SWINE INFLUENZA

Synonyms: pig influenza, swine flu, hog flu and pig flu

Swine influenza is a highly contagious viral infection of pigs. The disease in swine occurs within a herd either as an epizootic or enzootic form. In the epizootic form, the virus quickly moves through all phases of a swine unit with rapid recovery, provided there are not complicating factors such as secondary bacterial infections. In the enzootic form, clinical signs may be less obvious and not all pigs may demonstrate traditional clinical signs of infection. Morbidity rates can reach 100% with swine influenza infections, while mortality rates are generally low. The primary economic impact is related to retarded weight gain resulting in an increase in the number of days to reach market weight.

Etiology:

Swine influenza is caused by influenza A viruses in the family Orthomyxoviridae. Influenza A viruses are further characterised by subtype by the two major surface glycoproteins, haemagglutinin and neuraminidase. One relatively stable subtype, H1N1, was the etiologic agent of most swine influenza until the mid-1990s, and has been the strain historically most commonly associated with “classical swine influenza”. Since that time, established swine influenza viruses comprise various subtypes and variants, many of which are the result of substantial reassortment between influenza A viruses of several hosts. Currently circulating influenza viruses infecting swine also include genetic components, or entire viruses, of avian and human influenza viruses. The most common subtypes of influenza virus in swine are H1N1, H1N2, and H3N2. Other novel reassortants of swine influenza viruses continue to be discovered. New subtypes have also been found in some populations, including reassortments with equine influenza viruses.

Hosts:

Influenza viruses are found in a number of species including birds, humans, swine, horses and dogs. Swine influenza viruses are found mainly in pigs, but they have also been found in other species including humans, turkeys, and ducks.
Transmission:

Influenza viruses are readily transmitted between animals in the species to which they are adapted. Pigs may begin excreting swine influenza viruses within 24 hours of infection, and in the majority of cases shedding ceases by 7-10 days post infection. The primary route of virus transmission is through pig to pig contact via the nasopharyngeal route, most probably through none-to-nose contact or direct contact of mucus. The virus is shed in nasal secretions and disseminated through droplets or aerosols.

Pathogenesis:

Swine influenza viruses are usually introduced into a herd by an infected pig. In a newly infected herd, up to 100% of the animals may become ill, but most animals recover within 3-7 days if there are no secondary bacterial infections or other complications. In uncomplicated cases, the case fatality rate ranges from less than 1% to 4%. Many infections in enzootically infected herds are subclinical; typical signs of influenza may occur in only 25% to 30% of the pigs.

The spectrum of infection ranges from subclinical to acute. In the classic acute form, the virus multiplies in bronchial epithelium within 16 hr of infection and causes focal necrosis of the bronchial epithelium, focal atelectasis, and gross hyperaemia of the lungs. Bronchial exudates and widespread atelectasis, grossly appearing as plum-colored lesions affecting individual lobules of apical and intermediate lobes, are seen after 24 hr. The lesions continue to develop until 72 hr after infection, after which the virus becomes more difficult to demonstrate. Losses in reproduction associated with primary outbreaks appear to be secondary, because virus has been recovered only rarely from the fetus.

Clinical signs:

An acute upper respiratory disease characterised by fever, lethargy, anorexia, weight loss, nasal discharge, and laboured breathing. Coughing, sneezing, and nasal discharge are commonly seen. Conjunctivitis is a less common clinical sign. Decreased semen production in boars and abortions in sows may also occur due to secondary effects of fever. Some strains can circulate in pigs with few or no clinical signs. Complications may include secondary
bacterial or viral infections. Severe, potentially fatal bronchopneumonia is occasionally seen. All three virus subtypes (H1N1, H3N2, H1N2) have been associated with disease. Swine influenza viruses can also contribute to more chronic, multifactorial respiratory disease problems in combination with other viruses or bacteria.

Lesions:
In uncomplicated infections, the gross lesions are mainly those of a viral pneumonia and are usually confined to the respiratory tract. Affected parts of the lungs are clearly demarcated, and are atelectic or consolidated and dark red to purple-red. The lesions may be found distributed throughout the lungs but tend to be more extensive and confluent ventrally. Other areas of the lung may be pale and emphysematous. The airways are often dilated and filled with copious mucopurulent exudate. The bronchial and mediastinal lymph nodes are typically oedematous but not congested. Pulmonary oedema may also be seen. Some strains of swine influenza viruses produce more marked lesions than others. Generalised lymphadenopathy, hepatic congestion and pulmonary consolidation were reported in one outbreak of severe disease in swine.

Histologically, the fully developed lesions are primarily those of an exudative bronchiolitis with necrosis, metaplasia, or attenuation of the bronchiolar epithelial cells and varying degrees of some interstitial pneumonia. Exudative tracheitis and rhinitis may also be present.

Gross and Microscopic changes in lungs in swine influenza
Diagnosis:

**Identification of the agent:** Virus identification is best accomplished by collection of samples within 24-48 hours after development of clinical signs. The animal of choice is an untreated, acutely ill pig with an elevated rectal temperature. Virus can readily be detected in lung tissue and nasal swabs; deep nasal swabs are recommended. Virus isolation can be conducted on continuous cell lines and in embryonated chicken eggs. Isolated viruses can be subtyped using the haemagglutination inhibition (HI) and the neuraminidase inhibition tests, or by reverse transcription-polymerase chain reaction assays. Immunohistochemistry can be conducted on formalin-fixed tissue and a fluorescent antibody test can be conducted on fresh tissue. Enzyme-linked immunosorbent assays (ELISA) may be available for detection of type A influenza viruses, but may have variable performance depending on the circulating strains.

The primary serological test for detection of swine influenza virus antibodies is the HI test conducted on paired sera. The HI test is subtype and strain specific. Collection of paired sera is generally recommended 10-21 days apart. A four-fold or greater increase in titre between the first and second sample is suggestive of a recent swine influenza virus infection. Additional serological tests that have been described are the agar gel immunodiffusion test, indirect fluorescent antibody test, virus neutralisation, and ELISA. 

Newer molecular methods, particular RT-PCR (both real time and conventional) are used. Common screening real-time RT-PCRs used in North America for influenza diagnostics are directed against the Matrix protein or Nucleoprotein of the influenza virus.

