Contagious bovine pleuropneumonia (CBPP)

Author: Dr. Mary-Louise Penrith


Licensed under a Creative Commons Attribution license.

TABLE OF CONTENTS

Introduction ............................................................................................................................................. 2
Epidemiology .......................................................................................................................................... 4
Pathogenesis .......................................................................................................................................... 5
Diagnosis and differential diagnosis ............................................................................................ 7
  Clinical signs and pathology ................................................................................................................ 7
  Laboratory confirmation ..................................................................................................................... 11
  Differential diagnosis .......................................................................................................................... 12
Control/prevention.............................................................................................................................. 13
Socio-economics ................................................................................................................................ 15
References ............................................................................................................................................. 15
INTRODUCTION

Since the global eradication of rinderpest was declared in 2011, contagious bovine pleuropneumonia (CBPP) has been considered the most serious disease of cattle. It is an acute, subacute or chronic disease that affects only cattle and occasionally water buffalo (*Bubalus bubalis*). It is caused by a mycoplasma, *Mycoplasma mycoides* subspecies *mycoides* Small Colony (MmmSC). Cattle suffering from the acute to subacute disease develop serofibrinous pleuropneumonia and severe pleural effusion. In animals that develop the chronic form of the disease or recover from acute disease persistent pulmonary sequestra occur but their ability to transmit the disease is uncertain.

*Mycoplasma mycoides* subsp. *mycoides* SC is a pleomorphic bacterium that grows under aerobic and anaerobic conditions. It belongs to a group of closely related mycoplasmas known as the mycoides cluster that are all ruminant pathogens. Genetic studies indicated that the cluster became established and spread approximately 10,000 years ago, coinciding with the domestication of livestock.

Contagious bovine pleuropneumonia was first described in Europe in 1564 and has, with the exception of South America and Madagascar, occurred throughout the world. It has been eradicated in North America, Australia, Europe, and probably in Asia, as the last definite reports of CBPP to OIE from Asia were from Afghanistan in 2002 and Saudi Arabia in 2005, although reports of suspicion of CBPP, apparently either not confirmed or negated, emanated from Mongolia in 2005 and Afghanistan in 2009. The two outbreaks in Saudi Arabia may have been linked to importation of live cattle from the Horn of Africa. The reappearance of CBPP in Portugal in 1983 and in Italy between 1990 and 1993 after a lengthy absence caused considerable consternation, and it was only eradicated from Portugal in 1999 after 85,000 cattle had been slaughtered. It is an economically important disease in sub-Saharan Africa, where it has been reported from 29 countries in West, Central, East and southern Africa in the period 2005 to 2014, an increase over the 27 countries that reported it between 1995 and 2001. The southernmost countries currently affected are Angola, northern Namibia, western Zambia, DRC and Tanzania. The presence of CBPP is a constraint for economic and rural development and most countries lack the necessary resources to achieve control and eradication.

It is believed that CBPP was present in East Africa before the colonial era, but its introduction into South Africa is known to have resulted from a Friesland bull or bulls from the Netherlands landed at Mossel Bay in what is now the Western Cape Province in 1853. From Mossel Bay the disease was disseminated rapidly by trek oxen along transport routes throughout the country, soon reaching the northern provinces. Within two years it had killed over 100,000 head of cattle. By the time rinderpest appeared in 1896 to 1897, CBPP was widespread in southern Africa.

Namibia was infected in 1856 when a localized outbreak occurred at Warmbad in the south. This outbreak was contained by quarantine measures adopted by missionaries in the area, but further cattle introductions from either South Africa or Botswana resulted in the infection reaching the central cattle-raising districts in 1859. Very high mortalities resulted and the Herero people referred to 1860 as
‘otjipunga’, the year of the lung. In 1861 CBPP moved across the Limpopo River to cause heavy losses among the cattle of the Matabele in southern Zimbabwe.

The presence of CBPP was confirmed in Angola in 1888. It was probably introduced by infected cattle belonging to the Dorsland Trekkers who emigrated from South Africa and settled at Humpata in the Huila Province in the early 1880s. By 1914 the whole country had been infected, probably due to the extensive use of draught oxen. The disease also spread from Angola to Zambia, from which country it was eradicated in 1946, but it was again introduced in 1969 and resulted in 75 per cent morbidity and 68 per cent mortality in affected herds. According to OIE records it was eradicated by 1978 but was reintroduced in 1997, again from Angola, and continues to be reported regularly from the Western Province. While much of East Africa was considered to have been infected before the colonial era, it is reported that Tanzania (then Tanganyika) became infected for the first time in 1916 and the disease was only eradicated in 1964, but it was reintroduced in 1990 and subsequently has become widespread.

