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Contagious Bovine Pleuropneumonia: Epidemiology, Diagnosis, Prevention and Control Method

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Abstract: Contagious Bovine Pleuropneumonia (CBPP) is caused by Mycoplasma mycoides subspecies mycoides small colony variant and is characterized by difficulty in breathing, loss of condition, extensive sero-fibrinous pleurisy and edema of the interlobular septae. It is one of the major constraints to cattle production in Sub-saharan and South West Africa and also a threat to all countries currently free of the disease. Transmission occurs from direct and repeats contacts between sick and healthy animals. The epidemiology of CBPP is characterized by the occurrence of sub-acute and symptomless infections, the persistence of chronic carriers and the spread of the disease is associated with cattle movement. In Ethiopia, CBPP is known to be endemic and is rapidly spreading to cover the whole country in a few years' time, if adequate control measures are not taken. Diagnosis of CBPP in most developing countries of Africa is based on culture and isolation of the causal agent which is fastidious and slow growing, serology and postmortem examination of lungs affected animals. Although the complement fixation test and c-ELISA are commonly used as diagnostic methods in most CBPP endemic countries of Africa, their sensitivity in detecting chronically affected animals is low. The major obstacles for the eradication of CBPP are the absence of a field test for diagnosis, the difficulties in controlling cattle movement and applying quarantine and slaughter policies. The major possible strategies used for control in affected countries or regions are vaccinations, control the movements of cattle and slaughter of infected animals.

Key words: Contagious Bovine Pleuropneumonia · Control · Diagnosis · Epidemiology

INTRODUCTION

Ethiopia stands first in the livestock population in Africa, ranking ninth in the world. The country has about 59.5 million cattle populations [1]. It has a high livestock population which provides draught power, milk, meat, fuel and fertilizer and foreign currency from hide and skin, our country is not using from her livestock as much expected due to many animal diseases circulating in animal population [2]. Respiratory diseases are among the most economically important cattle disease. Among which contagious bovine pleuropneumonia (CBPP) is one of the most enzootic respiratory diseases prevailing in most parts of the world including Ethiopia [3]. CBPP was first described by Gallo in 1550 and occurs throughout the world with exception of South America and Madagascar [4].

Contagious bovine pleuropneumonia is caused by *Mycoplasma mycoides* subspecies *mycoides Small Colony* (MmmSC) variant and is characterized by difficulty in breathing, loss of condition, extensive sero-fibrinous pleurisy and edema of the interlobular septae. This Mycoplasma was isolated in the late 19th century and while eradicated from Europe, still presents immense problems in Africa. Following the eradication of Rinderpest from most parts of the African continent,

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CBPP is now the most important transboundary disease, along with Foot and Mouth disease, although its effect on the animals is far more severe [5].

Contagious bovine pleuropneumonia is an economically important disease of cattle that affects domestic ruminants of the genus *Bos*, mainly *Bos taurus* and *Bos indicus* and is an important disease in many of the principal pastoral areas of Africa [6]. The direct loss results from mortality, reduced milk yield, vaccination and treatment costs, disease surveillance and research programs. The disease also leads to loss of weight and working ability, delayed marketing, reduced fertility and due to quarantines reduced access to cattle trade. CBPP is endemic throughout much of semi-arid sub-Saharan Africa, particularly in a wide belt running from West Africa to Somalia. It also occurs in India, China, South East Asia, Southern and Eastern Europe and sporadic out breaks have occurred in other parts of Africa, Europe and Asia [7].

Epidemiology of CBPP in Africa associated with four factors: cattle are the only species affected, no reservoirs among wild animals, clinical cases (chronic carriers) are the usual source of infection and cattle movement plays a very important role in the maintenance and transmission of the disease [3]. Contagious bovine pleuropneumonia remains the most important infectious disease of cattle in Ethiopia. It is one of the major threats in Ethiopia hindering and challenging the livestock production system [9, 10]. After Renderpest has been brought under control CBPP is considered to be among the most important cattle disease and impediments to livestock development in Ethiopia, particularly in the low lands. The irregularity and low rate of vaccination since 1993 seem to contribute to the increased incidence of the disease and its further spread even towards the highlands and the traditional management system and cattle movement played vital role in the spread of the diseases [11, 12]. In countries such as Ethiopia where CBPP was reported to be prevalent, the knowledge of the diseases and factors associated to such important disease is crucial [11]. Therefore, the aim of this manuscript is to review the epidemiology and control strategies of contagious bovine pleuropneumonia.

Literature Review

Background of Contagious Bovine Pleuropneumonia

Definition: Contagious bovine pleuropneumonia is highly infectious septicemia characterized by localization in the lungs and pleura. It is one of the major plagues in cattle causing heavy losses in many parts of the world [13]. Also, the disease is characterized by a serofibrinous, pleuro-pneumonia and pulmonary sequestra which results in the chronic, sub-clinical carrier state in many recovered animals [14]. This highly contagious pneumonia is generally accompanied by pleurisy. It is present in Africa, the Iberian Peninsula and parts of India and China; minor out breaks occur in the Middle East [15].