**Differential diagnosis:**

Swine influenza virus is one of the several agents involved in acute respiratory disease in pigs, and can frequently be accompanied by other respiratory diseases such as PRRS virus, Aujesky’s disease virus, porcine circovirus type 2, *Actinobacillus pleuropneumoniae*, *Bordetella bronchiseptica*, *Pasteurella multocida*, and *Mycoplasma hyopneumoniae*.

**References:**

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EQUINE INFLUENZA

Equine Influenza (EI) is a highly contagious though rarely fatal respiratory disease of horses, donkeys and mules and other equidae. The disease has been recorded throughout history, and when horses were the main draft animals, outbreaks of EI crippled the economy. Nowadays outbreaks still have a severe impact on the horse industry.

Etiology:
Equine influenza is highly contagious and spreads rapidly among naive horses. Horses 1-5 yr old are the most susceptible to infection. Orthomyxovirus A/equine-2 was first recognized in 1963 as a cause of widespread epidemics and has subsequently become endemic in many countries, except for New Zealand and Iceland. China, Japan, and Australia experienced devastating epidemics of equine influenza affecting tens of thousands of horses in 2007. Equine influenza had not been reported in China since 1993, in Japan since 1972, and had never been reported in Australia.

Transmission:
Highly contagious, EI is spread by contact with infected animals, which in coughing excrete the virus. In fact animals can begin to excrete the virus as they develop a fever before showing clinical signs. It can also be spread by mechanical transmission of the virus on clothing, equipment, brushes etc carried by people working with horses.

Pathogenesis:
The incubation period of influenza is ~1-3 days. The disease is principally one of inflammation of the upper respiratory tract. The virus is inhaled, attaches to respiratory epithelial cells with it haemagglutinin spikes, fuses with the cell and is released into the cytoplasm where it replicates. Initial viral infection and replication occurs mainly in the nasopharyngeal mucosa, but by 3-7 days after infection, virus can be recovered from cells throughout the respiratory tract. Infection of the respiratory mucosa results in death of epithelial cells, inflammation, edema and loss of the protective mucocilliary clearance. Proliferation by bacteria may occur because of the disruption of normal clearance mechanisms and may cause the bronchopneumonia.

Clinical signs:
In fully susceptible animals, clinical signs include fever (up to 106°F [41.1°C]), and a harsh dry cough followed by a nasal discharge. Depression, loss of appetite, muscle pain and weakness are frequently observed. The clinical signs generally abate within a few days, but complications due to secondary infections are common. While most animals recover in two weeks, the cough may continue longer and it may take as much as six months for some horses
to regain their full ability. If animals are not rested adequately, the clinical course is prolonged. While the disease is rarely fatal, complications such as pneumonia are common, causing long term debility of horses, and death can occur due to pneumonia, especially in foals.

**Lesions:**

Influenza virus replicates within respiratory epithelial cells, resulting in destruction of tracheal and bronchial epithelium and cilia. Respiratory tract epithelium takes ~21 days to regenerate; during this time, horses are susceptible to development of secondary bacterial complications such as pneumonia, pleuropneumonia, and chronic bronchitis. Complications are minimized by restricting exercise, controlling dust, providing superior ventilation, and practicing good stable hygiene. Primary complications of vasculitis, myositis, and myocarditis are seen infrequently.

**Diagnosis:**

A diagnosis of influenza A used to be presumed based on history, clinical presentation, and by ruling out other causes of fever, cough, and nasal discharge (i.e., strangles, bacterial pneumonia). Definitive diagnosis can be determined by virus isolation, influenza A antigen detection (patient-side kit), or paired serum samples (hemagglutination inhibition). Nasopharyngeal swabs are obtained for virus isolation and antigen detection. These samples should be obtained soon after the onset of illness. Virus isolation in chick embryos is highly specific but less sensitive for detection of influenza because of bacterial contamination of the sample. Antigen detection is performed using a human influenza A kit, which provides immediate results that are not affected by bacterial contamination.

**References:**

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Poxvirus infection in animals

Pox diseases are acute viral diseases that affect many animals, including people and birds. Some poxviruses also cause zoonoses. Typically, lesions of the skin and mucosae are widespread and progress from macules to papules, vesicles, and pustules before encrusting and healing. Most lesions contain multiple intracytoplasmic inclusions, which represent sites of virus replication in infected cells. In some poxvirus infections, vesiculation is not clinically evident, but microvesicles can be seen on histologic examination and, in some, proliferative lesions are characteristic.

Infection is acquired either by inhalation or through the skin (eg, sheep pox). In certain instances (eg, fowl pox, swine pox), the virus is transmitted mechanically by biting arthropods. Infection may be followed by generalized lesions (eg, sheep pox) or remain localized (eg, pseudo cowpox). Strains of poxvirus with reduced virulence are used to immunize against some infections, the classic example being the global eradication of smallpox in people by immunization with strains of live vaccinia virus.

Classification:
The genus Orthopoxvirus contains a number of species that can infect animals and humans.

Orthopoxviruses
- Camelpox virus
- Cowpox virus
- Ectromelia virus
- Horsepox virus
- Monkeypox virus
- Raccoonpox virus
- Vaccinia virus (smallpox vaccine)
- Variola (smallpox) virus
- Volepox virus

The genus Parapoxviruses can infect a variety of livestock animals including sheep, goats, and cattle. Human infection is normally associated with an occupation involving sheep, goats, and cattle.

Parapoxviruses
- Bovine papular stomatitis virus
- Orf virus (sore mouth infection)
- Pseudocowpox virus
- Parapoxvirus of red deer
- Squirrel parapoxvirus

Tentative members
- Camel contagious ecthyma (Ausdyk) virus
- Chamois contagious ecthyma virus
- Parapoxvirus of reindeer virus
- Sealpox virus

The genus *Capripoxviruses* cause infection in cattle, sheep, and goats. Infection can cause high morbidity and outbreaks of Capripoxviruses can have profound economic impact for farmers. The viruses in this genus are listed by the World Organizations for Animal Health (OIE: Office International des Epizooties) as important animal diseases that require notification.

**Capripoxviruses**
- Sheeppox virus
- Goatpox virus
- Lumpy skin disease virus

The genus Swinepox virus is the sole member of the *Suipoxvirus* genus. Swine are the only known host for this virus.

