Contagious Caprine Pleuropneumonia

Disease Monograph Series – 03

Bacteria | *Mycoplasma capricolum capripneumoniae* | Goats

IDRC | Bartay

This monograph forms part of a series of disease monographs commissioned by the International Development Research Centre over the period Nov 2015 to April 2016 to inform funding priorities for the Livestock Vaccine Innovation Fund (LVIF). The LVIF is a seven-and-a-half year, CA$57 million partnership between the Bill & Melinda Gates Foundation, Global Affairs Canada and Canada's International Development Research Centre. It focuses on those animal diseases posing the greatest risk to poor livestock keepers in Sub-Saharan Africa, South and Southeast Asia, targeting transboundary diseases to achieve lasting regional impact.

Table of Contents

Acronyms

AU	African Union
AU-IBAR	African Union Inter-African Bureau for Animal Resources
AU-PANVAC	African Union – Pan African Vaccine Centre
CCPP	Contagious caprine pleuropneumonia
CFT	Complement fixation test
CI	Confidence Interval
CVO	Chief Veterinary Officer
DG	Director General
DoI	Duration of immunity
DVS	Director Veterinary Services
ELISA	Enzyme-linked immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
IM	Intramuscular
KEVEVAPI	Kenya veterinary vaccine production institute
LAMP	Isothermal loop-mediated amplification
LAT	Latex agglutination test
Mccp	*Mycoplasma capricolum* subspecies *capripneumoniae*
NGO	Non-governmental organization

OIE	World Animal Health Organization
PCR	Polymerase chain reaction
PPR	*Peste des petits ruminants*
RPA	Recombinase polymerase amplification
SAT	Slide agglutination test
SC	Subcutaneous
SHF	Small holder farmer
TPP	Target Product Profile
VACNADA	Vaccines for Neglected Animal Diseases in Africa (Project funded by EU, completed in 2012)

Executive Summary

The disease, etiology, epidemiology and impact

Contagious caprine pleuropneumonia (CCPP) is one of the most severe diseases of goats and is caused by *Mycoplasma capricolum* subsp *capripneumoniae (Mccp)*. It is strictly a respiratory disease, characterized by fever, coughing, severe respiratory distress and high mortality. Infected animals become very sick and mostly die within 7-10 days. It can reach 100% morbidity and 70% mortality. There has been quite a lot of confusion regarding the exact cause of the disease. It was only in 1976 that a mycoplasma designated F38 (later in 1993 called *Mycoplasma capricolum* subsp *capripneumoniae*) was confirmed as the primary cause of CCPP. *Mccp* belongs to the *Mycoplasma mycoides* cluster together with another 5 mycoplasmas. Respiratory diseases caused by other mycoplasmas of the same cluster, especially *M. mycoides capri* (*Mmc*) are still referred incorrectly as CCPP, particularly in the Middle East and India (this is quite relevant when reviewing the literature and the vaccine strains). See Table 1.

For a long time, goats were believed to be the only susceptible host for CCPP. In CCPP outbreaks in mixed goat and sheep herds, sheep may also be infected, as verified by isolation of *Mccp* or detection of antibodies from clinically affected sheep. CCPP is highly contagious. This disease is transmitted during close contact, by the inhalation of respiratory droplets. Chronic carriers may exist, but this remains unproven. No evidence of indirect transmission has been shown as the mycoplasma is highly fragile in the environment. In most goat production systems in Africa, goats are often an important source of income for women, and CCPP therefore negatively impacts on their ability to provide for their children and family needs. There is very little reliable information on the economic impact of the disease.

Incidence / Prevalence

The exact distribution of *Mccp* is not known and it may be much more widespread than the zone represented by the countries where *Mccp* has been isolated, as CCPP is often confused with other respiratory infections and also because the isolation of the causative organism is difficult. While the clinical disease has been reported in nearly 40 countries in Africa and Asia, *Mccp* has only been isolated in 20 countries because few laboratories have the expertise for isolating and growing mycoplasmas. *Mccp* was first isolated and shown to cause CCPP in Kenya; it has subsequently been isolated in the Chad, Eritrea, Ethiopia, Niger, Oman, Sudan, Tanzania, Tunisia,

Turkey, Uganda, the United Arab Emirates, and more recently in Mauritius, China and Tajikistan. In the countries of interest in Asia, the disease has only been described in India, but care is needed when interpreting the information, as much is based on *Mmc* and not on *Mccp*. In Africa, the disease is very significant in East Africa, but it has been expanding West (there is evidence of the disease in Mali although *Mccp* has not been isolated) and South. Attempts to confirm the presence of *Mccp* by isolation should be encouraged, as that will open control opportunities (some countries might fear using the vaccine for example, if there have been no isolates in the country).

Diagnostics

Definitive diagnosis can be difficult, as *Mccp* is one of the most fastidious mycoplasmas; faint turbidity in liquid medium or colonies on solid medium may appear only after 5–15 days and can be missed during routine bacteriological analysis. Isolation is often unsuccessful, and detection may be easier with specific molecular methods such as PCR.

Control

Treatment with antibiotics such as tetracyclines, fluoroquinolones and the macrolide family are generally clinically effective if used early enough. In remote areas and/or nomadic herds, long-acting formulations are preferred in order to achieve a complete treatment. However, the complete elimination of the mycoplasma is rarely achieved, and treated animals are considered to be potential carriers. Further work is necessary to determine whether such a risk actually exists.

Prevention and control of CCPP is undertaken through vaccination, quarantine, movement controls, slaughter of infected and exposed animals and cleaning and disinfection of premises. Vaccines for the prevention of CCPP can be very useful. Unfortunately, the vaccines are not easily available. Different countries adopt different control measures. For example, Tanzania and Uganda allow treatment, while Kenya and Ethiopia rely on vaccination – this might be due as the vaccine in only produced in Kenya and Ethiopia in Africa, and their availability is very limited.

Current vaccines for CCPP

An experimental attenuated live vaccine was developed in 1978, but it didn't progress. Since then, a number of different preparations have been produced, including a vaccine composed of sonicated antigens that did not progress either. An inactivated vaccine was developed in 1987 by Rurangirwa and colleagues. This is the vaccine that is currently being produced in Kenya, Ethiopia and Jordan. It is based on 0.15 mg of *Mccp* in saponin. Saponin inactivates the mycoplasma and provides the adjuvant effect. Duration of immunity is claimed 6-12

months depending on the manufacturer. Currently, there are only CCPP inactivated and adjuvanted vaccines commercially available. Some references mention live attenuated CCPP vaccines being manufactured in Turkey and China, however, those vaccines are based on *Mycoplasma mycoides* subsp *capri* (*Mmc*) and there is no reference of cross-protection in the literature. There was no evidence of a *Mccp* vaccine commercially produced in Asia.

Efficacy and safety of the inactivated vaccines are acceptable (care needs to be taken with the saponin quality). *Mccp* requires very rich media, the yield is low, the procedure involves a purification process and it requires large amounts of antigen (the current payload of a vaccine dose is very high), so the vaccines are costly. Process improvements aimed at increasing the yield, or research to determine the minimum protective dose of the current vaccine as to reduce the payload per dose, could help to decrease the price. There are only 2 manufacturers in Africa (Kenya and Ethiopia), and the Jordanian vaccine manufacturer JOVAC exports vaccines to Africa. The supply is very limited, and it doesn't seem to cover the needs. There is no clarity on whether the protective antigen should be the protein, the LPS or both. Currently, only protein estimation methods are used for quantifying the antigen load, but they measure all proteins (not only the one of interest) and do not ensure the identity of the antigen, nor its immunogenicity. During the VACNADA Project, some process and QC improvements were developed, but they never reached a point of implementation on the production lines. AU-PANVAC was planning to take it further, but the support seems to have ceased. AU-PANVAC also developed Immuno-Capture ELISA test, to use in QC of the CCPP vaccines which needs to have the final validation.

Potential new vaccines and the way forward

The current inactivated vaccines have some limitations as mentioned above, and could benefit from process improvement (some of which have already been identified). Better QC methods are critically needed. Correct measurement of the protective antigen would also allow to decrease the vaccine dose. The current inactivation method does not allow certain combinations, for example with a live PPR vaccine. CCPP vaccine combinations with other diseases relevant for goats from the production or zoonotic point of view, for example PPR, sheep and goat pox, pasteurellosis or brucellosis, might be of interest depending on the area.

Characteristics of an ideal CCPP vaccine, can be seen under the Target Product Profile in Section 9.

Clinical disease overview

Etiology & Epidemiology

Contagious caprine pleuropneumonia (CCPP) is a severe disease of goats caused by *Mycoplasma capricolum* subspecies *capripneumoniae* (*Mccp*), formerly known as *Mycoplasma* biotype F-38. It was only in 1976 that a mycoplasma designated F38 (renamed *Mccp* in 1993) was confirmed as the primary cause of CCPP. It is a highly contagious respiratory disease, and one of the most severe diseases of goats. CCPP causes major economic losses in Africa, Asia and the Middle East, where it is endemic.

