

CONTAGIOUS BOVINE PLEUROPNEUMONIA

AETIOLOGY

Classification of the causative agent

The causative agent of contagious bovine pleuropneumonia (CBPP) is *Mycoplasma mycoides* subsp. *mycoides* (Mmm), which belongs to the *Mycoplasma mycoides* cluster. This cluster consists of five mycoplasma species or subspecies from bovines and goats that share serological and genetic characteristics, creating difficulties for taxonomy and diagnostics by traditional techniques.

A number of Mmm strain genomes have been fully sequenced, including that of PG1, the reference strain. Molecular typing has been performed with an eMLST scheme, which showed that all European Mmm strains grouped in a single lineage. The emergence of Mmm has been determined around year 1700 by molecular dating studies. This emergence resulted from the adaptation of a *M. mycoides* subsp. *capri* strain, frequently found in goats, to a new host, cattle.

Mycoplasmas lack cell walls and are, therefore pleomorphic and resistant to antibiotics of the beta-lactamine group, such as penicillin. Growth of mycoplasma is relatively fastidious and requires special media rich in cholesterol (addition of horse serum).

Resistance to physical and chemical action

Mycoplasma mycoides subsp. *mycoides* does not survive for long in the environment and transmission requires close contact.

However, under favourable atmospheric conditions of humidity and wind, aerosols can transport the agent for longer distances.

Temperature:	Inactivated within 60 minutes at 56°C and 2 minutes at 60°C
pH:	Inactivated by acid and alkaline pH
Chemicals/Disinfectants:	Inactivated by many of the routinely used disinfectants. Susceptible to 1% sodium hypochlorite, 70% ethanol, iodophores, gluteraldehyde and peracetic acid. Inactivated by mercuric chloride (0.01%/1 minute), phenol (1%/3 minute), and formaldehyde solution (0.5%/30 seconds)
Survival:	Survives outside the host for up to 3 days in tropical areas and up to 2 weeks in temperate zones. May survive more than 10 years frozen

EPIDEMIOLOGY

Hosts

- Cattle, both *Bos taurus* and *Bos indicus*, are the main hosts
- Infections have also been reported from Asian buffalo (*Bubalus bubalis*) and yak (*Poephagus grunniens*, formerly *Bos grunniens*)
- Sheep and goats can also be naturally infected, but with no clear associated pathology
- Wild bovids and camels seem to be resistant, and, so far, do not appear to be important in the transmission of CBPP

Transmission

- CBPP is spread mainly by inhalation of droplets from infected coughing animals, especially if they are in the acute phase of the disease
- Although close and repeated contact is generally thought to be necessary for transmission, transmission may occur up to 200 metres under favourable climatic conditions
- The organism also occurs in saliva, urine, fetal membranes and uterine discharges
- Transplacental infection can occur
- Nonclinical bovine carriers with chronic infection are an important source of infection, and may retain viable organisms in encapsulated lung lesions (sequestra) for up to 2 years

- it is widely believed that recovered animals harbouring infectious organisms within pulmonary sequestra may become active shedders when stressed or immunodepressed
- Cattle movement and cattle gatherings are important factors in the spread of the disease
- Outbreaks usually begin as the result of movement and contact of an infected animal with a naive herd
- There are a few anecdotal reports of transmission on fomites, but Mycoplasmas do not survive for long periods in the environment, and indirect transmission is thought to be unimportant
- Close, repeated contact is generally thought to be necessary for transmission; however, Mmm might be spread over longer distances (up to 200 metres) if the climatic conditions are favourable

Sources of infection

- Bronchial secretions, nasal discharges, exhaled air and nasal aerosols
- Saliva, urine, fetal membranes and uterine discharges
- Spread of infection through urine droplets was not fully confirmed
- Microorganisms have also been isolated from bull semen, but transmission through semen requires further investigation
- Nonclinical bovine carriers, including subclinically infected cattle, can retain viable organisms in encapsulated lung lesions (sequestra) from several months up to two years. These animals are thought to be capable of shedding organisms, particularly when stressed or immunodepressed

Occurrence

CBPP has been unequivocally identified in Europe since the 18th century and it gained a world-wide distribution during the second half of the 19th century through cattle trade. CBPP was eradicated from many countries at the beginning of the 20th century, mostly through stamping-out strategies (UK, USA) or by vaccination campaigns followed by stamping-out strategies (Australia). Today, CBPP remains enzootic in many Sub-Saharan African countries including countries in the West, South, East, and Central regions of Africa, while in Europe the last CBPP cases were observed in Portugal in 1999. The situation in some Asian countries is unclear due to a lack of efficient CBPP surveillance.

