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→ are fragile and do not survive well outside the body.
 → requires close contact
 → sheep → Not disease causes
 → Latin → Creep & crawl

↗ ~~fect~~
 ↗ ~~gan~~
 ↗ ~~sapi~~
 ↗ grow
 ↗ Host range → Broad

Table 54.1 Herpesviridae

Virus

Bovine herpesvirus 1

Bovine herpesvirus 2

Bovine herpesvirus 5

Ovine herpesvirus 2

Alcelaphine herpesvirus

Herpes
CNS disease
affects pigs
herpesvirus
infections are p
are listed i

Infectious
vulvovag
Infection
cause of l
clinical c
(IBR), in
conjuncti

Table 54.

Virus

Porcine
herpesv
(Aujesz
disease
virus)

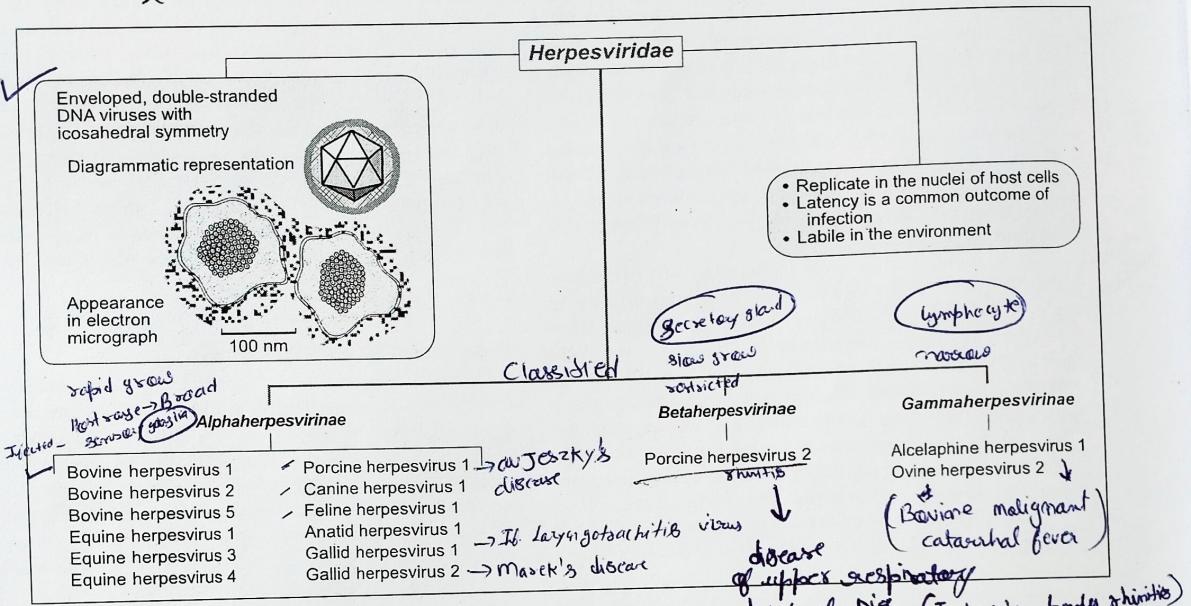
↓

mad
it

Porcine
herpes

54 Herpesviridae

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The family *Herpesviridae* contains more than 100 viruses. Fish, amphibians, reptiles, birds and mammals including humans are susceptible to herpesvirus infection. These viruses are of special importance because of their widespread occurrence, their evolutionary diversity and their involvement in many important diseases of domestic animals and humans. The name, herpesvirus (Greek *herpein*, to creep), refers to the sequential appearance and local extension of lesions in human infection. Herpesviruses are enveloped and range from 200 to 250 nm in diameter. They contain double-stranded DNA within an icosahedral capsid. Herpesviruses enter cells by fusing with the plasma membrane. Replication occurs in the cell nucleus. The envelope is probably derived from the nuclear membrane of the host cell, incorporating at least 10 viral-encoded glycoproteins. Release from the cell is by exocytosis. Active infection results in cell death. Intranuclear inclusions are characteristic of herpesvirus infections. Extension of viral infection occurs through points of cell contact without exposure of virus to neutralizing antibodies in blood or interstitial fluids. Protective antibody responses are usually directed against the envelope glycoproteins. Herpesvirus virions, which are fragile and sensitive to detergents and lipid solvents, are unstable in the environment.

The family is divided into three subfamilies comprising 13 genera. Alphaherpesviruses replicate and spread rapidly, destroying host cells and often establishing latent infections in

sensory ganglia. Betaherpesviruses, which replicate and spread slowly, cause infected cells to enlarge, hence their common name, cytomegaloviruses. They may become latent in cells of the monocyte series. Gammaherpesviruses, which infect lymphocytes, can produce latent infections in these cells. When lymphocytes become infected, there is minimal expression of viral antigen. Some gammaherpesvirus species also replicate in epithelial and fibroblastic cells, causing cytolysis. A number of herpesviruses are implicated in neoplastic transformation of lymphocytes.

Clinical infections

Herpesviruses establish lifelong infections with periodic reactivation resulting in bouts of clinical disease. Shedding of virus may be periodic or continuous. During latency, the episomal viral genome becomes circular and gene expression is limited. Reactivation of infection is associated with various stress factors including transportation, adverse weather conditions, overcrowding and intercurrent infection. Natural infections with particular herpesviruses are usually restricted to defined host species. Because these viruses are highly adapted to their natural hosts, infections may be inapparent or mild. However, in very young or immunosuppressed animals, infection can be life-threatening.

Effect → sensory
ganglia
grow → rapid
Hot & dry → Broad

- secretory
- gland
- slave
- restricted

- lymphocytes
- marrow

Table 54.1 Herpesvirus infections of ruminants

Virus	Genus	Comments
Bovine herpesvirus 1	<i>Varicellovirus</i>	Causes respiratory (infectious bovine rhinotracheitis) and genital (infectious pustular vulvovaginitis, balanoposthitis) infections. Occurs worldwide
Bovine herpesvirus 2	<i>Simplexvirus</i>	Causes ulcerative mammillitis in temperate regions and pseudo-lumpy-skin disease in tropical and subtropical regions
Bovine herpesvirus 5	<i>Varicellovirus</i>	Causes encephalitis in calves, described in several countries
Ovine herpesvirus 2	<i>Macavirus</i>	Causes subclinical infection in sheep and goats worldwide. Causes malignant catarrhal fever in cattle and in some wild ruminants
Alcelaphine herpesvirus 1	<i>Macavirus</i>	Causes subclinical infection in wildebeest in Africa and in zoos. Causes malignant catarrhal fever in cattle, deer and in other susceptible ruminants

Herpesviruses can cause respiratory, genital, mammary and CNS diseases in cattle (Table 54.1). Aujeszky's disease, which affects pigs and other domestic species, is the major porcine herpesvirus infection (Table 54.2). Equine herpesvirus infections are presented in Table 54.3; those of domestic carnivores are listed in Table 54.4 and those of birds in Table 54.5.

Infectious bovine rhinotracheitis and pustular vulvovaginitis

Infection with bovine herpesvirus 1 (BoHV-1) is an important cause of losses in cattle worldwide. It is associated with several clinical conditions including infectious bovine rhinotracheitis (IBR), infectious pustular vulvovaginitis (IPV), balanoposthitis, conjunctivitis and generalized disease in newborn calves. Iso-

Table 54.2 Herpesvirus infections of pigs.

Virus	Genus	Comments
<u>Porcine herpesvirus 1</u> <u>(Aujeszky's disease virus)</u> <p style="text-align: center;">↓</p> <p><u>mad itch</u></p>	<i>Varicellovirus</i>	Causes Aujeszky's disease in pigs. <u>Encephalitis, pneumonia and abortion</u> are features of the disease. In many species other than pigs, pseudorabies manifests as a neurological disease with marked pruritis. Occurs worldwide but USA (occurs in feral pigs), Canada, New Zealand and several EU states have eradicated this disease
Porcine herpesvirus 2	Unassigned	Causes disease of the upper respiratory tract in young pigs (inclusion body rhinitis)

Table 54.3 Herpesvirus infections of horses.

Virus	Genus	Comments
Equine herpesvirus 1	<i>Varicellovirus</i>	Causes abortion, respiratory disease, neonatal infection and neurological disease. Occurs worldwide
Equine herpesvirus 3	<i>Varicellovirus</i>	Causes mild venereal infection (equine coital exanthema) in both mares and stallions
Equine herpesvirus 4	<i>Varicellovirus</i>	Causes rhinopneumonitis in young horses. Occurs worldwide

Table 54.4 Herpesvirus infections of domestic carnivores.

Virus	Genus	Comments
Canine herpesvirus I	<i>Varicellovirus</i>	Causes a fatal generalized infection in neonatal pups
Feline herpesvirus I	<i>Varicellovirus</i>	Causes feline <u>viral rhinotracheitis</u> in young cats

lates of BoHV-1 can be divided into subtypes 1.1 (IBR-like) and 1.2 (IPV-like) using restriction endonuclease analysis of the genome.

The virus is usually acquired through aerosols (subtype 1.1) or genital secretions (subtypes 1.2a and 1.2b). Aerosol transmission is most efficient over short distances and is facilitated by the close proximity of animals. Replication occurs in the mucous membranes of the upper respiratory tract and large amounts of virus are shed in nasal secretions. Virus also enters local nerve cell endings and is transported intra-axonally to the trigeminal ganglion, where it remains latent. In most instances, infection is contained within two weeks by a strong immune response. However, tissue necrosis may facilitate secondary bacterial infection, with severe systemic effects and, possibly, death. Rarely, viraemia in pregnant cows may produce foetal

Table 54.5 Herpesvirus infections of birds.

Virus	Genus	Comments
Gallid herpesvirus 1	<i>Ilovirus</i>	Causes <u>infectious laryngotracheitis</u> . Present in many countries
Gallid herpesvirus 2 (Marek's disease virus)	<i>Mardivirus</i>	Causes Marek's disease, a lymphoproliferative condition in 12- to 24-week-old chickens. Occurs worldwide
Anatid herpesvirus 1	<i>Mardivirus</i>	Causes acute disease in ducks (duck plague), geese and swans characterized by oculonasal discharge, diarrhoea and high mortality. Occurs worldwide

↓ Duck plague

pups under four weeks of age, they are particularly dependent on ambient temperature and maternal contact for maintenance of normal body temperature. A cell-associated viraemia and widespread viral replication in visceral organs can occur in infected neonatal animals with subnormal body temperatures. Affected pups stop sucking, show signs of abdominal pain, whine incessantly and die within days. Morbidity and mortality rates in affected litters are high. Bitches whose pups are affected tend to produce healthy litters subsequently.

