cattle and thus is reportable in many countries. Regulatory officials should be contacted if the disease is suspected. Confirmed outbreaks are dealt with in many countries by strict quarantine and slaughter. The difficulty of eradicating the disease once established was strikingly evident in the recent outbreak in Britain.
- In areas where the disease is endemic, vaccination is practiced using killed vaccines, of cell culture origin, containing the appropriate serotypes of virus for the region. The most effective vaccines in current use contain inactivated virus with an oil-adjuvant. Although requiring periodic revaccination, this type of vaccine has been quite effective and has contributed markedly to eradication in a number of countries.

Hepatovirus

Avian Encephalomyelitis

(Epidemic tremor)

Cause

Avian encephalomyelitis virus of which there are 15 serotypes.

Occurrence

Avian encephalomyelitis is an important, frequently occurring disease with worldwide distribution. It affects chickens, pheasants, turkeys, and quail.

Transmission

The virus is transmitted via the egg and by the oral/fecal route.

Clinical & Pathologic Features

Avian encephalomyelitis is principally a disease of young chicks during the first six weeks of age. The typical clinical disease usually occurs between 1 - 3 weeks of age. In laying birds, clinical signs are not apparent other than a decline in egg production, which may last 2 - 3 weeks.

Signs in young birds include tremor of the head, in-coordination, and leg weakness with loss of condition followed frequently by prostration and death. Average mortality rate is about 20%.

Some infections are asymptomatic and are only diagnosed by the finding of brain lesions. The lesions in the brain and spinal cord consist of loss of neurons and perivascular cuffing that is mainly observed in the cerebellum, medulla, and pons. Diffuse lymphoid nodular hyperplasia is observed in the proventriculus, spleen, pancreas, and liver.

Diagnosis

- Clinical specimens: Brain and spinal cord.
- A presumptive diagnosis can be made clinically. Finding the typical microscopic lesions is supportive.
- Definitive diagnosis depends upon the demonstration of the virus by the intracerebral inoculation of day-old susceptible chicks. If virus is present, epidemic tremor develops in 10 - 12 days, and the brains can be harvested for histopathologic examination.
- Another diagnostic method is the inoculation of brain suspension into chicken embryos via the yolk sac; signs of encephalomyelitis infection in the chicks are observed after hatching. Tissues from these birds should be examined histologically after the signs appear.
- The virus can be cultivated in primary whole embryo cell cultures.
- Antibodies can be demonstrated by means of neutralization tests in chicken embryos employing an embryo-pathogenic strain of the virus.
- A commercial ELISA is available for the serologic monitoring of chicken flocks.

Prevention

A live virus vaccine is administered in the drinking water to 10 - 16 week-old birds. Killed vaccines are used to revaccinate breeders with poor antibody response. These vaccines are administered by the wing-web stick method.

Papillomaviridae

This family of double-stranded DNA viruses was once included with polyomaviruses in the discontinued family Papovaviridae. The myriad papilloma viruses cause papillomas (warts) of the skin and mucous membranes of most domestic animals and a wide variety of other mammals and birds.

Viral Characteristics

- These viruses are nonenveloped, circular dsDNA viruses with icosahedral symmetry.
- The genome consists of a single, circular molecule of double stranded DNA. The complete genome is ~8,000-nucleotide base pairs in length and encodes 12 genes, two of which are associated with the capsid. Only one strand of the dsDNA encodes the genes.
- The dsDNA serves as a template for transcription of mRNAs and progeny genomes by host enzymes. Replication and virion assembly occur in the nucleus and virions are released by destruction of the nuclear and cell membranes.
- Papillomaviruses replicate in the nucleus and new virions are released with the lysis of the cell.
- Because papillomaviruses grow poorly if at all in cell culture, it has taken significantly longer to understand how they replicate. Much has been learned recently by the study of bovine papillomavirus-1 (BPV-1). However, the scope and detail of the studies go beyond the scope of this book.
- Papillomaviruses produce diagnostically significant koilocytotic (vaculated) cells while replicating.
- The viruses are resistant and remain viable for long periods of time on contaminated premises.
- Transmission is mainly by direct contact and fomites.
- These viruses are host species-specific.
- Papillomaviruses target squamous epithelial cells of the skin and mucous membrane.
- The many papillomatoses are common and occur worldwide.
- The immune response to papillomaviruses associated with the spontaneous regression of warts and is mediated by both cellular and humoral immune responses.
- Some papillomaviruses cause neoplastic transformation of cells and have been implicated in the cause of bovine and human cancers.

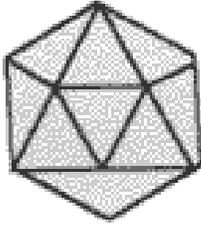


Figure 3. Papillomaviridae (~55 nm). Illustration of the icosahedral capsid.

Classification

This family has a single genus, *Papillomavirus*.

The papillomaviruses, which are species-specific, infect many animals including humans, chimpanzee, monkeys, cattle, deer, dog, horse, sheep, elephant, elk, opossum, rabbit and birds.

The genus consists of a number of antigenically distinct papillomaviruses:

- six types occur in cattle,
- three types in dogs,
- two in rabbits and more than 100 in humans.

Types are largely distinguished by the characteristic restriction endonuclease cleavage of their genome.

Bovine Papillomatosis

(Common warts of cattle)

Cause

Six types of papillomavirus cause bovine papillomatosis.

Occurrence

Bovine papillomatosis occurs frequently worldwide, mainly affecting young cattle. They occur with greater frequency in stabled cattle.

Clinical & Pathologic Features

Papillomas develop as small nodular growths of the skin or mucous membrane. They initially grow slowly, but then more rapidly and eventually become larger, horny, pendulant and sometimes cauliflower in shape. They ultimately necrose and fall off. The most common sites affected are the head (particularly around the eyes), neck, and shoulders. They may occur on the penis of the bull and in the vaginal mucosa of the female, resulting in breeding difficulty.

After about a year there is usually spontaneous recovery.

The recognized six types of bovine papillomaviruses are associated with particular sites as follows:

- Types 1 and 2: head, neck and shoulders; penis and vaginal mucosa.
- Type 3: persistent papillomas of the skin.
- Type 4: papillomas in the alimentary tract; malignant transformation associated with concomitant bracken fern ingestion has been reported.
- Type 5: "rice-grain type" papillomas of the teat.
- Type 6: flattened (frond-like) papillomas of the teat.

Diagnosis

- This is usually based on characteristic gross appearance. Laboratory diagnosis is not usually sought.
- Definitive diagnosis requires histological examination for the presence of koilocytes.
- Although not employed for diagnosis, types 1 and 2 bovine papillomaviruses can be cultivated in cell cultures and on the chorioallantoic membrane of chicken embryo.