The rinderpest pandemic overshadowed the effects of CBPP and killed many CBPP-infected cattle. It was only at the turn of the century that the persistence of CBPP in southern African cattle populations again became evident, and strict control measures were introduced in most countries of the region. These were, however, hampered by other events that occurred about that time, such as the South African War, the introduction of East Coast fever, the Herero War and the 1918 human influenza pandemic. The disease was eventually eradicated from Zimbabwe in 1904, South Africa in 1924 and Botswana in 1939. However, Angola and the adjacent part of Namibia remained infected. Botswana was reinfected in 1995 from Namibia, and the disease was eradicated by 1997 by the stamping out, with compensation, of all the cattle in the northern infected area, a measure considered mandatory in order to allow resumption of beef exports to the European Union.

Angola, DRC, Namibia, Tanzania and Zambia all reported CBPP to the OIE for most years from 2005 to 2013. In Namibia the high risk areas are the districts north of the veterinary cordon fence that separates the southern, foot and mouth disease (FMD) free area from the Northern Communal Areas; the Kunene and Kavango Districts that share borders with Angola are particularly at risk. The Zambezi District to the east of them experienced no CBPP outbreaks after 1939 until an outbreak occurred there in 2003, in spite of regular vaccination campaigns since 1997 that combine CBPP and FMD vaccination. By 2005 a survey showed that 15 herds were infected in spite of continued vaccination. The outbreak was finally eradicated after treatment of clinically affected and in-contact cattle with an effective antimicrobial was added to the control strategy.

West, Central and East Africa have in the last decades experienced increased numbers of outbreaks of CBPP, which may be the result of cessation of vaccination against rinderpest, as this was combined with vaccination against CBPP. Until that time, CBPP control was reasonably good, with few outbreaks reported. The decline in efficacy of control is also attributed to a decline in the economies of countries in sub-Saharan Africa, weakening of veterinary services and lack of investment in disease control.
Contagious bovine pleuropneumonia is a directly transmitted disease. Closeness of contact, intensity of infection and the number of susceptible animals determine the rate of spread of the disease. Large numbers of MMMSC are present in bronchial secretions, nasal discharges and exhaled air and are transmitted to susceptible animals in close contact by droplets emanating from either cattle with clinical disease or subclinical carriers that are actively excreting the organism. Closely stabled or trucked animals are therefore most prone to infection. However, aerosols containing infected droplets may spread the disease over distances of 20 m or more. In extensive sub-Saharan African farming conditions spread of the disease may nevertheless be rapid, facilitated by the common practice of penning the animals at night, and when large numbers of animals mingle at places such as watering points or live markets.

Transmission depends upon direct contact between infected and susceptible animals, with fomites apparently playing no role in the spread of the disease. Healthy animals introduced into crushes, sales yards or vehicles that have previously been occupied by infected animals do not become infected. Transmission does not occur through ingestion of contaminated feed or direct exposure to the organs of animals that have died of CBPP. Since the organisms may be excreted in the urine of severely diseased cattle, inhalation of aerosol droplets of infected urine may cause infection. The organism has also been isolated from semen but venereal transmission requires further investigation.

Apart from shedding of MMMSC by clinically ill animals, there are other sources of infection. Cattle in the incubatory phase of the disease may harbour MMMSC in their nasal passages for 40 days prior to developing clinical signs or antibodies and are considered to be a potent source of infection. It has also been postulated that recovered animals with sequestra in their lungs might pose a risk for infection, since viable MMMSC has been isolated from sequestra for up to 12 months. As long as the bacteria remain encapsulated by fibrous tissue in the intact sequestrum the animal will not be infective, but it is postulated that sequestra might rupture and permit shedding of the bacteria and consequent transmission of the disease. This is obviously difficult to reproduce. Most of the support for the contention that these animals play a role in transmission is based on attempts to explain outbreaks that have occurred when no obvious source of introduction could be identified and on models based on assumptions of infectivity, but limited experimental work suggested that carriers, if infectious at all, would only occasionally transmit the disease.