Diagnostically significant postmortem findings include focal areas of necrosis and haemorrhage, particularly in the kidneys. Intracellular inclusions are usually present. Specimens from liver, kidney, lung and spleen are suitable for virus isolation or detection of viral nucleic acid. A commercial vaccine is available. Affected bitches and their litters should be isolated to prevent infection of other whelping bitches.

Feline viral rhinotracheitis

This acute upper respiratory tract infection of young cats is caused by feline herpesvirus 1 (FHV-1). The virus, which occurs worldwide, accounts for about 40% of respiratory infections in cats.

Close contact is required for transmission. Most recovered cats are latently infected. Reactivation with virus replication and shedding is particularly associated with periods of stress such as parturition, lactation or change of housing. Initially, FHV-1 replicates in oronasal or conjunctival tissues before infecting the epithelium of the upper respiratory tract. Secondary bacterial infections, which commonly occur, exacerbate the clinical signs. Young cats display signs of acute upper respiratory tract infection including fever, sneezing, inappetence, hypersalivation, conjunctivitis and oculonasal discharge. In more severe disease, pneumonia or ulcerative keratitis may be evident. The mortality rate is low except in young or immunosuppressed animals.

Clinical differentiation of feline viral rhinotracheitis from feline calicivirus infection is difficult. Virus can be isolated from suitable tissue specimens or viral DNA can be detected in oropharyngeal or conjunctival swabs. Specific viral antigen can be demonstrated in acetone-fixed nasal and conjunctival smears using immunofluorescence. Good husbandry practices and disease control procedures should be implemented in

catteries together with regular vaccination to minimize the impact of clinical disease. Commercial vaccines also contain feline calicivirus. The protection provided by vaccination against these two viruses is incomplete as vaccinated cats can become infected but clinical signs tend to be much reduced.

Marek's disease

This contagious lymphoproliferative disease of chickens is caused by gallid herpesvirus 2 (Marek's disease virus), which is cell-associated and oncogenic. The disease, which is of major economic significance in the poultry industry, occurs worldwide. Productive replication with release of infective virus occurs only in the epithelium of the feather follicle. Cell-free virus is released from the follicles along with desquamated cells. This dander can remain infective for several months in dust and litter in poultry houses. Infected birds remain carriers for life and their chicks, which are protected initially by maternally-derived antibody, acquire infection within a few weeks, usually by the respiratory route. In addition to the virulence of the infecting strain of herpesvirus, host factors which contribute to the severity of the disease include the sex, age at the time of infection and genotype. Female birds are more susceptible than male birds, while resistance to the development of disease increases with age. The bird's genotype influences the susceptibility of T lymphocytes to transformation and development of lymphoid tumours. Birds between 12 and 24 weeks of age are most commonly affected when clinically affected birds present with partial or complete paralysis of the legs and wings.

The diagnosis of Marek's disease is based on clinical signs and pathological findings. Differentiation from lymphoid leukosis is based on the age of affected birds, the incidence of clinical cases and the histopathological findings. The use of appropriate management strategies, genetically resistant stock and vaccination have reduced losses from Marek's disease. Disinfection, all-in/all-out policies, and rearing young chicks away from older birds for the first two or three months of life reduce exposure to infection, decreasing the likelihood of serious disease. A range of modified live vaccines are commercially available. Although a single dose of virus injected into day-old chicks provides good lifelong protection, it does not prevent superinfection with virulent field viruses. Automated *in ovo* vaccination is used in large commercial units.

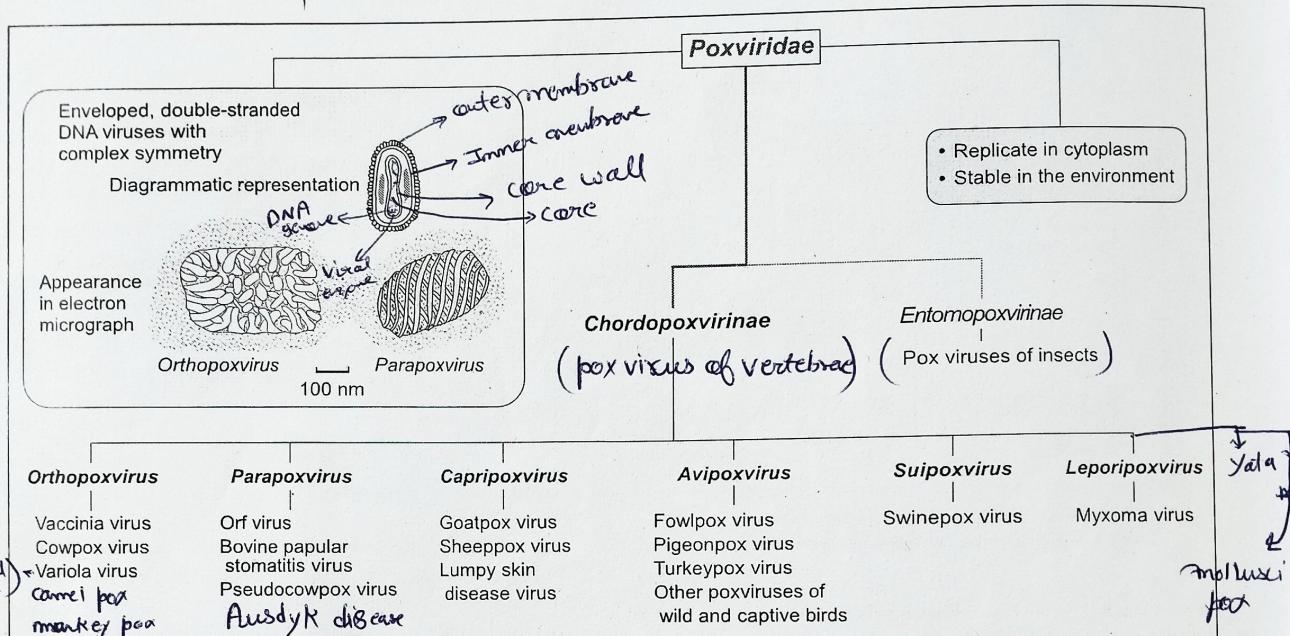
→ DNA genome is wrapped around a fibrous spiral like core. Which has the shape of a torus.

- ① pseudo lumpy skin disease → Bovine Herpes virus -2
 - skin disease
 - lesion → teat
- ② Aujeszky's disease → porcine Herpes virus → I
 - It is also known as pseudorabies
 - pigs ↗
 - Air-borne transmission
 - fomites
 - Host → pig, cattle, dog, cat, sheep

Respiratory tract → Brain
 Skin abrasion → Pneumonia
 → Inh → Head & Neck
 → Skin lesion & ulcer

Chicken pox virus → Herpes virus

57 Poxviridae



The family Poxviridae contains the largest viruses which cause disease in domestic animals. The family is divided into two sub-families, *Chordopoxvirinae*, the poxviruses of vertebrates, and *Entomopoxvirinae*, the poxviruses of insects. Genetic recombination within genera results in extensive serological cross-reactions and cross-protection. These double-stranded DNA viruses replicate in the cytoplasm and are stable in the environment under dry conditions.

Infections with poxviruses usually result in vesicular skin lesions (Table 57.1). Smallpox, caused by variola virus, was formerly a human disease of major international significance. The use of vaccinia virus for the prevention of smallpox, first introduced by Jenner in the late eighteenth century, eventually led to the global eradication of this highly contagious disease at the close of the twentieth century.

Clinical infections

Transmission of poxviruses can occur by aerosols, by direct contact, by mechanical transmission through arthropods and through fomites. Skin lesions are the principal feature of these infections. Several virus-encoded proteins are released from infected cells, including a homologue of epidermal growth factor which stimulates cell proliferation. Typically, pox lesions begin as macules and progress through papules, vesicles and pustules to scabs which detach, leaving a scar. In generalized infections there is a cell-associated viraemia and recovered ani-

mals have solid immunity. Some localized pox infections may induce transient immunity and reinfection can occur.

Three closely related parapoxviruses, namely pseudocowpox virus, bovine papular stomatitis virus and orf virus, infect ruminants. These viruses are transmissible to humans, producing lesions which are clinically similar. Moreover, the three viruses are morphologically indistinguishable and identification of the causal agent relies on nucleic acid analysis.

Capripoxviruses are economically important viruses producing generalized infections with significant mortality in domestic ruminants. Sheppox virus, goatpox virus and lumpy skin disease virus are closely related and share a group-specific structural protein (p32), which allows the same vaccine to be used against each virus.

Many avian species are susceptible to infection with members of the genus Avipoxvirus. Although antigenic relationships exist among avian poxviruses, this relatedness is variable. Virus species within the genus, named in accordance with their affinity for particular host species, include fowlpox virus, canarypox virus, pigeonpox virus and turkeypox virus. The type species of the genus is fowlpox virus.

Diagnosis

Diagnosis can often be made solely on clinical grounds. Skin biopsies or postmortem specimens may be used for laboratory confirmation. Eosinophilic intracytoplasmic inclusions may

→ Concatemer → Long continuous DNA molecules that contains multiple copies of the same DNA sequence linked in series

Table 57.1 Members of the Poxviridae of veterinary significance.