From a taxonomic point of view, *Mccp* belongs to the so-called "mycoides cluster" (see Table 1). Its closest relatives are *Mycoplasma capricolum* subsp. *capricolum* and *Mycoplasma leachii,* which may cross-react with *Mccp,* but the other members of the mycoides cluster, such as *Mycoplasma mycoides* subsp *capri* or *Mycoplasma mycoides* subsp. *mycoides,* may also share similarities.

Epidemiological studies of *Mccp* are still limited; however, genetic analyses have grouped *M. capripneumoniae* isolates into two major clusters representing two evolutionary lines of the organism, five lineages which correspond to geographic regions, or six genotypes (A to F).

M. mycoides subsp. *capri* (a species now containing both *M. mycoides* subsp. *capri* and the former *M. mycoides* subsp. *mycoides* Large Colony type) can cause a disease that resembles CCPP but may have extra pulmonary signs and lesions. Some texts consider *M. mycoides* subsp. *capri* to be a minor cause of contagious caprine pleuropneumonia; however, the World Organization for Animal Health (OIE) defines CCPP as only the disease caused by *M. capricolum subsp. capripneumoniae.* In spite of this evidence, respiratory diseases caused by *M. m. capri* are still referred to erroneously as CCPP, particularly in the Middle East and India[1]. This use of CCPP should be taken into account when reviewing the literature and the vaccine strains.

According to Nicholas[1], the OIE says that a case should only be defined as CCPP when the following criteria have been satisfied:

1. *Mycoplasma capricolum* subsp. *capripneumoniae* is isolated or there is strong serological evidence of the mycoplasma

2. Lesions are restricted to lung and pleura and consist of a pleuropneumonia

3. There is no enlargement of the interlobular septa of the lung

Table 1: *Mycoplasma mycoides* cluster. Adapted from various sources including: http://www.microbiologyresearch.org/docserver/fulltext/ijsem/59/6/1353.pdf?expires=1452577662&id=id&accname=guest&checksum=2F03A9A90406DCBDDA0514A8873B4D4F **and** http://vri.cz/docs/vetmed/58-8-389.pdf

Subcluster	Taxa		Species affected	Disease
	Previous name	Most recent name		
M. mycoides	*M. mycoides* subsp *mycoides* Small Colony (MmmSC)	*M. mycoides mycoide* s (Mmm)	Cattle	CBPP
	M. mycoides subsp *mycoides* Large Colony (MmmLC)	Reclassified as Mmc	Goats and sheep	MAKePS
	M. mycoides subsp *capri* (Mmc)	*M. mycoides* subsp *capri* (Mmc)		
M. capricolum	*M. capricolum* subs *capricolum* (Mcc)	*M. capricolum* subs *capricolum* (Mcc)	Goats and sheep	MAKePS
	***M. capricolum* subsp *capripneumoniae* (Mccp) - formerly known as F38 strain**	***M. capricolum* subsp *capripneumoniae* (Mccp)**	**Goats**	**CCPP**
M. leachii	*Mycoplasma* sp bovine group 7 of Leach (MBG7)	*M. leachii*	Cattle	Mastitis, arthritis
MAKePS: Mastitis, arthritis, keratitis, pneumonia and septicemia.				

Transmission

CCPP is highly contagious. This disease is transmitted during close contact, by the inhalation of respiratory droplets. Chronic carriers may exist, but this remains unproven. Some outbreaks have occurred in endemic areas when apparently healthy goats were introduced into flocks, and in one experiment, a goat developed clinical CCPP nearly three months after contact with infected goats and a month after all other animals had recovered. However, one study that followed a large flock of experimentally infected goats for up to 105 days did not find any chronic carriers.

No evidence of indirect transmission has been shown as the mycoplasma is highly fragile in the environment.

Clinical Signs

CCPP is strictly a respiratory disease. Goats of all ages and sexes are susceptible. Peracute, acute and chronic forms may be seen in endemic areas. Peracutely affected goats can die within 1 to 3 days with minimal clinical signs. The acute form of the disease is characterised by unilateral sero-fibrinous pleuropneumonia with severe pleural effusion. The initial signs are a very high fever, lethargy and anorexia, followed by coughing and labored respiration. The cough is frequent, violent and productive. In the final stages of disease, the goat may not be able to move, and stands with its front legs wide apart, and its neck stiff and extended. Saliva can drip continuously from the mouth, and the animal may grunt or bleat in pain. Frothy nasal discharge and stringy saliva may be seen terminally. Pregnant goats can abort. Acutely affected goats generally die within7 to 10 days.

Subacute or chronic cases tend to be milder, with coughing mainly following activity. Chronic CCPP is characterized by a chronic cough, nasal discharge and debilitation. Infected animals become very sick and mostly die, with high morbidity reaching 100% and mortality of 70%. In some naive flocks, the morbidity and mortality rates may reach 100%.

For a long time, goats were believed to be the only susceptible host for CCPP although it was reported that sheep could be infected and seroconvert in the face of close contact. In CCPP outbreaks in mixed goat and sheep herds, sheep may also be infected, as verified by isolation of *Mccp* or detection of antibodies from clinically affected sheep[2]. Following the introduction of CCPP into Eritrea with the livestock of returning refugees from Sudan, sheep mixing with affected goats were reported to be suffering from respiratory disease. There are also reports from sick sheep mixed with goats in Uganda suffering from the disease and detection of antibodies in sheep in Ethiopia make sheep to be suspected potential carrier of *Mccp*. The role of sheep as a reservoir for the disease has to be considered.

More recently, there have been confirmed reports from Qatar of CCPP in wild captive ungulates including wild goat, Nubian ibex, *Larisstan mouflon* and gerenuk kept in animal breeding parks. Clinical signs in wild or captive wild ungulates have been similar to cases in goats. Even more surprisingly however were the outbreaks of acute respiratory disease in a private collection of captive but free-ranging gazelles and other deer species in the United Arab Emirates in which above 10% died. The disease was almost certainly introduced via sick goats and spread by close contact with the gazelles at feed stations. It is likely that CCPP is far more widespread in wildlife species in the Middle East as a result of infected escapees from these parks[1].

Diagnosis

The diagnosis of outbreaks of respiratory disease in goats, and of CCPP in particular, is complicated, especially where it is enzootic. Definitive diagnosis can be difficult, as *Mccp* is one of the most fastidious mycoplasmas and faint turbidity in liquid medium or colonies on solid medium may appear only after 5–15 days and can be missed

during routine bacteriological analysis. Isolation is often unsuccessful, and detection may be easier with specific molecular methods such as the PCR.

OIE listed tests

Identification of the agent:

- Bacteriology and confirmation by PCR
- Nucleic acid detection: PCR

- Serology: Complement fixation test (CFT), Latex agglutination test (LAT) and cELISA.

Table 2 shows the laboratory methods currently used for the diagnosis of CCPP and their purpose, as specified by the OIE.

Table 2: Tests recommended by the OIE. Source: OIE Terrestrial Manual of Diagnostic tests and vaccines for terrestrial animals, 2015.

Method	Purpose					
	Population freedom from infection	Individual animal freedom from infection prior to movement	Contribution to eradication policies	Confirmation of clinical cases	Prevalence of infection - surveillance	Immune status in individual animals or populations post-vaccination
Agent detection and identification[1]						
In-vitro culture[2]	-	-	-	++	-	-
Molecular tests (PCR)	-	-	-	+++	-	-
Detection of immune response[3]						
CFT	++	++	-	++	++	+
Latex agglutination	+	+	-	+++	+	-
C-ELISA	+++	++	-	++	+++	+++

1- A combination of agent identification methods applied on the same clinical sample is recommended
2- Organisms isolated should be subjected to confirmatory molecular, biochemical or immunological methods
3- One of the listed serological tests is sufficient

Key: +++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; – = not appropriate for this purpose.

Although not all of the tests listed as category +++ or ++ have undergone formal validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable.

Comments on the tests

The gold standard remains the direct isolation and cultivation of *Mccp* from infected lung tissues or pleural fluid collected post-mortem. However, the process is cumbersome and time-consuming. In addition, isolation of the mycoplasma may be hampered by sample contamination and prior antibiotic treatment of the diseased animals.

Moreover, DNA-based confirmation of the cultures using PCR methods is still needed. Thus, culture, isolation, and molecular characterization of *MCCP* is not feasible for rapid containment of a CCPP outbreak.

The development of PCR has greatly improved CCPP diagnosis as it is now possible to detect the mycoplasma quickly even in mixed cultures, directly from clinical material such as pleural fluid and lung samples, or from this material dried on filter paper. Serodiagnosis of CCPP, is a relatively easy task, thanks to the LAT, a rapid, specific and relatively sensitive test developed in Kenya. It uses a carbohydrate extracted from *M. c. capripneumoniae* linked to latex particles, which agglutinate in the presence of specific antibodies in the blood of affected goats[3]. The test, which takes minutes to perform, is more sensitive and easier to perform than the CFT or indirect or competitive ELISA, which should be used for confirmation. Although rapid and applicable for field use, this test is not specific for *Mccp*[4].