Etiology: Mycoplasma *mycoides* subspecies *mycoides small colony* is the cause of the diseases in cattle. The organisms belong to the '*mycoides cluster'* (Table 1) which consists of six closely related mycoplasma. Members of *mycoides* cluster are pathogens of cattle, sheep and goats but the agent of CBPP is not communicable to other species. It is very similar culturally and antigenically to the causative organisms of caprine contagious pleuropneumonia (CCPP) but the two can be differentiated culturally and biochemically. Large colony types are pathogenic for sheep and goats, but not for cattle. Small colony types have been isolated from milk of sheep with mastitis and goats with pneumonia [16].

The mycoplasmas are the smallest and simplest prokaryotic cells and are devoid of cell wall. They belong to the class Mollicutes (soft skin) which consists of six genera: Acholeplasma, Anaeroplasma, Asteroplasma, Mycoplasma, Spiroplasma and Ureaplasma. Only members of the genera Mycoplasmas and Ureaplasma are important in veterinary medicine [17]. The Ureaplasma are distinctive in that they hydrolyze urea. The genus Acholepla-sma is separated from the genera Mycoplasma and Ureaplasma because the latter two require cholesterol [18].

The cell morphology of mollicutes is extremely pleomorphic. Cell shapes includes spherical, pear shaped, spiral shaped and filamentous forms. Cells sometimes appear as chains of beads, the results of a synchronized genome replication and cell division. The diameter of the spherical form ranges from 0.3-0.8 μm. Although classified as gram negative, mollicutes stain poorly by the Gram method. Giemsa, Castaneda, Dienes and new methylene blue stains are preferred. The mollicutes are not only devoid of cell walls but lack the genetic capacity to produce one. They are bound by single trilaminar membrane composed of proteins glycoproteins, glycolipids, phospholipids and sterols. Cholesterols in the membranes provides for osmotic stability. A polar bleb has been demonstrated in some species and has a role in adherence the host cell surfaces. Capsules have also been described for some species [17, 19].

Table 1: Members of the *Mycoplasma mycoides* cluster

Name	Main disease	Host
MmmSC variant	CBPP	Cattle (goats, sheep and buffalo)
MmmLC variant	Caprine pneumonia Contagious agalactiae	Goats (sheep, cattle)
M. mycoides subsp. *capri*	Caprine pneumonia	Goats (sheep)
M. capricolum subsp. *capricolum*	Caprine pneumonia, Contagious agalactiae	Goats (sheep, cattle)
M. capricolum subsp. *capripneumoniae*	CCPP	Goats (sheep)
M. bovis group 7 (Bg 7)	Arthritis, Calf pneumonia, mastitis,	Cattle

Source: [20]

The mollicutes grow slowly and generally require 3 to 7 days incubation before colonies are apparent. The growth is best at 37°C in an atmosphere of 5% carbon dioxide and on nutrient media which contains 10-30% horse serum and 0.2% glucose. Sterols are required by all genera except Acholeplasma and Anaeroplasma. Most genera are facultative anaerobes and microaerophiles except of Anaeroplasma and Asteroplasma, which are obligate anaerobes [4].

The lack of cell wall renders mollicutes resistant to the action of antimicrobial agents that affect the cell wall or its synthesis. They are sensitive to compounds that interfere with protein and nucleic acid synthesis. In general, mollicutes survive outside the host for substantial periods in moist, cool environments. They are very susceptible to heat and most detergent and disinfectants (quaternary ammonium, iodine and phenol-based compound) [20].

Epidemiology: Under natural conditions, CBPP occurs in cattle of the species Bos and allied animals including Buffalo, Yak, Bison and even Reider. While buffaloes can be infected by artificial means and pulmonary lesions and the organism have been found in seropositive buffaloes that have been in contact with CBPP infected cattle in Italy, it is uncertain if they can spread the disease to cattle [4].

In groups of susceptible cattle, the morbidity approaches 90%; the case mortality may be as high as 50% and 25% of infected cattle remain as recovered carriers with or without clinical signs. The source of infection is often provided by recovered 'carrier' animals in which a pulmonary sequestrum preserves a potential source of organisms for periods as long as 3 years. For many years it was thought that conditions of stress due to starvation or exhaustion disease can cause the sequestrum to an active case. Experimental evidence throws some doubt on this explanation, but droplet infection is usually associated with a donor lesion in the lungs. Renal lesions are not uncommon and large numbers of viable *Mycoplasma mycoides* are passed in the urine of infected animals and inhalation of urine droplets may be a route of infection. The organism has been isolated from the semen and preputial washings of two young bulls which were the result of frozen embryos implanted into Portuguese cows and were being considered for entry into a breeding center [16].