Virus	Genus	Host species	Significance of infection
Vaccinia virus	<i>Orthopoxvirus</i>	Wide host range	Infections in sheep, water buffaloes, rabbits, cattle, horses and humans. Used as a recombinant virus vector for rabies vaccine
Cowpox virus	<i>Orthopoxvirus</i>	Rodents, cats, cattle	Species of small rodents are the likely reservoir hosts. Cats are the principal incidental hosts; infection results in skin lesions. Rare cause of teat lesions in cattle. Transmissible to humans
Uzain gishu virus	<i>Orthopoxvirus</i>	Unknown wildlife reservoir, horses	Rare disease, reported in Kenya and neighbouring African countries. Causes papilloma-like skin lesions in horses
Camelpox virus	<i>Orthopoxvirus</i>	Camel	Widely distributed in Asia and Africa. Causes systemic infection with typical pox lesions; severe infection in young camels
Pseudocowpox virus	<i>Parapoxvirus</i>	Cattle	Common cause of teat lesions in milking cows; causes milker's nodule in humans
Bovine papular stomatitis virus	<i>Parapoxvirus</i>	Cattle	Produces papular lesions on the muzzle and in the oral cavity of young cattle. Transmissible to humans
Orf virus	<i>Parapoxvirus</i>	Sheep, goats	Primarily affects young lambs; causes proliferative lesions on the muzzle and lips. Transmissible to humans
Sheppox/goatpox virus	<i>Capripoxvirus</i>	Sheep, goats	Endemic in Africa, Middle East and India. Causes generalized infection with characteristic skin lesions and variable mortality
Lumpy skin disease virus	<i>Capripoxvirus</i>	Cattle	Endemic in Africa. Causes generalized infection with severe lesions and variable mortality
Swinepox virus	<i>Suipoxvirus</i>	Pigs	Causes mild skin disease. Occurs worldwide. Transmitted by the pig louse (<i>Haematopinus suis</i>)
Fowlpox virus	<i>Avipoxvirus</i>	Chickens, turkeys	Causes lesions on the head and on the oral mucous membrane. Occurs worldwide. Transmitted by biting arthropods
Myxoma virus	<i>Leporipoxvirus</i>	Rabbits	Causes mild disease in cottontail rabbits, the natural host, and severe disease in European rabbits (myxomatosis). Introduced into Europe, Australia and Chile as a biological control measure
Squirrelpox virus	Unassigned	Red and grey squirrels	Important factor in decline of native red squirrels (<i>Sciurus vulgaris</i>) in Great Britain; carried by grey squirrel (<i>Sciurus carolinensis</i>) introduced from North America
Nile crocodilepox virus	<i>Crocodylidpoxvirus</i>	Nile crocodile	Cause of skin lesions in wild and farmed crocodiles

SECTION IV

be demonstrable histologically in epidermal cells. Electron microscopy can be used for the rapid identification of poxvirus particles in material from lesions. Parapoxviruses can be readily distinguished from members of the other genera. For some species, virus may be isolated in testis or kidney cell monolayers. An antigen-trapping ELISA has been developed for the detection of capripoxvirus antigen. Protocols for PCR assays for the detection of viral DNA are also available.

Control

Vaccines are available for a number of poxviruses and control is based on annual vaccination. Inactivated vaccines are

less effective than modified live vaccines because cell-mediated immunity is the predominant protective response. A recombinant vaccine providing protection against lumpy skin disease and peste des petits ruminants has been developed. In flocks endemically infected with orf virus, control is based on the use of a fully virulent live vaccine derived from scab material or cell culture. Ewes should be vaccinated by scarification in the axilla at least eight weeks before lambing. Close to lambing, ewes must be moved to a new grazing area in order to minimize exposure of lambs to infectious vaccinal scab material.

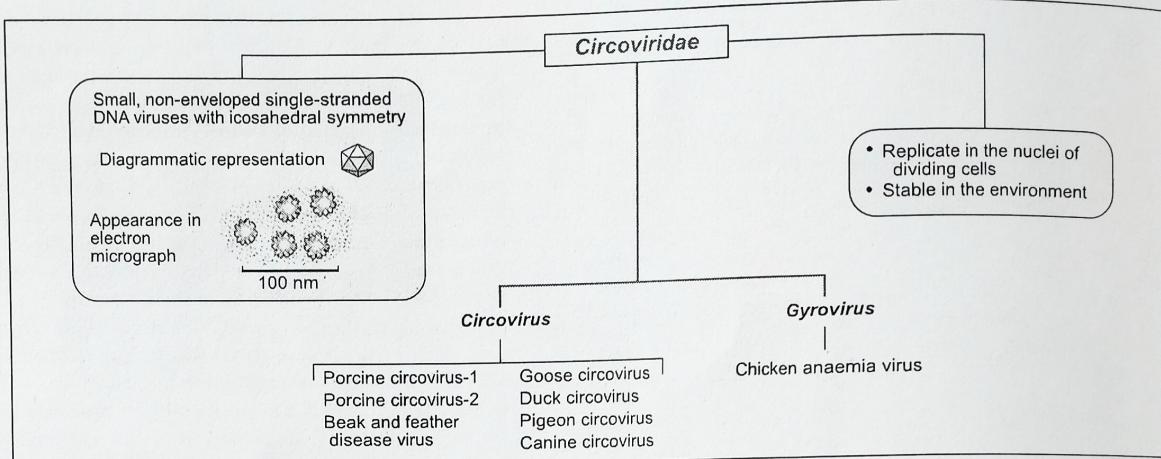
→ Viral Replication

- attachment
- penetration
- uncoating
- transcription of early m-RNA
- translation - *Poxviridae* protein
- Replication of viral DNA
- late transcription of late m-RNA
- translation
- Assembly of viruses

- Vision → Brick shaped
- parapoxvirus → ... → Coccus shaped
- outer layer encloses a dumbbell-shaped core and two lateral bodies
-

61 Circoviridae

Circular



SECTION IV

Circoviruses (20 to 25 nm in diameter) are non-enveloped with icosahedral symmetry. The genome consists of a molecule of circular single-stranded DNA. Replication occurs in the nuclei of dividing cells and these viruses are stable in the environment. Circoviruses are host-specific, have a worldwide distribution and infect cells of the haemolymphatic system. The majority of circoviruses identified have been isolated from avian species. Infections with chicken anaemia virus and with porcine circovirus are of particular veterinary interest. Beak and feather disease virus is associated with a debilitating, immunosuppressive disease of young psittacine birds, particularly cockatoos. Canine circovirus has been identified in dogs suffering from severe haemorrhagic gastroenteritis, vasculitis and granulomatous lymphadenitis.

Chicken anaemia virus infection

Young birds infected with chicken anaemia virus (CAV) develop aplastic anaemia and generalized lymphoid atrophy. This virus is present in poultry flocks worldwide. Both horizontal and vertical transmission occur. Infection is by the faecal-oral route. Once infection is established in a breeder flock, most birds develop antibodies before laying begins. Maternally-derived antibodies do not prevent chicks from becoming infected and shedding the virus. However, they prevent the development of clinical disease. An age-related resistance to disease but not to infection develops in chicks at about two weeks of age. However, age-related resistance and the protective effect of maternally-derived antibodies do not prevent clinical disease if immunosuppressive viruses such as infectious bursal disease virus or gallid herpesvirus 2 are present in the flock. The principal target cells are in the thymus and in the bone marrow. Chickens develop clinical signs at about two weeks of age. The mortality rate is usually about 10%. Subclinical infection in broilers from breeder flocks can adversely affect weight gains.

A presumptive diagnosis is based on the clinical signs and gross lesions at postmortem. Laboratory confirmation relies on detection of viral antigen by immunocytochemical techniques. Viral DNA can be demonstrated in bone marrow and thymus by *in situ* hybridization, by dot-blot hybridization or by PCR. Serum antibodies can be detected using virus neutralization, indirect immunofluorescence and ELISA. Commercial live vaccines are available and are designed to prevent vertical transmission of the virus from breeder hens. Vaccination does not prevent economic losses in broilers due to subclinical infection.

Pig circovirus infection

Porcine circovirus 2 (PCV-2) is consistently isolated from piglets with post-weaning multi-systemic wasting syndrome (PMWS). Sero-epidemiological studies indicate that infection is widespread in pig populations worldwide. The virus has also been linked to porcine dermatitis and nephropathy syndrome and to reproductive problems.

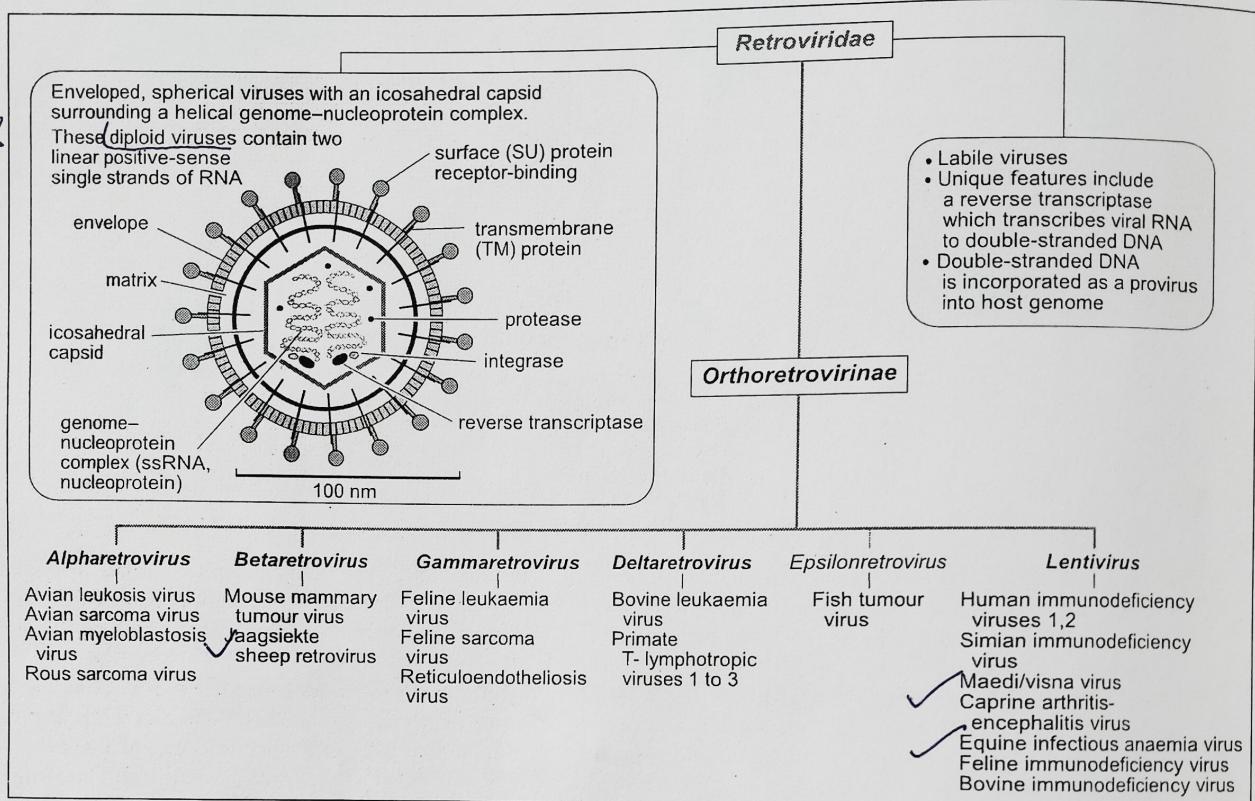
Co-factors appear to be necessary for the development of the full clinical disease. It is thought that immune stimulation may be an important trigger. A generalized depletion of lymphocytes resulting in immunosuppression is a consistent feature of the disease.