A LAT has also been described for circulating antigen and could provide earlier detection in affected animals before antibodies have appeared[3].

Recent developments

In 2014, Peyraud et al[5] published data on a newly formatted CCPP cELISA modified to create a heat stable kit. They concluded that the new formatted CCPP cELISA kit has retained the high specificity of the original kit and can be used to evaluate CCPP prevalence in countries or regions without vaccination programs. However, the paper does not include data comparing the new format with the old format (or with CFT), sensitivity is not evaluated, and specificity is only evaluated using animals from France, a CCPP free country, that might have different disease background that the goats in Africa and/or Asia. Further data might be needed for this kit. This kit is not suitable for detecting acute disease in the field.

Advanced molecular techniques, such as real time PCR, are both sensitive and specific. However, these methods require well-equipped laboratory, expensive equipment, and trained personnel. A loop-mediated isothermal amplification (LAMP) assay for the detection of *M. capricolum subsp. capripneumoniae* has been reported recently[4]. This assay transcends the limitations associated with thermocyclers; however, it still requires DNA extraction protocols and gel electrophoresis to separate DNA products on horizontal agarose gels, which limits the applicability of this method as a field test. Recombinase polymerase amplification (RPA) is another isothermal technique for detecting DNA. Recently, the development of a specific and sensitive assay using RPA for the rapid diagnosis of CCPP directly from clinical caprine specimens (i.e., pleural fluid and lung tissue samples) has been published[4]. They demonstrated the assay to be suitable for field testing using lyophilized test reagents, a car battery for power, and a portable fluorescent illuminator to read the assay output.

Differential diagnosis

Differential diagnosis may be difficult in the field as goats may be infected with a number of mycoplasma species that may induce similar signs. However, CCPP may be suspected when lesions are restricted to the respiratory tract, affect only one lung and when animals present a conspicuous pleurisy with profuse effusion of pleural fluid. CCPP could also be confused with *peste des petits ruminants* (PPR) or pasteurellosis.

Zoonotic disease

CCPP is not a zoonotic infection. There is no known risk of human infection with *Mccp*.

Incidence and Prevalence in Selected Countries

Global

While the clinical disease has been reported in nearly 40 countries in Africa and Asia, *M. c. capripneumoniae* has only been isolated in 20 countries because few laboratories have the expertise for isolating and growing mycoplasmas[1].

The disease was first described in 1873 in Algeria. Shortly after, in 1881, the disease was introduced to South Africa by a shipment of Angora goats. The disease was eradicated using a policy of slaughter of the infected goats coupled with a traditional vaccination procedure for the in-contact goats. The organism was first isolated and shown to cause CCPP in Kenya; it has subsequently been isolated in the Chad, Eritrea, Ethiopia, Niger, Oman, Sudan, Tanzania, Tunisia, Turkey, Uganda, the United Arab Emirates, and more recently in Mauritius, China and Tajikistan. See Figure 1 and Table 3.

Sequence analysis done by Manso-Silvan[6], showed a distinct Asian cluster, indicating that CCPP was not recently imported to continental Asia. It is more likely that the disease has been endemic in the area for a long time, as supported by historical clinical descriptions. There are historical clinical descriptions from India in 1914.

In 2003, CCPP was diagnosed in Thrace, the region of Turkey on the European mainland bordering Greece and Bulgaria, with losses of up to 25% of kids and adults in some herds. Prior to this infection, the only report of CCPP in Europe dates to the 1920s when an outbreak occurred in Greece following the seizure of goats from Turkey although the exact cause was never confirmed. Interestingly, Greece reported two outbreaks of CCPP in 2006 but it seems likely that this was caused by *M. m. capri* which is endemic in Greece rather than *M. c. capripneumoniae* as the mortality rate was <1% of goats in a herd of above 150 (OIE, 2008). It is also likely that the outbreak of CCPP in Czech Republic in 1902 was similarly misdiagnosed; though, it is clearly impossible to confirm over a century later[1].

There have been no reports of the isolation of *M. c. capripneumoniae* on the American continent although other closely related mycoplasmas have been described there.

Serious problems caused by CCPP exist in Oman where nearly 600 outbreaks were reported between 2008 and 2009 with mortality rates of nearly 10% of 30,000 cases. In Iran, 478 outbreaks were seen affecting more than

16,000 goats between 2006 and 2007 (OIE, 2008/2009). New outbreaks were reported in Tajikistan in 2009 with four outbreaks affecting 166 goats, most of which died. A dozen new outbreaks occurred in Yemen affecting more than 800 goats of which just above 200 died. Mauritius became infected for the first time in 2009 following the introduction of goats from the African mainland, and within one month, just more than 300 home-bred goats had died[7].

There have been very few declarations of CCPP outbreaks to the OIE in the last 15 years, due to a lack of awareness of this disease, and possibly confusion with other diseases such as *peste des petits ruminants* or *Pasteurella* infections[5]. The exact distribution of the disease is not known and it may be much more widespread than the zone represented by the countries where *Mccp* has been isolated, as CCPP as already indicated, is often confused with other respiratory infections and also because the isolation of the causative organism is difficult.

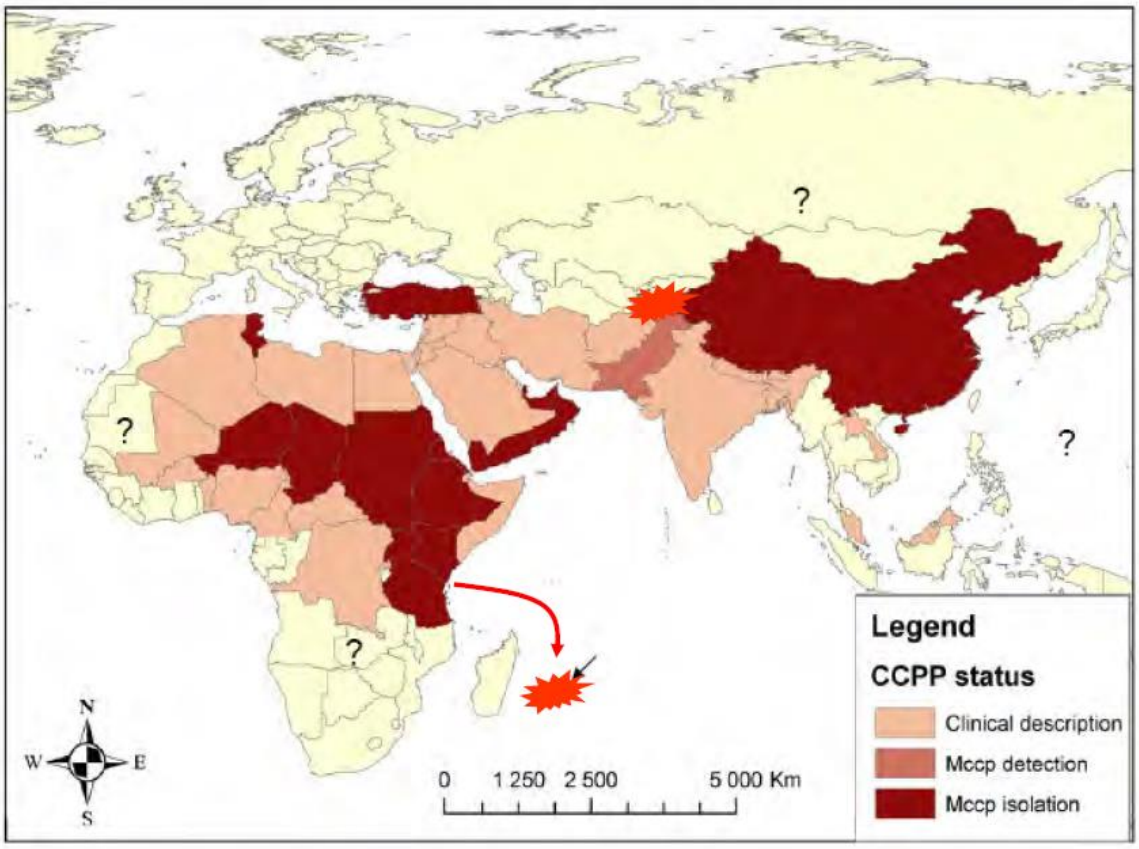

Figure 1: CCPP distribution. Source: F. Thiaucourt. VACNADA Workshop, October 2011, modified from Manso-Silvan, 2011. Spiked areas show the relatively recent outbreaks in Mauritius and Tajikistan.

