Classical Swine Fever (CSF)

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INTRODUCTION

Classical swine fever (CSF), known in the United States of America as hog cholera, is an acute to chronic disease of pigs. In its acute form it presents as a highly lethal haemorrhagic fever that is indistinguishable from African swine fever (ASF). It is caused by a small, single-stranded enveloped RNA virus of the genus *Pestivirus*, family *Flaviviridae*, which is closely related to the viruses that cause bovine viral diarrhoea (BVD)/mucosal disease in cattle and border disease in sheep. Although both viruses can infect pigs, no clinical signs have been observed to develop, but BVD viral particles have been detected in pig faeces and infected pigs or pig manure could therefore be a source of infection for cattle. CSF is considered to be the most feared and important disease of pigs worldwide.

CSF was first reported from the USA in 1830 and soon became widespread throughout the American continent, Europe and Asia. It has been eradicated from North America and from Western Europe apart from some reservoirs in wild boars, but is still present in several South American countries and in much of Eastern Europe and Asia. Outbreaks were reported in South Africa in 1905 and eradication was only accomplished by 1918. CSF appears to be absent from continental Africa, but there is long-time endemic infection in Madagascar. Mauritius suffered outbreaks from 2000-2002, apparently due to an introduction from Madagascar, and outbreaks occurred in the Western and Eastern Cape provinces of South Africa from 2005 until 2007. At present CSF occurs concurrently with ASF only in Sardinia, Madagascar and Russia.

EPIDEMIOLOGY

CSF is strictly a disease of pigs. It does not affect humans or domestic livestock other than pigs. Its natural hosts are domestic pigs and European wild boars, which belong to the same species and are ancestral to domestic pigs. Limited experimental studies carried out after the CSF outbreaks in South Africa indicated that the virus can be transmitted to bush pigs and warthogs and can cause lethal disease in bush pigs.

It is highly contagious and is easily transmitted between pigs. The most important sources of virus are live infected pigs and meat and tissues derived from infected pigs. European wild boars are equally susceptible to infection with CSF virus and as in domestic pigs infections result in subclinical to acute fatal disease depending on the virulence of the virus and the immunity of the pigs. Like ASF, CSF affects pigs of all ages, but in endemic areas even infection with virulent virus may produce overt disease only in the younger pigs because the older pigs have developed a degree of immunity.

Molecular studies have revealed two major types of CSF virus, one in Europe and the other in Asia, which makes it possible to trace the probable origin of outbreaks.
Domestic and wild pigs

Maintenance of the virus in domestic pigs and wild boars is similar to that of ASF virus. There is no long-term carrier state in recovered pigs, but large continuous populations of either free-ranging domestic pigs or wild boars can maintain indefinite circulation of the virus. In North America and Western Europe CSF has been eradicated in domestic pigs, but it has not been possible to eradicate the virus from all the wild boar populations in Western Europe, and occasional outbreaks are registered when careless husbandry allows domestic pigs to come into contact with wild boars, or the entrails of wild boars infected with CSF are fed to domestic pigs. Such outbreaks are generally limited in extent and easily controlled. More serious outbreaks have occurred in recent decades in Belgium, The Netherlands and the United Kingdom, where molecular studies revealed the cause to be viruses of Asian origin that most probably came in with illegally imported pork that was subsequently fed as swill.

Wild boar

Maintenance of the virus outside the host

CSF virus is resistant to a wide range of temperature and pH changes. It is therefore able to persist for long periods in meat and tissues derived from viraemic pigs. More detailed studies have been made on the survival of CSF virus in meat than on ASF virus, and have demonstrated that the virus can survive for up to 85 days in chilled pork and more than four years in frozen pork. It can also survive for 140 – 312 days in cured hams depending on the curing process. It is destroyed by exposure to 70˚C for 30 minutes. It is sensitive to desiccation and exposure to sunlight and does not survive long in the environment in the absence of sufficient moisture and organic material. There are no biological vectors.
Transmission