**Suipoxviruses**
- Swinepox

Members of the *Leporipoxvirus* genus infect rabbits, hares, and squirrels. Myxoma virus was used in Australia in the 1950s as a pest control to try and eradicate feral European rabbits. Transmission of leporipoxviruses is primarily through the mosquito although other biting insects such as fleas may also transmit virus.

**Leporipoxviruses**
- Myxoma virus
- Shope fibroma virus (Rabbit fibroma)
- Squirrel fibroma virus
- Hare fibroma virus

The genus *Avipoxviruses* infect a number of domestic and wild birds and can be identified as causing disease in at least 232 species in 23 orders. Transmission usually occurs by skin abrasions, inhalation, or by biting insects, such as mosquitoes.

**Avipoxviruses**
- Canarypox virus
- Fowlpox virus
- Juncopox virus
- Mynahpox virus
- Pigeonpox virus
- Psittacinepox virus
- Quailpox virus
- Sparrowpox virus
- Starlingpox virus
- Turkeypox virus

**Tentative members**
- Crowpox virus
- Peacockpox virus
- Penguinpox virus
COWPOX

In this mild, eruptive disease of dairy cows, lesions are seen on the udder and teats. Although once common, cowpox is now extremely rare and reported only in Western Europe.

The virus of cowpox is closely related antigenically to vaccinia and smallpox viruses. Indeed, the first two can be differentiated only by sophisticated laboratory techniques. Before vaccination of the general population against smallpox was discontinued, some outbreaks of cowpox in cows in North America and Europe were due to infection with vaccinia from recently vaccinated persons. Vaccinia-related viruses continue to cause occasional outbreaks of teat infections in dairy cattle in South America and buffalo in the Indian subcontinent. These viruses often spread to people in contact with cattle. The epidemiology of these viruses is unknown, but it has been suggested that they are vaccine viruses that spread to animals during the smallpox vaccination campaigns.

The disease spreads by contact during milking. After an incubation period of 3–7 days, during which cows may be mildly febrile, papules appear on the teats and udder. Vesicles may not be evident or may rupture readily, leaving raw, ulcerated areas that form scabs. Lesions heal within 1 mo. Most cows in a milking herd may become affected. Milkers may develop fever and have lesions on the hands, arms, or face. Occasionally, cowpox in people can cause generalized disease, and fatalities have been recorded.

Cowpox or vaccinia infection may be confused with bovine herpes mammillitis because the lesions of these two conditions are superficially similar, laboratory confirmation is required. The viruses of cowpox and vaccinia can be easily visualized by electron microscopy. Although they cannot be distinguished from each other, their morphology by electron microscopy is distinct from that of pseudocowpox virus and bovine herpes mammillitis virus. Both vaccinia and cowpox viruses grow readily in cell cultures

Reference:
en.wikipedia.org › wiki › Cowpox
**SHEEP POX and GOAT POX**

Sheep pox virus (SPV) and goat pox virus (GPV) were once believed to be strains of the same virus, but genetic sequencing has now demonstrated them to be separate viruses. Most strains are host specific and cause severe clinical disease in either sheep or goats, while some strains have equal virulence in both species. Further complicating this is that recombination can occur between sheep and goat strains, which produce a spectrum with intermediate host preference and range of virulence SPV and GPV cannot be distinguished from each other with serological techniques, including viral neutralisation. SPV and GPV are also closely related to lumpy skin disease virus in cattle (LSDV), but there is no evidence LSDV causes disease in sheep and goats. It has a different transmission mechanism (insects) and partially different geographic distribution.

**Hosts:**

All breeds of domestic and wild sheep and goats, although most strains cause more severe clinical disease in only one species. Native breeds in endemic areas are far less susceptible than introduced breeds of European or Australian origin-morbidity and mortality may approach 100%.

**Transmission:**

Transmission is usually by aerosol after close contact with severely affected animals containing ulcerated papules on the mucous membranes. There is no transmission in the prepapular stage, e.g. animals early in disease or those dying peracutely (e.g. Soay breed of European sheep). There is reduced transmission once papules have become necrotic and neutralising antibody produced (about one week after onset). Animals with mild localised infections also rarely transmit disease. Infection may also occur through other mucous membranes or abraded skin. Chronically infected carriers do not occur. Indirect transmission by contaminated implements, vehicles or products (litter, fodder) occurs. Indirect transmission by insects (mechanical vectors) has been established (minor role).

**Pathogenesis:**

The virus enters the host cell via endocytosis which is initiated by the attachment of viral proteins to host glycosaminoglycans. Then, SPV fuses with the plasma membrane which releases the viral core into the cytoplasm. Viral proteins help contribute to early gene
transcription in the host cytoplasm and expression begins 30 minutes post infection. After early expression, the viral genome becomes free in the cytoplasm due to the core no longer being coated with the capsid.

The intermediate phase, approximately 100 minutes post infection, stimulates genomic replication as the intermediate genes are expressed. 140 minutes to 48 hours post infection is considered the late phase which is when all structural proteins are produced. Virion assembly begins in the cytoplasm with the formation of an immature spherical particle. Once maturation occurs, it is considered an intracellular mature virion. These are brick-shaped particles that can then be released from the cell either by budding or cell lysis.

Clinical signs:

Vary from mild to severe, depending on host factors (e.g. age, breed, immunity) and viral factors (e.g. species predilection and virulence of viral strain). Inapparent infections also occur.

Early clinical signs- included rise in rectal temperature to above 40°C. Macules develop in 2-5 days – small circumscribed areas of hyperaemia, most obvious on unpigmented skin. Papules develop from macules – hard swellings of between 0.5 and 1 cm in diameter – which may cover the body or be restricted to the groin, axilla and perineum. Papules may be covered by fluid-filled vesicles, but this is rare. A flat haemorrhagic form of capripox has been observed in some breeds of European goat, in which all the papules appear to coalesce over the body; this form is always fatal.

Acute phase: within 24 hours after appearance of generalised papules. Affected animals develop rhinitis, conjunctivitis and enlargement of all superficial lymph nodes, especially prescapular lymph nodes. Papules on the eyelids cause blepharitis of varying severity. Papules on the mucous membranes of the eyes and nose ulcerate, creating mucopurulent discharge. Mucosae of the mouth, anus, and prepuce or vagina become necrotic. Breathing may become laboured and noisy due to pressure on the upper respiratory tract from the swollen retropharyngeal lymph nodes draining developing lung lesions.