Table 3: Distribution of CCPP. Source: Mycoplasma diseases of ruminants, 2008. Editors: Nicholas R, Ayling R, McAuliffe L. Page 115. http://www.cabi.org/cabebooks/ebook/20093002833

	Confirmed by isolation of mycoplasma	Clinical disease reported or suspected
Africa	Chad, Eritrea, Ethiopia, Kenya, Niger, Sudan, Tunisia, Uganda	Algeria, Benin, Burkina Faso, Cameroon, Central African Republic, Djibouti, Egypt, Libya, Mali, Nigeria, Somalia, Zaire
Asia	Nepal, Oman, Turkey, United Arab Emirates, Yemen	Afghanistan, Bangladesh, India, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Pakistan, Saudi Arabia, Syria
Europe	Thrace (Turkey)	

Regional

There are two main sources, OIE and AU-IBAR (which includes only Africa), but data are not always similar.

1- Source: OIE.
Data of outbreaks reported to the World Animal Health Organization (OIE) are shown in Tables 4 and 5. Data are not always reliable, as many countries doesn't seem to report, or to be reporting consistently over time.
http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/statusdetail

Similar information but presented in a different manner can be seen in Annex 1.

Number of cases reported to the OIE by disease and by country:

- No information, + Present but quantitative data not known, ? Disease suspected

Table 4: ASIA – CCPP outbreaks notified to OIE from the Asian countries of interest.

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Bangladesh	-	-	?	0	0	0	0	0	0	0	-
India	12	>1	>2	3	+	21	>1	>2	3	2	-
Indonesia	0	0	-	0	0	0	0	0	0	-	-
Myanmar	0	0	0	0	0	0	0	0	0	0	-
Nepal	0	0	0	0	0	0	0	0	0	0	-
Vietnam	0	0	0	0	0	0	0	0	0	0	-

Table 5: ASIA – AFRICA – CCPP outbreaks notified to OIE from the Asian countries of interest.

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso	-	-	-	-	-	-	-	-	-	-	-
Ethiopia	30	31	35	16	6	14	14	23	16	6	-
Ivory Coast	-	-	-	0	0	0	0	0	0	+	-
Kenya	1?	5	6	7	17	5	8	5	6	28	5?
Madagascar	0	0	0	0	0	0	0	0	0	0	-
Malawi	0	0	-	-	0	0	0	0	-	-	-
Mali	-	-	-	-	-	-	-	-	-	-	-
Mozambique	0	0	0	0	0	0	0	0	0	0	-
Rwanda	-	0	?	-	0	?	?	?	?	-	-
Senegal	-	-	-	-	-	-	-	-	-	-	-
South Africa	0	0	0	0	0	0	0	0	0	0	-
Tanzania	>26	22	50	21	10	9	8	5	6	7	6?
Uganda	+	0	0	+	0	0	0	+	+	+	-

Zambia	-	-	-	-	-	-	-	-	-	-	-

2- Source: AU-IBAR.

Number of outbreaks per year as reported to AU-IBAR and published in the Pan African Animal Resources YearBook. (**http://www.au-ibar.org/pan-african-animal-resources-yearbook?showall=&limitstart**=)

Table 6 shows the number of CCPP outbreaks reported to AU-IBAR. Below the table, there are some relevant notes for specific years, that were included in the AU-IBAR reports. Table 7 shows the total number of outbreaks, number of cases, number of deaths and number of slaughtered animals, from all the African countries that reported the disease during the specified periods.

Table 6: Number of CCPP outbreaks per year as reported to AU-IBAR and published in the Pan African Animal Resources YearBook. Please see notes below the table for each year.
NS= Not specified

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso	-	-	-	-	-	-	-	-	-	-	-
Ethiopia	30	31	35	16	6	14	14	23	16	6	-
Ivory Coast	-	-	-	0	0	0	0	0	0	+	-
Kenya	1?	5	6	7	17	5	8	5	6	28	5?
Madagascar	0	0	0	0	0	0	0	0	0	0	-
Malawi	0	0	-	-	0	0	0	0	-	-	-
Mali	-	-	-	-	-	-	-	-	-	-	-
Mozambique	0	0	0	0	0	0	0	0	0	0	-
Rwanda	-	0	?	-	0	?	?	?	?	-	-
Senegal	-	-	-	-	-	-	-	-	-	-	-

South Africa	0	0	0	0	0	0	0	0	0	0	-
Tanzania	>26	22	50	21	10	9	8	5	6	7	6?
Uganda	+	0	0	+	0	0	0	+	+	+	-
Zambia	-	-	-	-	-	-	-	-	-	-	-

2005: No mention of CCPP in the report.

2006: CCPP was reported in three countries only. Out of 289 outbreaks, a total of 3,439 deaths were recorded. Somalia had the highest number of outbreaks (246), followed by Tanzania (41) and Eritrea (2).

2007: Even if Uganda only recorded one outbreak, Uganda reported the highest number of cases (6,403), followed by Tanzania (2,893). Kenya reported only 154 cases and Ethiopia 93.

2008: Uganda again reported the highest number of cases (90,102) but only 1,238 deaths. Ethiopia reported the highest number of deaths (11,244). Tanzania didn't report any outbreaks, but reported 1,536 cases, presumably due to an ongoing outbreak from the previous year.

Table 7: CCPP data as reported in the AU-IBAR Yearbooks.

	2006	2007	2008	2009	2010	2011	2012	2013	2014
# countries	3	5	7	7	8	7	5	7	6
# outbreaks	289	68	68	57	256	280	335	152	117
# cases		10,650	117,651	3,155	12,889	5,833	21,149	4,171	3,729
# deaths	3,439	1,488	12,849	1,037	1,380	1,342	6,124	672	594
# Slaughtered/destroyed		1,648			546	227	439	126	77

Note: 2008 seems exceptionally high for number of cases and number of deaths. Uganda with only 3 outbreaks reported 90,102 cases, but only 1,238 deaths. Ethiopia reported 53 outbreaks, 25,651 cases and 11,244 deaths.

Prevalence data by country

- Sources: PubMed, and internet engine searches (English and French when applicable).
- Efforts have been made to include the year of the study, and not the year of the publication. If they are known to be different, the year of publication is included in the reference.
- Note that not all papers have been read in full. In many cases, only the abstracts have been read. Critical evaluation of the papers for inclusion has not been conducted. If a review paper included some references, the source of the review is mentioned.

ASIA

There is no evidence of CCPP in Indonesia, Vietnam and Myanmar. In Bangladesh, India and Nepal, there are clinical descriptions of the disease, but no isolations or *Mccp* detections[6]. However, Nicholas mentions in the book "Mycoplasma diseases of ruminants", chapter 9, that in Nepal there has been confirmation by isolation.

Bangladesh

Kabir 2015: Report on isolation of mycoplasma from the respiratory system of goats, but no confirmation of species (work done in 2010, published in 2015):

http://www.netjournals.org/pdf/MRI/2015/2/14-021.pdf

India

It would seem that finally *Mccp* has been confirmed in India (Kerala), according to a 2015 abstract. The full paper has been requested to the authors but has not been received so far.

http://www.indianjournals.com/ijor.aspx?target=ijor:ijvp&volume=39&issue=2&article=002T

There is a paper from Ingle et al, 2008 titled "Seroprevalence of Contagious Caprine Pleuropneumonia in goats in Nagpur district of Vidarbha region". However, when reading the paper, it is clear that they were looking for *Mycoplasma mycoides* var *capri* and not for *Mccp*.

http://www.veterinaryworld.org/2008/September/Seroprevalence%20of%20Contagious%20Caprine%20Pleuropneumonia%20in%20goat.pdf

Thiaucourt reported in 1996[8] that numerous publications have documented the presence of goat pleuropneumonia in India without the isolation of *Mccp*. Usually the isolated mycoplasmas belong to *M. mycoides* subsp. *capri*. The only description of *Mccp* isolation in India has been recorded from cattle milk, but doubts have been raised on the exactness of this identification.

http://www.oie.int/doc/ged/D9103.PDF

AFRICA

There is no evidence of CCPP in Ivory Coast, Madagascar, Malawi, Mozambique, Senegal, South Africa and Zambia.

Burkina Faso

Clinical disease has been reported or suspected but no details available. See Table 2 and reference[5]

Ethiopia

The presence of CCPP in Ethiopia was suspected since 1980 and confirmed later in 1990. Since then, the disease has become endemic in different regions of the country with repeated outbreaks being reported in Tigray, Afar, Dire Dawa, SNNP, Oromiya, Benishangul-Gumz, and Amhara regional states. It is more prevalent in the arid and semi- arid low land areas of Rift Valley, Borena range lands, South Omo, Afar and other pastoral areas of Ethiopia. These same regions are home to about 70% of the national goat population.

According to the outbreak reports map for CCPP from 2007 to 2011 (Figure 2), the highest number of outbreaks were reported in Oromiya, Afar, Somali and SNNP Regional states. It is notable that the areas with the highest number of reported outbreaks are bordering Northern Kenya, Somalia and South Sudan. The outbreaks are also concentrated along the borders between regions. This distribution is attributed to pastoral nature of the production system with animals moving freely within and across the country the borders.