Transmission occurs from direct and repeated contacts between sick and health animals. The principal route of infection is by inhalation of infective droplets from active or carrier case of the disease. Mediate infection by contamination of inanimate objects is unlikely under natural conditions, but it has been infected experimentally, the infected hay remaining infective up to 144 hours. A separation of 6m between animals is usually considered to be sufficient, but transmission over 45m has been suspected to occur. The spread of the disease may also occur by discharges from local tail lesions resulting from vaccination with virulent culture. Cattle may be exposed to infection for periods of up to 8 months before the disease becomes established and this necessitates a long period of quarantine before a herd can be declared to be free of the disease. Other inanimate objects such as placenta and urine can also remain infective for long periods [8, 12].

The occurrence and incidence of CBPP is heavily influenced by management systems, disease control policies and regulations of country, knowledge of the disease by farmers and veterinarians and livestock field officers. The diagnostic capability of veterinary laboratories, disease-surveillance and monitoring systems, adequacy of vaccination programs, government budgets allocated to control programs and the desire of cattle owners and traders to control the disease are critically important management factors which influence the effectiveness of control of disease in a country [16].

Geographical Distribution of Contagious Bovine Pleuropneumonia: In Africa, the control of CBPP greatly benefitted from the efforts toward the control of Rinderpest in the 1980s. At that time the geographical distribution of CBPP was limited and almost no outbreaks were observed thanks to annual combined vaccinations that given as a camping. CBPP gained a wider extension

in Africa in the 1990s as its re-invaded countries, such as Botswana, Tanzania and Rwanda that had eliminated the disease in the past [21]. In Africa Botswana was the only country that succeeded in regaining a free status after very strict sanitary measures were applied. In the rest of the continent, CBPP continued to spread gradually to various countries such as Gabon, the Republic of Congo, the Gambia and Senegal. In 2015, CBPP was considered present in all countries of the south Sahara. The southern part of the continent is still free thanks to physical barriers [22]. As the recent report revealed that based on data generated through reports submitted to AU-IBAR monthly by African union member states, CBPP is endemic in most pastoral areas of West, Central and East Africa, with at least 24 countries (45%) regularly reporting outbreaks every year for the last 10 years [21]. The disease is also encroaching on new areas such as Gambia reporting an outbreak in 2013 for the first time after being free of the disease for 45 years. CBPP has also been reported in a few countries in Southern Africa (Angola, Namibia and Zambia). The reported morbidity and mortality as well as case fatality rates have been variable and there appears to be no clear seasonal pattern of outbreaks (no defined temporal trend). The reported fatality rates range between 17-20% [22, 23].

Zimbabwe eradicated the disease in 1904, South Africa did so in 1924 and Botswana completed eradication in 1939. Namibia and Angola have remained infected to this day and the infection was reintroduced into Botswana in 1994. North African countries have been infected only on a sporadic basis, the most recent being Egypt in 1972, however, Egypt rapidly eradicated the disease. The origin of the disease in Central, West and East Africa is obscure. It has been suggested that the infection was introduced by zebu cattle when they first migrated to the African continent. There is a strong possibility that CBPP was introduced into East Africa from India by the army of Field Marshal Napier when he invaded Ethiopia in 1867-1868 [24].

The reasons for increase in incidence of CBPP in Africa are related specifically to reduce funding for vaccination, possibly linked to the success of rinderpest campaign, changes in vaccines and vaccine usage, cost recovery for CBPP vaccination and reduced disease surveillance [16]. In Asia CBPP has been reported in recent times in the Far East but it is now believed to be absent, with India, Myanmar and Pakistan. However, as recently as the late 1970s, high incidences of CBPP were being reported in the Brahmaputra Valley districts of Akajan, Sissiborgaon, Dhemaji and Dhakuakhana. Sporadic outbreaks occur in the Middle East, including United Arab Emirates (1990), Kuwait (1991) and Saudi Arabia (1995), largely as a result of importation of cattle from north-east Africa [5]. Epidemiological and clinical observations indicate that the European outbreaks of CBPP are less virulent than the disease encountered in Africa. Furthermore, CBPP in Europe seems to be far more insidious, as it is usually chronic and affected cattle show few distinctive clinical signs and rarely die [25].

Status in Ethiopia: Contagious Bovine Pleuropneumonia is considered to be among the most important cattle disease and impediments to livestock development in Ethiopia particularly in the low lands. During the past years the level of the disease is reduced in the high land due to unfavorable environment conditions for the development of the organism. The irregularity and low rate of vaccination since 1992/93 and vaccination with combined Rinderpest and CBPP contribute to the increased incidence of the disease and its further spread [3].