The intensity of infection is determined by the concentration of infective organisms in a herd at a given time. It is highest during an acute outbreak but low intensities of infection, which may occur in the early stages of an outbreak and result in slower spread, are more complicated for control and account for the insidious nature of CBPP. Low intensities of infection also result later in an outbreak when only the clinically sick animals in a herd are treated with antimicrobials.

Not all cattle within a herd are equally susceptible to CBPP, and from 10 to 60 per cent of the cattle may be naturally resistant to it, and an even lower number of animals may develop clinical signs. Animals that
survive outbreaks have substantial resistance, and in a closed herd, although it may take a long time, the disease may disappear completely, leaving only the young, new calves susceptible. However, studies in pastoral cattle in East Africa suggest that CBPP would persist indefinitely even in an isolated herd of the size typical for the area. In Africa herds are rarely closed, with considerable between-herd movement and contact, and new introductions are therefore probably common. It was observed that young calves that were infected developed arthritis, particularly of the carpal and tarsal joints and it was believed that they did not develop pneumonia. However, in the 1995 Botswana outbreak, which occurred in fully naive cattle, calves aged three to six months developed severe lung lesions, and it is probable that calves in endemic situations are protected by colostral immunity that slowly wanes. In mixed crop-livestock systems in East Africa it was also observed that the calves are generally kept away from the rest of the herd except when suckling and therefore are at lower risk of exposure.

There is no evidence that MmmSC causes clinical disease in any species other than cattle under natural conditions. The disease is abortive in water buffaloes although seroconversion occurs, and transmission to cattle from this species has not been demonstrated. Natural infection has been demonstrated in goats by recovery of the agent from their lungs but experimental inoculation suggested that their susceptibility to the disease is low, and the fact that CBPP was eradicated from Botswana by culling only the cattle, although large numbers of goats are present in the affected area, suggests that they do not serve as a reservoir for the disease. Surveillance for CBPP in goats in countries free of the disease has, however, been suggested based largely on the resurgence of CBPP in southern Europe in the 1980s and 90s from a source that has never been identified. Molecular genetic characterization of the mycoplasmas isolated during those outbreaks demonstrated conclusively that the disease was not introduced from Africa or Asia and must therefore have originated from one or more unknown reservoirs of infection in the affected area. The disease has never been recorded in wild ruminants and it is believed that positive serology from various wild species using the complement fixation test (CFT) was due to cross reactions with other mycoplasmas. Two African buffaloes experimentally infected with MmmSC died after seroconverting with high antibody titres but did not develop lesions of CBPP so that the cause of death was questionable.

PATHOGENESIS

Natural infection is by inhalation and results in bronchiolitis and pneumonia. Some experimental studies have shown that infection of cattle by endotracheal intubation resulted in chronic disease, while natural infection by close contact with infected animals induced severe infection that was more likely to result in mortality, although other studies indicated that the only difference observed was in the incubation period, which was more variable in naturally infected cattle. It appears that the route of infection determines the outcome. While the typical respiratory lesions result from infection via the respiratory route, subcutaneous inoculation results in the development of an invasive local oedema known as the ‘Willems reaction’ after the person who performed the first inoculation trials in 1852. Intraperitoneal inoculation results in
Livestock Health, Management and Production › High Impact Diseases › Contagious diseases › Contagious bovine pleuropneumonia

peritonitis. In natural infection the lesions are confined to the lungs in both the acute and chronic forms of the disease, apart from the arthritis that has been described in calves.

The result of the multiplication of MmmSC in the lung is severe inflammation that causes respiratory distress and can result in the death of 30 per cent or more of the affected cattle. The pathogenesis of CBPP has not been fully elucidated because of the high cost of experimental work in cattle and the lack of a laboratory animal model. Given the severity of the disease, there are also ethical considerations. However, individual molecular mechanisms that contribute to virulence can be studied using a variety of techniques such as in vitro immunoassays, cellular studies and mouse infection bioassays.