The outbreak reports alone do not give the true picture of the disease prevalence due to the poor disease reporting across the country and the fact that the reports are based on clinical signs. However, the trends of the outbreak reports when combined with the available different serological studies done overtime and consultation with stakeholders, give a clear indication that the regions where CCPP is highly prevalent are Afar, SNNP and Oromiya, especially along the border with Kenya and Somali. Discussions with key informants also emphasized that the Somali and Gambella regions could be other hot spots but there was no data to support this. The two regions are somewhat marginalized, which could explain the lack of data.

Year	Area	Species of animal	No. samples tested	% positive	Reference
2014	Dassenech (South Omo)	Goats	184	87	Molla, 2015
2012-2013	Borana pastoral area	Goats	510	31.6	Lakew et al, 2014
2012*	Dubti and Hadar (Afar region)	Goats	1,000	cELISA Individual: 14.6	Peyraud et al, 2014[5]

2011-2012	Dire Dawa (Eastern Ethiopia)	Goats	244	4.92	Yousuf et al, 2012
2011-2012	Jijiga, Kebri Beyah and Tuli Guled Districts of Jijida.	Goats	334	Jijiga 34 Kebri Beyah: 33.64 Tuli-Guled: 28.38 Total: 32.63	Sheirf et al, 2012
2011	Lare, Itang and Gambella Zuria (Gambella Regional State)	Goats	Lare: 389 Itang: 497 Gambella: 266 Total: 1,152	Lare: 12.6 Itang: 24.3 Gambella Zuria: 14.7 Total: 18.1	Fasil et al, 2015
2011	Borana and Guji lowland	Goats	900 (300 per location)	Moyale: 9.7 Teltale: 11.7 Liban: 18.3 Total: 13.2	Bekele et al, 2011
2009	Kefta Humera, Alamata (Tigray) and Aba-'ala (Afar)	Goats and sheep	Goats: 863 Sheep: 137	CFT Goats: 32.68 Sheep: 18.25	Hadush, 2009
2008	Afambo, Assaita, Dubti, Mille, Gewane, Amibara, Dewe and Telalak (Afar region)	Goats	Afambo: 135 Assaita: 11 Dubti: 16 Mille: 8 Gewane: 74 Amibara: 30 Dewe: 9 Telalak: 46 Total: 329	Afambo: 31.85 Assaita: 36.36 Dubti: 18.75 Mille: 12.50 Gewane: 12.16 Amibara: 10 Dewe: 22.22 Telalak: 19.56 Total: 22.49	Regassa et al, 2010
2007	Abattoir receiving animals from Borena, Bale, Afar and Jinka.	Goats	300	CFT. 31	Eshetu, 2007

2005-2006	Southern Ethiopia	Goats	913	18.61 Sedentary: 27.78 Pastoral: 15.46	**Mekuria, 2010**
2005-2006	ELFORA export abattoir	Goats	Serology: Awash: 224 Dire Dawa: 200 Borana: 280 Lung inspection: 704	CFT Overall: 48.3 Awash: 47.3 Dire Dawa: 44.5 Borana: 51.8 cELISA: 11.8 Awash: 17 Dire Dawa: 5,6 Borana 11.7 Lung inspection: Awash: 14.7 Dire Dawa: 9 Borana: 15.5	**Gizaw et al, 2009**
2004-2005	Hammer and Benna-Tsemay (Southern Omo)	Goats	679	15.5	**Mekuria et al, 2008**
2003	CCPP not reported before: N. Shoa and Wollo. CCPP reported before: Afar, Yabello, Metehara, Arsi, Borena, Konso, Awash.	Goats	767	Areas CCPP not reported: CFT *Mccp*: 23 Blocking ELISA: 2 CFT MmmSC: 12 Areas CCPP reported: CFT *Mccp*: 60 Blocking ELISA: 83 CFT MmmSC: 87	**Sharew et al, 2005**

* Year of sampling not specified, but suspected based on the relation to VACNADA project sampling

Ivory Coast

According to the OIE database, the disease was reported in 2014, but no other evidence has been found of CCPP presence or suspicion in the country, neither searching the web in French, which creates doubts about the OIE report.

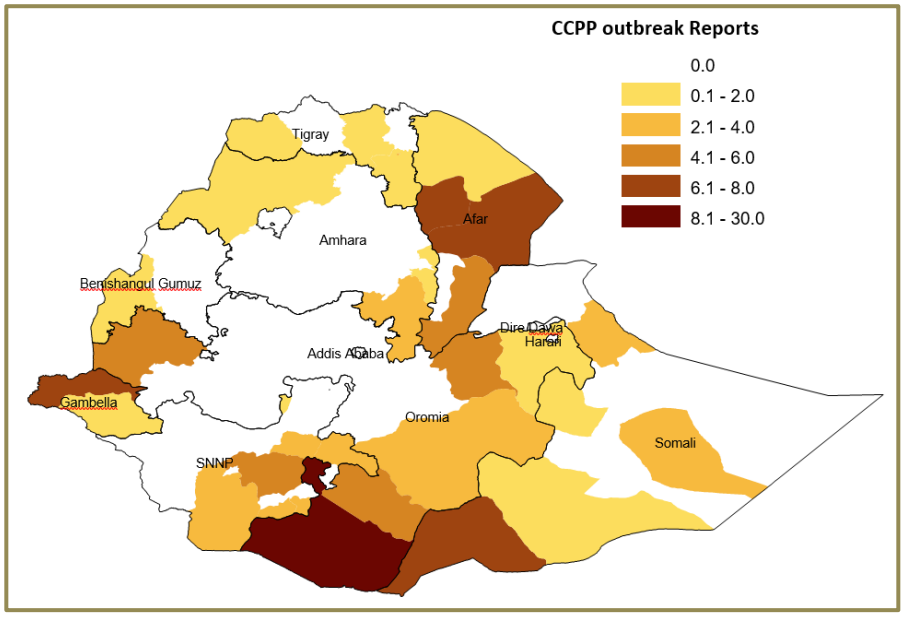

Figure 2: CCPP outbreaks in Ethiopia, 2007 – 2011. Source: Ministry of Agriculture, Animal and Plant Health Regulatory Directorate, 2007-2011. Animal Health Service Status in Ethiopia. Epidemiology unit data on diseases outbreaks, Addis Ababa, Ethiopia.

Kenya

Mccp was first isolated from the lungs of goats with pleuropneumonia in Kenya and demonstrated to cause CCPP in 1976.

Despite frequent reports to OIE and AU-IBAR, there information about prevalence is very limited.

Year	Area	Species of animal	No. of samples tested	% positive	Reference

2014-2015	Rift Valley Region	Goats	432 from 54 flocks	Turkana West: 63.9 Kajiado Central: 48.6 Pokot East: 29.2	Kipronoh et al, 2015
2012?	Area around Narok	Goats	895 (10 herds)	6-90% depending on the herd	Peyraud et al, 2014

Mali

In Mali, goats have been suspected of infection based on serological evidence (Rurangirwa et al., 1990 http://www.cabdirect.org/abstracts/19902214660.html) when using the LAT test, 37% out of 954 goats tested positive. However, the causal agent has never been isolated up to today.

During implementation of the VACNADA project in 2012, a serological survey using c-ELISA showed a prevalence of 2.03% nationwide with the highest prevalence in Koulikoro (4.69%), Segou (2.41%) and the Bamako District (2.38%) as indicated in the Table below.

Seroprevalence of CCP in Mali

Régions	Cercles	Sites	%
Kayes	Kayes	Kayes	3.33
	Kita	Kita	15.38
	Nioro	Nioro	1.48
		Tourourou	0
		Diandioume	0
Koulikoro	Banamba	Banamba	5.56
	Kati	Kati	4.49
	Nara	Nara	4.76
Sikasso	Bougouni	Bombala	0
		Bougouni	0
		Kologo	1.43

	Kolondieba	Kolondieba	1.18
	Sikasso	Sikasso	20
	Yanfolila	Yanfolila	0
Ségou	Baroueli	Bando	0
		Boboti III	2
		Diabougou	6.17
	Bla	Bla	0
	Macina	Kerimetomo	0
		Kossala	0.78
		Macina	5.56
		Sarro	0
		Yiribadougou	0.65
		Souleye	1.34
	Niono	Niono	3.77
	Ségou	Ségou	1.03
	Tominian	Tominia	5
Mopti	Koro	Briga dogon	5.88
		Briga peul	0
Tombouctou	Tombouctou	Tombouctou	0
Bamako	Bamako	Commune I	0
		Commune II	0
		Commune III	0
		Commune IV	0

		Commune V	0
		Commune VI	14.29
Total			2,03

Rwanda

There seems to be clinical description of the disease, but *Mccp* has not been detected or isolated[6] in Rwanda.

Tanzania

CCPP is thought to have been in Tanzania since 1980s. It was only confirmed in 1998 and is now assumed to be endemic in most of goat rearing regions of Tanzania[9].