According to Malicha *et al.* [26] and Tolesa *et al*. [27] there was report 25% and 32% prevalence in Sidama and Amaro zone respectively. Agew Awi Zone and West Gojam Zones are the two major seriously affected zones of Amhara regional state, followed by South Gonder and East Gojam. In 1989/90, there was major epidemic of CBPP in Dangila and Ankesha districts of Agew Awi zone. This was suspected to be introduced from Metekel zone of Beneshangul Gumiz region. Since CBPP has progressed far to the east and reached Dembecha district of Western Gojam zone. Of Oromia regional state, all the Borena Zone and West Wollega Zones boarding the Sudan are- considered to be CBPP endemic areas. CBPP is found to be enzootic in all the districts of West Wollega [3]. The same study indicated that in West Oromia overall prevalence rate of 29% [28].

According to disease outbreak reports CBPP is widely spread in different regions of the Ethiopia. Outbreaks and enzootic situations in the western, south western and north-west parts of the country are described for several years. Based on data compiled by the MOA, the country may be divided into three CBPP epidemiological areas (Table 2) [27]. According to Najash and Nesradin [29] analysis of 20 Years (1996–2016) the existence of the disease in different parts of the country with prevalence that range from 0.4% (from bull at finishing phase for export in East Shewa zone that brought from Borena pastoral area) to 96% in Western Gojjam. The current distribution of CBPP in different areas of Ethiopia is shown in Figure (1).

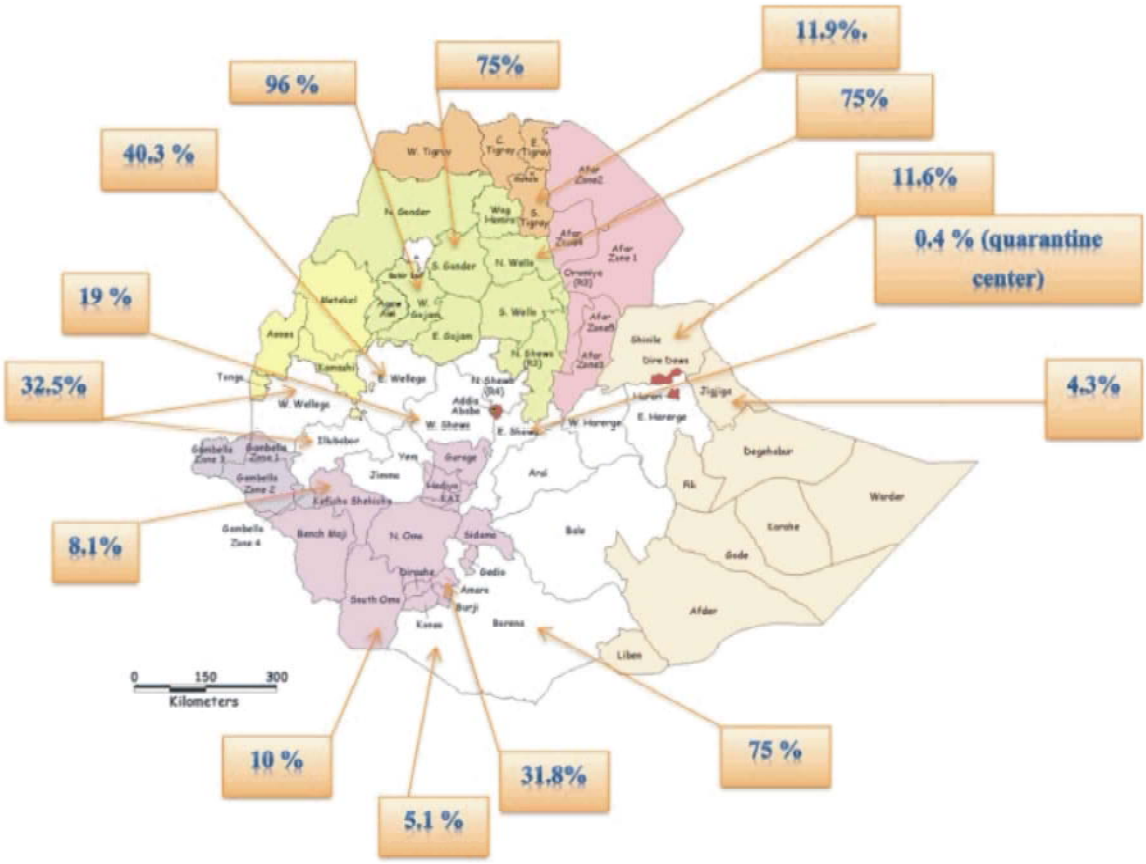

Fig. 1: Current distribution of CBPP in different areas of Ethiopia
Source: [29]

Table 2: Prevalence of Contagious Bovine Pleuropneumonia in different district of Ethiopia

Site of study (different district)	Prevalence (%)	Author
North west Ethiopia	9.1	[30]
Southern Ethiopia (Shashemenne and Arbaminch	6.14	[31]
Borena	9.4	[21]
Somali regional state	39	[11]
Southern zone of Tigray region	11.9	[32]
Adama	4	[33]
Amaro zone, Southern Ethiopia	31.8	[27]
Western oromia	28.5	[28]
Sidama Zone, Southern Ethiopia	25.3	[26]
Gimbo district, southwest Ethiopia	8.1	[34]

Economic Importance: Contagious Bovine Pleuropneumonia is the most economically important disease of cattle in Africa. The direct losses are from mortality, reduced milk yield, vaccination costs, disease surveillance and research programs. The indirect costs are due to the chronic nature of the disease including: loss of weight and working ability, delayed marketing, reduced fertility, loss due to quarantine and loss of cattle trade. In the affected countries, enormous losses are experienced each year from the death of animals and the loss of production during convalescence [16].