Prevention

- Commercial wart vaccines and autogenous wart vaccines, both consisting of finely ground warts, are used. Formalin is often used to kill the virus and a preservative is added. Their value is questionable.
- To prevent spread, affected animals should be isolated.

The BPV-1 is currently being investigated as a potential shuttle vector for moving genes into animals. In addition to BPV-1, human papillomavirus (HPV)-6b, -11, -16, -18, and -31 are also being investigated for use in this manner.

Bovine Papilloma Virus 2 and 4

The combined action of bracken fern and BPV 2 or 4 are thought to produce tumors in the upper digestive track of cattle.

Enzootic hematuria due to ingestion of bracken fern occurs in cattle worldwide. The hematuria results from hemorrhages caused by tumors in the bladder wall. Studies suggest that the oncogenesis is due to the combined action of bracken compounds and BPV 2.

Equine Papillomatosis

(Common warts of horses)

Cause

A papillomavirus.

Occurrence

Worldwide in horses, mules and donkeys usually up to three years of age. Warts in older horses persist longer.

Clinical Features

Warts generally occur on the nose and lips, vary in size and number and usually disappear within three months. Congenital papillomatosis has been reported but occurs rarely.

A different papillomavirus is associated with genital lesions in both male and female horses.

Diagnosis

- This is usually based on the characteristic gross lesions.
- Histologic examination of affected tissue provides confirmation.

Prevention

- Autogenous formalin-inactivated wart vaccines are sometimes administered but their value is questionable; repeated doses are recommended.
- Surgical removal of warts may be helpful.
- Equine warts, like the warts of other species, will frequently disappear spontaneously.

Equine Sarcoids

Cause

There is some evidence that bovine papillomavirus types 1 and 2 may be involved in the etiology of sarcoid. This is mainly based on the demonstration of viral DNA sequences in sarcoid tissue, and the fact that experimental infection with these viruses in horses results in sarcoid-like lesions.

Occurrence

Sarcoid, a fibroblastic tumor that occurs frequently worldwide, is the most common neoplasm of horses, mules and donkeys less than four years of age.

Transmission

Evidence suggests that sarcoids are transmitted by direct contact fomites and probably by arthropod vectors.

Clinical & Pathologic Features

These cutaneous tumors, which occur most commonly on the head and neck regions, ventral abdomen and limbs, are relatively benign. Most animals will have multiple lesions. They vary in size from 1 - 20 cm and are flat, raised, pedunculated or verrucous, firm and adherent to the underlying connective tissue.

They do not metastasize, but as high as 50% may recur after surgical removal.

Diagnosis

- Diagnosis is usually based on the characteristic appearance.
- Definitive diagnosis requires histologic examination.

Treatment

- Cryosurgery is the preferred treatment; two freeze-thaw cycles are used.
- Immunotherapy using BCG vaccine or an extract of *Mycobacterium bovis* (commercial preparations are available); the control rate is about 50%.
- Radiation and chemotherapy are also used with varying success.
- Some untreated lesions regress spontaneously.

Prevention

Vaccines are not available.

Canine Oral Papillomatosis

(Common warts of dogs)

Cause

Three types of papillomavirus cause canine warts, a common worldwide disease of young dogs.

Clinical & Pathologic Features

Numerous papillomas may occur on the mucous membrane of the mouth, lips, tongue, and pharynx of young dogs. Infections begin as small, white elevated areas that enlarge to form small cauliflower-like lesions. Warts may occasionally involve the eyelid.

Skin warts are seen in older dogs and may be caused by a particular type of papillomavirus.

Warts usually regress spontaneously in several months. Recovered dogs are immune, and dogs older than two years are usually immune.

Diagnosis

- The disease is clinically characteristic.
- Histologic examination of warts or biopsies is confirmatory.

Treatment

- Surgical excision may be employed.
- Autogenous wart vaccines are considered of questionable value in treatment.

Prevention

Vaccination for prevention is not generally practiced.

Papillomaviruses and Human Cancer

Although not of direct veterinary significance, it is of interest that some papillomaviruses are implicated in the cause of human cancers. There are at least 30 human types of papilloma viruses that infect the genital tract. Human papillomavirus 16 and 18 (HPV-16 and HPV-18) has been implicated as a cause of cervical cancer. Two papillomavirus genes (E6 and E7) are involved in carcinogenesis. These genes encode proteins responsible for inactivating proteins encoded by the tumor suppressor gene p53 and the retinoblastoma (RB) gene.

Human genital warts are usually caused by types HPV-1 and HPV-6.

Bunyaviridae and Bornaviridae

Both families consist of negative-sense, single-stranded RNA viruses. Bunyaviridae is a large family of mainly arthropod-borne viruses (arboviruses) with several significant veterinary pathogens. Bornaviridae has only one species and horses and sheep appear to be the principal natural hosts.

Bunyaviridae

Bunyaviridae is the largest family of vertebrate viruses. Most bunyaviruses are transmitted by biting arthropods and, with the exceptions of Akabane disease, Cache valley, Rift valley fever, and Nairobi sheep disease, are of limited veterinary importance.

Viral Characteristics

- These viruses are 80 - 120 nm in diameter, have a helical nucleocapsid surrounded by an envelope, on the surface of which are glycoprotein projections. See Fig 4.
- The genome consists of three segments of negative-sense single-stranded RNA.
- The segmented RNA genome may undergo genetic reassortment leading to new strains.
- With most of these viruses, genes are expressed in two disparate host systems, vertebrate and arthropod.
- The virus replicates in the cytoplasm and matures by budding into vesicles in the Golgi region and then released by exocytosis at the cell surface.
- These viruses are labile outside the host.



Figure 4. Bunyaviridae (80 to 120 nm). Helical nucleocapsid surrounded by an envelope with glycoprotein spikes.

Classification

The term arbovirus (arthropod-borne virus) is often used to refer to any virus of vertebrates transmitted by an arthropod. It thus includes in addition to the viruses in Bunyaviridae, viruses in the families Arenaviridae, Togaviridae, Flaviviridae, Reoviridae and Rhabdoviridae. The name "arbovirus" is therefore not considered a legitimate taxonomic term.

There are presently five genera assigned to the Bunyaviridae and these genera contain serogroups. The genera are:

- ***Bunyavirus*** - This genus consists of a large number of serologically grouped and ungrouped viruses. Most are mosquito-borne; some are tick-borne and some show transovarial transmission. Included of veterinary and human significance are:
 - Akabane, Peaton and Aino viruses (members of the Simbu serogroup), which cause disease in sheep and cattle.
 - California encephalitis virus: Consists of more than a dozen serologically related mosquito-borne viruses that can occasionally cause encephalitis in humans in the USA.
 - La Crosse virus is a strain of California encephalitis virus that was isolated from a fatal case of human meningoencephalitis in Wisconsin.