CBPP is one of the diseases for which the OIE has a procedure for the recognition of disease-free areas within a country or at national level. For more information, visit the status portal on the OIE website [<http://www.oie.int/en/animal-health-in-the-world/official-disease-status/>]

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE *World Animal Health Information Database (WAHID)* Interface [<http://www.oie.int/wahis/public.php?page=home>]

DIAGNOSIS

The incubation period for contagious bovine pleuropneumonia can be 3 weeks to 6 months, with most cases becoming apparent in 3–8 weeks. After experimental inoculation of large doses into the trachea, the clinical signs appeared in 2 to 3 weeks.

For the purposes of the *Terrestrial Code*, the incubation period for CBPP is 6 months.

Clinical diagnosis

- Clinical diagnosis of CBPP is unreliable as initial signs may be slight or non-existent and may be indistinguishable from any severe pneumonia. Therefore, CBPP should be investigated by pathological, microbiological, molecular or serological diagnostic methods

The disease may occur in peracute, acute, subclinical and chronic forms

- A few cattle with CBPP may die peracutely with no clinical signs other than fever
- Acute cases in cattle are characterised by nonspecific signs of fever, loss of appetite, depression and a drop in milk production, followed by respiratory signs, which may include coughing, purulent or mucoid nasal discharges, and rapid respiration. Clinical signs can differ in severity between outbreaks, but some cases progress rapidly to dyspnea. Respiration can be painful, and animals

may react intensely if pressed between the ribs. Respiration can be painful, and animals may react intensely if pressed between the ribs

- Epistaxis and diarrhoea have been reported, and pregnant animals may abort or give birth to stillborn calves. Severely affected cattle often die, typically within 3 weeks

In adults

- Initial signs are usually a depressed, inappetent animal with moderate fever, followed by coughing, thoracic pain and increased respiratory rate
- As pneumonia progresses, there is laboured respiration and dyspnoea, and animals prefer to stand with elbows abducted to decrease thoracic pain and increase chest capacity
- Auscultation of the lungs may reveal a wide variety of sounds, depending on how severely the subjacent pulmonary parenchyma is affected
 - crepitation, rales, and pleuretic friction rubs are all possible
 - at percussion, dull sounds can be noticed in the low areas of the thorax
- CBPP often evolves into a chronic disease, characterised by ill thrift and recurrent low-grade fever that may be difficult to recognise as pneumonia
- Forced exercise may precipitate coughing

In calves

- Pulmonary tropism is not the general rule, and infected calves present arthritis with swelling of the joints
 - Co-existence of pulmonary signs in adults and arthritis in young animals should alert the clinician to a diagnosis of CBPP

Lesions

- Gross pathologic lesions of the lung are characteristic and often unilateral; the affected pulmonary parenchyma is odourless
- The predominant gross change is consolidation, or thickening, of individual lobules that become encased in markedly widened interlobular septa, resulting in the characteristic marbled appearance
- Interlobular septa become distended first by oedema, then by fibrin, and finally by fibrosis; the organism produces a necrotising toxin, galactan, which allows for this extensive spread through septa
- Abundant yellow or turbid exudate in the pleural cavity (up to 30 litres in severe cases) that coagulates to form large fibrinous clots
- Fibrinous pleurisy: thickening and inflammation of the pleura with fibrous deposits
- Interlobular oedema, marbled appearance due to hepatisation and consolidation at different stages of evolution usually confined to one lung
- Sequestra with fibrous capsule surrounding grey necrotic tissue (coagulative necrosis) in recovered animals
- *Mmm* can survive within these sequestra for months or longer, facilitating spread

Differential diagnosis

Acute form

- Acute bovine pasteurellosis
- Hemorrhagic septicaemia
- East Coast fever (theileriosis)
- Bovine ephemeral fever
- Traumatic pericarditis

Chronic form

- Echinococcosis (hydatid cyst)
- Actinobacillosis
- Abscesses
- Tuberculosis
- Bovine farcy

Laboratory diagnosis

Samples

- Samples from live animals include nasal swabs and/or broncho-alveolar washings, or pleural fluid obtained by puncture; blood and sera should also be collected
- Samples to be taken at necropsy are lung lesions, lymph nodes, pleural fluid and synovial fluid from those animals with arthritis
- Samples should be shipped cool but may be frozen if transport to the laboratory is delayed

Procedures

Identification of the agent

In-vitro culture isolation

- Isolation of pathogen from clinical samples and colony identification by polymerase chain reaction (PCR). The presence of the pathogen varies greatly with the stage of development of the lesions, and a negative result is not conclusive, particularly if the animal was treated with an antibiotic
- The growth of *Mmm* takes can take up to 7 days. In specific culture media (agar and broth), growth is visible within 2–7 days as a homogeneous cloudiness with whirls when shaken; on agar, small colonies develop, 1 mm in diameter, with the classical 'fried-egg' appearance
- The organism is then identified routinely with dot immunobinding on a membrane filter [MF-dot] or PCR

PCR

- PCR has become the method of choice for the rapid, sensitive and specific detection and identification of *Mmm* directly from a pathological sample or when the organism is isolated. These tests have to be performed in accordance with appropriate quality assurance requirements

Definitive identification is best done by an OIE Reference Laboratory (<https://www.oie.int/en/scientific-expertise/reference-laboratories/list-of-laboratories/>), which may use PCR as well as fine genotyping.