If animal survives acute phase then papules become necrotic from vascular thrombosis and ischaemic necrosis. Papules form scabs in the next 5–10 days, which persist for up to 6 weeks, leaving small scars. Skin lesions are susceptible to fly strike. Secondary pneumonia is common. Anorexia is unusual unless mouth lesions physically interfere with feeding. Abortion is rare.
Lesions:  
**Skin lesions:** congestion, haemorrhage, oedema, vasculitis and necrosis. All the layers of epidermis, dermis and sometimes musculature are involved. The underlying edematous dermis and subcutis contain many distinctive cells called “cellules claveleuses” of Borrel or “sheep pox cells”. Most of the cells contain cytoplasmic eosinophilic inclusion bodies.

**Lymph nodes draining infected areas:** enlargement (up to eight times normal size), lymphoid proliferation, oedema, congestion, haemorrhage

**Pox lesions:** on mucous membranes of the eyes, mouth, nose, pharynx, epiglottis, trachea, on the rumenal and abomasal mucosae, and on the muzzle, nares, in the vulva, prepuce, testicles, udder, and teats. Lesions may coalesce in severe cases

**Lung lesions:** severe and extensive pox lesions, focal and uniformly distributed throughout the lungs; congestion, oedema, focal areas of proliferation with necrosis, lobular atelectasis. Enlargement, congestion, oedema and haemorrhages of mediastinal lymph nodes is also observed.

**Diagnosis:**

Samples for virus isolation must be sent to the laboratory as soon as possible. They should be kept cold and shipped on gel packs. If these samples must be shipped long distances without refrigeration, glycerol (10%) can be added; tissue samples must be large enough that glycerol does not penetrate into the centre of the tissue and destroy the virus. Neutralising antibodies can interfere with virus isolation and some antigen-detection tests; samples for these tests must be collected during the first week of illness. Samples for PCR can be taken after neutralising antibodies have developed. Paired serum samples should be collected for serology.

**Live animals:** Full skin thickness biopsies; vesicular fluid if available; scabs; skin scrapings; lymph node aspirates; whole blood collected into heparin or EDTA; paired sera

**Animals at necropsy:** skin lesions; lymph nodes; lung lesions; histology: full set of tissues, especially those with lesions.
**Differential diagnosis:**
The clinical signs of severe sheep pox and goat pox are highly characteristic. However, in their mild form they can be confused with parapoxvirus causing orf or urticaria from multiple insect bites.

- Contagious eczema (contagious pustular dermatitis or orf)
- Insect bites
- Bluetongue
- Peste des petits ruminants
- Photosensitisation
- Dermatophilosis
- Parasitic pneumonia
- Caseous lymphadenitis
- Mange

**References:**

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[en.wikipedia.org/wiki/Sheeppox](en.wikipedia.org/wiki/Sheeppox)

[www.msdvetmanual.com/goat/sheeppox](www.msdvetmanual.com/goat/sheeppox)
**SWINEPOX (Suipoxvirus)**

Swinepox is a worldwide disease of the pig, caused by a virus of the family *Poxviridae* and the genus *Suipoxvirus*. It is the most common cause of pox disease in pigs, with vaccinia virus being the next most common cause of outbreaks. It is a mild to severe disease depending on the louse it was contracted from. Symptoms include papules and pustules on the skin of the abdomen. Characteristic lesions on the lower abdomen have dark hemorrhagic centers. Swinepox is transmitted by direct contact and by the pig louse, *Hematopinus suis*. Often the hooves go crusty due to the animals water content in its body being used for fighting the infection. This in serious Swine pox cases can cause malformed hoofs and damage the ability for the pig to walk properly. In some extremely rare cases, the genetics of the animal can be changed by this disease but go unnoticed in terms of physical symptoms; this, if contracted by breeding pigs is very threatening for the potential baby piglets to be born. Piglets born from parents that both have the severest strain of the disease will be born frequently with disfigurements such as a tail that is bulbous, and crooked snouts. The inside of the animal is also affected by the genetic strain by making the muscles and fat of the animal pus filled and also weakens the piglets organs over time resulting in death.

![Image](https://ars.elscdn.com/content/image/3-s2.0-B9780323357753000175-f017-069-9780323357753.jpg)

**A.** Note the four umbilicated pustules in the abdominal skin. **B.** Note keratinocytes with ballooning degeneration and eosinophilic cytoplasmic viral inclusion bodies (arrowheads). Ballooning degeneration develops before vesicle formation. H&E stain. **Source:** https://ars.els-cdn.com/content/image/3-s2.0-B9780323357753000175-f017-069-9780323357753.jpg
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www.oie.int › fileadmin › Home › eng › docs › pdf › Disease_cards

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Rota virus infection

Rotavirus diarrhea is the major cause of death of millions of children in developing countries besides causing economically significant malady in neonates of many domestic animals. In neonates, the infection is non-viremic, have very short incubation period, and manifests profuse diarrhea and severe dehydration. Concurrent infection with secondary pathogens may augment the disease severity.

Neonatal calf diarrhoea (scours)

Rotavirus is the most common viral cause of diarrhea in calves and lambs. Neonatal calf diarrhea (calf scours) is an enteric disease complex. Newborn calves are susceptible to neonatal calf diarrhea (calf scours) especially during their first 28 days of life. Bacteria, viruses and parasites, by attacking the lining of the calf’s intestine, give rise to diarrhea.

Etiology:

Groups A and B rotavirus are involved, but group A is most prevalent and clinically important and contains several serotypes of differing virulence.

Transmission:

As the infected animals shed a high concentration of virus via feces, and the infectious dose needed is less, the minimal environmental contamination can cause widespread infection in calves. Also, aggregation of calves can hasten the transmission through direct contact and cows or buffaloes may excrete virus in feces during late stages of pregnancy, thus providing a source of infection to their offsprings. But it has been suggested that the major mode of virus spread is from infected calves to other susceptible ones. Calves are known to excrete the virus through feces by the second day of infection, which continues for 7-8 days; and susceptible calves of 2-3 weeks age may get contracted. After 3 months of age, calves are not usually infected. However, in buffalo calves, the infection has been recorded up to an age of six months.