Actions involved in virulence include evasion of the host’s immune system, tight adhesion to the surface of the host’s cells, dissemination and persistence in the host, efficient importation of required nutrients and induction of cytotoxicity in the host. Mycoplasmas have the smallest genomes of all self-replicating organisms. Complete sequencing of the genome of MmmSC in 2004 has revealed a lack of genes encoding primary virulence factors like toxins, cytolysins and invasins that are generally found in other bacteria, so that virulence depends on intrinsic metabolic and catabolic functions as well as surface proteins and their regulation. For example, recent studies have confirmed that the production of large amounts of hydrogen peroxide \( \text{H}_2\text{O}_2 \) due to a gene that facilitates active uptake of glycerol, which is phosphorylated and then metabolised further to release \( \text{H}_2\text{O}_2 \) which is then transported into the host cell, is important for virulence. The MmmSC strain that caused the outbreaks of CBPP in Europe in the last decades of the 20th century lacked the genes necessary for this process and caused mild disease. Tight adhesion of the pathogen to the host cell is required for the \( \text{H}_2\text{O}_2 \) to be released into the host cell and produce a cytotoxic effect, since a strain that produced large amounts of \( \text{H}_2\text{O}_2 \) but did not adhere well to the surface was unable to cause cytotoxicity.

Evasion of the host immune system and the ability to disseminate and persist in the host appear to be related to effects of the pathogen on cells responsible for the immune response. In vitro experiments indicated that MmmSC is capable of inducing apoptosis in all types of blood leucocytes (all lymphocyte and monocyte/granulocyte subsets), although no genetic basis for this was found; production of TN-alpha by MmmSC may be involved, as in association with NF-kappa-B it is associated with induction of apoptosis. Furthermore, the progression of clinical signs in acute disease was associated with decreased interferon production by peripheral blood mononuclear cells.

Virulence appears to depend strongly on surface antigens that protect the organism and cause various reactions in the host. The capsular polysaccharide galactan has cytopathic and vaso-active effects and contributes to the ability of the organism to spread and persist in the host, probably owing to its ability to protect the organism. Surface lipoproteins have been identified that are strongly antigenic and are believed to have important roles in virulence. Several have been identified as promising candidates for mediation of adhesion, including a variable surface lipoprotein that appears to be specific to MmmSC. Although adhesins have been found in other mycoplasmas and are considered to be central to their pathogenicity, enabling transport into the host cell of substances that induce the inflammatory reaction as well as being responsible for species specificity and tissue tropism, none have to date been found in
MmmSC. Lipoproteins are also considered to play an important role in immunopathogenicity. The membrane protein L-alpha-glycerophosphate oxidase (GlpO) has been identified as playing a central role in cytotoxicity by catalysing the oxidation of glycerol-3-phosphate, which results in the release of H₂O₂. The presence of H₂O₂ and/or reactive oxygen species in the host cell may cause direct damage as well as triggering an inflammatory reaction. Some of the differences in virulence between strains including vaccine and field strains may be explained by a single nucleotide polymorphism in the gene encoding 6-phospho-beta-glucosidase (Bgl) that determines the isoform in which Bgl occurs.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Although CBPP was eradicated from North America and most of Europe in the 19th century by a process of clinical diagnosis, movement control and stamping out even before the causative organism had been characterised in 1898, diagnosis presents challenges in areas where the disease is endemic and most often is subclinical or chronic. In the acute form clinical signs and pathology are highly suggestive of the disease but laboratory confirmation is always essential. As detailed a history as possible of the herd should be obtained as the introduction of new animals to the herd or mixing of herds would add to the level of suspicion that the disease might be CBPP.

Clinical signs and pathology

The incubation period for CBPP is highly variable. Under natural conditions it is seldom less than 21 to 42 days and may be several months, but if there is massive aerosol infection it can be as short as 15 to 35 days or even shorter in experimental infection where large doses are administered. Cattle can remain infected for six months or longer after exposure to the organism.