- ***Hantavirus*** At least 20 serologically related viruses that cause natural infection in small rodents (including mice). They are transmitted to humans by inhalation often causing fatal hemorrhagic fever.
- ***Nairovirus***
 - Nairobi sheep disease virus.
- ***Phlebovirus***
 - Rift Valley fever virus.

Phlebovirus

Rift Valley Fever

Cause

Rift Valley fever virus.

Occurrence

Rift Valley fever occurs in Africa and the Middle East in sheep, goats, cattle, camels, antelopes and humans. Large outbreaks have occurred in Africa, Saudi Arabia and Yemen and considerable humans have succumbed.

Transmission

By mosquitoes but probably also by contact.

Clinical & Pathologic Features

Infection is most severe in young animals, and is characterized by a high fever, anorexia, weakness, and rapid death. Some affected animals may have nasal discharge and hemorrhagic diarrhea. Adult animals are less severely affected, but pregnant animals are likely to abort. Cattle are less severely affected than sheep.

The mortality rate may exceed 70% in young animals but is considerably less in adults.

Humans may become infected by mosquitoes and through contact with diseased tissues.

Infections are "flu-like", and can infrequently be severe and fatal.

A consistent and characteristic necropsy finding is severe liver necrosis.

Diagnosis

- Clinical specimens: Liver and spleen.
- A presumptive diagnosis is made on the basis of clinical signs and gross and microscopic lesions observed in the liver.
- Confirmation requires isolation and identification of the virus. The virus replicates on the chorioallantoic membrane of chicken embryos and in various cell cultures.

Prevention

- Modified live virus and killed virus vaccines are used in countries where the virus is endemic. The modified live vaccine should not be used in pregnant animals.
- Mosquito control reduces the chances of infection. In countries where the disease does not occur, outbreaks are dealt with by strict quarantine and slaughter.

Herpesviridae

This is a large, diverse family of DNA viruses that infect humans and a wide variety of animal hosts. They are large in size and are noted for their ability to cause latent infections. They are divergent with regard to genome sequence and proteins, biological properties, but are similar in overall virion structure and genome organization.

Viral Characteristics

- They are enveloped, double stranded DNA viruses (100 - 200nm in diameter) with an icosahedral capsid.
- The virions consist of four structural units: 1) the core of DNA around that is wrapped a protein fibrillar spool; 2) a capsid composed of 12 pentameric and 150 hexameric capsomeres; 3) an amorphous protein layer between the capsid and the envelope; and 4) the envelope.
- The envelope has projections (spikes) evenly distributed over its surface (see Fig 5).
- The dsDNA is used as a template for the production of progeny genomes and mRNAs,
- Following fusion of the viral envelope with the cell membrane, the nucleocapsid migrates to the cell nucleus, where replication takes place.
- Viral transcription is divided into immediate early, early, and late transcription. The structural proteins and the genome (DNA or RNA) are assembled into icosahedral or helical virions, then released.
- Certain host cells can prevent the transcription of genes and thus the viral genome persists, does not replicate, and the host cell doesn't die. This constitutes a form of viral latency.
- All herpesviruses thus far examined have the capacity for latency in host cells.
- There is no common antigen for all members.

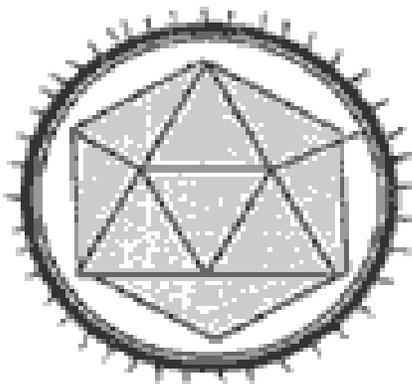


Figure 5. Herpesviridae (100 - 200 nm). Between the capsid and the envelope there is a protein-filled region known as the tegument.



Figure 5.1. Equine "slow herpesvirus" intranuclear inclusions. *Courtesy of A. Wayne Roberts.*

Herpesvirus Infections: General

All herpesviruses are thought to be capable of establishing latent infections. The classic example is human herpesvirus 1 (HSV-1) which infects of the dorsal root ganglia. The virus is latent between episodes of "cold sores". During latency only a small region of the viral genome is expressed, although no protein has been unequivocally identified as a product of this transcription. The mechanism of reactivation of infection is not understood.

Some virus species infecting eukaryotic hosts are cell-associated and a small number are oncogenic. Many infections are silent or mild in natural hosts but serious in other hosts. For example, pseudorabies virus is a broad host range herpesvirus that causes fatal encephalitis in a wide variety of animal species but not in its natural host, the adult pig. Herpesviruses are widespread and are frequently recovered in the diagnostic laboratory as they can be readily cultivated in cell cultures; some produce pocks on the chorioallantoic membrane. Only those herpesviruses causing significant animal diseases are discussed below.

A general rule is that every animal species harbors at least one herpesvirus.

Classification

The family Herpesviridae is divided into three subfamilies, Alphaherpesvirinae, Betaherpesvirinae, and Gammaherpesvirinae.

Alphaherpesvirinae have a relatively short replication cycle (< 24 h), a variable host range, and usually cause rapid destruction of cultured cells. Viruses belonging to this subfamily establish latent infections in neural cells. Most herpesviruses of veterinary importance are found in the genus *Varicellovirus*.

Betaherpesvirinae contains the genera *Cytomegalovirus*, *Muromegalovirus*, and *Roseolovirus* of little veterinary significance. Unlike the Alphaherpesvirinae, this group of viruses has a relatively slow replication cycle (>24 h), a narrow host range, and causes a slow destruction of cultured cells. Infected cells are often greatly enlarged and may contain cytoplasmic as well as nuclear inclusions. These viruses establish latent infections in lymphoreticular and secretory gland cells.

Gammaherpesvirinae contains the genera *Lymphocryptovirus* (marine and fresh water fish) and *Rhadinovirus* (disease in marmosets and monkeys).

- **Alphaherpesvirinae (Subfamily)**

- ***Simplexvirus*:**

- Bovine herpesvirus 2:
 - Bovine ulcerative mammillitis, pseudolumpy-skin disease