Pathogenesis:

Rotavirus replicates in the mature absorptive and enzyme-producing enterocytes on the villi of the small intestine, leading to rupture and sloughing of the enterocytes with release of virus to infect adjacent cells. Rotavirus does not infect the immature cells of the crypts. With virulent strains of rotavirus, the loss of enterocytes exceeds the ability of the
intestinal crypts to replace them; hence, villous height is reduced, with a consequent decrease in intestinal absorptive surface area and intestinal digestive enzyme activity. Diarrhea prevents the absorption of fluids from the intestines; also, body fluids pass from the scouring calf body into the intestines. A calf is approximately 70 percent water at birth. The scouring calf loses fluids and rapidly dehydrates. In addition, dehydration is associated with loss of essential body chemicals (electrolytes)-sodium and potassium-and the build up of acid. The scouring calf becomes dehydrated and suffers from electrolyte loss and acidosis. Infectious agents cause the primary damage to the intestine, but death from scours usually results from dehydration, acidosis, and loss of electrolytes. The identification of infectious agents which cause scours, however, is essential for implementing effective preventive measures.

Figure. The pathogenesis of rotavirus-induced diarrhea, including the role of the enteric nervous system (ENS) and the rotavirus nonstructural protein, NSP4. (A) Immunoelectron microscopic (IEM) of rotavirus particles. (B) Detection of rotavirus infection by immunofluorescence staining; note staining of rotavirus-infected cells lining the intestinal villi. (C) Mechanisms of rotavirus-induced diarrhea including destruction of enterocytes lining intestinal villi leading to maldigestion/malabsorption as well as NSP4 mediated secretory diarrhea. IEM, immunoelectron microscopy. Courtesy of L. Saif, The Ohio State University.
Clinical signs:

Watery stools yellow in color. Occasionally, flecks of blood and mucus may be evident in the stools. The calves are often weak and depressed, and may lose their desire to nurse. The calves develop a sunken-eyed appearance as a result of dehydration. The bony prominences of their hips, shoulders, and ribs may become more apparent as the calves dehydrate and burn their body fat supplies. The calves may stagger or sway as they walk; this often reflects weakness, low blood sugar concentrations, and/or alteration of the acid-base balance of their bodily fluids. The calves may become too weak to stand. Death typically occurs within a day if treatment is not initiated.

Lesions: Lesions and signs follow an extremely short incubation period and develop within hours. The first changes are visible under the electron microscopy with swollen mitochondria and cisternae development in ER. Microscopically, epithelial cells become vacuolated and shed prematurely. Villus thus become atrophic and shorten.

Diagnosis:

Rapid and accurate detection of the etiological agent is important to further contain the spread of infection in animals. Generally, the diagnosis of rotavirus is based on isolation and identification of the virus in intestinal contents or feces. Isolation of virus has been performed in rotavirus specific cell line MA 104 (Simian origin), and direct detection has been facilitated by electron microscopy. Immunofluorescence test (IFT), immunoperoxidase test (IPT) and viral RNA-based PAGE have also been employed to detect the infectious agent. Latex agglutination test (LAT) has also been used for the rapid detection of rotavirus antigens. ELISA, being a highly sensitive and specific test, has been developed by many workers and used for the identification of rotaviruses.

References:

www.researchgate.net › publication › 322856673_Rotavirus_infections ..
Corona virus infection

Coronal calf diarrhoea

Coronaviruses possess a distinctive morphology, the name being derived from the outer fringe, or “corona” of embedded envelope protein. Members of the family Coronaviridae cause a broad spectrum of animal and human diseases. Coronavirus and coronavirus-like infections are described in swine, cattle, horses, cats, dogs, rats, birds, bats, rabbits, ferrets, mink, and various wildlife species, although many coronavirus infections are subclinical or asymptomatic.

Clinical signs:

Clinical signs begin approximately 2 d after exposure and continue for 3 to 6 d. Typically, coronavirus infection causes profuse watery diarrhea, and feces can contain blood clots. Calves become moderately depressed, the suckling reflex is weak, and dehydration can develop rapidly. Decreased food intake, fluids, and electrolyte loss can result in dehydration, metabolic acidosis, and hypoglycemia.

Lesions:

The virus has an affinity for the epithelial cells of the villi of the small intestine. Replication of the virus in these cells results in loss of epithelium and blunting and fusion of villi. In the colon, surface and crypt epithelial cells are attacked, with loss of surface cells and cystic dilatation and accumulation of cellular debris in underlying crypt.

Figure. Bovine coronavirus infection. A. Blunt, fused villi with cuboidal surface epithelium in small intestine. B. Attenuation of surface epithelium and necrosis of gland epithelium in colon

Source: https://ars.els-cdn.com/content/image/3-s2.0-B9780702053184000073-f001v002-114b-9780702053184.jpg?_
Diagnosis:
Can be achieved using viral culture, antigen-capture ELISA, hemagglutination assay using mouse erythrocytes, and PCR. Recently, a pancoronavirus reverse transcription (RT) PCR assay (PanCoV-RT) was described to identify human CoV from samples of humans with respiratory diseases.

Differential diagnosis of calf diarrhoea

<table>
<thead>
<tr>
<th>Infectious agent</th>
<th>Age affected</th>
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<tbody>
<tr>
<td>Bacteria</td>
<td></td>
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<tr>
<td>E. coli (ETEC)</td>
<td>1-5 days</td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td>4-28 days and older</td>
</tr>
<tr>
<td>Cl. perfringens Types A, B &amp; C</td>
<td>1-15 days and older</td>
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<tr>
<td>Virus</td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>5-14 days</td>
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<tr>
<td>Coronavirus</td>
<td>5-30 days</td>
</tr>
<tr>
<td>Protozoa</td>
<td></td>
</tr>
<tr>
<td>Cryptosporidium parvum</td>
<td>5-20 days</td>
</tr>
</tbody>
</table>

References:

www.ncbi.nlm.nih.gov › books › NBK92442

en.wikipedia.org › wiki › Bovine_coronavirus
**Prion Disease**

"Prion" is a proteinaceous infective particle. Recent work has revealed that prion is a heavily glycosylated specific protein (a polypeptide) of 30 kilo Daltons (30-kD), called "prion protein (PrP)". Since it is a proteinaceous particle closely associated with infectivity, the term "proin" was coined from "proteinaceous infective particle". The word "proin" thus formed from "pro" and "in" was changed to "prion" to sound rhythmic.