The disease may be acute, subacute or chronic, and during an epidemic a progression from acute manifestations to mainly subacute and chronic disease is observed. Acute CBPP starts with fever, listlessness and signs of respiratory distress, with grunts and moist coughs becoming more frequent as the disease progresses. Animals with severe lung lesions are reluctant to move and adopt a typical stance with the neck extended, elbows abducted and the mouth open with the tongue protruding; breathing is abdominal and exhalation may be accompanied by grunting. A mucoid nasal discharge and frothy saliva around the mouth may be observed. Later the nasal discharge becomes mucopurulent, and the animal becomes emaciated with ventral oedema. Percussion of the lung fields elicits dull sounds over affected areas. In the subacute form of the disease the only clinical sign is an infrequent cough, as the lung lesions are more localised, while chronic disease is characterised by emaciation and coughing when the animal gets up. Calves up to the age of six months may only develop carpal and tarsal arthritis, but lung lesions have been described in calves as young as three months during an epidemic in a naïve herd in Botswana in 1995.
The pathology of the lungs and pleural cavity in severe acute cases is striking. The lesions usually affect only one side of the thorax, although bilateral lesions may be seen in up to 20 per cent or more animals. A large volume (sometimes more than 10 litres) of yellow to greyish yellow clear or turbid fluid exudate containing pieces of fibrin may be present in the pleural cavity, usually accompanied by localised to diffuse fibrinous visceral and parietal pleuritis.

Pneumonic lesions are observed in the lung and may affect part of a lobe, a whole lobe or more than one lobe. They consist of demarcated areas of consolidation that progress to areas of red and grey hepatisation, giving the lung a marbled appearance.
The interlobular septa are distended by a serofibrinous exudate, sometimes containing blood, which is also present in the perivascular and peribronchiolar interstitium. Massive haemorrhage may be present in severely affected animals. The cut surface of the lung yields copious clear yellow fluid, and oedema, thrombosis and infarcts may be present. The infarcts are well demarcated areas of necrotic tissue that progress to sequestra when they become encapsulated by fibrous tissue. Chronic cases usually have one or more sequestra that may be present in one or more lung lobes and can even be very large and occupy a whole lung lobe. Smaller sequestra may resolve within three to four months to form fibrotic scars, but larger ones can persist for a year or more. Recent sequestra consist of firm pinkish to yellowish grey necrotic material surrounded by a thin capsule, which thickens as the lesion ages and may be separated from the necrotic content by a layer of semi-solid yellow material. Purulent liquefied content indicates secondary bacterial infection of the sequestrum, which may rupture.

The healed lungs and pleura of animal that recover completely, usually after a lengthy period of time, are characterised by fibrous scars and areas of scar tissue, and the pleura may be thickened, with adhesions between the parietal and visceral pleura.
Extensive serofibrinous pleuritis of the parietal and visceral pleura

Although the lesions are largely confined to the lungs and pleura, acute cases may have swollen mediastinal and bronchial lymph nodes with multiple necrotic foci, serofibrinous pericarditis and multiple small whitish infarcts in the kidneys. Cases have been described in which only the mediastinal lymph nodes were oedematous, in the absence of lung lesions, but MmmSC could be isolated from the lymph nodes.

Calves may develop serofibrinous polyarthritis and tendosynovitis, particularly of the carpal and tarsal joints, which in animals that recover may be seen as swollen joints due to fibrosis of the joint capsule. Vegetative valvular endocarditis may result in necrogranulomatous lesions in calves, which may also develop mainly atrial myocarditis.

Microscopic lesions depend on the stage of the disease, with the early stages characterised by capillary congestion and flooding of the alveoli with serofibrinous fluid containing neutrophils and macrophages. As the disease progresses there is an increase in the amount of fibrin and neutrophils, which become necrotic, and the septa are widened by exudate and distended lymphatics. The exudate also infiltrates peribronchial, peribronchiolar and perivascular spaces. Oedema and infiltrations of neutrophils and macrophages are present in the bronchial mucosa and submucosa. The early exudates are gradually replaced by fibrosis and infiltrating lymphocytes and plasma cells.

Vasculitis and thrombosis are common and often result in infarction in the lungs as well as the kidneys. The fibrous walls of the sequestra that develop as a result of infarction of lung tissue may contain follicular accumulations of lymphocytes.
Affected lymph nodes are hyperplastic, with oedema, fibrin and infiltration of neutrophils, vasculitis, thrombosis and necrosis. Arthritic lesions are characterised in the acute stage by infiltration of mainly lymphocytes and macrophages into the hyperaemic and oedematous synovial membranes, with thrombosis and deposition of fibrin. Chronic cases have the joint capsule thickened and fibrous, sometimes with hypertrophy of the villi.