- Cercopithecine herpes 1 (B virus of monkeys):
 - Infects Asian macaque monkeys naturally; has caused rare fatal encephalitis in monkey handlers.
- **Varicellovirus:**
 - Bovine herpesvirus 1:
 - Infectious bovine rhinotracheitis, pustular vulvovaginitis / balanoposthitis
 - Bovine herpesvirus 5:
 - Causes meningo-encephalitis in cattle, particularly in South America
 - Porcine herpesvirus 1:
 - Pseudorabies or Aujeszky's disease
 - Canine herpesvirus 1:
 - Canine herpesvirus infection
 - Equine herpesvirus 1:
 - Equine herpesvirus abortion
 - Equine herpesvirus 3:
 - Equine coital exanthema
 - Equine herpesvirus 4:
 - Equine rhinopneumonitis
 - Feline herpesvirus 1:
 - Feline viral rhinotracheitis
- **Marek's disease-like viruses:**
 - Gallid herpesvirus 2:
 - Marek's disease
- **Infectious laryngo-tracheitis-like viruses:**
 - Gallid herpesvirus 1:
 - Infectious laryngotracheitis
- **Betaherpesvirinae (Subfamily)**
 - No viruses of significance in domestic and farm animals.
- **Gammaherpesvirinae (Subfamily)**
 - **Rhadinovirus**
 - Alcelaphine herpesvirus 1:
 - Malignant catarrhal fever in cattle, deer and other ruminants in Africa; natural host is the wildebeest.
 - **Ovine herpesvirus 2**
 - Malignant catarrhal fever in cattle and some wild ruminants; sheep are natural host; occurs worldwide.
- **Unassigned Genera**
 - Porcine herpesvirus 2:
 - Inclusion body rhinitis
 - Anatid herpesvirus 1:
 - Duck viral enteritis

Malignant Catarrhal Fever (MCF)

(Snotsiekte - Africa)

Cause

Alcelaphine herpesvirus 1 causes malignant catarrhal fever (MCF) in Africa. Ovine herpesvirus 2 causes MCF in cattle in regions other than Africa.

Occurrence

Malignant catarrhal fever is a wide spread, infrequent, usually sporadic, often fatal disease.

It is caused by:

- Alcelaphine herpesvirus 1 causes the disease in Africa. Latent infections are present in the wildebeest and other wild ruminants; it spreads from these to cattle.
- Ovine herpesvirus 2 causes the disease in sheep (natural host; subclinical infection) and goats worldwide; the disease is transmitted from sheep to cattle.
The non-African form (Europe, North and South America and other regions) of MCF may be transmitted to cattle and deer from sheep that shed virus during lambing. This form is sometimes referred to as sheep associated MCF.
The incidence is not high. Except for feedlots, there are usually only one or two cases in a herd at one time.

Transmission

As mentioned above the non-African MCF is considered to be transmitted to cattle and deer from sheep that shed virus during lambing. Infection probably takes place via the respiratory route.

Pathogenesis

This is little understood. There is a cell-associated viremia and a dearth of virus in lesions. The latter are thought to have an immunological basis. Although latency probably occurs there is no evidence of recrudescence of infection.

Clinical & Pathologic Features

Most affected cattle may have the following signs: fever, depression, diarrhea, anorexia, rhinitis with nasal discharge that becomes mucopurulent and encrusted. The skin of the muzzle becomes eroded, and there is stomatitis, pharyngitis, laryngitis, and parotitis with salivation. After a short febrile period; most cattle with the severe disease die within 10 days.

In addition to the lesions referred to the above, there may be edema of the meninges, perivascular cuffing in other areas of the brain, enteritis, general lymphoid hyperplasia, and corneal opacity. Gray foci may be seen in the kidneys and liver. The anterior cervical and retropharyngeal lymph nodes may be hemorrhagic and edematous. Vasculitis is widespread.

Diagnosis

- Clinical specimens: Fresh leukocytes (buffy coat), fresh thyroid and adrenal tissue, serum.

- Diagnosis is usually based on clinical signs and pathologic changes. The usual sporadic nature of the disease helps distinguish MCF from bovine virus diarrhea and rinderpest. The history of sheep associated with cattle supports a diagnosis.
- Laboratory confirmation of MCF is difficult. Serologic tests, virus isolation, and molecular techniques (polymerase chain reaction) are used, but these procedures are not available in most diagnostic laboratories.
- The virus of the wildebeest-associated MCF has been isolated but is not ovine *herpesvirus 2*.

Prevention

- Vaccines are not available. The infrequency of the disease does not warrant use of a vaccine.
- Cattle should be kept separate from sheep.
- A PCR assay has been used to detect infection in sheep.

Flaviviridae

This large family consists of enveloped, positive-sense single-stranded RNA viruses. There are three genera, two of which include important veterinary pathogens. One of these, *Flavivirus*, has more than 50 species, many of which are mosquito and tick-borne.

Viral Characteristics

- The Flaviviridae are similar to each other in virion morphology, genome organization, and replication strategy, but lack serological cross-reactivity across the family.
- The envelope contains at least two viral envelope proteins that are thought to be involved in receptor-mediated endocytosis. However, the target receptor has not yet been identified.
- Once the genome has entered the cytoplasm, it is translated by host ribosomes into a large polyprotein (a polypeptide comprised of several proteins). The polyprotein is then cleaved by viral and host proteases into approximately ten individual proteins.
- The complementary RNA (negative sense) is synthesized by virus non-structural proteins for use as the template for progeny genomes.
- The positive-sense RNA genome is divided into two basic regions: 5'- structural genes - nonstructural genes - 3'. However, the genera differ as far as modification of the genome is concerned: *Flavivirus* have a 5'-cap, but no poly A tail, *Pestivirus* have no 5'-cap but have a poly C tail, and the *Hepacivirus* have no 5'-cap but have either a poly U or polypyrimidine tail.
- A great deal about the replication strategy is currently unknown. This has unfortunately limited vaccine and antiviral drug development.



Figure 6. Flaviviridae (40 - 60 nm). Complex virion structure, enveloped, nucleocapsid has icosahedral/polyhedral symmetry.

Classification

The Flaviviridae consists of three genera, *Flavivirus*, *Pestivirus*, and *Hepacivirus*. The viruses of these genera causing significant diseases are listed below:

- ***Flavivirus*** Consists of more than 50 antigenically related viruses. Some are mosquito-borne, some tick-borne and others have not been associated with any arthropod. A number cause disease in animals and humans. Some have been recovered from bats, marsupials, rodents and birds.
 - Louping ill virus
 - West Nile virus
 - Japanese B encephalitis virus
 - Wesselsbron virus
 - St. Louis encephalitis virus: The host is birds. Transmitted by mosquitoes. Causes human encephalitis in the Americas.
- ***Pestivirus*** Viruses of this genus are not related antigenically to the viruses of the other genera.
 - Bovine viral diarrhea virus
 - Swine fever virus
 - Border disease virus
- ***Hepacivirus***
 - Hepatitis C virus: A major cause of hepatitis in humans.

Pestivirus

- **Bovine Viral Diarrhea**
(Mucosal disease)
- **Border Disease**
(Hairy shaker disease)
- **Swine Fever**
(Hog Cholera)

Cause

Swine fever virus.

Occurrence

Although swine fever still occurs in many countries its incidence has been much reduced in recent years. The eradication program initiated in the United States in 1962 has resulted in complete eradication of the disease. Other countries free of the virus are Canada, Great Britain, New Zealand, Australia, Iceland, and Switzerland. Although the disease still occurs in South America, outbreaks are infrequent to rare.