Pigs are usually infected by the oronasal route either through contact with the excretions and secretions of infected pigs or by consuming the tissues of infected pigs. Fomites may transmit infection but this is considered to be less important than direct contact, scavenging or swill feeding. Vertical transmission occurs readily. In the case of infection with highly pathogenic viruses the foetuses usually die and will be resorbed or aborted. CSF is therefore considered to be one of the diseases that contribute to the SMEDI syndrome. Infection with less virulent viruses is not fatal to the piglets. If it occurs during the first trimester, before the foetuses have developed immune competence, it can result in the birth of persistently infected piglets. These piglets are born apparently normal and without antibodies to CSF. They shed virus intermittently until suddenly they develop clinical signs of acute CSF and die. Usually they do not survive for many months but survival up to 11 months has been recorded. These piglets are therefore potentially dangerous as unapparent transmitters of the virus. Sexual transmission has been demonstrated to occur and the virus can persist in chilled or frozen semen, but its importance in the epidemiology of the disease has not been established.

Other means of viral transmission have been investigated. Airborne transmission over a distance of less than 2 km may be possible in pig-dense areas under conditions of low temperature and high humidity. Mechanical transmission by biting flies may be possible. A study indicated that birds, rodents and domestic animals such as dogs and cats are not able to transmit the virus in infective quantities.

**PATHOGENESIS**

Pigs are usually infected with CSF virus via the oro-nasal route under natural conditions, although infection via the conjunctiva, genital mucosa and abraded skin may occur, as well as transplacental infection of foetuses in utero.

The primary site of replication is the oro-pharyngeal tonsillar tissue. Virus may be present in a variety of cell types, including tonsillar epithelium, but studies have demonstrated that the target cells for the virus are monocyte-macrophages, and that the pathogenesis of the disease as far as it is known results mainly from the release of cytokines by these cells as a result of viral replication within them. Cytokines that have been identified as particularly important include tumour necrosis factor α (TNF-α), interleukin 1α (IL-1α) and interleukin 6 (IL-6). In spite of the fact that the viruses that cause ASF and CSF are very different, the pathogenesis of the two diseases appears to be almost identical, which explains the similarity in presentation of the two diseases in pigs.

After primary replication in the tonsils, the virus is disseminated to other lymphoid tissues via lymphatics, where further replication takes place. A viraemic phase with haematogenous spread to parenchymatous...
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organs follows. Although virus titres are generally lower in parenchymatous organs than in lymphoid tissues, macrophages in the liver (Kupffer cells and intravascular macrophages) and in the lung have demonstrated to play an important role in the pathogenesis of CSF.

CSF is characterised by lymphopenia and thrombocytopenia, which were initially ascribed to direct effects of the virus on lymphocytes and thrombocytes, but have been demonstrated to be due to apoptosis of lymphocytes and aggregation of thrombocytes as a result of cytokines released by infected macrophages. Particularly in the acute form of CSF, haemorrhages are a prominent feature of the infection. These were thought to be due to direct damage to endothelial cells as a result of virus replication, but in fact the damage to endothelium has been found to be minimal, and the haemorrhages are most likely to be due to increased vascular permeability as a result of inflammatory mediators and impaired clotting ability owing to consumption coagulopathy. Death from acute CSF is most likely due to the severe circulatory disturbances that result in widespread haemorrhages.

The pathogenesis of chronic CSF, resulting from infection with moderately virulent viruses, is similar to that of acute ASF but viraemia is generally low. The course of disease is characterised by a phase during which virus may be detected in serum followed by one when circulating virus is not detectable, after which another viraemic phase occurs. This is attributed to possible immune exhaustion, although antibodies are present. The simultaneous presence of antibodies and circulating virus can result in the deposition of immune complexes in the kidneys, causing glomerulonephritis. During the second phase of viraemia the pigs may suffer secondary bacterial infections.

Infection of pregnant sows in the first trimester with CSF viruses of low virulence can result in persistently infected foetuses. These foetuses develop into piglets that have a persistent viraemia and do not develop antibodies to the virus as they are immunotolerant. The factors that trigger acute fatal CSF in these pigs are unknown.

**DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS**

**Clinical signs and pathology**

Diagnosis of CSF is complicated by the lack of specificity of the clinical signs and pathological lesions as well as by the presence of secondary infection in disease of longer duration. Acute CSF manifests as a haemorrhagic fever that is indistinguishable from ASF. In a naïve herd it can cause up to 100% mortality. In endemically infected areas mortality will generally be much lower, with mainly the younger pigs being affected. The clinical signs of high fever, loss of appetite, lethargy, skin flushing progressing to bluish discoloration of particularly the ventral parts and extremities, and hindquarter weakness resulting in a
swaying gait are similar to those of ASF, and may also be accompanied by ocular discharges, constipation or diarrhoea, vomiting, and respiratory signs.

Pigs huddle together, often lying on top of each other, and are poorly responsive to external stimuli.

The skin may show multiple infarcts (black slightly raised well circumscribed crusty plaques) with the eventual formation of necrotic “button” ulcers.
Pathological lesions include haemorrhages in skin, mucosa and multiple organs, oedematous and haemorrhagic lymph nodes, accumulation of fluid in body cavities, enlargement and frequently (but not consistently) infarction of the spleen and congestion of the gastro-intestinal tract and other organs. Ulceration at the ileo-caecal valve has been described but is inconsistently present. The pharyngeal tonsils may appear congested or necrotic. Histopathologically there is karyorrhexis in lymphoid tissues, as observed in ASF. A detailed survey carried out in The Netherlands indicated that no single lesion was consistent or even predominant, and concluded that pigs presented at a laboratory for diagnosis of any disease should also be tested for CSF. It was also determined in various studies that detection of CSF on farms was likely to take 2 – 5 months after the initial outbreak.

Subacute and chronic forms of CSF are even more difficult to diagnose. As the virus targets the immune system, secondary infections are common and may cloud the original picture.
The primary site of viral replication is the oro-pharyngeal tonsillar tissue with resultant necrosis.

Enlarged haemorrhagic lymph node

Splenic infarcts

Laboratory confirmation

The diagnostic samples of choice from live pigs are whole blood in EDTA and serum, and tonsils, lymph nodes and spleen from dead pigs, on ice. Pigs suffering from severe acute CSF are unlikely to have measurable antibodies, as these only appear after 9 – 11 days, but tests are available to detect viral antigen in serum.

The most sensitive, specific and rapid diagnostic assay for CSF is a reverse-transcription polymerase chain reaction (RT-PCR) to detect viral genome. Prior to the development of the PCR the first test of choice was a fluorescent antibody test (FAT). It is less sensitive than PCR and does not distinguish between CSF virus and the pestiviruses that infect ruminants (BVD and border disease) and can also infect pigs. False negatives are also possible and the FAT should be followed by a more sensitive
confirmatory test, for example viral isolation. The antigen-capture enzyme-linked immunosorbent assay (ELISA) is less sensitive than PCR but is useful for screening large numbers of sera, particularly in an outbreak. It should not be used to test individual pigs.

In terms of antibody detection, the ELISA test does not distinguish between antibodies to CSF virus and antibodies to BVD virus, which are sometimes present in pigs unless monoclonal antibodies are used. Virus neutralisation is also used for the specific identification of antibodies to CSF virus. Serology is mainly useful for screening herds that may have been infected with viruses of low virulence or to detect persistent pockets of infection after an outbreak, although the presence of antibodies does not necessarily indicate active infection. The time lapse between infection and development of measurable antibody levels can be as long as 21 days and therefore serology is of no use in the early detection of outbreaks.

**Differential diagnosis**

The most important differential diagnosis for CSF is ASF, and laboratory tests are essential to distinguish between the two diseases. Bacterial septicaemias, in particular erysipelas and porcine salmonellosis, are also important. The early history of CSF in the United States is blurred by confusion that occurred between CSF and *Salmonella choleraesuis*, which was prevalent at the time and also occurred concurrently with CSF. Other differential diagnoses include porcine reproductive and respiratory syndrome (PRRS), porcine dermatitis/nephropathy syndrome (PDNS), and a range of causes of abortion, diarrhoea, respiratory disease or ill thrift in the case of less pathogenic viruses.