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2013	Manyara Region	goats	Mbulu: 82 Babati: 100 Hanang: 81 Kiteto: 80 Simanjiro: 56 Total: 399	Mbulu: 29.3 Babati: 65 Hanang: 54.3 Kiteto: 77.5 Simanjiro: 71.4 Total: 58.9	Wambura, 2014
2013	Kongwa (Dodoma) and Mvomero (Morogoro)	Dairy goats	129	26.4	Shija et al, 2014
2012	Musma district (Mara region)	Goats	320	64.4	Nyanja et al, 2013
2010	Babati and Arumeru	Goats	337	Animal level: 3.3 Flock level: 9.6 Village level: 31.5	Swat et al, 2013
2007 and 2009	Mtwara and Lindi regions (Southern Tanzania). Retrospective studies	Goats and sheep	2007: Goats 447, sheep 30 2009:	2007: Goats: 52.1 Sheep: 36.7 2009:	Mbyuzi et al, 2014

			Goats 434, sheep 70.	Goats: 35.5 Sheep: 22.9	

Uganda

The disease was first confirmed in Uganda in 1995 in Karamoja region (**http://www.ncbi.nlm.nih.gov/pubmed/8748175**).

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2013	Karamoja region (Kotido, Kabong, Abim and Amudat)	goats	220	33.18	**Emmanuel, 2013**
2011	Agago and Otuke districts	Goats	Agago: 181 Otuke: 223	Agago: 17.7 Otuke: 23.3	**Atim, 2013**

Economic and Social Impacts at Global and Regional Levels, and in Selected Countries

CCPP is a highly contagious and fatal disease of goats and it has been described as the most serious infection of goats in East Africa. Goats are important animals providing meat, milk, and hides. CCPP has both direct and indirect effects on goat production. A specific risk for CCPP is that it has been spreading beyond its traditional distribution area due to lack of diagnostic capacity in most countries; poor transportation access to the affected areas and inadequate availability of control tools.

Morbidity, mortality and production

Direct losses due to CCPP are associated with the high morbidity and mortality rates (100% and > 60% respectively) which results in loss of income from sales of live animals and animal products (meat, milk and skins) and reduced productivity of the affected animals in the form of reduced weight gains and decreased milk production. The costs of diagnosis, treatment, and control all have a direct effect on the goat owners.

Indirect losses

Indirect losses are associated with the extra cost of treatment, increased risk associated with antibiotic residues and reproductive wastage.

There are also indirect losses due to the implementation of trade restrictions. Because CCPP is a transboundary animal disease (TAD), which can easily spread to other countries through uncontrolled movement of animals, it is a major constraint to international trade in the affected countries.

Social impact

In most goat production systems in Africa, goats are often an important source of income for women and CCPP therefore negatively impacts on the ability of women to provide for their children and family needs. Goats have the advantage over cattle of recovering faster following droughts.

- Kenya: Kabaka et al reported a participatory epidemiological Research conducted in Turkana in 2011 to identify the two most important livestock diseases, and then characterize their incidence and the economic impact. The research focused on PPR and CCPP. CCPP was described to be an endemic disease known by the community for a long time and had a median morbidity rate of 50% (with range of 39 to 75%) and a median and range case fatality rate of 62% and 40 to 85%, respectively. These losses led to reduced income and food insecurity at the household levels. The biggest challenge to livestock farming (which contributed to 75% of the livelihood) was recurrent drought, insecurity and diseases, with CCPP and PPR being considered as having the largest impact. Respondents indicated that these challenges have made people worse off than they were 20 and 10 years ago and more reliant on external food aid.

http://www.ajol.info/index.php/bahpa/article/view/84380

Economic impact

Very little information is available on the quantification of the economic losses due to CCPP.

- GALVmed website mentions that CCPP causes major economic losses in endemic areas, and the total yearly cost of the disease is estimated to be US $507 million. There is no reference or any details in how the calculation has been made so it is not clear if it includes indirect costs or not. Literature searches have not yielded any similar results. (**https://www.galvmed.org/?s=contagious+caprine+pleuropneumonia**)

- India: A publication from Dr Singh in 2008 (**http://ageconsearch.umn.edu/bitstream/47686/2/18-B-Singh.pdf**) that models the economic losses due to some important diseases in goats in India, includes calculations for CCPP. It is not clear if it is "only" CCPP, or if it also includes losses due *Mycoplasma mycoides* var *capri*, as there is a frequent confusion in India.

His estimations were that from the years 1991 to 2005, the average annual losses due to CCPP were 17.04 lakh (which is 1,704,000 million, and in June 2008 would have been the equivalent to USD 39,767). The cost for CCPP is in fourth place, well behind FMD (37.9 lakh), Sheep and goat pox (37.25 lakh), and PPR (91.42 lakh).

Disease Prevention and Control Methods

Treatment (Control)

Antibiotics such as tetracyclines, fluoroquinolones and the macrolide family are generally clinically effective if used early enough. Streptomycin is not advisable because of rapid appearance of streptomycin-resistant strains. The duration of the treatment should always be at least 5 days, and all the animals that have been exposed should be treated. In remote areas and/or nomadic herds, long-acting formulations are preferred in order to achieve a complete treatment.

However, the complete elimination of the mycoplasma is rarely achieved, and treated animals are considered to be potential carriers. Further work is necessary to determine whether such a risk actually exists as the infection window in goats appears to be quite small[1].

Unfortunately, failures of treatment and recurrence of the disease in the long term are not infrequent, especially when recommendations are not followed, as sometimes occur under field situations.

Prophylaxis (Prevention)

Sanitary Prophylaxis

Prevention and control of CCPP is undertaken through vaccination, quarantine, movement controls, slaughter of infected and exposed animals and cleaning and disinfection of premises.

Quarantine of infected stock is very important. Markets might have to be temporarily closed and goat movements banned.

Vaccines for the prevention of CCPP can be useful. Unfortunately, they are not easily available. In some countries like Tanzania, they do not have a market authorization. For more details, see Section 6.

Options and strategies for control programs at national, sub-national or regional level

AU-IBAR in its recently published Standard Methods and Procedures (SMPs) for control of CCPP in the Greater Horn of Africa recommends as part of the disease response (**http://www.au-ibar.org/training-manuals-and-tools**):

1. Movement control

   Regulate movement for index flock and contact flocks by monitoring livestock movement control (checks posts, stock routes and border posts); control and regulate livestock markets in the infected and surrounding areas; any goat movement will be as directed by an authorized veterinary officer and a movement permit shall accompany moving animals; develop a harmonized regional policy enabling veterinary authorities to enforce movement control.

2. Quarantine

   Identify area to be quarantined and apply quarantine measures as laboratory confirmation is awaited. Once CCPP is confirmed apply full quarantine in the identified area.

3. Vaccines and Vaccination

   There is an effective vaccine, inactivated *Mccp* vaccine (Formerly F38), for the effective control of CCPP. Vaccination should aim at covering 100% of the population to control CCPP. Coordination between neighboring geographical areas and countries in vaccination is very important to control the spread of disease across the region. It is recommended to use the quality assured/certified vaccine (AU-PANVAC Certificate). Sero-monitoring before and after field vaccination will be required.

AU-IBAR also suggests different disease prevention and control approaches in the different areas depending on the disease status:

1. Area of no known disease status

   Efforts in this area will be undertaken to determine the disease status that will hence advice control measures.

2. Disease-free area

   Vaccinations for CCPP will not be carried out in this area. However, intense surveillance involving clinical examination and certification of goats in the area will be undertaken. Goats movement to and from the area will be closely monitored by the authorized veterinary personnel.

3. Endemic Areas

All goats over 6 months of age will be vaccinated bi-annually. Use only certified vaccine to control outbreak (AU-PANVAC). Records of all vaccinated livestock must be properly kept; sero-monitoring shall be conducted on a randomly sampled population to confirm vaccination efficiency and vaccine efficacy. Further vaccination is carried out as determined by epidemiology and risk analysis. Mobilization of the community and awareness creation is required. There should be immediate notification of the diseases to OIE, AU-IBAR and RECs. Resource mobilization (financial and human)/ operationalization of contingency plans are required; and lastly, there is permanent identification of vaccinated animals using approved official methods.

4. Epizootic Phase

In case an area is declared infected as a result of confirmed CCPP outbreak in any one of the described diseases status areas, the following measures can be put in place: Mass vaccination in the infected area through ring vaccination, and markets closed in response to the outbreak.

Both quarantine and movement control as disease control tools should be enhanced. The objective of movement control and quarantine is to minimize the spread of disease and to mitigate its spread.

- Movement control: Regulation of livestock movement is a routine activity and animals are only moved when their health status does not pose a risk to animals in their destination.
- Quarantine: The application of quarantine is not very useful as it is difficult to enforce in pastoral systems.

5. Test and slaughter and treatment of sick animals

Test and slaughter policy can be considered whenever applicable. If some animals test positive the 'test and slaughter' principle may apply, where owners sell the animals for slaughter under supervision. Re-stocking should require all entries to test negative for CCPP.

