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 staranded 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 is 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
   - Jaagsietate sheep retrovirus (ovine pulmonary adenocercinome virus)

3. Gamma retrovirus
   - Feline sarcoma virus
   - Feline leukaemia virus
   - Avian reticuloendotheliosis virus (Turkey, ducks, chicken, snail, pheasants)

4. Delta rerovirus
   - Bovine leukaemia virus
   - Human T-lymphotropic virus 1,2

5. Epislonretrovirus
   - 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

<u>Clinical infection</u>

- 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 inection 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/transducting 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: avain leucosis virus (ALV) group
- Causes neoplastic conditions including lymphoid, erythroid and mycloid leucosis in chickens. Also associated with fribrobarcoma, haemangiosarcoma, and nephroblastoma
- Lymphoid leucosis, a B-cell lymphoma, is the most common and most economically important of the condition
- Avian leukoses 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 viraemia
- 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 develops transcient viraemia before neutralizing antibodies
- Such bird become carrier and shed virus intermittently and produce infected chick
- 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 chick offering passive immunity to infection for the first few weeks of life

C.S:

- mutation period usually more that four months. Diseases usually sporadic in infected flock but occasional epidemics have been described
- Inappetint
- Weakness
- Emaciation
- Pale hatther
- Enlarged liver and horse of fabrisios
- 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 tumur
- Differential diagnosis: Marek's disease (based on age of affected birds, presence of bursed 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 immunoflourescence

- 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 envelop 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, malase lymphadenopathy
- Non-specific clinical signs: anaemia, reduced reproductive performance, enteric secondary infections due to immunosurpressive effect
- Myeloid and fibrosarcoma tumour

Diagnosis

- Sample: blood, saliva
- Commercial ELISA for antigen detection (major capsid protein p27)

- Immunoflourescent 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 has anti FeLV antibodies. Detection of neutralizing antibodies indicates that a cat is immuned and resistant to infection
- An antigen termed feline oniovirus-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, subvant and recombinants 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 bile

- Transmitted in uterus from green to kitten during partrution 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 immunoflourescence
- 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 colostral antibodies
- Virus may be isolated from saliva and blood but it is not a realistic procedure for routine diagnosis
- Proviral DNA detectible 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 haemato insets particularly *Tabanus spp* and *Stomaxys 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 reccudenscence 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 eyelips and ear, erosion and ulceration of oral mucosa, excessive salivation and watery nasal discharges which later becomes mucopurulent, swollen and cyanotic tongue, lameness from coronotis and laminitis, tortocillis, 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.