Serological tests

Serological tests for CBPP are valid at the herd level only because false positive or false negative results may occur in individual animals. Tests on single animals can be misleading; an important cause of false positives is serological cross-reactions with other mycoplasmas, particularly other members of the *M. mycoides* cluster.

The validity of the results has to be confirmed by post-mortem and bacteriological examination, and serological tests on blood taken at the time of slaughter.

Complement fixation test (CFT)

- With a sensitivity of 63.8% and a specificity of 98% (Bellini *et al.*, 1998), the CFT can detect nearly all sick animals with acute lesions, but a rather smaller proportion of animals in the early stages of the disease or of animals with chronic lesions
- Modified Campbell & Turner complement fixation (CF) test is suitable for determining existence of disease and is a prescribed test in the OIE *Terrestrial Manual*. However, it has low sensitivity

(70%), and may miss animals in early infection, those with chronic lesions, and those where therapy has been given; for herds, however, it can detect nearly 100% of infected groups

- In a CBPP-free country, the predictive value of a positive CFT test is very low, unless high titres are found on multiple animals from the same herd

Latex agglutination and slide agglutination tests

- Rapid confirmation of CBPP acute outbreaks can be achieved in the field with coloured antigen or sensitised latex beads, which will yield agglutination in the presence of positive sera containing IgMs.

Immunoblotting

- The highly specific immunoblotting test is useful as a confirmatory test for doubtful CFT
- Not fit for mass screening as it is difficult to standardise and is time consuming
- A field evaluation indicated a higher specificity than the CFT enabling the detection of CFT false positives

C-ELISA

- Is recommended in the OIE *Terrestrial Manual* to certify animals as free from infection prior to movement, including international trade purposes
- Compared with the CFT, the C-ELISA has greater specificity (99.8%) and it is able to detect antibodies for a longer time as it detects mostly IgGs when the CFT detects IgMs
- It can now be purchased commercially and it is easier to perform it under quality management

For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 3.4.8 Contagious bovine pleuropneumonia in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Diagnostic Techniques".

PREVENTION AND CONTROL

Antibiotic treatment is not recommended in countries that wish to eradicate the disease because it may delay recognition of the disease and encourage emergence of resistant *Mmm* strains. In Africa, countries where CBPP is enzootic do not have the means to achieve eradication and cattle owners frequently treat their sick animals with antibiotics when observing respiratory signs (including when it is CBPP then). In fact, antibiotics which are effective against mycoplasmas reduce the clinical signs and shedding of mycoplasmas but do not allow a complete cure. In those countries, control of CBPP should be based primarily on vaccination but prudent use of antibiotherapy could be advocated as a substitute for slaughter when slaughter cannot be achieved. The methods used for control depend on the epidemiological situation, animal husbandry methods in effect, and the availability and efficacy of veterinary services in a specific country.

Sanitary prophylaxis

- In disease-free areas: quarantine, movement controls, serological screening and slaughtering of all positive herds
- Control of cattle movements is the most efficient way of limiting the spread of CBPP
- Surveillance for CBPP should be in the form of a continuing programme designed to establish that the whole territory or part of it is free from CBPP infection
- As the pathological lesions of CBPP are distinctive, and pathognomonic, abattoir surveillance for CBPP involving lung examination is a practical method for disease monitoring. It is recommended to isolate and identify the causative organism in order to confirm an outbreak

Medical prophylaxis

- In enzootic areas vaccination is very important in the control of CBPP to reduce its prevalence before eradication can be foreseen
- The only vaccines commonly used today are produced with attenuated *Mmm* strains called T1 (T1/44 and T1sr)

- T1/44 induces a 1-year long protection but may have some residual virulence upon primary vaccination. Reacting animals should be treated with antibiotics. T1sr has no virulence left but afford only 6 months protection
- Vaccination campaigns must be implemented under quality management so that an effective vaccine dose is really injected to the animals

All CBPP-free countries should prepare an emergency intervention plan in the case CBPP is suspected. This plan should include means for rapid confirmation, both in the field and in the laboratory, as well as a rapid intervention strategy and legislation.

For more detailed information regarding vaccines please refer to Chapter 3.4.8 Contagious bovine pleuropneumonia in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading “Requirements for Vaccines and Diagnostic Biologicals”.

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the *Terrestrial Animal Health Code*.

REFERENCES AND OTHER INFORMATION

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated December 2020.