Disease situation and government policies by country

Tables 8 and 9 below have been completed with the information received from the questionnaires sent to the DG and DVS for CCPP.

Table 8 covers the disease situation (if it is notifiable or not), the presence of official surveillance and/or control programs, and the treatment situation. Table 9 refers to the vaccination situation.

The definitions that were given to the respondents are:

[1]Surveillance: is the systematic ongoing collection, collation and analysis of data and the timely dissemination of information to those who need to know so that action can be taken.

[2]Control: a program which is approved, and managed or supervised by the Veterinary Authority of a country for the purpose of controlling a vector, pathogen or disease by specific measures applied throughout that country, or within a zone or compartment of that country.

It is interesting to note that for example Kenya produces the vaccine, and does not allow treatment, while Tanzania does not produce the vaccine, and authorizes treatment. For more information on the use of the CCPP vaccine in Tanzania, please see Wambura 2014 Report.
http://vetvac.org/galvmed/docRep/docs/40_Promoting_Access_to_CCP_Vaccine_and_Vaccination_in_Tanzania_Baseline_Study_in_Manyara_Region._Draft_Report.pdf

Table 8: Official status, official programs and treatment for CCPP in the countries of interest. Information provided by the questionnaire sent to the DG/DVS as part of this monograph. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa.

Country	Notifiable (yes/no)	Official surveillance[1] program (yes/no) (if yes, active or passive)	Official control[2] program (yes/no)	Treatment (Chemotherapy)	
				Treatment authorised (yes/no)	Frequently practiced (yes/no)
ASIA					
Bangladesh	No	no	No	No	No
Myanmar (Burma)	No	No	No	No	No
Nepal	Yes	Yes, passive	No	No	No
Vietnam	No	No	No	-	-
AFRICA					
Côte d'Ivoire (Ivory Coast)	Yes	Yes, passive but active in case of an outbreak	-	-	-
Kenya	No	Yes	No	No	No

Malawi	Yes	Yes, passive	No	N/A	N/A
Mali	-	-	-	-	-
Rwanda	Yes	Yes, active and passive	Yes	No	No
Tanzania	Yes	Yes, passive and active	No	Yes	Yes
Uganda	Yes	No	No	Yes	Yes
Zambia	Yes	Yes, passive	No	N/A	N/A

Table 9: Vaccination for CCPP in the countries of interest. Information provided by the questionnaire sent to the DG/DVS as part of this monograph. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa.

Country	Vaccination			
	Compulsory vaccination (yes/no)	Who pays for the vaccine (Government, farmers, combination, others-specify)	Who delivers the vaccine (official, private vaccinators or both)	Species vaccinated (cattle, sheep, goats, pigs, poultry)
ASIA				
Bangladesh	No	N/A	N/A	N/A
Myanmar (Burma)	No	-	-	-
Nepal	No	N/A	N/A	N/A
Vietnam	No	-	-	-
AFRICA				
Côte d'Ivoire (Ivory Coast)	-	-	-	-
Kenya	No	Farmers	Both	Goats

Malawi	No	N/A	N/A	N/A
Mali	-	-	-	-
Rwanda*	Yes	Farmers	Official	Cattle
Tanzania	No	Farmers	Private	Goats
Uganda	No	Combination	Official	Goats
Zambia	No	N/A	N/A	N/A

*: There seem to be a confusion with the reply from Rwanda as they mention vaccinating cattle. Also the vaccine is not produced in the country, and they did not mention that were importing the vaccine (see Table 12).

Vaccines Available

An experimental attenuated live vaccine was tested with some encouraging results in 1978 by MacOwan and Minette[10]. In that study, 20 inoculated goats received 10 ml of a 24 h log phase culture of mycoplasma strain F38 at the 235th passage in broth containing 10^9 colony forming units, by the intratracheal route. They were challenged by an in-contact method, and 9 were clinically affected and one died. In the control group, all 20 were clinically affected, and 7 died[10]. However, this vaccine didn't progress.

Since then, a number of different preparations have been produced, including a vaccine composed of sonicated antigens emulsified with incomplete Freund's adjuvant, that did not progress either.

An inactivated vaccine was developed later, in 1987 by Rurangirwa et al[11]. Several experiments demonstrated that an effective vaccine for CCPP could be made with inactivated F38 mycoplasma. Evaluation of the amounts of lyophilised F38 mycoplasma plus saponin showed that the optimum formulation was 0.15 mg of *Mccp* in saponin. Saponin inactivates the mycoplasma and provides the adjuvant effect necessary to stimulate a protective immune response. In the original publication, the concentrated antigen was freeze dried and reconstituted extemporaneously with a diluent containing 3 mg of saponin per ml. Such a procedure ensured a very long shelf life for the concentrated antigen (>14 months) at either 4°C or 22°C without losing its immunising potential. A single immunisation with the optimum formulation produced a protective immune response in goats that lasted for longer than one year. This vaccine based on the F38 strain, is the one currently being used to produce vaccines in Kenya and Ethiopia. It is also the one being used in Jordan.

According to the OIE Terrestrial Manual, due to the fastidious nature of *Mccp*, the production of CCPP vaccines is costly. *Mccp* requires very rich media, the yield is limited, the procedure involves a purification processs, and inactivated vaccines also require larger amounts of antigen compared with live vaccines.

CCPP vaccines should be safe. The fact that live *Mccp* strains do not induce post-vaccine reactions could be an advantage for this kind of vaccine. For inactivated vaccines containing saponin, the pro-inflammatory effect of the saponin has to be verified as it may vary according to the producers or batches. It is not recommended to vaccinate pregnant animals because of a possible reaction to saponin

Currently, there are only CCPP inactivated and adjuvanted vaccines commercially available. For more details see Table 10.

It is of interest to note that there are some references in the literature and in the databases searched, that mention live attenuated CCPP vaccines being currently manufactured in Turkey. They are Pulmovac (manufactured by Vetal) and Capridoll (manufactured by Dollvet). However, looking at the web information in detail, it comes clear that they include the BQT Mycoplasma, that is not a *Mccp*, but *Mycoplasma mycoides* subsp *capri* (Mmc) – See Table 1.

Pulmovac: http://www.vetal.com.tr/Urun/PULMOVAC/59

Capridoll: http://www.dollvet.com.tr/urun-detay/Capridoll.html

CCPP vaccines in China

There seems to be some CCPP vaccines available in China: at least one from Harbin Pharmaceutical Group, and one from CAHIC (China Agriculture Vet. Bo. Science and Technology Co. Ltd). http://www.cahic.com/pham/index.php?optionid=357&auto_id=532

According to the research conducted by Shumin Li, the vaccine manufactured by Harbin Pharmaceutical group, is an inactivated vaccine based on the C87-1 strain, which is a *Mycoplasma mycoides* subsp *capri.* CAHIC does no longer produces the vaccine, but they were also using the strain 87-1.

Vaccine improvements

The inactivated vaccines require a large amount of antigen, and Kenya and Ethiopia (the only two African manufacturers of CCPP vaccines) are struggling to satisfy the demand. Vaccine improvements will make possible to ultimately reduce the input of antigen from 0.15 mg/dose to something more common like 25 to 70 µg/dose.

During the VACNADA Project, GALVmed supported several process improvements for the CCPP vaccines conducted at KEVEVAPI (supported by consultant Keith Haffer), NVI Ethiopia (supported by Pfizer fellow Paul Dominowsky) and the Process Development Lab at AU-PANVAC (Cellution was engaged to develop a simple process to increase the productivity). The plans going forward were to combine and re-evaluate the different processes at the PDL, but this activity is no longer supported.

Quality control

Current methods for quantifying specifically the antigen load (vaccine potency) are not reliable. The current essay used is the total protein quantification, using the bicinchonic acid (BCA) protein test, that is not specific for the protein of interest. Any irrelevant protein present in the final product will also be measured.

There is also no certainty whether the protective antigen should be just the protein, the LPS or both. Methods to quantify the 2 were developed under VACNADA (Keith Haffer worked on a test to estimate the capsular polysaccharide, and AU-PANVAC on the protein measurement), but they have not been assessed and correlated to vaccine potency and efficacy.

AU-PANVAC developed an immunocapture ELISA (ICE) to detect and quantify specifically *Mccp* protein in CCPP vaccine and to use this essay as an alternative to assess vaccine potency. Dr Charles Sanne-Bodjo from AU-PANVAC confirmed that they are planning to work for the validation, and assistance would be appreciated.

Table 10 summarises the characteristics of the current *Mccp* vaccines.

Table 10: Vaccination for CCPP in the countries of interest. Information provided by the questionnaire sent to the DG/DVS as part of this monograph. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa.