**Laboratory confirmation**

If CBPP is suspected in an area considered free of the disease it is important to determine whether the national laboratory is able to test for the disease, as not all laboratories retain capacity for diseases that are considered not to be present in the country. If unable to do the tests the laboratory should be able to transmit the samples to a reference laboratory.

Successful diagnosis depends on the quality of the samples submitted and also on the presence of the causative organism in the animals sampled. The amount of organisms present varies with the stage of the disease and whether the animals have been treated with antimicrobials; samples should be taken from animals that have not been treated if at all possible, and if they have been treated this should be mentioned in the history supplied to the laboratory. A negative result does not necessarily mean that the animal did not have CBPP.

Samples that can be taken from live animals for confirmation of the agent are nasal swabs in transport medium, broncho-alveolar washings or pleural fluid obtained by thoracic puncture. Samples to be taken at necropsy are samples of lung lesions taken at the interface with normal tissue, mediastinal or bronchial lymph nodes and pleural fluid, or synovial fluid from calves with arthritis. Samples should be taken aseptically and if available placed in transport medium obtained from the laboratory, otherwise the addition of ampicillin to especially the pleural fluid samples, which are the samples of choice for culture, will prevent overgrowth of other bacteria. The samples can be kept at 4°C for a few days or frozen at -20°C or below for a longer period. Samples of pleural fluid can also be taken using sterile filter paper strips that are allowed to dry before dispatch; these can be stored at room temperature. In addition, samples of lesions from the interface with normal tissue should be preserved in 10% buffered formalin for histopathology and immunohistochemistry, especially if the distance from the laboratory is great and/or if there are potential difficulties in maintaining the cold chain.

The OIE Terrestrial Manual for Diagnostic Tests and Vaccines describes the tests that are available for diagnosis of CBPP. These include culture, immunological tests to detect antigen, and tests to detect nucleic acid. Once typical ‘fried egg’ cultures of the organism have been obtained they can be confirmed as MmmSC by immunological tests or polymerase chain reaction (PCR), but if these tests yield doubtful results biochemical tests can be used after subcultures have confirmed the colonies as a mycoplasma and at least three colonies have been cloned.

Immunological tests and PCR assays can also be used to test field samples and have the advantage of being able to detect mycoplasmas that are no longer viable. The course of the disease after the acute
stage is such that several tests may be necessary, depending on the quantity and viability of the organisms, but PCR, which detects genomic material, is useful as long as this is available. A number of PCR assays have been developed including real-time PCRs that are highly sensitive and specific and less susceptible to contamination than earlier PCRs. PCRs including a real-time PCR have also been developed that can distinguish between different strains of MmmSC (e.g. the recent European strains and the earlier strains that infected Africa and Australia) and may have future applications in distinguishing between infected and vaccinated animals (DIVA).

The serological tests prescribed by OIE for export testing are the complement fixation test (CFT) and a competitive ELISA (c-ELISA). Both are regarded as herd screening tests and should not be used for testing individual animals owing to the possibility of those animals being either in an early stage of the disease before detectible antibodies have been produced or in a chronic stage when only a few animals remain positive. A more sensitive immunoblotting test can be used for confirmation of CFT and c-ELISA results.

Various tests have been developed for use in the field to detect MmmSC. These include a slide agglutination test (SAT) and a latex agglutination test (LAT) that according to the OIE Manual is easier to interpret than the SAT test. These tests detect antibodies and are herd tests of relatively low sensitivity that will detect MmmSC in the acute phase of the disease provided that antibodies are present. More recently, a diagnostic tool using isothermal loop-mediated amplification (LAMP) has been developed to detect DNA that can be used directly on field samples because all stages are performed on a battery-run instrument. Sensitivity and specificity are comparable to or better than PCR and the methodology appears to be ideal for rapid outbreak diagnosis or abattoir monitoring for prevalence.

**Differential diagnosis**

The main differential diagnosis for CBPP is pneumonic pasteurellosis or ‘shipping fever’ caused by *Mannheimia haemolytica* and less commonly *Pasteurella multocida*, which at necropsy is characterised by a serofibrinous pleural exudate and fibrinous to fibrinopurulent bronchopneumonia. The lesions are bilateral and stained impression smears of affected lung tissue reveal the typical bipolar rod-like bacteria, which will usually be isolated in pure culture. Aspiration of foreign material into the lung can result in acute serofibrinous pneumonia that resembles the early acute phase of CBPP. Haemorrhagic septicaemia caused by *Pasteurella multocida* types B and E is an acute and rapidly fatal disease that can cause swelling in the laryngeal area and brisket, pulmonary oedema and acute serofibrinous bronchopneumonia. The organisms can be cultured and visualised on stained smears.