Diagnosis of PMWS is based on clinical signs and pathological findings. A definitive diagnosis requires demonstration of PCV-2 antigen or viral nucleic acid in association with lesions. Due to the widespread nature of the virus, control is largely directed towards eliminating the co-factors and triggers of the disease that may be present on individual farms: good husbandry, rapid removal of affected animals and the elimination of other infectious agents. Commercial inactivated and subunit vaccines are available.

63 Retroviridae

LvN

SECTION IV



Retroviruses (Latin *retro*, backwards) are labile enveloped RNA viruses, 80 to 100 nm in diameter. The family name refers to the presence in the virion of a reverse transcriptase which is encoded in the viral genome. Reverse transcriptase acts as an RNA-dependent DNA polymerase, which transcribes RNA to DNA. Under the influence of the reverse transcriptase, double-stranded DNA copies of the viral genome are synthesized in the cytoplasm of the host cell. During this process, repeat base sequences called long terminal repeats (LTR), containing several hundred base pairs, are added to the ends of the DNA transcripts. Transcripts are integrated into the chromosomal DNA as provirus, through the action of viral integrase. Integration occurs at random sites in the DNA and the sites of proviral integration determine the extent and nature of cellular changes. The LTR contain important promoter and enhancer sequences. Infectious viruses have four main genes: 5'-gag-pro-pol-env-3' as illustrated.

Because errors are relatively frequent during reverse transcription, a high mutation rate is a feature of retroviral replication. Recombination between retroviral genomes in doubly-infected cells can occur due to transfer of reverse transcriptase from one RNA template to another. Consequently,

quasispecies frequently form and definitive classification at the level of species or below often proves difficult.

Retroviruses can be categorized as exogenous or endogenous. Exogenous retroviruses are capable of horizontal transmission between members of the host species. Endogenous retroviruses occur widely among vertebrates, constituting up to 10% of the genomic DNA of the host. They are consistently present in germline cells and are transmitted (inherited in Mendelian fashion) only as provirus in germ-cell DNA from parent to offspring. They are regulated by cellular genes and are usually silent but may recombine with exogenous retroviruses.

Retroviruses in the genera *Alpharetrovirus*, *Betaretrovirus*, *Gammaretrovirus* and *Deltaretrovirus* are frequently referred to as oncogenic retroviruses because they can induce neoplastic transformation in cells which they infect (Table 63.1). On the basis of the interval between exposure to the virus and tumour development, exogenous oncogenic retroviruses are designated either as slowly transforming (*cis*-activating) viruses or as rapidly transforming (transducing) viruses. Slowly transforming retroviruses induce B-cell, T-cell or myeloid tumours after long incubation periods. For malignant transformation to occur,

Jaagsiekte → pulmonary oedema
 → pulmonary carcinoma
 → neoplastic disease → old sheep
 → Nasal discharge (catareathal)

wheel barrow test
 Hold the Sheep up by hind legs
 mucus run out of nostrils

Table 63.1 Oncogenic retroviruses of veterinary importance.

Genus	Virus	Hosts	Comments
Alpharetrovirus	Avian leukosis virus	Chickens, pheasants, partridge, quail	Endemic in commercial flocks. Exogenous and endogenous transmission of virus can occur. Causes lymphoid leukosis in birds between 5 and 9 months of age
Betaretrovirus	Jaagsiekte sheep retrovirus	Sheep	Causes jaagsiekte, a slowly progressive neoplastic lung disease of adult sheep which is invariably fatal. Occurs worldwide except in Australasia
	Enzootic nasal tumour virus	Sheep, goats	Closely related to jaagsiekte sheep retrovirus. Causes adenocarcinoma of low-grade malignancy, which affects the nares
Gammaretrovirus	Feline leukaemia virus	Cats	Important cause of chronic illness and death in young adult cats. Causes immunosuppression, enteritis, reproductive failure, anaemia and neoplasia. Worldwide distribution
	Reticuloendotheliosis virus	Turkeys, ducks, chickens, quail, pheasants	Infection usually subclinical. Sporadic disease may present with anaemia, feathering defects, impaired growth or neoplasia. Disease outbreaks have occurred following use of vaccine contaminated with reticuloendotheliosis virus
Deltaretrovirus	Bovine leukaemia virus	Cattle	Causes enzootic bovine leukosis in adult cattle. A small percentage of infected cattle develop lymphosarcoma

the provirus must be integrated into the host cell DNA close to a cellular oncogene (*c-onc*, protooncogene), resulting in interference with the regulation of cell division (insertional mutagenesis). Multiple insertions of the provirus into the host cell genome results in exaggerated gene expression and over-production of a transformation-associated protein. Rapidly transforming retroviruses, which can induce tumour formation after short incubation periods, contain viral oncogenes (*v-onc*). More than a dozen different oncogenes have been identified in transforming avian retroviruses. Viral oncogenes are considered to be cellular oncogenes acquired by recombination during virus evolution. If the oncogene is integrated into the viral genome without loss of replicative virus genes, as in Rous sarcoma virus, the retrovirus is described as replication-competent. Frequently, as a consequence of cellular oncogene integration, existing viral sequences necessary for replication are deleted. Such replication-defective retroviruses, which cannot multiply without helper viruses, are rarely transmitted under normal field conditions. The protein products of oncogenes may act as hormone or growth factor receptors, transcription control factors and kinases in signal transduction pathways. A third method of tumour induction is exemplified by bovine leukaemia virus, which depends on the *tax* gene encoding a protein capable of up-regulating both viral LTR and cellular promoter sequences, even when the provirus is integrated into a different chromosome (*trans*-activation).

genes of FeLV-A and endogenous FeLV-related proviral DNA, are present in about 50% of isolates. Cats that are infected with both FeLV-A and FeLV-B have a higher risk of developing tumours than those infected with FeLV-A alone. Each FeLV-C isolate is unique, arising *de novo* in a FeLV-A infected cat through mutations in the receptor-binding region of the FeLV-A *env* gene. Once generated, FeLV-C viruses rapidly cause a fatal anaemia and consequently are not transmitted to other cats. Conversion of FeLV-A to FeLV-T requires a combination of an insertion and single amino acid changes to the envelope protein, giving rise to a T-cell tropic, cytopathic virus capable of inducing immunodeficiency.

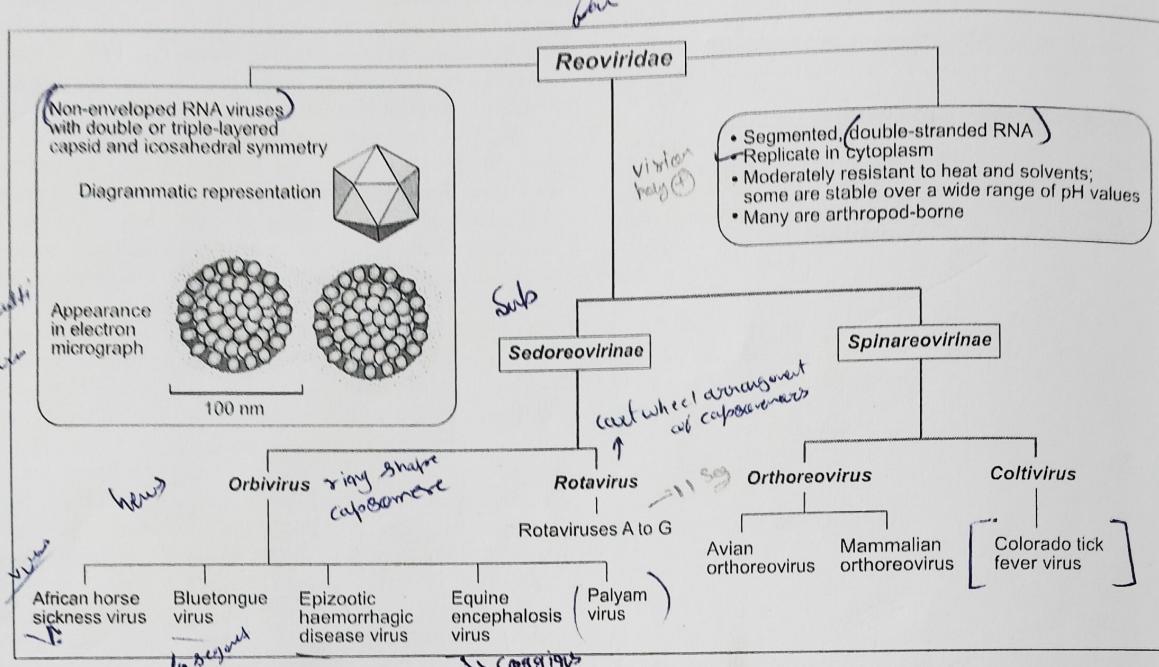
Close contact is required for transmission of this labile virus and the incidence of infection is related to population density. Highest infection rates are found in catteries and multi-cat households. Large amounts of virus are shed in saliva. Infection is usually acquired by licking, grooming and through bite wounds. Young kittens are more susceptible to infection than adults and a significant proportion of those exposed before 14 weeks of age become persistently infected. Such animals constitute the main reservoir of FeLV and are prone to develop an FeLV-related disease. Because the production of virus particles requires cellular DNA synthesis, tissues with high mitotic activity, such as bone marrow and epithelia, are targeted. The virus causes tumours, particularly lymphosarcoma, by several means, including insertional mutagenesis and recombination with a variety of cellular protooncogenes, producing rapidly transforming, replication-defective viruses. Examples of the latter are FeLVs isolated from thymic lymphomas and also feline sarcoma viruses (FeSV) that are isolated from rare multicentric fibrosarcomas in young cats. These viruses are not transmitted under natural conditions. The majority of persistently infected cats die within three years of infection. About 80% of these cats die from non-neoplastic FeLV-associated disease.

