Contagious bovine pleuropneumonia (CBPP)

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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
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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.

![Image of a cow with extended head and neck]

Typical stance of an animal suffering from contagious bovine pleuropneumonia: the head and neck are extended as a result of dyspnoea

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.

![Image of healed lungs and 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 pneumatic 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 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.