Pathogenesis: Even after more than 100 years since CBPP was discovered, the pathogenesis is not well understood. The possible role of the carbohydrate cell capsule and hydrogen peroxide production in *MmmSC* has been

reviewed. The disease is an acute lobar pneumonia and pleurisy. The organism invades the lungs of cattle and causes a mycoplasmemia, this results in localization in numerous other sites including the kidneys and brain, resulting in high morbidity and mortality. An essential part of the pathogenesis of the disease is thrombosis in the pulmonary vessels, probably prior to the development of the thrombosis is not understood, but there is no general increase in blood coagulability and no generalized tendency to spontaneous thrombosis [14].

The production of hydrogen peroxide and active oxygen species (e.g. super oxygen) is widely believed to play an important role in mycoplasma pathogenecity and has been demonstrated to result in lysis of erythrocytes, the per oxidation of lipids in *Mycoplasma mycoides* infected fibroblasts and inhibition of ciliary movement in tracheal organ cultures infected with *Mycoplasma mycoides* and *Mycoplasma ovipneumoniae*. Death results from anoxia and presumably from toxemia. Under natural conditions a proportion of animals in a group do not became infected, either because of natural immunity or because they are not exposed to a sufficiently large infective dose. The animals may show a transient positive reaction to the complement fixation test [16].

Diagnosis: Diagnosis of CBPP in most developing countries of Africa is based on clinical signs, culture and isolation of the causal agent which is fastidious and slow growing, serology and post mortem examination of affected animals lung is commonly used as a diagnostic methods in most CBPP-endemic countries of Africa, their sensitivity in detecting chronically affected animals is low [35].

Clinical Signs: After an incubation period of 3 to 6 weeks (in occasional instances up to 6 months) there is a sudden onset of high fever 40°C, a fall in milk yield in milking cows, anoxia and cessation of rumination. There is severe depression and the animals stand a part or lag behind a traveling group. Coughing, at first only on exercise and thoracic pain are evident, affected animals are disinclined to move, standing the elbows out, the back arched and head extended. Respirations are shallow, rapid and accompanied by expiratory grunting. Pain is evidenced on percussion of the chest [14]. Auscultation reviews pleuritic friction sounds in the early stages of acute inflammation and dullness, fluid sounds and moist gurgling crackles in the later stages of effusion. Recovered animals may be clinically normal but in some an inactive sequestrum forms in the lung, with a necrotic center of sufficient size to produce toxemia causing unthrifteness, a chronic cough, mild respiratory distress on exercise. These sequestra commonly break down when the animal is exposed to environmental stress and cause an acute attack of the disease [13].

Laboratory Diagnosis: No single laboratory test is capable of detecting all CBPP affected animals in the field and which are useful for diagnosis at the herd level only. In the absence of a 'gold standard' test for the serological diagnosis of CBPP, some uncertainty remains unresolved. Suspicious CBPP cases identified by positive serology must be confirmed by further investigations which demonstrate the presence of antigen in the respiratory tissues of animals [19]. In CBPP free countries like Botswana, CFT should be used in conjunction with other serological tests where possible, so that every stage of disease could be followed serologically should the disease enter the country [16].

Isolation and Identification of the Etiological Agent: Isolation of the organism is essential for the diagnosis. The organism is nutritionally fastidious and special laboratory media is required for growth and identification. Final identification of mycoplasmas is usually made by growth inhibition or immunoflourescence tests on agar [16]. To culture *MmmSC,* samples to be taken from live animals are nasal swabs and secretions, tracheal and bronchoalveolar washes and pleural fluid and occasionally blood, urine and synovial fluid should be obtained. From the dead animal: pleural fluid, portions of affected lungs and lung sequestra (scrapings from inside the capsule) and lung-associated lymph nodes and kidneys should be taken. Tissues should be transported in insulated containers at temperatures between 0 and +4°C, to reach the laboratory within 48 hours after collection. For a period of time over 48 hours before dispatching, keep the tissues frozen at -20°C although some loss of viability of the agent occurs. Swabs should be sent in a suitable- medium also refrigerated between 0 and +4°C, to arrive at the laboratory within 48 hours after collection. These conditions are crucial and often overlooked in the success of mycoplasma isolation particularly in hot climate [36].