Feline leukaemia and associated clinical conditions
 Infection with feline leukaemia virus (FeLV) not only results in feline leukaemia but is also associated with a variety of other clinical conditions. Isolates of FeLV are assigned to four subgroups (A, B, C and T) on the basis of differences in the gp70 envelope glycoprotein. FeLV-A, the predominant subgroup, is isolated from all FeLV-infected cats. Viruses of subgroup B, which arise through recombination between the *env*

64

Reoviridae

SECTION IV



The family name *Reoviridae* is based on the acronym 'reov' because the initial isolates came from respiratory and enteric sources without any associated disease, so-called orphan viruses. These icosahedral viruses, 60 to 80 nm in diameter, are non-enveloped and possess a layered capsid which is composed of up to three concentric protein shells. The genome of the virion is composed of nine to twelve segments of double-stranded RNA. Genetic reassortment readily takes place in cells co-infected with viruses of the same species (genetic shift). There is also a high rate of mutation (genetic drift). As a result, there are numerous serotypes and strains of each virus species. Replication occurs in the cytoplasm of host cells, often with the formation of intracytoplasmic inclusions. The family contains 15 genera in two subfamilies, *Sedoreovirinae* (six genera) and *Spinareovirinae* (nine genera). Members of the genera *Orthoreovirus*, *Rotavirus* and *Orbivirus* infect animals and humans. Members of the genera *Coltivirus* and *Seadornavirus* are arboviruses that may occasionally cause disease in humans. Other genera in the family contain viruses of plants, arthropods and fish. Viruses in the family are moderately resistant to heat, organic solvents and non-ionic detergents.

Clinical infections

Reoviruses, which are widespread in nature, have been isolated from many animal species (Table 64.1). Avian orthoreoviruses

have been implicated in arthritis, tenosynovitis, chronic respiratory disease and enteritis. Rotaviruses cause acute diarrhoea in young intensively reared farm animals. Transmission of orthoreoviruses and rotaviruses occurs through contact with contaminated faeces.

African horse sickness and bluetongue are particularly important diseases caused by orbiviruses. Epizootic haemorrhagic disease of deer and Ibaraki disease in cattle, both caused by members of the epizootic haemorrhagic disease virus (EHDV) serogroup, have clinical effects in these species similar to those of bluetongue in sheep. The viruses of African horse sickness, bluetongue and epizootic haemorrhagic disease of deer are transmitted by blood-sucking arthropods, especially by *Culicoides* species.

Enteric disease caused by rotaviruses in young animals

Rotaviruses cause diarrhoea in intensively reared young farm animals worldwide. Isolates are divided into several antigenically distinct groups (A-G), also termed species, based on differences in the major capsid protein, VP6. Most isolates belong to group A. High titres of virus (10^9 virus particles per gram of faeces) are excreted by clinically affected animals. Because the virus is stable in the environment, premises may be heavily contaminated and, accordingly, intensively reared animals are those

Table 64.1 Viruses of veterinary importance in the family *Reoviridae*.

Genus	Virus	Comments
<i>Oribivirus</i>	African horse sickness virus	Arthropod-borne infection of <i>Equidae</i> , principal vector <i>Culicoides</i> species. Endemic in Africa. High mortality rate
	Bluetongue virus	Arthropod-borne infection of sheep, cattle, goats and wild ruminants. Principal vector <i>Culicoides</i> species. Severe disease in sheep. Clinical disease uncommon in cattle except for serotype 8. Teratogenic effects
	Epizootic haemorrhagic disease virus	Arthropod-borne infection of deer, cattle and buffalo. At least seven serotypes recognized. Principal vector <i>Culicoides</i> species. Clinically similar to bluetongue. Important disease of white-tailed deer in North America. Generally subclinical or mild infections in cattle except for Ibaraki virus (EHDV-2) in south-east Asia which causes an acute febrile disease
	Equine encephalosis virus	Reported in South Africa and Israel. Majority of infections subclinical. Sporadic cases of acute fatal disease. Cerebral oedema, fatty liver and enteritis are prominent features
	Palyam virus	Arthropod-borne disease of cattle. Causes abortion and teratogenic effects. Recorded in southern Africa, south-east Asia and Australia. Many viruses in the serogroup
	Peruvian horse sickness virus	Isolated from horses (neurological disease) in Peru and Northern Territories of Australia (Elsey virus). Mosquito vector
<i>Rotavirus</i>	Rotaviruses	Outbreaks occur in intensively reared neonatal animals. Mild to severe diarrhoea, severity influenced by virulence of viral strain, age, colostral intake and management factors
<i>Orthoreovirus</i>	Avian orthoreoviruses	Important cause of viral arthritis/tenosynovitis in chickens. Multiple serotypes described. Turkeys and other avian species susceptible
	Mammalian orthoreoviruses	Associated with mild enteric and respiratory disease in many species, severity dependent on secondary infections. Four serotypes recognized
<i>Coltivirus</i>	Colorado tick fever virus	Rodent species act as reservoirs. Arthropod-borne, mainly ticks and also mosquitoes. Primarily of significance in humans

SECTION IV

most often affected. Diagnosis is based on electron microscopy or demonstration of viral antigen in faeces by ELISA or latex agglutination. Control involves measures aimed at reducing the levels of virus challenge in young animals while vaccination of pregnant dams can be used to raise antibody levels in mammary secretions.

African horse sickness

This is a non-contagious OIE-listed disease of *Equidae* caused by African horse sickness virus. Nine serotypes of this orbivirus constitute the African horse sickness serogroup. The disease is endemic in sub-Saharan Africa. The virus is transmitted by haematophagous insects, principally *Culicoides imicola*. Four forms of this febrile disease are recognized. A peracute pulmonary form is characterized by depression and nasal discharge, rapid progression to severe respiratory distress. Mortality rates may approach 100%. A subacute cardiac form manifests as conjunctivitis, abdominal pain and progressive dyspnoea. Subcutaneous swellings of the head and neck are most obvious in the supraorbital fossae, palpebral conjunctiva and intermandibular space. In this form of the disease, the mortality rate is about 50%. A mixed form of intermediate severity (up to 70% mortality rate) presents with both cardiac and pulmonary features. A mild or subclinical form, termed horse sickness fever, may be observed in zebras and donkeys. Vector control, quarantining of affected animals and vaccination are the main methods of preventing disease transmission.

Bluetongue

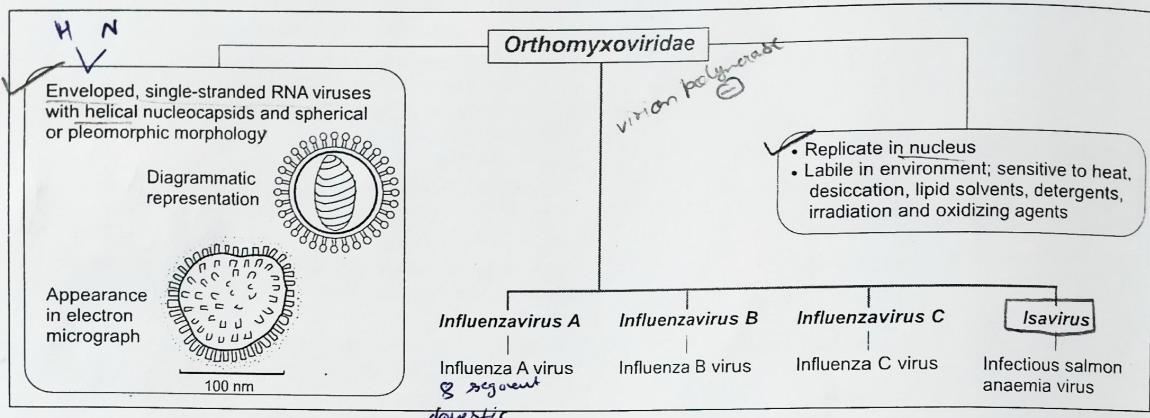
This non-contagious OIE-listed disease of sheep and other domestic and wild ruminants is transmitted by a range of *Culicoides* species. Twenty-six serotypes of bluetongue virus (BTV) have been described. Infection is of greatest significance in sheep and deer. In 2006, BTV-8 appeared in northern Europe and caused a severe epizootic. Clinical disease in cattle has been a feature of this epizootic with clinical signs similar but generally milder than those observed in sheep. The clinical presentation is highly variable, ranging from subclinical to severe disease with high mortality. Affected animals are febrile and depressed with vascular congestion of the lips and muzzle. Oedema of the lips, face, eyelids and ears develops. Lameness may result from coronary and laminitis. Mortality rate may be up to 30%. A presumptive diagnosis may be based on clinical findings and postmortem lesions. Confirmation generally relies on detection of viral RNA by RT-PCR or demonstration of BTV-specific antibodies. Live attenuated vaccines have been used successfully for many years and provide protection against virulent viruses of homologous serotype. Polyvalent vaccines are essential in regions where a number of serotypes are present. Killed adjuvanted vaccines can induce protection but are more expensive to produce and require two inoculations.

~~genetic reassortment (antigenic shift) (host switch)~~

When a virus undergoes a sudden changes in genetic makeup, creating a new strain

65

Orthomyxoviridae



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The family *Orthomyxoviridae* (Greek *orthos*, proper and *myxa*, mucus) contains those viruses which cause influenza in humans and animals. Orthomyxoviruses are spherical or pleomorphic, enveloped viruses, 80 to 120 nm in diameter. Long filamentous forms also occur. The envelope, which is derived from host cell membrane lipids, contains glycosylated and non-glycosylated viral proteins. Surface projections of glycoproteins form 'spikes' or peplomers which, in influenza A and B viruses, are of two types: a haemagglutinin (H) responsible for virus attachment and envelope fusion, and a neuraminidase (N) capable of cleaving viral receptors thus promoting both entry of virus into cells and release of virions from infected cells.

Influenza viruses haemagglutinate erythrocytes from a wide range of species. Antibodies to the H glycoprotein are mainly responsible for virus neutralization. The nucleocapsid has a helical symmetry. The genome, which is composed of six to eight segments, consists of linear, negative-sense, single-stranded RNA. Replication occurs in cell nuclei with release of virions by budding from plasma membranes. Virions are labile in the environment and are sensitive to heat, lipid solvents, detergents, irradiation and oxidizing agents.

The family contains six genera, namely *Influenzavirus A*, *Influenzavirus B*, *Influenzavirus C*, *Thogotovirus*, *Quaranjavirus* and *Isavirus*. Influenza B and C viruses are pathogens of humans; Thogoto virus and Dhori virus are tick-borne arboviruses isolated from camels, cattle and humans in parts of Africa, Europe and Asia; infectious salmon anaemia virus affects farmed salmon. Influenza A virus, the most important member of the family, is a significant pathogen of animals and humans.