**CONTROL / PREVENTION**

Unlike ASF, CSF can be well controlled by vaccination. The most widely used vaccines are live vaccines, most of which are based on the Chinese ‘C’ strain. They are highly effective and safe and have been successfully used in eradication programmes in many countries.

In countries where CSF has been eradicated, and particularly those which export pigs and/or pork, vaccination is generally prohibited. This is partly because absence without vaccination is considered the ideal situation, and partly because it is not possible to distinguish serologically between pigs vaccinated with the live vaccine and pigs that have been naturally infected. The occurrence of major outbreaks in countries that were free without vaccination (e.g. The Netherlands in 1997 and the United Kingdom in 2000), necessitating massive culling of pigs at high cost in order to regain their free status, as well as the fact that some countries where CSF is endemic nevertheless have the potential to export pork, makes the development of marker vaccines that will enable differentiation between infected and vaccinated animals (DIVA) attractive. To this end a number of subunit marker vaccines have been developed where for
example an immunogenic protein is expressed in cell cultures, separated and combined with an adjuvant to form the vaccine. Some of the problems encountered have been lower protection than that afforded by the live vaccines, viral circulation in the presence of vaccination, failure to protect against vertical transmission of the virus, and the length of time required for immunity to develop, which precluded the use of this type of vaccine in emergency control of outbreaks. While the live vaccine apparently stimulates cellular as well as humoral immunity, since vaccinated pigs are protected before measurable antibodies develop, this has not been the case with marker vaccines. However, ongoing efforts to improve marker vaccines are reported to be yielding more promising results.

Like ASF, CSF can largely be prevented by biosecurity measures on farms. This would include limiting access to the pigs, supplying a change of footwear at least to people who have to approach the pigs, and not feeding swill that could contain raw or undercooked pork to pigs. This includes not feeding the entrails or other remains of wild boars that have been found dead or killed by hunters, as well as not permitting pigs to roam freely in areas where encounters with wild boars are likely. The 1997 outbreaks in The Netherlands suggested a possibility of airborne transmission over relatively short distances in areas with dense and contiguous pig farms in cool, moist conditions, and this is difficult to overcome by biosecurity measures unless pigs are permanently confined in barns with virus-proof air filters. Under these conditions vaccination would be a necessary adjunct to biosecurity measures. Because subclinical disease is not uncommon in herds with well-developed immunity, quarantine of new pigs would be an important measure to prevent the introduction of CSF into a naïve herd.

Dead pigs going to burial

In countries where wild boars are known to be infected, oral vaccination using baits with live vaccine has been implemented. While the results were promising, it is recommended that this approach should be combined with other approaches such as controlling the size of wild boar populations through hunting and
taking the normal precautions to prevent exposure of domestic pigs to wild boars or their remains. A particular problem was that, while the infection circulates in the younger members of the wild boar population, the larger boars tended to ‘hog’ the oral baits so that the younger pigs were not exposed to the vaccine.

During an outbreak, particularly in countries that have eradicated the disease, massive culling tends to be applied. During the 1997 outbreak in The Netherlands 11 million pigs were culled, of which only 0.7 million were from infected herds and 1.2 million from ‘dangerous contact’ herds; the remaining pigs had to be killed for welfare reasons due to overcrowding on farms when all movement and sales were banned. This kind of exercise is not only unpopular with farmers and public alike; it also creates massive challenges in terms of disposal of such a large number of carcasses. Modelling applied after the event suggested that some costs would have been saved by including vaccination as part of the control strategy. The vaccinated pigs could then have been removed from the population by commercial slaughter and the appalling waste of high quality protein that results from disposal avoided. When South Africa experienced CSF in the Western and Eastern Cape in 2005 the disease was eventually brought under control by a massive and logistically difficult culling operation that involved finding and culling an unknown number of free-ranging pigs in challenging terrain. The cost of compensating owners for close to half a million pigs slaughtered would likely make it difficult to justify another such operation should the same situation arise again. An alternative approach would be to vaccinate as many pigs as possible with the live vaccine, which requires only one vaccination, thus saving the costs of disposal and compensation. The saving would need to be balanced against factors like the value of South Africa’s pork export market. However, resistance to massive culling operations is growing and it is probable that in the future less drastic alternatives will become the norm rather than the exception.