As culturing of *MmmSC* takes several days, desiccation of the solid medium should be limited by sealing the Petri dishes hermetically or by using controlled humunity incubator. The media should contain basic medium based on heart infusion or peptone, 10% yeast extract to provide group B-vitamins, 10% antibody

free serum and several other components such as glucose, glycerol and fatty acids. To avoid growth of other bacterial and fungal contaminants inhibitors are necessary such as penicillin and thallium acetate. The media can be used as broth or solid medium with 1.0 to 1.2% agars [37].

In fluid medium a homogenous cloudiness usually appears within 3-5 days frequently with silky, fragile filament called a 'comet' which is characteristics of *MmmSC*. During growth on agar media, the colonies are small (1mm in diameter) and have the classical appearance of 'fried eggs' with a dense center. Colonial morphology and isolation should be accompanied by some biochemical tests. After two or three sub-cultures are omitted from the medium so as to check whether the isolates are mycoplasmas or L-form bacteria. Biochemical identification is done after a pure culture of the isolated mycoplasma is obtained [20].

Polymerase Chain Reaction: The polymerase chain reaction (PCR) has been used to identify the specific organism and differentiate it from other members of the cluster. The test can be used to detect small numbers of organisms in nasal mucous, pleural fluid and pulmonary tissue. The PCR can identify the organism in bacterial isolates or clinical material within 2 day of extraction and is highly specific. The organism can also be identified using the PCR on nasal filter strips placed into the nasal cavities of cattle to be tested [16]

Complement Fixation Test: The complement fixation test (CFT) on serum is still the most useful method of detecting infection. It is rapid, simple to perform and easy to interpret the result. It is more specific than the ELISA tests; it lacks sensitivity for serum samples having a very low antibody level. ELISA tests detect late and persistent infections while CFT detects early infections. In small proportion of animals the results may be deceptive [14, 25]. Early cases may give a negative reaction and some positive reactors show no lesions on necropsy' High levels of circulating capsular polysaccharide antigen can leads to false-negative diagnoses due to antibody 'making' and in up to 36% of CBPP positive animals may detectable by the CFT. The test is particularly effective in detecting carriers. Animals recovering from the disease gradually become negative and vaccinated animals give a positive reaction for about 6 weeks, although this period may be much longer if severe vaccination reactions occur. A slide flocculation test and a rapid slide agglutinatin test have been used but their sensitivity is lower than that of the complement fixation test and they are recommended for herd diagnosis rather than for use in individual animals. A modified complement fixation test, the 'plate CFT' is more accurate than the standard CFT and is much more economical of time and equipment [16].

Enzyme Linked Immune-Sorbent Assay: Enzyme linked immune-sorbent assay (ELISA) appeared to be very sensitive but showed false-positive results. An ELISA developed in France also detected antibodies in more chronically infected cattle than did CFT. An indirect ELISA for the detection of antibody to *MmmSC* has been developed jointly by FAO and the International Atomic Energy Agency (IAEA) and ELISA kit is now available, but no data were available on the sensitivity and specificity of this test detecting CBPP cases at all stages of the disease [38].

A competitive ELISA test has undergone evaluation and is possible to apply at animal level (for interpretation) and compared with CFT, the c-ELISA has equal sensitivity and greater specificity. The c-ELISA is an individual test but you can aggregate the results and therefore interpret it at herd and it is easier to perform than the CFT but its performance characteristics have not yet been fully assessed [11].

Latex Agglutination Test: A latex agglutination test (LAT) for the diagnosis of CBPP uses latex microspheres coated with anti-*MmmSC* capsular polysaccharide antigen in the serum of infected animals is useful for detection of acutely infected animals compared to the CFT which is not highly sensitive in the early stages of the disease or for animals with chronic lesions. In comparison to the CFT, the *MmmSC* IgG-coated LAT exhibited 62 and 61% correlation in diagnosis at 2 to 3 min of incubation, respectively. The LAT combines low cost and high specificity with ease of application in the field, without the need for any specialist training or equipment and allows rapid and primarily herd screening prior to confirmatory laboratory diagnosis (PCR or ELISA) [16].

Immuno Binding, Immunohistochemistry and Immunoblotting Tests: At present, immunobinding assays are the most reliable tests for routine identification of mycoplasma species isolated from clinical material. All these assays are based on the detection of mycoplasma surface antigens which are believed to be highly specific. However, sensitivity and specificity can be affected in certain circumstances. Since the number of mycoplasm species is increasing, each isolate has to be

tested with several sera for complete identification and immunobinding assays involving mycoplasma colonies or imprints of colonies are becoming highly laborious. Immunobinding assays with broth culture bound onto nitrocellulose paper can be affected by a high level of background staining [5].