Isolates of influenza A virus are grouped into subtypes on the basis of their H and N antigens. Currently, 18 H antigens and 11 N antigens are recognized and new subtypes of influenza A virus emerge periodically. A number of mechanisms – point

mutation and recombination (genetic reassortment) – are responsible for the emergence of new strains and new subtypes respectively. Point mutations give rise to antigenic drift, in which variation occurs within a subtype. Genetic reassortment, a more complex process in which the genome segments of two or more related viruses infecting the same cell are exchanged, results in the development of new subtypes (antigenic shift). To assess the risk posed by the emergence of new variant viruses, a precise classification of isolates has been adopted by the World Health Organization. This system is based on the influenza virus type, host, geographical origin, strain number, year of isolation and subtype. An example of this classification system, influenza virus A/equine/Prague/1/56 (H7N7), indicates that this virus was isolated from a horse in Prague during 1956. Antigenic subtypes of influenza A virus which cause disease in humans and farm animals are presented in Table 65.1.

Clinical infections

Influenza A viruses cause significant infections in humans, pigs, horses and birds. All known subtypes (except H17N10 and H18N11, which have been found only in bats) can infect birds. Aquatic birds, particularly ducks which are reservoirs of influenza A virus, provide a genetic pool for the generation of the new subtypes capable of infecting mammals. Migratory waterfowl and trade in poultry and poultry products may disseminate avian viruses across international borders. Although isolates of influenza A virus are usually species specific, there are well-documented instances of transfer between species. The viruses replicate in the intestinal tract of birds and transmission of low pathogenic influenza viruses is mainly by the faecal-oral route. Human infection with avian influenza viruses has been attributed to the combined effects of poor hygiene and the close association of concentrated human populations with domestic

→ cap snatching → orthomyxoviridae → ⚡ endonuclease
as a primer for RNA synthesis ← steal (प्राप्ति)
help methylated cap off host cell m-RNA

- ← genetic reassortment (antigenic shift) (antigenic shift)
- point mutation (antigenic drift) (genetic drift)

↳ when a virus undergoes a gradual change in genetic makeup causing a diff but genetic makeup similar to previous virus

Table 65.1 Antigenic subtypes of influenza A virus isolated from humans and animals.

Hosts	Antigenic subtypes	Comments
Humans	H1N1 (1918, 1977, 2009) ^a H2N2 (1957) H3N2 (1968)	Subtypes which have been found in pigs such as H1N1 have been implicated in human pandemics. Sporadic or limited transmission of infections reported with H5N1, H7N2, H7N3, H7N7, H7N9, H9N2 and H10N8 in recent years
Birds	Many antigenic subtypes represented by different combinations of haemagglutinin (H) and neuraminidase (N) neoplamers have been recognized	Disease is usually associated with subtypes expressing H5 or H7. Wild birds, especially migrating ducks, act as carriers
Pigs	Predominantly H1N1, H1N2 and H3N2	
Horses	Usually H7N7 or H3N8 (H7N7 has not been detected in horses for more than 20 years. H3N8 has replaced H7N7 as the predominant subtype)	Severity of disease is determined by the antigenic subtype Subtypes associated with disease, which are widely distributed geographically, are absent from Australia, New Zealand and Iceland
Dogs	H3N8 (originated from an equine H3N8 lineage), H3N2	H3N8 first reported in Florida in 2004. Large outbreak of influenza (H3N2) in dogs in USA in 2014

^aYear of recognition. genetic drift
 genetic shift

fowl and pigs. Genetic reassortment in these animal populations can lead to the emergence of novel virulent influenza virus subtypes which are capable of infecting humans, thereby initiating pandemics. Avian influenza viruses usually replicate poorly in humans. However, both human and avian influenza subtypes replicate in pigs, a species in which genetic reassortment readily occurs with the emergence of new subtypes. Such novel subtypes may be implicated in major pandemics which occur at intervals of about 20 years. As there is limited immunity in the human population to new subtypes, spread from country to country tends to occur rapidly.

Subtypes of influenza A virus, which are well established as pathogens in particular animal populations, have also been implicated in crossing species barriers without genetic reassortment. An H1N1 avian subtype appeared in pigs in Europe in 1979. In 1997, following a large epidemic of avian influenza in chickens, a highly pathogenic avian influenza (HPAI) H5N1 subtype (first isolated from a goose in southern China in 1996) was isolated from a fatal case in a young child in Hong Kong. This subtype had not previously been described outside of avian species. Human health fears prompted the destruction of 1.2 million birds in Hong Kong. The virus reappeared in members of a Hong Kong family in 2003 and was subsequently found to be circulating across south-east Asia resulting in spread to the Middle East, Africa and Europe. Fortunately human-to-human transmission has not been demonstrated to any significant extent to date, although human cases (mortality rate approximately 60%) have continued to occur as a result of contact with infected poultry. Other subtypes of avian origin have caused human infections (Table 65.1), particularly in China where factors such as live bird markets appear to be important in disease transmission.

* Avian influenza (fowl plague) \rightarrow H5N1
Avian influenza subtypes occur worldwide. Outbreaks of severe clinical disease, usually caused by subtypes expressing H5 and

- Highly contagious
- viral disease of poultry
- characterised by \approx pneumonia
- Caseous exudate in upper respiratory tract
- paralysis

oedema of face
Haemorrhage in breast muscles, navel

H7 determinants, occur periodically in chickens and turkeys. In these species, acute infection is often referred to as fowl plague or HPAI and is categorized as a listed disease by the OIE. It is likely that the HPAI viruses in these acute outbreaks arise by mutation from low pathogenic avian influenza viruses. Spread of influenza virus in tissues is dependent on the type of proteases present in a given tissue and the structure of the viral haemagglutinin molecule. The production of infectious virions requires cleavage of the viral haemagglutinin. In the majority of influenza A virus subtypes, haemagglutinin cleavage takes place only in the epithelial cells of the respiratory and digestive tracts. Because of the amino acid composition at their cleavage sites, haemagglutinins of virulent subtypes are susceptible to cleavage in many tissues, facilitating the development of generalized infection. Highly virulent subtypes cause explosive outbreaks of disease with high mortality. Clinical signs are more apparent in birds which survive for a few days. Respiratory distress, diarrhoea, oedema in the cranial region, cyanosis, sinusitis and lacrimation are features of the clinical presentation. In countries free of the disease, test and slaughter policies are implemented. Vaccination is permitted in those countries with recurring outbreaks of disease but is prohibited in countries implementing a slaughter policy.

\rightarrow H5N1, H3N8

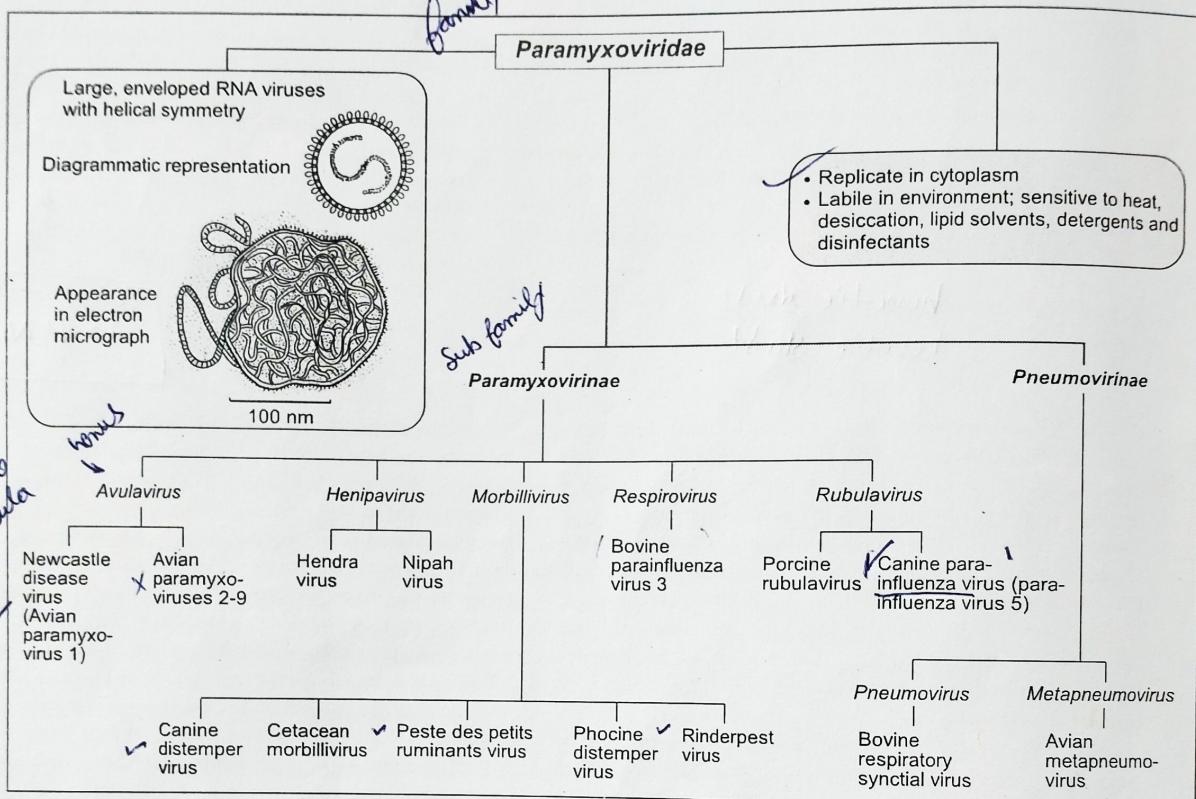
Equine influenza

Equine influenza is an economically important respiratory disease of horses. Outbreaks of disease are associated with the assembly of horses at shows, sales, racing or training. Affected animals develop a high temperature with nasal discharge and a dry cough. A number of inactivated vaccines are commercially available, but as immunity is short-lived, regular booster injections are required. Vaccinated horses, exposed to field virus, exhibit milder clinical signs than unvaccinated animals.

fowl plague

first reported Italy \rightarrow H5N1, (H5 H7 H9)
vertical transmission \rightarrow morbidity or mortality 100%
swallow \rightarrow comb, wattle

66 Paramyxoviridae



Paramyxoviruses and orthomyxoviruses were formerly grouped together as the 'myxoviruses' (Greek *myxa*, mucus), a name which describes their affinity for mucous membranes. Paramyxoviruses are pleomorphic, 150 nm or more in diameter and enveloped. They contain a single molecule of negative-sense, single-stranded RNA. Two types of glycoprotein 'spikes' or peplomers are present in the envelope, an attachment protein and a fusion protein (F). The attachment protein may be either a haemagglutinin-neuraminidase protein (HN) or a protein without neuraminidase activity (G or H). The attachment proteins allow the virus to bind to cell surface receptors and the fusion protein causes the virus envelope to fuse with the host cell membrane. However, there is significant variation between different paramyxoviruses in the mechanism of viral attachment, stimulation of the fusion protein and the process of viral entry into the cell. Both types of peplomers can induce production of virus neutralizing antibodies. Paramyxoviruses may exhibit haemagglutinating, haemolytic and neuraminidase activities. The nucleocapsid, which has helical symmetry, is 13 to 18 nm in diameter and has a characteristic herring-bone appearance. Replication

occurs in the cell cytoplasm and acidophilic inclusions are a feature of paramyxovirus infections. Virions are released by budding from the plasma membrane at sites containing virus envelope proteins. The labile virions are sensitive to heat, desiccation, lipid solvents, non-ionic detergents and disinfectants.