Sequestra in chronic cases of CBPP must be differentiated from abscesses caused by pyogenic bacteria and will be difficult in cases in which secondary bacterial infection of the sequestra has occurred.

Clinical signs of respiratory distress and fever may resemble those of East Coast fever and Corridor disease caused by *Theileria parva*, in which there is severe lung oedema. Occasional cases of bronchopneumonia with necrotic bronchitis and atelectasis may result from infection with bovine
Livestock Health, Management and Production › High Impact Diseases › Contagious diseases › Contagious bovine pleuropneumonia

herpesvirus 1 (infectious bovine rhinotracheitis virus), and a patchy pneumonia may be seen in cases of bovine malignant catarrhal fever caused by alcelaphine herpesvirus 2.

**CONTROL/PREVENTION**

Eradication of CBPP has been achieved in North America, Europe, Australia and apparently in Asia, with only sub-Saharan African continent remaining significantly infected. Methods used have generally involved movement control and stamping out of infected herds, although eradication in China, in which infection was widespread, was finally achieved by the use of an attenuated vaccine involving numerous passages in rabbits that was apparently effective, although it took more than 30 years to achieve eradication.

Efforts to control CBPP in Africa have a long history in especially West Africa, where cattle keepers are reported to have vaccinated cattle against CBPP by inserting pleural fluid or a piece of infected lung tissue under the skin either of the tail or on the bridge of the nose. Lack of the necessary resources as well as resistance by cattle-owning populations preclude the use of massive culling as a control measure for CBPP in most countries and vaccination is usually regarded as the only alternative. The use of antimicrobials is controversial because of fears that it could result in more carriers, but cattle owners nevertheless do use antimicrobials to cure clinical disease and save the lives of their cattle. It is widely agreed that vaccination will play a central role in reducing the impact of CBPP in Africa and that it may be necessary to combine vaccination with therapy using approved antimicrobials. For this approach to succeed, a more effective vaccine than those currently available would be a great advantage.

The only commercial vaccines available are live attenuated vaccines using the T1/44 and T1sr strains. The former is more widely used, as it provides coverage for a year, while the duration of immunity of the T1sr vaccine is shorter. The latter has the advantage of inducing fewer adverse reactions and being unlikely to cause clinical disease, as sometimes occurs with T1/44, where especially first time vaccination may induce a Willems reaction that is sufficiently severe to require treatment. Additionally, suspicion that T1/44 subcutaneous vaccination could cause outbreaks of clinical disease was supported by an experimental study. The level of protection provided by T1/44 has also not been determined as it appears not always to correlate well with the humoral immune response, and animals without antibodies may also be protected. Studies have suggested that a reduced ability to produce interferon-gamma in the early phase of the disease leads to the development of severe lesions. There are also practical problems of vaccine delivery in less developed areas. Both T1sr and T1/44 are freeze-dried vaccines that are thermostable until reconstituted, but after reconstitution they have to be used within a short period of time, approximately one hour. This is a serious disadvantage when undertaking vaccination in areas with poor infrastructure and relative small herds, as it may only be possible to vaccinate a small number of cattle during the recommended period after reconstitution. Farmer resistance on account of adverse reactions
has also been reported from various countries including Kenya, Namibia and Zambia, leading to lower vaccine coverage.

Investigation of the immune responses of cattle to infection with MmmSC as well as molecular studies of the pathogen to determine the genes coding for antigens have provided information that may lead to development of improved vaccines. It has been proposed that mucosal subunit vaccines would probably be the best option, since IgA appears to be important in mitigating the effects of the infection. However, it is apparent that new generation vaccines are still a long way from becoming available. Some candidate vaccines tested in cattle apparently enhanced the pathogenic effects of MmmSC. Even if an excellent new generation vaccine can be developed, questions have been raised about the practical implications of producing and delivering it. T1/44 is a relatively low tech vaccine that can be produced at a reasonable cost, while high tech vaccines are inevitably more expensive. Willingness on the part of cattle owners in Africa when it has been investigated has been variable, but given that most of them have limited resources it is unlikely that they would be able to buy a more expensive vaccine.