Immunohistochemistry has proved to be a robust assay in the diagnosis of CBPP, particularly where the causative organism is not recoverable (e.g. following long transport distances), where the animal has died of acute disease or where serology cannot be performed or is inconclusive. The sensitivity of IHC using polyclonal serum can be low and non-specific results occur frequently identified a monoclonal antibody, M92/20, for use in IHC confirmation of suspected CBPP cases. These monoclonal show no background noise, but some cross reactivity with other mycoplasmas from the '*M. mycoides* cluster' is known; other monoclonal can be evaluated in this test. IHC is the test of choice when the diagnostic laboratory is presented with a carcass in which lung lesions are suggestive of CBPP while serum is not available and mycoplasma culture from lung is unreliable. Samples are taken from lung lymph nodes or lung tissue with suspected macroscopic lesions, fresh or already formalin fixed and embedded in paraffin wax [36].

An immunoenzymatic test based on immunoblotting has been recently developed and is considered of diagnostic value due to its specificity. A core profile of antigenic bands, present both in experimentally and naturally infected cattle, was considered to be immune dominant. The more accurate picture of the immune status of animals given by this test is due to the electrophoretic profile of *MmmSC* antigens, thus the test outcomes problems related to none specific binding [37].

Necropsy: The detection of specific lesions is an important factor in identifying cattle infected subclinically. The "organising centres" observed in the interlobular septa of lungs with lesions are considered pathognomonic for CBPP [36]. CBPP is manifested as a fibrinonecrotic bronchopneumonia with abundant serofibrinous pleuritis. The gross lesions are similar to the bronchopneumonia of pasteurellosis, but CBPP differs as follows: often only one lung is affected, the lesions are never symmetric when both lungs are involved, lesions are more common in caudal lung lobes, the marbled appearance on cut sections is more pronounced and sequestra are more common [39].

Histologically, in the early stages the typical lesion consists of bronchiolar necrosis and edema, progressing to exudative serofibrinous bronchiolitis with extension to the alveoli and adjacent lymphatics. This process extends to the tracheobroncial lymph nodes and pleural lymphatics. The mediastinal, sterna, aortic and intercostals lymph nodes are enlarged, edematous and hemorrhagic. Lymphatic become thrombosed and fibrosed. The pulmonary lobules become consolidated with alveolar edema, fibrin and inflammatory cells. Coagulation necrosis is common and the organism can be demonstrated in these lobules by immunohistochemistry [5].

Treatment, Control and Prevention

Treatment: *Mycoplasma mycoides*, the agent of CBPP are sensitive to antibiotics such as tetracyclines and chloramphenicol. Oxytetracycline at usual dosage rates for three days has been recommended, while tylosin at the dosage rate of 7.5mg/kg body weight administered at 12 hours intervals for three to five days has been used successfully. Chemotherapy is not used in the control of CBPP as it is highly likely that carriers will develop. Antibiotics have, however, been used to control post-vaccinal reactions, such as those caused by the V-5 vaccine used in kavango region of Namibia in 1984, Schneider *et al.* [14].

Little research work has been carried out on the effect of antibiotics on the pathogenesis of the disease but it is likely that the sequence of events is as follows: Treatment during the incubation period (before clinical signs) - treatment should kill the causative organism and it may be that a single treatment is sufficient. The animal will recover but may not develop resistance to the disease nor develop a serological response. Treatment of clinical cases- early clinical cases may respond to prolonged treatment but advanced cases may not. In both cases, if the animal survives, it is possible but not certain that the treatment will result in a chronic carrier condition [34]. The consensus is that such animals will not easily be detectable by serological test. Treatment of chronic case or "lungers" - the consensus of opinion is that treatment will have little effect on these cases as the causative organism, if present, is walled up in the sequestrum. Treatment of vaccinated animals - treatment in recently vaccinated animals will kill the vaccine strain and thus abort the development of immunity. Animals vaccinated sometime in the past will have little remaining resistance and can be regarded as susceptible animals [40].

The treatment is only of value if cattle are in the incubation stage and is contraindicated if they have been recently vaccinated [36]. It follows that treatment may be of value in two particular situations: (a) where cattle are moving from infected areas into frees areas

(but only when the herd of origin is disease free). Some may be incubating the disease and treatment of all animals in the herd may abort the epidemic. (b) An outbreak of disease where cattle are quarantined waiting for slaughter [24]. Some of the cattle will be advanced cases and will die, but others will be incubating the disease [40].

Control and Prevention: The major obstacles to the control and eradication of the disease are: difficulty in controlling the movement of cattle especially in sub-Sahara Africa, complications of applying quarantine and slaughter policies, lack of rapid pen-side diagnostic tests, ineffective vaccines, insufficient funds to implement control policies and civil strife and drought, which have an effect on the spread of the disease in Africa [16].