In countries where CSF is endemic, efforts to eradicate it are supported by vaccination with the live vaccine to limit virus circulation as well as by attempts to improve pig husbandry and ensure permanent confinement of pigs. In a relatively recent development, the OIE has added biosecure compartments to the options that support export of livestock commodities (http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.08.03_CSF.pdf). The concept is particularly applicable to intensive production systems and offers the opportunity to commercial pig farms to enter the export market in spite of endemic CSF provided that they can prove that the measures in place are sufficient to ensure that the compartment is free of CSF. In response to the outbreak in the Eastern Cape, guidelines for CSF-free compartments were developed by the national authorities in collaboration with the private sector to at least permit some movement within the country for producers who were able to comply with the measures stipulated. Provided the measures applied to compartments are accepted by prospective trading partners, export from areas that are not geographically free of CSF becomes a reality.
MARKETING AND TRADE / SOCIO-ECONOMICS

CSF has serious economic consequences wherever it occurs. These are due to direct losses, the cost of prevention and control, and, in the case of outbreaks in countries that export pigs and/or pork, trade bans.

In countries where CSF is endemic outbreaks are relatively rarely characterised by high mortality, clinical disease may be seen only in young pigs that were not previously exposed and the clinical signs may be mild. CSF viruses range from highly virulent to only mildly or moderately virulent. However, studies have indicated that they are relatively stable in terms of pathogenicity and mild disease caused by highly virulent viruses is the result of good immunity on the part of the pigs. If the same virus is introduced into a naïve herd, severe acute disease with high mortality will occur. The main costs in CSF endemic countries are those associated with control and eradication. Since most of the countries where CSF is endemic are developing countries and countries where there is a significant smallholder pig farming sector, the erosive effects of the disease are felt at household level in terms of lower production and consequent loss of income.

The eradication of CSF from industrialized countries with the consequent cessation of vaccination has resulted in large naïve populations of pigs that are highly susceptible to CSF. It is possible that the welfare requirement to produce pigs under more natural conditions has increased the risk of CSF in countries that do not practise vaccination, since the outbreaks that occurred in 2000 in the UK apparently started in outdoor herds. These pigs may be exposed to food that might include the type of pork products in which CSF virus is able to survive for long periods carelessly discarded by picnickers. When CSF outbreaks occur in large commercial piggeries the costs of eradication can be enormous. The loss to producers, even if compensation is available, is devastating, because they will have to start from scratch after losing a herd that may have taken decades to build up in order to achieve the desired genetic composition. In vertically integrated industries the indirect costs to feed factories in terms of loss of sales, as well as to abattoirs, processors and retailers may also be considerable. Consumers often have to pay more for pork because it has to be imported. Most countries with industrialized pig industries are exporters and suffer severe losses in terms of revenues from export. The economy of these industries is such that even a temporary slowing of pork sales can have a significant effect on revenues. During the H1N1 influenza pandemic in 2009 when, in spite of reassurances from national and international organizations, the insistence of the media on calling the illness ‘swine ‘flu’ resulted in a marked drop in pork sales worldwide, the loss to the United States of America pork export industry was $1.3 billion as 27 countries banned pork from the USA. Based on pork export revenue in 2008, this would have been $4.9 billion if a total ban had been imposed, as would likely be the case if a CSF outbreak occurred.
The incursion of CSF into the Eastern Cape in 2005 had marked socio-economic effects because, apart from commercial piggeries that were affected, pig-keeping is traditional in the Eastern Cape and almost every family had a few pigs which were free-ranging scavengers, costing almost nothing to raise and providing a very important source of protein in communities that are very poor. The cost at national level was very high because the eradication operation was logistically difficult and required the use of helicopters to track down the pigs in the hilly terrain, the pig population was much larger than estimates had suggested, and to obtain the cooperation of the owners they were compensated at market price for pigs culled. In spite of this, the operation caused great suffering at household level because payment was often delayed, and in remote areas with few facilities financial compensation may not bring immediate relief when it is paid. In order to prevent a recurrence, the government has laid down stringent requirements for pig-keeping in future that may make it impossible for many of the people to keep pigs, when many are not able to afford cement housing or high quality food for themselves and their families.
IMPORTANT OUTBREAKS