The family is divided into two subfamilies, *Paramyxovirinae* and *Pneumovirinae*, containing seven and two genera respectively. The genera *Aquaparamyxovirus* (viruses of fish) and *Herlavirus* (viruses of reptiles) are the most recent members of the family to be designated as genera in a family that continues to expand as new virus species in wild animals are discovered. Although paramyxoviruses are genetically relatively stable and do not appear to undergo recombination, some antigenic variation occurs through mutational changes and selection.

Clinical infections

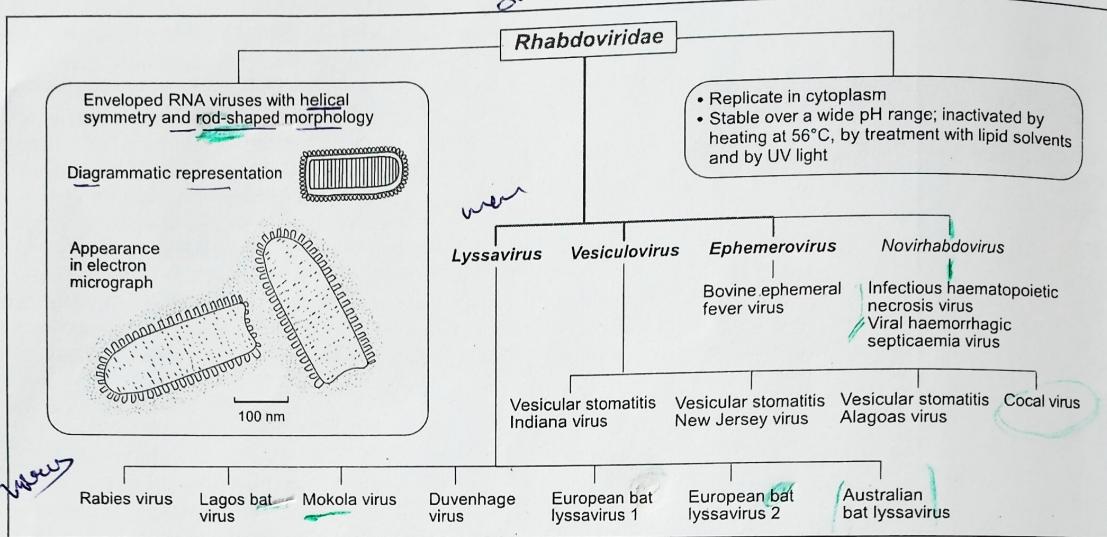
Paramyxoviruses, which typically have a narrow host range, infect mainly mammals and birds (Table 66.1). Following transmission through close contact or by aerosols, replication occurs

67

Rhabdoviridae

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Members of the family *Rhabdoviridae* (Greek *rhabdos*, rod) have characteristic rod shapes. Rhabdoviruses possess a linear, non-segmented RNA genome of negative polarity encased in a ribonucleoprotein complex. This large family contains viruses of vertebrates, invertebrates and plants. Rhabdoviruses of vertebrates appear bullet- or cone-shaped. The family *Rhabdoviridae* comprises 11 genera. The genera *Vesiculovirus*, *Lyssavirus* and *Ephemerovirus* contain viruses of veterinary significance. Rhabdoviruses of importance in fish belong to the genera *Novirhabdovirus*, *Vesiculovirus* and *Perhabdovirus*. Replication occurs in the cytoplasm (with the exception of nucleorhabdoviruses of plants). Newly synthesized nucleocapsids acquire envelopes from the plasma membrane as virions bud from the cell. Virions (100 to 430 nm × 45 to 100 nm) are stable in the pH range 5 to 10. They are rapidly inactivated by heating at 56°C, by treatment with lipid solvents and by exposure to UV light.

Clinical infections

Rhabdoviruses of veterinary importance are presented in Tables 67.1 and 67.2. They can be transmitted by bites of mammals, arthropod vectors or direct contact. Infection may also be acquired through environmental contamination. The best-known and most important member of the *Rhabdoviridae* is rabies virus, a *Lyssavirus* (Greek *lyssa*, rage or fury). A number of distinct lyssaviruses, many isolated from bats, produce clinical signs indistinguishable from rabies. Novel lyssaviruses continue to be isolated from wildlife sources. The most important vesiculoviruses which infect domestic

animals are the vesicular stomatitis Indiana virus and the vesicular stomatitis New Jersey virus. Bovine ephemeral fever virus, of significance in the tropics and subtropics of Africa, Asia and Australia, is the type species of the genus *Ephemerovirus*.

Rabies

This viral infection, which affects the central nervous system of most mammals including humans, is invariably fatal. However, mammalian species vary widely in their susceptibility. Most clinical cases are due to infection with rabies virus (genotype 1). A number of other neurotropic lyssaviruses, closely related to the rabies virus, produce clinical signs indistinguishable from rabies. Classical rabies caused by rabies virus is endemic on continental land masses, with the exception of Australia and Antarctica. Many island countries are also free of the disease.

Several species-adapted genotypes or strains of rabies virus have been described. Strains affecting a particular species are transmitted more readily to members of that species than to other animal species. In a given geographical region, rabies is usually maintained and transmitted by particular mammalian reservoir hosts. Two epidemiologically important infectious cycles are recognized, urban rabies in dogs and sylvatic rabies in wildlife. More than 95% of human cases in developing countries are as a result of bites from rabid dogs. Racoons, skunks, foxes and bats are important reservoirs of rabies virus in North America. In continental Europe, the principal reservoir is the red fox. The vampire bat is an important reservoir of the virus in Central and South America and in the Caribbean islands. Although virus may be transmitted through scratching and licking, transmission

Genus

Enterovirus

Teschovirus

Sapelovirus

Tremovirus

Aphthovirus

Cardiovirus

Erbovirus

Avihepatovirus

confer i
subtypes

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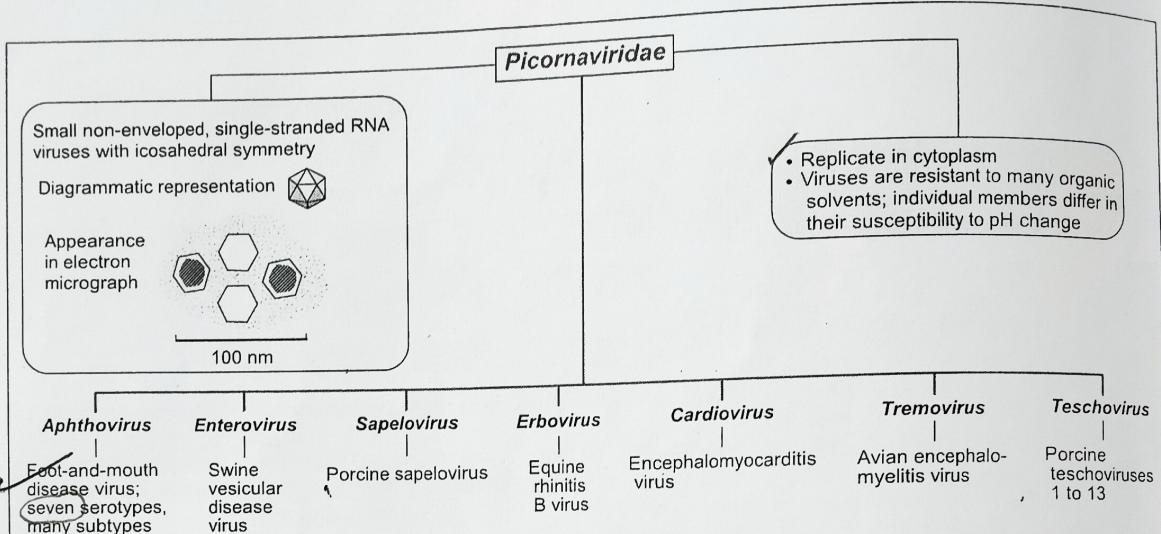
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70 Picornaviridae



SECTION IV

Picornaviruses (Spanish *pico*, very small), which are icosahedral and non-enveloped, contain a molecule of single-stranded RNA. Virions are 30 nm in diameter. The capsid is composed of 60 identical subunits, each containing four major proteins, VP1, VP2, VP3 and VP4. The VP4 protein is located on the inner surface of the capsid. Viral replication occurs in the cytoplasm in membrane-associated complexes and infection is usually cytotytic. The family has expanded greatly in recent years and now comprises 29 genera. Viruses of veterinary importance are contained in the genera *Enterovirus*, *Cardiovirus*, *Aphthovirus*, *Avihepatovirus*, *Erbovirus*, *Sapelovirus*, *Tremovirus* and *Teschovirus*. Several enteroviruses of pigs and poultry have been reassigned: porcine enteroviruses 1 to 7 and 11 to 13, which are associated with nervous disease and reproductive problems in pigs, have been reassigned to the genus *Teschovirus* while avian encephalomyelitis virus has been placed in the newly created genus *Tremovirus*. The genus *Rhinovirus* has been removed and human rhinoviruses have been placed in the genus *Enterovirus*.

Viruses of veterinary importance in the family *Picornaviridae* are presented in Table 70.1. Important human pathogens in the family include hepatitis A virus (genus *Hepadnavirus*) and enterovirus C (genus *Enterovirus*) the cause of poliomyelitis, a serious neurological disease in humans. Picornaviruses are resistant to ether, chloroform and non-ionic detergents. Individual genera differ in their thermal lability and pH stability. Aphthoviruses are unstable at pH values below 6.5. Viruses in the other genera are stable at acid pH values.