Transmission

The virus is present in saliva, nasal secretions, faeces, blood, and urine. Spread is by direct and indirect contact. Pigs are infected by ingestion or inhalation; birds and haematophagous arthropods may be mechanical vectors. The disease has been spread by consumption of uncooked pork scraps.

Clinical & Pathologic Features

In susceptible swine, the disease is usually acute and characterized by a high temperature, depression, and anorexia. The morbidity is high and the mortality is usually about 90% in fully susceptible pigs.

Neurological signs are not uncommon, and abortions and stillbirths may occur.

Typical hog cholera is frequently complicated with secondary bacterial infections. The two most common are *Pasteurella multocida* and *Salmonella choleraesuis*. Those with secondary infections often have bronchopneumonia and severe enteritis. Leukopenia is common.

The changes observed in affected pigs are related to the strong affinity of the virus for the vascular system. Among the more common lesions are: petechial and ecchymotic hemorrhages involving all the serous surfaces; petechial hemorrhages of the kidney ("turkey egg kidney"), hemorrhagic lymphadenitis ("strawberry" lymph nodes), and the so-called "button" ulcers of the intestinal mucosa.

The most striking microscopic change observed is the accumulation of lymphocytes in the perivascular spaces. Infection of fetuses may result in malformations, such as cerebellar hypoplasia and microencephalopathy.

A less severe chronic form of the disease may be seen that often escapes detection and makes eradication difficult. This may be due to some immunity or to a less virulent strain of virus.

Diagnosis

- Clinical specimens: Kidney, spleen, tonsil, lymph nodes, brain, and blood.
- The diagnosis is based on clinical signs, gross and microscopic lesions, and laboratory tests. The fluorescent antibody (FA) test on frozen sections of spleen, tonsil, and lymph nodes is the simplest and most reliable means of diagnosis.
- The virus can be cultivated in cell cultures of swine origin but grows without discernible CPE. Cell culture coverslips are stained with specific FA to confirm the presence of virus.
- Reverse transcription (RT)-PCR is being used to detect swine fever virus in clinical specimens. This method converts viral RNA to DNA and allows for specific amplification of swine fever virus nucleic acid. This method is rapid and highly sensitive, but has yet to be accepted for routine clinical diagnostic use.

- Virus-specific monoclonal antibodies are used to distinguish the viruses of swine fever, BVD and border disease. Virus characterization in this manner confirms any antigen detection or virus isolation tests that may be performed.

Prevention

- Countries free of hog cholera have strict importation and quarantine requirements to prevent entry of the disease.
- Live attenuated virus vaccines are used in countries where the virus is endemic. Such vaccines are inappropriate where eradication is being attempted in that the virus may continue to circulate subclinically in vaccinates.
- A marker vaccine (gene-deleted vaccine) has been developed that doesn't express one of the viral glycoproteins. Thus the vaccinated animals can be differentiated from infected (wild type virus) by the lack of an antibody response to the viral glycoprotein. Marker vaccines are not yet widely used in eradication programs.

Coronaviridae

Viruses of this family are enveloped with a positive-sense, single-stranded, linear RNA molecule as genome. The term "corona" refers to the halo of spikes extending outwards from the envelope. These viruses infect the respiratory, gastrointestinal tracts and the CNS of many mammals, including humans, and birds.

Viral Characteristics

- Virions are enveloped (80 - 120 nm in diameter), with club-shaped surface spikes (about 20 nm from the envelope surface) that give the appearance of a crown .
- The nucleocapsid has helical symmetry. This feature is unique to the coronaviruses, as most positive- sense RNA viruses have icosahedral nucleocapsids.
- The spike protein is associated with attachment to target cells, which is usually species specific, and is antigenic.
- Coronaviruses replicate in the cytoplasm and bud into cytoplasmic vesicles from which the virions obtain the envelope.
- Coronaviruses have the largest genome of any RNA virus (26 - 32 kb in size).
- The genome is positive-sense ssRNA that is nonsegmented. The genome has a 5' cap and a 3' polyadenylated (poly A) tail.
- Coronaviruses have a high frequency of mutation and a high frequency of recombination, resulting in rapid strain formation within an individual.
- In the cytoplasm, the genomic RNA is copied to a complementary negative-sense RNA strand. This is used as the template for more genomic positive-sense RNA strands and for the formation of viral mRNAs of various sizes (all have a common

- 3' end), known as subgenomic RNAs. The production of subgenomic RNAs is characteristic of coronaviruses.
- These viruses can be propagated in cell culture but often with difficulty.
- They are labile in the environment.

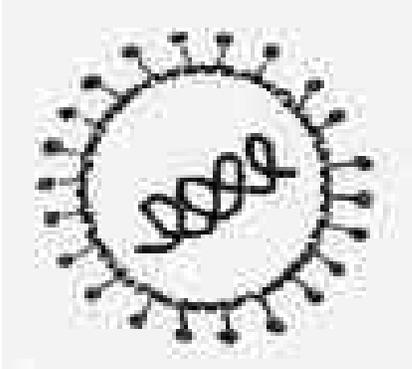


Figure 7 Coronaviridae (80 - 120 nm in diameter). Distinguishing features are the club-shaped surface spikes (about 20 nm from the envelope surface) that give the appearance of a crown and a nucleocapsid that has helical symmetry.

Classification

The family Coronaviridae has two genera, *Coronavirus* and *Torovirus*. The genus *Coronavirus* is divided into three groups on the basis of several features, including the presence or absence of a hemagglutinin-esterase (HE) protein and the number and arrangement of non-essential genes.

Important viruses in these genera are as follows:

- ***Coronavirus***
- Group 1
 - Porcine transmissible gastroenteritis virus
 - Porcine epidemic diarrhea virus
 - Feline infectious peritonitis virus
 - Canine coronavirus
- Group 2
 - Bovine coronavirus
 - Porcine hemagglutinating encephalomyelitis virus
- Group 3
 - Infectious bronchitis virus
 - Turkey coronavirus
- ***Torovirus***
 - Bovine torovirus (Breda virus-Iowa): Associated with severe diarrhea in neonatal calves.

- Equine torovirus: Isolated from a horse with diarrhea in Switzerland, although it was probably not the etiological agent responsible for the disease. The isolate was antigenically related to bovine torovirus.

Coronaviruses cause human respiratory infections, including the common cold and recently a disease called severe acute respiratory syndrome (SARS) that was first recognized in Asia in 2003. It spread to a number of countries in Europe, the Americas and Asia but was finally contained by strict control measures. The fatality rate was ~ 3%. The virus is genetically and antigenically different from other previous known animal or human coronaviruses and has not yet been assigned to a genus.

Coronavirus

Transmissible Gastroenteritis

Cause

Transmissible gastroenteritis virus. There is only one antigenic type. The virus is serologically related to porcine respiratory coronavirus, canine coronavirus, and feline infectious peritonitis virus. The virus may remain viable on premises for up to three days.