While outbreaks of CSF are always important to the victims, they assume a particular importance when they occur in countries that are considered to be free of CSF. Most countries in Western Europe had eradicated CSF by the 1980s and had ceased vaccination. Small outbreaks sporadically occurred in countries like Germany and Italy where the wild boar population was known to be infected and unsafe practices resulted in domestic pigs becoming infected. However, in 1997 an outbreak of CSF occurred in the Netherlands in areas of dense pig farming that resulted in the loss of 11 million pigs and cost $2.3 billion to eradicate. Although the outbreak originated in Germany and was believed to have been introduced into The Netherlands by a contaminated truck used for transporting pigs, molecular genetic studies of the German and Netherlands outbreak viruses demonstrated that it differed at group level from the viruses circulating in European wild boar populations and most likely came from in Asia. In 2001 the United Kingdom suffered an outbreak and although the origin was not traced with certainty, the first confirmed case occurred in outdoor pigs and the virus was again of the Asian type.

An outbreak of CSF was documented in South Africa in 1900 in the Western Cape that spread and was only eradicated in 1918, three years before African swine fever was described for the first time as a different disease. Apart from Madagascar, where CSF was introduced during the colonial period and became endemic, CSF was not reported from Africa again until 2000, when the island of Mauritius suffered an outbreak apparently due to an introduction from Madagascar. Eradication was accomplished.
by 2002 with the help of vaccination. In 2005 CSF was reported from South Africa, first in the Western Cape and then in the Eastern Cape. Although only a few commercial farms were infected, the disease spread rapidly among pigs in the smallholder sectors. In the Western Cape smallholder pig farmers were just recovering from a devastating outbreak of porcine reproductive and respiratory syndrome (PRRS) when once again all their pigs had to be culled to control CSF. In the Eastern Cape, as indicated above, almost half a million pigs belonging to nearly as many households were culled, an operation that continued until 2007.

FAQs

1. What is the difference between CSF and ASF?

   The two diseases are caused by completely different and unrelated viruses; vertical and sexual transmission of the virus have been demonstrated for CSF virus but not for ASF; there are effective vaccines to control CSF but no vaccine exists for ASF.

2. Can CSF affect livestock species other than pigs?

   Pigs are the only target species for CSF.

3. Is CSF a zoonosis?

   CSF is not a zoonosis so people are not affected.

4. Since there are vaccines, why are all the pigs killed when there is an outbreak of CSF?

   Whether or not all the pigs are killed depends on national or regional policy. In the EU, for example, vaccination is not permitted for diseases that have been eradicated so all infected and in-contact herds have to be killed. The reason for a policy of no vaccination is that exporting countries want to regain free status as quickly as possible in order to be able recover their export markets. Although there are now marker vaccines that make it possible to distinguish between pigs that have been vaccinated and pigs that were naturally infected, fears that vaccination could mask infection and prolong the course of the disease have so far prevented a change in policy.

5. Are many countries in Africa infected with CSF?

   At present as far as is known the only country in the African region that is infected with CSF is Madagascar.

6. Is CSF easy to diagnose?
Field diagnosis of CSF is difficult because the clinical signs and pathological lesions are similar to those of many other diseases, including ASF, but there are good laboratory tests that enable a rapid diagnosis to be made so in any suspected case samples should be sent to a capable laboratory as soon as possible for confirmation.

REFERENCES