The major possible strategies used for control in affected countries or regions are movement controls: CBPP is spread by direct close contact between animals and epidemics if the disease is entirely due to the movement of infected livestock. These movements must be controlled and by three methods: the quarantine of infected herds until the infection has died out, Radostitis *et al.* [16]. This may take several months, controlling long distance movement of livestock. By ensuring that cattle do not move without health certificates (indicating that they have been examined and are free of clinical disease) and vaccination certificates (indicating vaccination within the last 3 months), controlling local movements example trans-humans by identifying areas within which cattle may move freely but which they cannot move out of FAO [40].

Vaccination: Vaccination in endemic areas should be on an annual basis while newly infected areas requires more intensive programs such as a repeat vaccination after 3, 9, 21 and 36 months aimed at the eradication of the disease within this period. Treatment with antibiotics and other chemotherapeutic drugs in association with the vaccination against CBPP has been shown to reduce the efficacy of the vaccines and must be avoided. Calves born to vaccinated cows received antibodies in the colostrums which has suppressed the response to vaccine for up to 60 days. CBPP Vaccination of individual animals increases their resistance but may not prevent them becoming infected. Vaccinating whole population will gradually extinguish infection circulating in that population but only if vaccination covers approaching 100% is achieved. Anything less means that there is the risk of susceptible cattle contracting the disease and by close contact with vaccinated stock overcoming (vaccinal) resistance. In such a situation the livestock owners and the authorities lose faith in the vaccination campaign and it fails [37].

Over the years, vaccines commonly used against CBPP were based on four strains of *MmmSC*: namely T_1, KH_3J, F-strain and V_5. Australian strain V_5 causes severe side reaction. The Australian strains V5 and the Sudanese strain F were naturally attenuated strains probably due to long term passages in natural hosts. Strains T_1 and KH_3J are thus the most widely used *MmmSC s*trains for production of CBPP vaccines [41].

All effective CBPP vaccines have been based up on live versions of the disease-causing mycoplasma, either attenuated or not. Current vaccine strains ($T_1$44 and T_1SR) for CBPP are made from freeze dried broth cultures of live attenuated *mycoplasma mycoides* subspecies *mycoides small colony* and are generally considered to exhibit poor efficacy and stability. Protection is low (only 30 to 60% of animals are protected) and short-lived (6 to 12 months) and repeat vaccination is necessary [42].

Recent experience with the $T_1$44 vaccine in Namibia showed that it was highly effective in bringing CBPP under control. The current vaccine is highly effective when administered as part of well conducted vaccination campaign, in which the vaccine is rapidly used following reconstitution (before a significant loss in titer occurred). The $T_1$44 vaccine which is given subcutaneously has been successfully used to control CBPP in different regions of Africa and has advantages and disadvantages. A number of posts vaccinal reactions may occur. Within two to four weeks following injection, an invading edema develops known as the 'Willems' reactions [16].

The reversion to virulence $T_1$44 vaccine has also been observed when it was serially passaged by endobronchial intubation resulting in the development of lesions of CBPP in animals which were infectious to in-contact animals. This suggests animals given the currently used vaccines ($T_1$44 and T_1SR) subcutaneously could be reservoirs for *MmmSC* and infect other animals in areas previously free of CBPP [27]. Similarly, vaccination with V_5 vaccine was abandoned in Australia when the prevalence of CBPP was sufficiently low, because the vaccine is responsible for erratic foci. In some situation, the $T_1$44 vaccine induces a good immunity, especially when herds are revaccinated annually in which case the level of protection exceeds 85% which compares favorably with a number of other bacterial vaccines. T_1SR strain is completely devoid of residual virulence and the level of protection afforded since to be similar to that provided by the $T_1$44 vaccine after three months [41].

Slaughter of infected animals: this is the quickest way of eradicating the disease provided it is accompanied by effective movement control. Herds containing clinically affected cattle are identified by inspection and

sub-clinically infected livestock detected by serological tests. The cost of these measures means that slaughter should be a strategy of last resort to be used in critical epidemiological situations e.g. in the case of outbreaks in the free area or the surveillance zone or on major trade routes [5].

CONCLUSION

Generally, Contagious Bovine Pleuropneumonia is highly infectious septicemia characterized by a serofibrinous pleuro-pneumonia and pulmonary sequestra which results in the chronic, sub-clinical carrier state in many recovered animals. The disease is caused by *Mycoplasma mycoides* subspecies *mycoides small colony* which belongs to the 'mycoid cluster'. Under natural conditions, CBPP occurs in cattle of the species Bos and allied animals including Buffalo, Yak, Bison and even Reider. Transmission occurs from direct and repeated contact between sick and health animals. Diagnosis of CBPP in most developing countries of Africa is based on culture and isolation of the causal agent which is fastidious and slow growing, serology and post mortem examination of lungs affected animals although the complement fixation test and c-ELISA are commonly used as diagnostic methods in most CBPP-endemic countries of Africa, their sensitivity in detecting chronically affected animals is low. The major obstacles to the eradication of CBPP are the absence of a field test for diagnosis, the difficulties in controlling cattle movement and applying quarantine and slaughter policies.

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