Occurrence

Although transmissible gastroenteritis (TGE) virus only causes serious disease in pigs; it can infect dogs subclinically. The disease, which is highly contagious and destructive, occurs frequently in swine worldwide. The majority of outbreaks occur during the colder months of the year.

Transmission

The virus is present in feces and nasal secretions and may also be present in the milk of infected sows. Spread is by direct and indirect contact.

Clinical & Pathologic Features

The severity of the disease depends to a large extent on the level of the sow's immunity. In previously unexposed swine herds, TGE is highly fatal to pigs less than 10 days old and usually spreads rapidly through the whole herd. Young pigs have a severe diarrhea with a watery, whitish or whitish-green stool. Vomiting is fairly common. Dehydration is especially marked, and deaths occur in 2 - 5 days after the onset of clinical signs.

The TGE virus selectively multiplies and destroys absorptive epithelial cells of the villi, giving rise to villous atrophy and impaired absorption (malabsorption). The disease in adult animals may include elevated temperature, poor appetite, mild diarrhea and depression. Vomiting may also occur in some animals.

In herds where the virus is endemic, due to pre-existing immunity in most individuals, clinical signs are milder and mortality is relatively low. Clinical signs are often seen in these pigs during the post-weaning period when passive immunity has declined. Although clinical signs of respiratory infection are not common, the virus can be recovered from lung tissue. The virus has been shown to persist in the intestine of pigs for extended periods of time.

Diagnosis

- Clinical specimens: Portions of jejunum and ileum with contents.

- Because various other agents cause clinically similar gastroenteritis, confirmation of diagnosis by laboratory means is recommended.
- The laboratory method most often used to diagnose TGE is the fluorescent antibody examination of cryostat sections or scrapings of affected intestine.
- The virus can be cultivated in cell cultures of swine origin, but may produce little or no discernible cytopathology.

Prevention

- Both live attenuated and killed vaccines are available for the immunization of sows prior to farrowing. Their value seems to depend on their capacity to produce colostral and colostrum-derived immunity.
- Stronger and long lasting immunity is achieved via natural infection, and one empirical procedure has been to feed infectious intestine and feces to pregnant sows about a month before farrowing.
- Application of strict sanitary measures to prevent spread to susceptible swine.

Infectious Bronchitis

Cause

Infectious bronchitis virus. Neutralization tests in chicken embryos have shown there are many antigenic types of the virus. They are not related antigenically to other coronavirus species.

Occurrence

This highly contagious disease of chickens occurs worldwide.

Transmission

The virus is present in respiratory discharges and transmission is by direct and indirect contact and aerosol.

Clinical & Pathologic Features

Infectious bronchitis is a highly contagious disease of sudden onset and high morbidity. The disease is most severe in chicks and young birds; older birds are susceptible, although the disease is mild. Mortality may be high in baby chicks infected with nephrotropic strains.

The cardinal clinical signs are coughing and gasping. Changes include cloudiness of the air sacs, exudative bronchitis, and excess serous or catarrhal exudate in the trachea. Principal loss in affected flocks is the lowered egg production. The egg-laying capacity of survivors may be permanently impaired; eggs may be misshapen, rough, and soft-shelled. Some strains of the virus are nephrotrophic and cause interstitial nephritis with sudden death.

Diagnosis

- Clinical specimens: Trachea, lungs, and kidneys.
- The virus can be cultivated in susceptible chicken embryos and in chicken epithelial cell cultures. Serotype identification is accomplished by virus neutralization tests with specific antisera.

- The changes occurring in the inoculated embryos are usually seen after several passages. They are characterized by death or dwarfing, curling of the embryo, and crystal urate deposits in the meso-nephrons.
- Fluorescent antibody tests on tracheal scrapings from infected birds have been used for rapid diagnosis.

Prevention

Vaccination is practiced widely. A live attenuated virus is usually administered to birds at 1 - 2 weeks of age via drinking water with revaccination 3 - 4 weeks later, often with a killed vaccine injected subcutaneously. Since there are numerous types of virus, the vaccine used should include the appropriate type(s) for a given area.

Orthomyxoviridae

This is a family of negative-sense, single-stranded RNA viruses. They are smaller than the paramyxoviruses and their genome is segmented (7 to 8 segments) rather than consisting of a single piece of RNA. Influenza viruses are the only members of Orthomyxoviridae.

Viruses of this family have a predilection for the respiratory tract, but usually do not cause a serious disease in uncomplicated cases. Exceptions are human infections with viruses of avian origin. Principal viruses of veterinary importance are type A influenza viruses, which cause equine, swine, and avian influenza.

Viral Characteristics

- Viruses have a segmented single-stranded RNA genome, helical nucleocapsids (each RNA segment + proteins form a nucleocapsid) and an outer lipoprotein envelope.
- The segmented genome facilitates genetic reassortment, which accounts for antigenic shifts. Point mutations in the RNA genome accounts for antigenic drifts that are often associated with epidemics. In either case, the changes are frequently associated with the HA (hemmagglutinin) and NA (neuraminidase) antigens.
- The envelope is covered with two different kinds of spikes, a hemagglutinin (HA antigen) and a neuraminidase (NA antigen). In contrast, the hemagglutinin and neuraminidase activities of paramyxoviruses are in the same protein spike.
- In the laboratory, the virus replicates best in the epithelial cells lining the allantoic cavity of chicken embryos.
- The viruses agglutinate red blood cells of a variety of species.
- Replication takes place in the nucleus.
- The viral RNA-dependent RNA polymerase transcribes the negative-sense genome into mRNA.
- Influenza viruses are labile and do not survive long on premises.

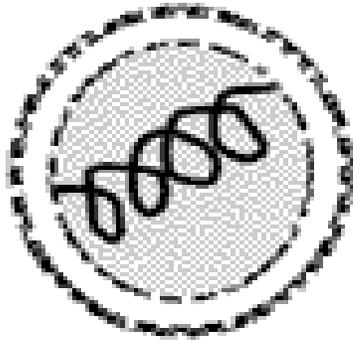


Figure 8. Orthomyxoviridae (80 to 120 nm). Helical nucleocapsid surrounded by an envelope with hyaluronidase and neuraminidase spikes.

Immune Response

The host immune response to influenza viruses includes:

- *non-specific immune response*: the release of interferons by infected cells aids in preventing viral spread to neighboring cells.
- *humoral immune response*: IgA in the upper respiratory tract and IgG in the lower respiratory tract. These antibodies are typically directed against the HA and NA antigens.
- *cell-mediated immune response*: cytotoxic T lymphocytes are important in recovery.