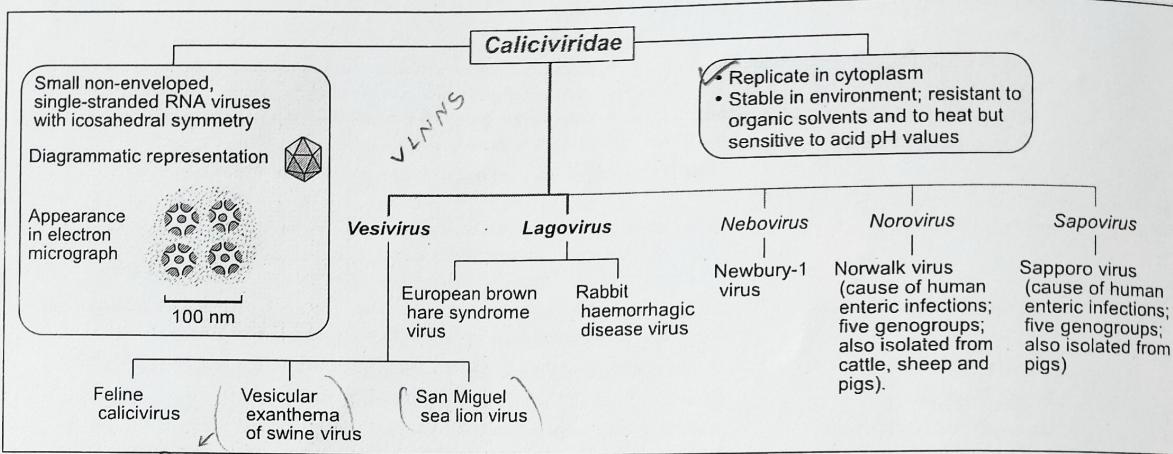
Clinical infections

With the exception of foot-and-mouth disease virus and encephalomyocarditis virus, picornaviruses typically infect a single, or a limited number of, host species. Transmission usually occurs by the faecal-oral route but may also occur by fomites or by aerosols. Some picornaviruses, notably foot-and-mouth disease virus and swine vesicular disease virus, can produce persistent infections. Antigenic variation, which may contribute to the development of persistent infection, has been attributed to a number of molecular mechanisms including genetic recombination. Mixed infections with different serotypes of foot-and-mouth disease virus are known to occur in individual animals, particularly in African Cape buffaloes. Porcine teschovirus infections are widespread in pig populations and frequently subclinical in nature but may result in encephalomyelitis, diarrhoea, pneumonia, pericarditis/myocarditis and reproductive disorders.

Foot-and-mouth disease

This highly contagious disease of even-toed ungulates is characterized by fever and the formation of vesicles on epithelial surfaces. Foot-and-mouth disease (FMD) is a listed disease of the OIE. It is of major importance internationally on account of its rapid spread and the dramatic economic losses which it causes in susceptible animals. Isolates of foot-and-mouth disease virus (FMDV) are grouped in seven serotypes with differing geographical distributions. Infection with one serotype does not

71 Caliciviridae



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Caliciviruses (Latin *calix*, cup) have cup-shaped depressions on the surface of virions, demonstrable by electron microscopy. The virions, 27 to 40 nm in diameter, are icosahedral and non-enveloped. The genome consists of a single molecule of linear, positive-sense, single-stranded RNA. Replication takes place in the cytoplasm of infected cells and virions are released by cell lysis. Many caliciviruses have not yet been cultured. The virions are resistant to ether, chloroform and mild detergents. They are relatively resistant to heat but are sensitive to acid pH values.

The family *Caliciviridae* is divided into five genera: *Vesivirus*, *Lagovirus*, *Nebrovirus*, *Sapovirus* and *Norovirus*. Caliciviruses belonging to the *Norovirus* and *Sapovirus* genera include viruses which cause acute gastroenteritis in humans.

Clinical infections

Caliciviruses have been recovered from many species including humans, cats, pigs, marine mammals, fish, rabbits, hares, cattle, dogs, reptiles, amphibians, shellfish and insects. They are associated with a wide range of conditions including respiratory disease, vesicular lesions, necrotizing hepatitis and gastroenteritis (Table 71.1). Infections with caliciviruses, which are frequently persistent, may be inapparent, mild or acute. Transmission occurs directly or indirectly without vector involvement. However, mechanical transmission of rabbit haemorrhagic disease virus by mosquitoes and fleas has been described.

Feline calicivirus infection

Infections caused by feline calicivirus (FCV) account for about 40% of upper respiratory tract inflammatory disease in cats worldwide. All species of *Felidae* are considered to be susceptible but natural disease tends to be confined to domestic cats

and to cheetahs in captivity. There is a high degree of antigenic heterogeneity among FCV isolates. Sequence analysis studies have shown that individual isolates of FCV exist as quasispecies which evolve and exhibit antigenic drift. Significant alterations in the antigenic profiles of sequential virus isolates from carrier cats are thought to be influenced by immune selection and this may play an important part in viral persistence.

Virus replication occurs primarily in the oropharynx with rapid spread throughout the upper respiratory tract and to the conjunctivae. A transient viraemia occurs. Infections range from subclinical to severe, reflecting differences in strain virulence and host immunity. Virulent strains of FCV can cause interstitial pneumonia in young kittens. The virus has been recovered from the joints of lame cats. Highly virulent strains of the virus associated with virulent systemic disease (VSD) have been reported periodically.

The incubation period is up to five days. Clinical signs, which are usually confined to the upper respiratory tract and the conjunctivae, are often less severe than those caused by feline herpesvirus 1 infection. Fever, oculonasal discharge and conjunctivitis are accompanied by the development of characteristic vesicles on the tongue and oral mucosa. These vesicles rupture leaving shallow ulcers. Morbidity may be high but mortality is usually low. Stiffness and shifting lameness, which usually resolve within a few days, are sometimes seen during the acute phase of FCV infection or following inoculation with FCV vaccine. The VSD form of FCV infection is characterized by severe upper respiratory tract disease, facial oedema, ulceration of the skin, vasculitis, multi-organ involvement and high mortality.

Although cats of all ages are susceptible to infection with FCV, acute disease occurs most commonly in kittens as maternally derived antibody wanes between two and three months

Table 7.1 Caliciviruses of veterinary importance.

Virus	Hosts	Comments
Vesicular exanthema of swine virus	Pigs	Acute, contagious vesicular disease, clinically similar to foot-and-mouth disease. Occurred in the USA before 1956. May have arisen from feeding sea lion and seal meat contaminated with San Miguel sea lion virus
San Miguel sea lion virus	Marine mammals, opal eye fish	Associated with cutaneous vesicles and premature parturition in pinnipeds; when inoculated into pigs, causes vesicular exanthema
Feline calicivirus	Domestic and wild cats	Important cause of upper respiratory tract infection in cats worldwide. Virulent systemic disease described in some outbreaks
Rabbit haemorrhagic disease virus	European rabbits	Acute fatal disease in European rabbits over 2 months of age
European brown hare syndrome virus	European brown hares	Related to rabbit haemorrhagic disease virus. Causes hepatic necrosis and widespread haemorrhages with high mortality
Canine calicivirus	Dogs	Occasionally associated with diarrhoea
Newbury-1 virus	Cattle	Has been linked to diarrhoea in calves

of age. Infected cats excrete large amounts of virus in oronasal secretions. Many cats continue to shed virus continuously from the oropharynx for weeks after recovery from acute infection or following subclinical infection while protected by maternally derived antibody or by response to vaccination. A minority of cats shed virus for months and, occasionally, for years. Infection is maintained in the cat population by these asymptomatic FCV carriers. The highest prevalence of infection is seen in large groups of cats living in colonies or shelters.

Due to the similarity of clinical signs caused by infection with feline herpesvirus 1 and FCV, laboratory tests are required to differentiate these two diseases. Feline calicivirus can be isolated in feline cell lines from oropharyngeal swabs or from lung tissue. Viral RNA can be detected in clinical specimens using RT-PCR. However, detection of FCV may not be aetiologically significant in every instance because of the presence of carrier animals in cat populations. Demonstration of a rising antibody titre in paired serum samples is required for laboratory confirmation.

Vaccination and management practices aimed at reducing exposure to the virus are the main methods of control. Inactivated vaccines for parenteral administration and modified live vaccines for either parenteral or intranasal administration are available. Although vaccination protects effectively against clinical disease in most instances, it does not prevent subclinical infection or the development of a carrier state. Vaccines are based on a limited number of FCV isolates which cross-react with a broad spectrum of field isolates. Live vaccines, for administration by injection, may cause clinical signs of disease if given by other routes.

Rabbit haemorrhagic disease

This is a highly contagious, acute and often fatal disease of European rabbits (*Oryctolagus cuniculus*). Rabbit haemorrhagic disease (RHD) was first reported in China in 1984 and has since been encountered in many parts of the world. This virus is considered to be a mutant form of a non-pathogenic virus, termed rabbit calicivirus, which has been endemic in commercial and

wild rabbits in Europe for many years. Rabbit haemorrhagic disease virus (RHDV) has been used for biological control of rabbits in Australia and New Zealand.

Virus is shed in all excretions and secretions. Among rabbits in close contact, transmission is mainly by the faecal-oral route. Infection may also occur by inhalation or through the conjunctiva. Mechanical transmission by a variety of insects, including mosquitoes and fleas, has been demonstrated. The virus survives in the environment and indirect transmission through contaminated foodstuffs or fomites may occur.

Cells of the mononuclear phagocyte lineage are considered to be the major targets of the virus. Rabbits under two months of age do not develop clinical signs. The reason for this resistance is unclear, but it may have a physiological basis. Severe hepatic necrosis is the most obvious lesion in affected rabbits. In addition, there may be evidence of disseminated intravascular coagulation.

The incubation period is up to three days. The disease is characterized by high morbidity and high mortality. The course is short, with death occurring within 36 hours of the onset of clinical signs. Rabbits may be found dead or die in convulsions. A few rabbits may present with milder, subacute signs during the later stages of a major outbreak.

High mortality in rabbits along with characteristic gross lesions including necrotic hepatitis and congestion of spleen and lungs are suggestive of RHD. Culture of RHDV has been unsuccessful. High concentrations of virus are present in affected livers. Confirmation is based on detection of virus by electron microscopy or of viral antigen by ELISA, immunofluorescence or haemagglutination using human erythrocytes. Reverse transcriptase PCR has been developed for the detection of RHDV nucleic acid. Suitable serological tests for the detection of specific antibodies to the virus include haemagglutination-inhibition and ELISA.

In countries where RHD is endemic, control is achieved by vaccination. Inactivated and adjuvanted vaccines are available. A live myxoma virus expressing the capsid protein gene of RHDV is available for the vaccination and protection of rabbits against both viruses.