**Transmissible spongiform encephalopathies (TSEs)** are a group of progressive, invariably fatal, conditions that are associated with prions and affect the brain (encephalopathies) and nervous system of many animals, including humans, cattle, and sheep.

<table>
<thead>
<tr>
<th>Disease name</th>
<th>Natural host</th>
<th>Prion name</th>
<th>PrP isoform</th>
<th>Ruminant</th>
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<tr>
<td>Scrapie</td>
<td>Sheep and goats</td>
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<td>Fatal familial insomnia (FFI)</td>
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<td>PrPFFI</td>
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Bovine Spongiform Encephalopathy (BSE):

Also known as Mad Cow Disease represents a group of symptoms that occur due to fatal neurodegeneration with a long preclinical phase and affects several mammalian species including humans. This is an a febrile, non-inflammatory disease of CNS, which is believed to be the bovine equivalent of scrapie disease in sheep that has occurred as a result of the exposure of cattle to animal protein feeds containing the scrapie agent.

Etiology:

The disease is thought to be caused by conversion of endogenous host encoded prion protein (PrP) to an abnormal conformation designated PrPsc.

Although both "prions" and "viruses" replicate, their properties, structure, and modes of replication are fundamentally different. Prions lack nucleic acid (RNA or DNA), and also do not produce any inflammatory or immune reaction in the host. Thus, prions are the most unconventional agents. Because they lack nucleic acids, prions are remarkably resistant to many agents that normally inactivate viruses, such as ultraviolet light and standard disinfectants. In fact, they can be classified as an entirely separate category. For his discovery of "prions", Stanley Prusiner, Professor of Biochemistry at the University of California, San Francisco, USA, won the 1997 Nobel Prize in Physiology and Medicine.

Transmission:

1. Ingestion of Meat and Bone Meal (MBM):

The initial epidemiological studies suggested that the disease in Britain was an extended common-source epidemic and the only common source identified in these initial studies was the feeding of proprietary concentrate feedstuffs containing meat and bone meal. Meat and bone is manufactured by rendering industry from tissue discarded in
slaughterhouses, and also from down and dead livestock. The outbreak of BSE in Britain was temporarily preceded by a change in the method of processing of meat and bone meal to a continuous process with a cessation of the use of hydrocarbon fat solvents. The marked fall in disease incidence following the introduction of the feed ban has substantiated the importance of meat and bone as the major method of infection.

2. Non-feed borne transmission:

This type of transmission can occur but is of minor importance. To date there is no evidence of animal-to-animal transmission of BSE. Semen, chemicals, autosomal inheritance, biologics and pharmaceuticals have been ruled out as the common source.

3. Vertical transmission:

In the absence of other mechanism of transmission, vertical transmission is not considered significant for the perpetuation of the disease in an epidemic form. There is little evidence for vertical transmission of BSE from dam to fetus; however calves born in close contact with BSE infected cow may be infected within days after calving.

Pathogenesis:

Animal may develop PrPsc-based disease 1) by ingestion of PrPsc; 2) by peripheral exposure to PrPsc, most commonly by an iatrogenic route (surgery, cadaveric growth hormone infection, corneal transplantation); 3) by hereditary transmission as an autosomal, dominant trait; or 4) sporadically by unknown origin.

Prions consumed in the feed, being unfilterable agents, cross the blood brain barrier and accumulate in the endosome-lysosome apparatus of the neuron. The normal protein (PrPc) after detaching from the cell surface is normally carried to the endosome lysosome apparatus for degradation but in the presence of extraneous prion particles, the PrPc is converted into its diseased homologue, the PrPsc. Some low molecular weight heat shock proteins or molecular chaperones of HSP- 70 family are thought to play role in the autocatalytic event where the abnormal isoform of the PrP protein PrPsc, catalyses the formation of PrPsc from normal cellular protein (PrPsc) (Prusiner, 1982 and 1994). Formation of a homotypic PrPc-PrPsc complex, therefore, is necessary for the exponential multiplication of PrPsc. This complex formation is assisted by Cathepsin B, cation dependent mannose-6-phosphate receptor, ubiquitin protein conjugate and B-glucuronidase, which are present in endosome-lysosome apparatus. The PrPc-PrPsc complex is subsequently transformed into two molecule of PrPsc. In the next cycle, two PrPsc will combine with two fresh PrPc molecules .The resulting two complexes then dissociate to combine with four PrPc molecules thus creating an exponential process. The faulty product
of PrP gene produced due to point mutations is as efficient as PrPsc in forming the PrPc-PrPsc complex and can produce thousands of copies of PrPsc. The PrPsc or prion molecules then co-polymerise to form amyloid, which is deposited into the cytoplasm of neurons. This leads to neuronal degeneration and vacuolation. Neuronal vacuolations are thought to be pathognomonic of the disease and are responsible for spongiform change.

Heterodimer model of prion propagation


Fibril model of prion propagation
Clinical signs:

The disease is insidious in onset and the clinical course progresses over several weeks, varying from 1 to 6 months in duration. There is a constellation of clinical signs with alterations in behavior, temperament, posture, sensorium and movement, but the clinical signs are variable from day to day although they are progressive over time.

The predominant neurological signs are apprehensive behavior, hyperesthesia and ataxia, and a high proportion of cases loses body condition and has a diminishing milk yield during the clinical course of the disease. Behavioral changes are gradual in onset and include changes, such as a reluctance to pass through the milking shed, a change in milking order and a reluctance to pass through passageways. Affected cattle are disoriented and may stare, presumably at imaginary objects, for long periods. There is hyperesthesia to sound and touch, with twitching of the ears or more general muscle fasciculation and tremors. Many throw their head sideways and show head shaking when the head or neck is touched.

Other changes in the temperament include the avoidance of other cows in loose housing. But antagonistic behavior to herd mates and humans when in confined situation. Affected animals may kick during milking and show resistance to handling. Some cows show excessive grooming and licking and may show the equivalent of the scrapie scratch reflex.