Classification

The family consists of four genera:

- **Influenza virus A**: Viruses cause avian, equine and swine influenza; associated with both epidemics and pandemics; both antigen shift and antigen drift noted. High antigenic variability in the surface glycoproteins HA and NA.
- **Influenza virus B**: Members infect only humans; associated with epidemics; antigenic drift noted.
- **Influenza virus C**: Viruses cause mild, sporadic respiratory infections in humans. May also infect swine.
- **"Thogoto-like viruses"**: The two species Thogoto and Dhori viruses are tick-borne viruses recovered from cattle, camels and humans in regions of Asia, Africa and Europe. They are not considered to be of pathogenic significance for animals.

Antigenic Composition

Knowledge of the antigenic nature of influenza viruses is necessary for an understanding of the epidemiology of influenza.

The internal proteins consist mainly of nucleocapsid protein (NC), some matrix proteins (M1) and three polymerases (PA, PB1 and PB2). The proteins NC and M1 determine type specificity. Even being internal, these proteins (or peptides derived from them) may elicit cytotoxic T cells that are important in recovery from infection.

The nucleoprotein antigen (A, B, C) determines the virus type. The HA and NA antigens determine subtypes.

The hemagglutinin (HA) is an envelope antigen (spike) that can attach to erythrocytes and cause agglutination. It is responsible for the attachment of the virion to cell surface receptors (neuraminic acid, sialic acid). If blocked by antibody, attachment of the virus to a susceptible cell is prevented; thus it is very important in protective immunity mediated by neutralizing antibody. A hemagglutination-inhibition titer of 1/40 is considered to be protective.

Neuraminidase is an envelope protein whose enzymatic activity results in the liquefaction of mucus thus contributing to viral spread. Specific antibody slows down the spread of virus. Neuraminidase also cleaves neuraminic acid to release progeny virus from the infected cell.

Influenza viruses are designated as follows: type/place/time of isolation/H and N content. In birds, there are approximately 15 H antigens (H1 - H15) and 9 N antigens (N1 - N9), which can be found in all possible combinations. An example would be H7N3. Therefore, the type A virus: A/Bangkok/3/79 (H3N2) denotes, respectively, type A, isolated in Bangkok, local laboratory designate of number 3, first isolated in 1979, and envelope antigens of H3N2.

Antigenic Variation

In brief there are two kinds of antigenic changes:

Antigenic shifts: These are major changes based on reassortment of segments of the genome. In reassortment, entire segments of RNA are exchanged between two viruses infecting the same host, each of which codes for a single protein, e.g., the hemagglutinin. As a result of co-infection by two viruses, a third one may arise.

Antigenic drifts: These are minor changes caused by point mutations in the genes encoding the HA and NA glycoproteins.

Genetic Basis for Antigenic Variation

- The genes of the type A viral hemagglutinin and neuraminidase are polymorphic, subject to extensive variation. This not the case for types B or C.
- The HA and NA genes of types A and B viruses undergo point mutations. When developing a vaccine, the effect of change can be determined by the reciprocal inhibition test. As a result of the change, the immune response generated against the vaccine HA or NA is now less effective against the mutated (variant progeny) HA or NA.

Swine Influenza

(Swine flu, Hog flu)

Cause

Influenza virus A. Subtypes H1N1 and H3N2 have been frequent causes of swine influenza. More virulent variants of H1N1 have appeared in recent years. The H1N2 subtype has also been implicated as a cause of acute swine influenza. It has been suggested that all porcine influenza viruses were derived originally from birds. Secondary infection with *Haemophilus parasuis* and other bacteria may contribute to a more severe disease.

Occurrence

Swine influenza occurs worldwide. Influenza strains from swine may produce serious infections in humans, other mammals, and birds.

Transmission

Swine influenza is widespread, occurring most commonly in the colder months. Aerosol droplets, contact, and fomites are the means of spread. In swineherds where the virus is endemic, young susceptible pigs are continually infected, thereby maintaining the virus. Explosive outbreaks of acute disease occur when the virus is introduced into susceptible, naive herds.

Clinical & Pathologic Features

Morbidity is high but the mortality is usually no greater than 2%. Virus infection is mild without secondary bacteria. In a typical outbreak, there is an incubation period of about three days followed by an acute onset of respiratory distress with rapid respiration, coughing, anorexia, and prostration. The clinical course is usually 2 - 6 days with rapid recovery in uncomplicated cases. With secondary invaders and particularly *Haemophilus suis* the disease is much more serious and some deaths may occur.

Necropsy in acute cases discloses edematous mediastinal lymph nodes and pneumonic lesions usually limited to the apical and cardiac lobes. Affected areas are firm and purplish in color and there is often a sharp line of demarcation between normal and affected tissue. Exudative bronchitis and interstitial pneumonia are common microscopic findings.

Diagnosis

- Clinical specimens: Nasal swabs and lungs, acute and convalescent sera.
- Given the often mild character of the disease, laboratory diagnosis may not be sought.
- A presumptive diagnosis is made on the basis of clinical and pathologic findings. Confirmation requires isolation and identification of the virus, demonstration of seroconversion or detection of viral infected cells in frozen sections of lung tissue by immunofluorescence.
- Swine influenza virus is most easily isolated by the inoculation of embryonated eggs via the allantoic cavity.

Prevention

- Swine influenza virus is usually introduced into herds via replacement stock or returning show animals.
- Vaccination is not practiced.

- In the event the disease is particularly severe, antibiotics may be used to control secondary bacteria.
- Recovery from swine influenza infection confers immunity, but the duration is probably less than a year.

Circoviridae

This is a newly established family of very small, non-enveloped DNA viruses that contains three virus species of veterinary significance.

Viral Characteristics

- Very small (17 - 22 nm in diameter), naked icosahedral viruses with a circular, single-stranded DNA genome. The genome encodes a single capsid protein. See illustration of capsid (fig 9).
- Replication takes place in the nucleus of dividing cells and is similar to the parvoviruses.
- The single-stranded circular DNA of circoviruses is thought to be replicated by a rolling circle mechanism.
- In the cell nucleus, the ssDNA (either negative sense or ambisense) is used as a template for the formation of dsDNA by host repair enzymes. The dsDNA is then used as a template for both mRNA production (for translation of proteins) and copies of the genome for progeny virions. These products are self-assembled into complete progeny virions.
- Circoviruses are very stable in the environment; resistant to some disinfectants, including detergents.

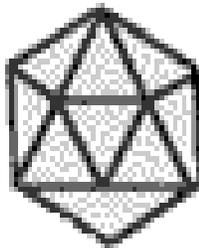


Figure 9. Illustration of the capsid of a circovirus (17 - 22 nm).

Classification

The family has two genera based on genetic studies. *Gyrovirus* also differs from *Circovirus* in the replication cycle and the virions being larger. They are with their species as follows:

- *Circovirus*

- porcine *circovirus* type 1
- porcine *circovirus* type 2
- beak and feather disease virus
- ***Gyrovirus***
 - chicken anemia virus

Gyrovirus

Chicken Anemia Virus Infection

Cause

Chicken anemia virus (*Gyrovirus*).