Modelling to determine the best approach to control of CBPP in pastoralist cattle in East Africa based on published data and participatory research to obtain information on the knowledge and perceptions of cattle owners indicated that vaccination alone would be insufficient to eradicate the disease as it could persist indefinitely even in small closed herds. In practice pastoralist herds are never closed and there is a high level of inter-herd exchange and interaction. An approach combining vaccination and prudent, effective antimicrobial treatment was therefore proposed. In spite of the fact that antimicrobial treatment is officially discouraged at international level and is prohibited in many countries, it is widely used to limit damage due to the disease and is regarded as effective by livestock owners and field veterinarians. Effectiveness and sustainability would be increased by the involvement of private and community-based service providers.

Oxytetracyclines (OTC) are the antimicrobials most widely used in Africa to treat CBPP. In spite of widespread and probably sub-optimal use over a long period of time resistance has not been detected, but a number of other products have been investigated. In vitro studies have indicated that relatively few drugs are efficacious against MmmSC, and some of these, for example Ciprofloxacin, are not recommended for use in food animals to prevent possible resistance developing in humans. The most effective drugs, according to the in vitro trials, were OTCs and tilimicosin, a macrolide. Further investigations included newer generation macrolides danofloxacin, which proved an effective contributor to eradicating an outbreak in northern Namibia, tulathromycin and gamithromycin. The studies concluded that OTC and all the macrolides studied showed good activity against MmmSC and that the macrolides would be good candidates for clinical trials. Both OTCs and macrolides are mycoplasmastatic and therefore do not necessarily sterilise the infection. It has been suggested that a mycoplamscidal effect would be ideal but so far no suitable candidate medicine has been reported.

Although the use of plants to treat CBPP has not been documented but is to an extent preserved in oral tradition, with at least one specific example in Niger, a recent investigation demonstrated good potential for various Nigerian plants tested in vitro. In particular a plant known as giant milkweed, Calotropis
Livestock Health, Management and Production › High Impact Diseases › Contagious diseases › Contagious bovine pleuropneumonia

_procera_ (family Asclepiadaceae), showed antimicrobial activity against MmmSC that was comparable with that of the macrolide tylosin.

**SOCI-O-ECONOMICS**

The effects of CBPP include variable mortality and morbidity that results in reduced production, low fertility, loss of capacity to work and trade bans. The OIE Terrestrial Animal Health Code provides standards for trade in live animals, semen and embryos but specifies that trade in milk and milk products, hides and skins, and meat and meat products other than lung should be free of any restrictions. This international recommendation may, however, be overridden by more stringent national standards. For example, the 1995 outbreak of CBPP in Botswana resulted in loss of access to the EU market, although the product involved was deboned beef. To regain access as soon as possible Botswana resorted to mass culling with compensation to the owners. More than 300,000 cattle were destroyed in the affected area, on the southern boundary of which additional veterinary cordon fences were erected, also with high costs. The massive cull and movement control resulted in eradication of the outbreak, but socio-economic assessments indicated that the effects on the human population were negative and included malnutrition in children who were under the age of five years at the time owing to a total lack of cow’s milk. Apart from its negative effects, such an approach would be financially impossible for most African countries.

The economic burden of CBPP is generally difficult to compute, but a recent study in 12 countries in West, Central and East Africa that reported a total of 2,612 outbreaks to OIE during the period 1996 to 2002, accounting for 96% of the reports of CBPP for that period, suggested an amount of 44.8 million euros in direct losses and control costs. Based on an approach using mass vaccination for five years to attain 80% coverage and including an estimated cost of treating about the same percentage of animals, the cost-benefit ratios of controlling CBPP were favourable for the countries studied. Various studies have indicated that CBPP is regarded as an important disease in the region and most cattle owners were prepared to treat sick cattle at their own expense although willingness to pay for vaccination, which has traditionally been provided by the governments, was more variable. Since rational and prudent use of antimicrobials would involve treating the whole herd and not just sick animals, owners might require some financial assistance to assure effective treatment, at least until control of CBPP had provided tangible economic benefits.

**REFERENCES**