Relatively early in the course of the disease there is hind limb ataxia with a shortened stride, swaying gait, and difficulty in negotiating turns. Knuckling, stumbling and falling, with subsequent difficulty in rising is common in the later stages of the disease. Cows show progressive weakness, with ataxia and weight loss, and prior to the common recognition of
the disease, they were sent to slaughter because of locomotor disabilities or changes in temperament.

Lesions:

BSE was initially diagnosed in 1986 by histological examination of sections of brain. The characteristic changes comprise discrete (separate) ovoid and spherical vacuoles, or microcavities, in the neuropil. This spongiosis (i.e., neuropil vacuolation) is a predominant form of vacuolar change observed, and is a feature of TSEs. Subsequently it was established that the pathognomonic vacuolar changes are consistently present in the brain stem facilitating routine diagnosis of the disease. Neuronal perikarya and neurites (axons) of certain brain stem nuclei contain large well defined intracytoplasmic vacuoles. These are single or multiple, and sometimes distend the soma (body) to produce ballooned neurons with a narrow rim of cytoplasm. The contents of vacuoles, both in the neuropil and in neurons remain unstained and clear, after histological staining for glycogen in paraffin and for lipids in fixed cryostat sections. A mild gliosis sometimes accompanies the degenerative changes. Also, now established, an additional diagnostic criterion for the spongiform encephalopathies is the detection by electron microscopy in extracts of affected brain of abnormal fibrils, which have been called "scrapie-associated fibrils".

Microscopic "holes" are characteristic in prion-affected tissue sections, causing the tissue to develop a "spongy" architecture. This causes deterioration of that "spongy" tissue in the brain. Source: https://upload.wikimedia.org/wikipedia/commons/2/23/Histology_bse.jpg
Neuronal vacuolation in Brainstem tissue section (dorsal motor nucleus of the vagus nerve).

**Source:** https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcQz0RZmY307m5s31ASE7l0xI7nVjWeJueHJw0Rrx8vMuiGfqoT&usqp=CAU

**Diagnosis:**

1. **Clinical signs:** It may be confusing due to fact that most of the symptoms are commonly seen in other CNS diseases. So it should be differentiated from:

   - Hypomagnesaemia.
   - Nervous acetonemia
   - Rabies
   - Lead poisoning
   - Listeriosis
   - Polioencephalomalacia
   - Tremorogenic toxin

2. **Immunological Test:**

   - Western blotting
   - 14-3-3-protein immunoassay in CSF
   - Assay based on polyclonal antibodies produced in PrP gene knockouts.
   - Assay based on monoclonal antibodies produced against engineered prion protein isotopes.

3. **Rodent Bioassay** (Mice or Hamster).

4. **Brain Biopsy:**

   - Immuno histochemistry- immunodetection of PrPsc.
   - Immunogold electron microscopy
   - Histopathology after Congo Red staining-imparts a pink or red color to amyloids.

Reference:

Scrapie

Scrapie is an insidious, degenerative disease affecting the central nervous system (CNS) of sheep and goats. The disease was first recognised as affecting sheep in Great Britain and other countries of Western Europe over 250 years ago. Scrapie is the prototype of the group of diseases known as the sub-acute, transmissible spongiform encephalopathies which affect man and some animal species, notably ruminants. Of the three human spongiform encephalopathies in this group: kuru, Gerstmann-Sträussler-Scheinker (GSS) syndrome and Creutzfeldt-Jakob disease (CJD), GSS and familial CJD have a hereditary cause but are also transmissible. Host genes can exert a major effect on the length of the incubation period and on clinical disease occurrence in some of the diseases, including natural scrapie in sheep. The cause of the animal diseases and kuru, a geographically localised human disease, is a polymorphic transmissible agent which has yet to be characterised.

Etiology:

Scrapie infectivity is associated with an abnormal form of a cellular sialoglycoprotein PrP0 coded by the host PrP gene. The transition to the abnormal isoform (PrPSc) is a posttranslational event and results from infection. The presence of PrPSc is specific for the diseased state. Hypotheses of scrapie agent structure include that:

a) PrPSc is the agent (prion hypothesis)
b) PrPSc is part of the agent coupled to the agent genome (virino hypothesis) and
c) the agent is an unconventional virus with the protein coded by the viral genome.

Transmission:

Although it is generally accepted that scrapie is an infectious, contagious disease, the means of natural transmission are not understood. To avoid semantic confusion, the following terms will be used as defined below:

a) lateral or horizontal transmission - the spread of infection between unrelated animals via direct or indirect contact at any time or to offspring after parturition;
b) vertical transmission - the spread of infection or genes responsible for disease from parent to offspring via germ plasm at the time of fertilisation or in utero during embryonic and fetal development;
c) maternal transmission - the spread of infection from a dam to her offspring either vertically from female germ plasm, from infection of the embryo, conceptus, placenta or fetus, or laterally, in the immediate post-parturient period.
**Pathogenesis:**

A significant amount of work has been conducted to investigate the pathogenesis of scrapie, using a wide variety of experimental models of scrapie in mice and hamsters. For details, refer to pathogenesis discussed under BSE.

**Clinical signs:**

Scrapie is a non-febrile, insidious disease in sheep and goats. Due to the damage to nerve cells, affected animals will usually show behavioural changes, tremor (especially of head and neck), pruritus and locomotor incoordination which progresses to recumbency and death. The clinical course of scrapie is usually of significant duration (one to six months). However, there has been one report of a case with only a two-week duration. The onset of clinical signs is often marked by a slight change in behaviour. For example, an animal may become more nervous or aggressive, and may separate itself from the rest of the flock. In many instances, these subtle changes may pass unnoticed. Some sheep appear to be demented, or exhibit head pressing, or "star gazing". Hypersensitivity is another characteristic of scrapie. An affected animal may appear normal if left undisturbed, but when handled, tremor may become excessive and the animal may even fall in a convulsive-like state. Scrapie-affected sheep, but not goats, have a tendency to lose much weight, despite retaining a normal appetite. Scrapie acquired its name from the characteristic sign of "scraping" or rubbing against fixed objects. Pruritus may be so subtle as to go undetected or can be so dramatic that an animal will rub off most of its wool. The areas of wool loss may sometimes be rubbed raw. Some sheep will pull wool from their sides or bite at their legs. Affected goats are less likely to rub against fixed objects, but scratch vigorously with hind feet and horns. Some sheep may exhibit a "nibble reflex" when rubbing themselves or when scratched by hand.