Occurrence

A worldwide, common infection of chickens, particularly of commercial flocks and broilers. The virus may infect chickens of all ages.

Infections are most serious when there is concurrent infection with the infectious bursal disease virus, avian adenovirus, or reticuloendotheliosis virus.

Transmission

Direct and indirect spread by the oral-fecal and respiratory routes; also, vertically via the egg and via the semen of infected roosters. Laying hens thus infected are viremic for a period of 1 - 3 weeks. Chicks hatched from infected eggs are viremic and thus a source of infection.

Pathogenesis

The viremia developing in infected day-old chicks leads to infection of many organs and specifically T cells in the thymic cortex and bursa, and hemocytoblasts in the bone marrow.

Clinical & Pathologic Features

Overt disease is seen only in young chicks within the first 2 - 3 weeks of life. The virus is present in many organs and feces.

There follows immunosuppression and aplastic anemia with atrophy of lymphoid tissue. Clinical signs begin at about two weeks of age and include anemia (pale), diarrhea, anorexia, depression and weight loss.

The mortality rate is usually about 10% but may be as high as 50% if there is dual infection.

Maternal antibodies prevent the development of clinical disease in chicks.

Necropsy lesions often noted are subcutaneous and muscle hemorrhages, pale visceral organs, an abnormal fatty-appearing bone marrow and thymic atrophy. Consistent microscopic lesions are found in the bone marrow where erythrocytes and other cells are replaced by fat cells and in the thymus, which is depleted of lymphocytes.

Diagnosis

- Clinical specimens: whole chicken, serum.
- Clinical signs, lesions and the aplastic anemia suggest chicken anemia virus infection.
- The virus can be cultivated in cells but isolation is not usually diagnostically feasible.

- Definitive diagnosis depends on the detection of viral DNA in the thymus or bursa by PCR, dot-blot hybridization or *in situ* hybridization.
- Serum antibodies can be detected by conventional procedures, such as ELISA.
- ELISA kits are available and are used to identify and eliminate positive hens before laying.

Prevention

- It is difficult to maintain laying flocks free of infection.
- A procedure used, is to deliberately expose layers before laying begins to infected tissue homogenates or litter from positive flocks.
- Losses are lessened if flocks are kept free of other immunosuppressive viruses.
- Antibiotics may be used to control secondary bacterial infections.
- Live vaccines are administered by injection or in drinking water to antibody-negative breeder flocks prior to the start of egg production.

Adenoviridae

This family consists of double-stranded DNA viruses with an icosahedral nucleocapsid. They have been recovered from many mammalian and avian species. Many are found in the respiratory tract and infections are often persistent. Only a small number cause significant veterinary diseases.

Viral Characteristics

- Non-enveloped, viruses with icosahedral symmetry containing a single, linear molecule of double-stranded DNA.
- The capsid consists of capsomeres (called *hexons*) and 12 vertex capsomeres (called *pentons*). These are the only viruses with a fiber (the fiber antigen) protruding from each of the 12 pentons (see Fig 10).
- The fiber is the structure of attachment to host cells and is also a type specific hemagglutinin.
- The hexon of mammalian adenoviruses contains a cross-reacting group antigen.
- The fiber antigen attaches to a specific cell receptor and initiates replication.
- The dsDNA encodes approximately 30 proteins. Viral DNA replication, mRNA transcription and virion assembly occur in the nucleus, utilizing both host and virus-encoded factors. This results in the formation of basophilic and / or acidophilic intranuclear inclusions.
- Many adenoviruses agglutinate red cells of various animal species and some are capable of malignant transformation in tissue culture cell and oncogenesis when inoculated into laboratory animals.
- They are resistant to trypsin and lipid solvents, and moderately resistant on premises.

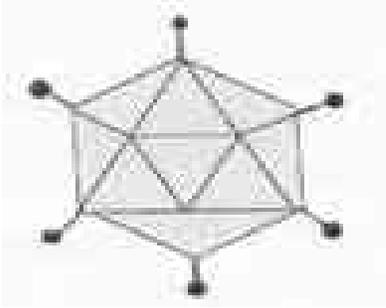


Figure 10. Adenoviridae (70 - 90 nm). Note the fiber proteins protruding from the vertices of the 12 pentons. To

Classification

This family originally consisted of only two genera, *Mastadenovirus*, which infect mammals, and *Aviadenovirus*, which infect birds. There are also several as yet unassigned and recently assigned viruses in the family.

Mastadenovirus

This genus consists of 20 virus species that infect mammals including canine, equine, bovine, ovine and porcine adenoviruses. All 20 species share a common antigen. Important diseases are infectious canine hepatitis, canine adenovirus 2 infection, and equine adenovirus A infection.

Aviadenovirus

This genus includes the viruses of inclusion body hepatitis, quail bronchitis, marble spleen disease and a number of adenoviruses of poultry and birds that are not associated with significant diseases. Members of the genus share a common antigen.

Previously Unassigned Adenoviruses

Included in this category are the viruses that have recently (2002) been placed in the genera *Atadenovirus* and *Siadenovirus*. These viruses include the egg drop syndrome virus (*Atadenovirus*), turkey hemorrhagic enteritis (*Siadenovirus*), adenoviral splenomegaly of chickens (*Atadenovirus*) and ovine adenovirus 287 (*Atadenovirus*; of research interest, but of no disease significance) and some bovine adenovirus types 4 to 8 (*Atadenovirus*).

Atadenovirus

Egg Drop Syndrome

Cause

Duck adenovirus 1.

Occurrence

Egg drop syndrome (EDS) is common and worldwide in distribution. It occurs most frequently in broiler chicken breeder flocks 5 - 6 weeks of age.

Transmission

It is mainly transmitted vertically through the egg. The virus is shed in the feces and spread can be by contaminated water and fomites. Sporadic outbreaks have been attributed to wild birds contaminating water.

Clinical & Pathologic Features

Infected birds appear healthy. Egg production is variably depressed and abnormal eggs are produced. Shells of the latter may be absent, thin, underpigmented and rough surfaced. Outbreaks last 4 to 10 weeks.

Among the effects noted are inactive ovaries, atrophied oviducts, edema of the uterus, exudates in the cell gland and intranuclear inclusions in tissue of the cell gland.

Diagnosis

- Loss of egg production with abnormal eggshells suggest EDS.
- Clinical specimens: eggs and reproductive tissues including the shell gland.
- Virus can be cultivated in duck and goose embryonated eggs (preferred) and also in duck kidney or fibroblast cell lines. The presence of virus is indicated by hemagglutination of avian red cells.
- Diagnosis is made with the hemagglutination inhibition test. It is used to screen flocks but negative tests do not indicate that birds are necessarily free of infection.

Prevention

- Replacement birds should be from uninfected flocks.
- An oil adjuvant inactivated vaccine provides immunity for a year.
- Good hygiene to prevent lateral spread particularly from infected egg contamination.