**Lesions:**

The pathological changes of scrapie in sheep and goats are confined to microscopic changes in the CNS. The lesions are characteristically found in the grey matter of the brain stem. They include neuronal vacuolation, other forms of neuronal degeneration including some cell loss, astrocytosis, and generalised vacuolar or spongiform lesions of the grey matter neuropil. The majority of vacuoles are intraneural either in the perikaryon or in neurites but some may be paraneural, perineural or not associated with perikarya at all. Vacuolation is most often found in the medulla, pons, midbrain, and thalamus. Usually a most prominent change is cytoplasmic vacuolation of the neurons in the medulla, pons and mesencephalon. The nucleus is often displaced to the cell periphery by large, single or
multilocular vacuoles. On occasions, the vacuoles may contain eosinophilic fibrillar, globular or finely granular material. Neuronal vacuolation may exist in apparently healthy sheep. However, the number of vacuoles is very small and they exist without the other pathological changes of scrapie. Other degenerative changes of neurons exist throughout the midbrain and include chromatolysis, pyknosis and sclerosis. Neurons often appear shrunken and angular. There is usually an increased basophilia of the cell body. The above lesions are accompanied by a glial cell proliferation or hypertrophy usually affecting astrocytes. The astrocytosis may be demonstrated by Cajal's stain or by immunocytochemical staining for glial fibrillary acid protein (GFAP). Information of astrocytosis is of limited diagnostic value as it is non-specifically associated with many other infections and insults to the CNS. Nevertheless, it is of value in experimental studies in mice because other causes are most unlikely.

**Diagnosis:**

There are several methods which may be used to diagnose scrapie in sheep and goats. At present, however, they depend on the occurrence of clinical signs in combination with histopathological confirmation. In addition, one or another of the following methods provides supporting evidence for a diagnosis of scrapie:

- immunohistochemical detection of PrPSc in paraffin sections of the CNS
- immunoblotting for PrPSc
- the detection of SAF in brain extracts by electron microscopy.

Transmissibility of the disease (e.g. by mouse bioassay) is a sound but impractical method of disease confirmation due to the long incubation period for positive cases and the potential inaccuracy of a negative result. However, it may have value in confirming the first introduction of scrapie into indigenous sheep in a country.

**Histopathology**

For a full examination, sections of the medulla, pons, cerebrum, midbrain, thalamus, cerebellum and anterior spinal cord should be examined, although findings are most prominent in the medulla, pons, midbrain and thalamus. The lesions characteristically found in scrapie are:

- neuronal vacuolation
- neuronal degeneration and loss
- vacuolation of grey matter neuropil
- astrocytosis
- occurrence of amyloid plaques (sometimes).
There is evidence that not all breeds of sheep exhibit the same severity or distribution of lesions making it more difficult to obtain a definitive diagnosis in some cases. It should be noted that brain tissue from apparently normal sheep may display occasional vacuolated neurons. However, when present, these are few in number and are not accompanied by the other characteristic changes.

Recently, an eyelid test has been developed in United States to detect scrapie in living animals suspected for the disease. It was discovered that, beside brain, PrP also accumulates in lymphatic tissues of the inner eyelid of sheep during incubation period of the disease. The lymphatic structure is present in sheep and cows, but not humans. A skin sample is taken from a sheep’s eyelid and tested for PrP using monoclonal antibody that binds tightly to the protein. The test could thus prove to be an important tool in the eradication of scrapie.

**Differential diagnosis:**

The clinical signs of many cases of scrapie are quite distinct and can be easily recognised (see chapter entitled "Clinical signs"). They include behavioural changes, tremor, pruritus and incoordination, progressing to recumbency and death. However, in the early stages of the disease, there are several other conditions which could be confused with scrapie including:

- ectoparasites (lice and mites) - can be eliminated by parasitological examination;
- Pseudorabies (Aujeszky's disease) - can be ruled out by an extremely short clinical course in ruminants (36-48 h) and the finding of a high fever;
- rabies - not a problem in rabies-free countries, but it should be considered in rabies endemic areas if the clinical course of the suspect has been shorter than ten days; because of the human health risk, rabies should be investigated in a specialist laboratory by brain examination in all animals dying in this period in a rabies-affected region;
- listeriosis - a febrile condition but usually a short clinical course in sheep and goats may eliminate this possibility; often associated with silage feeding; circling is a common feature;
- ovine progressive pneumonia (maedi-visna) - can be ruled out by a serological testing;
- pregnancy toxaemia (ovine ketosis) - is a seasonal disease of malnourished pregnant ewes and can be diagnosed by serum analysis;
- chemical and plant toxins - may also be difficult to eliminate on ante-mortem inspection if no source of toxin can be positively identified; liver function tests and specific tests (e.g. for lead or organophosphorous toxicity) may be helpful;
- hypomagnesaemia - short clinical course and may be diagnosed by plasma magnesium levels.

References:
www.britannica.com › science › scrapie
www.msdvetmanual.com

Zoonotic Importance of prion disease:
Creutzfeldt-Jacob Disease (CJD):

CJD is the most important spongiform encephalopathy of human, and also the best characterized. It is now feared that people may contract this disease from eating beef. CJD has been in existence much before BSE was discovered. Typically, the classical (sporadic, idiopathic) cases of CJD begin in the sixth or seventh decade of life with amnesia (loss of memory), or less commonly, with behavioral changes, or higher cortical function disturbances such as dysphasia (impairment of speech), or dyslexia (difficulty in reading). With time, patients develop rapidly progressive dementia (mental deterioration) and myoclonus (i.e., twitching or clonic spasm of a muscle or group of muscles characterized by muscular rigidity and then relaxation.) associated with various neurological signs. In about 10% of cases the initial clinical symptom is a behavioral disturbance or personality change often resulting in psychiatric problems. Other signs include abnormalities of vision or coordination, rigidity and involuntary movements. Death occurs usually within six months, and at autopsy, the brain shows pathognomonic spongiosis with neuronal loss and gliosis in the cortex, deep nuclei, and cerebellum.