	Mccp (F38 biotype)	Mmc C87-1 Strain
Status	Currently manufactured in Kenya, Ethiopia and Jordan	Developed in China.
Type	Inactivated *Mccp* , using F-38 Kenyan isolate	Inactivated *Mmc* , using C87-1 strain
Origen	Strain isolated in Kenya	
Target species	Goats	Goats
Indications	Vaccinate animals over 3 months of age (in case of an outbreak, can be 2 months)	
Immunity	Revaccinate every 6 months (Kenya, Jordan), 1 year (Ethiopia). According to the OIE manual, should be 1 year.	Revaccinate annually
Route	SC (thoracic wall area or elbow is advisable)	SC or IM
Dose & volume	Each dose contains a minimum of 0.15 mg of mycoplasma (1 ml)	Adult goats: 5 ml Kids 6 months of age: 3 ml Vaccine concentration: 0.1 g/ml
Adjuvant	Saponin (inactivating agent and adjuvant). 3 mg per dose	
Serology on standard tests		
Withdrawal period	Zero days	
Efficacy	At least 90% protection	
Zoonotic characteristics	No	No
Use in pregnant animals	No (potential reactins to saponin)	
Other side effects	A slight oedematous reaction is induced by saponin in less 5% of the animals, which normally disappears in 48 hours.	Generally no adverse reactions
First used	1989	
Large scale use	Yes. Over 10 years ago	
Others	Supply not enough to cover needs	Still available in China by at least one manufacturer

Main vaccine needs:
There is a need for a vaccine that has/is:
1- Easier and cheaper to produce
2- Longer duration of immunity
3- Compatible for combinations

Table 11: Manufacturers of CCPP vaccines in Asia and Africa.

Manufacturer	Country	Name & Strain	Vaccine Type	Countries distribution
ASIA				
China Animal Husbandry Group	China		Killed	
AFRICA				
KEVEVAPI	Kenya	Caprivax TM *Mccp* (F38)	Killed	Ethiopia, Kenya, Somalia, Uganda, UAE.
National Veterinary Institute - NVI	Ethiopia	CCPP vaccine *Mccp* (F-38) Kenyan	Killed	Ethiopia
Jordan Bio-Industries Center (JOVAC)	Jordan	Jovaplasm C Mycoplasma capricolum (formerly F38 biotype)	Killed	Ethiopia, and Middle East

Commercial vaccines manufactured in Africa and Asia

The information summarized in Table 12 is based on the questionnaire sent to the Directors of Veterinary Services office and regulators of the countries of interest. Note that some vaccines might have been imported under DVS dispensation, and they are not necessary licensed in the country. Replies were not received from India, Indonesia, Burkina Faso, Ethiopia, Madagascar, Mozambique, Senegal and South Africa.

Table 12: Commercial CCPP vaccines imported into the countries of interest

Country	Vaccine name	Strain or type	Country of origin	Doses imported 2015	Doses imported 2014	Doses imported 2013	Doses imported 2012
ASIA							
Bangladesh	-	-	-	-	-	-	-
Myanmar (Burma)	-	-	-	-	-	-	-
Nepal	-	-	-	-	-	-	-
Vietnam	-	-	-	-	-	-	-
AFRICA							
Burkina Faso							
Côte d'Ivoire (Ivory Coast)	-	-	-	-	-	-	-
Kenya	-	-	-	-	-	-	-
Madagascar							
Malawi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Mali	-	-	-	-	-	-	-
Rwanda	-	-	-	-	-	-	-
Tanzania	-	-	-	-	-	-	-
Uganda*			Kenya	0	0	500,000	0
Uganda**	CCPP vaccine	F38-biotype	Kenya	400,000	0	0	0
Zambia	-	-	-	-	-	-	-

- Questionnaire received, no information provided.

*: Information provided by the Regulatory Agency

**: Information provided by the DVS office. They also added that they imported 1,080,000 doses in 2011 from KEVEVAPI/KENYA

Other comments:

- JOVAC, the manufacturer from Jordan was also sent a questionnaire designed for key importers into the region. They confirmed that they export CCPP vaccine to Africa. They did not specify the countries or the volumes.

Combination vaccines

- Current use: There are no commercial vaccines including CCPP as combination.
- Desirable combinations: A combined vaccine with PPR will be desirable in view of the imminent PPR global eradication campaign. Combination with other diseases relevant for goats in the specific areas from the production or zoonotic point, for example sheep and goat pox, pasteurellosis or brucellosis, might also be of interest.

Characteristics of Ideal Vaccine Candidates for Smallholders

The Target Product Profiles (TPPs) reflect the availability and utility of current agents and incorporate features that will be necessary to improve on the current products and to address unmet needs, taking into account the particular requirements of the poorest livestock keepers.

The TPPs are more robust when they include the opinions and consider the needs of the different stakeholders. While efforts have been made to encompass them, the TPP showed in Table 13 below, should be considered a proposal, a live document subject to improvements.

Information on current vaccines has been obtained from the datasheet of different products as per links below:

Caprivax TM (Kenya): **http://www.kevevapi.org/index.php/products/item/16-caprivax-tm**

CCPP vaccine (Ethiopia): **http://www.nvi.com.et/products/vaccines-against/ruminant-and-equine-diseases/ccpp-2/**

Jovaplasm C (Jordan): **http://www.jovaccenter.com/userfiles/file/9-06-2014/Large%20Animals%20Vaccines%20/Jovaplasm%20C-En.pdf**

Table 13: Target Product Profile (TPP) CCPP vaccine – Proposal:

	Attribute	Minimum (current available vaccine)	Ideal
1	Antigen	Immunogen with protective antigens for *Mccp*	Immunogen with protective antigens for *Mccp*
2	Indication for use	For active immunization of goats to prevent incidence of CCPP	For active immunization of goats to prevent infection with *Mccp*

3	Recommended species	Goats	Goats (and sheep if their carrier role was demonstrated)
4	Recommended dose	0.15 mg of mycoplasma (1 ml)	<0.15 mg mycoplasma 1 ml
5	Pharmaceutical form	Suspension	Ready to use solution/suspension
6	Route of administration	SC	SC or IM
7	Regimen - primary vaccination	One dose	One dose
8	Regimen - booster	6 -12 months booster (depending on manufacturer)	Lifelong immunity after primary vaccination
9	Epidemiological relevance	Single vaccine for global use	Single vaccine for global use
10	Recommended age at first vaccination	3 months of age (can be 2 in the face of an outbreak)	1 -2 months of age
11	Onset of immunity		One week following primary vaccination
12	Duration of immunity	6 – 12 months	Lifelong immunity
13	Expected efficacy	Claims for current vaccines are not clear. OIE says protection rate should reach at least 90%.	To prevent infection and transmission in 100% of the animals.
14	Expected safety	Small reaction at injection site might occur in less than 5% of the animals. Do not use in pregnant animals.	No local or systemic post-vaccinal reactions. Safe for pregnant animals.
15	Withdrawal period	Nil	Nil
16	Special requirements for animals	Do not vaccinate un-healthy animals or during an outbreak.	Vaccinate all animals

17	Special requirements for persons	None	None
18	Package size	50 - 100 doses	Multiple pack size from 50 doses
19	Price to end user		
20	Storage condition and shelf-life as packaged for sale	Store at +4°C. Do not freeze. If stored at between +2°C and +8°C the shelf life is one year.	≥ 24 months 4-8° C and 48 hours at 30° C
21	In-use stability		48 hours or greater
22	Other		

Key Conclusions Related to Vaccination

Short-term Solutions: Live, attenuated and killed, inactivated NDV vaccines are effective, and can produce protective titers when applied properly. The first approach would be to 1) improve disease detection using rapid test kits; 2) improve reporting; 3) and optimize the access and delivery of vaccines in the field since it is a limiting gap regardless of the vaccine that is used. Thermostable vaccines currently are closest to the ideal vaccine for use in smallholder poultry. Proper delivery of vaccine to smallholder with community engagement is a key gap to overcome logistical challenges for the safe and effective delivery of vaccine.

Medium-term Solutions: 1) The further development of reverse genetics vaccines antigenically matched with the field strain genotype will optimize the immune response (level and duration of immunity) in typical currently available vaccine strains. Investment in the collection and molecular analysis of country-specific field strains will be required. 2) Improvement in diagnostic tests in vitro (cell culture) and rapid tests in the field will also be needed.

Long-term Solutions: There are two main needs: 1) Further refinement of a vaccination model multivalent, non-replicating, antigenically matched and epidemiologically appropriate; 2) Development of breed lines of native poultry with high levels of innate genetic resistance to further reduce replication and to increase vaccine efficacy. Needs assessments are recommended to assess the need for a multivalent NDV vaccine in combination

with infectious bursal disease (IBD) vaccine or other priority poultry disease, which also result in significant losses in some regions.

Limitations

Scientific quality: The publications and data from the different research groups, should be carefully evaluated. The use of good science and good experimental design with use of proper controls, adequate numbers, suitable challenge model, reproduction of results by them and by independent groups, and appropriate analysis has not been verified for this monograph. If any of these projects were to be pursued, a detailed peer review taking into account the above considerations is strongly recommended.

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ANNEX 1: Additional data on disease presence and incidence

Key to colours

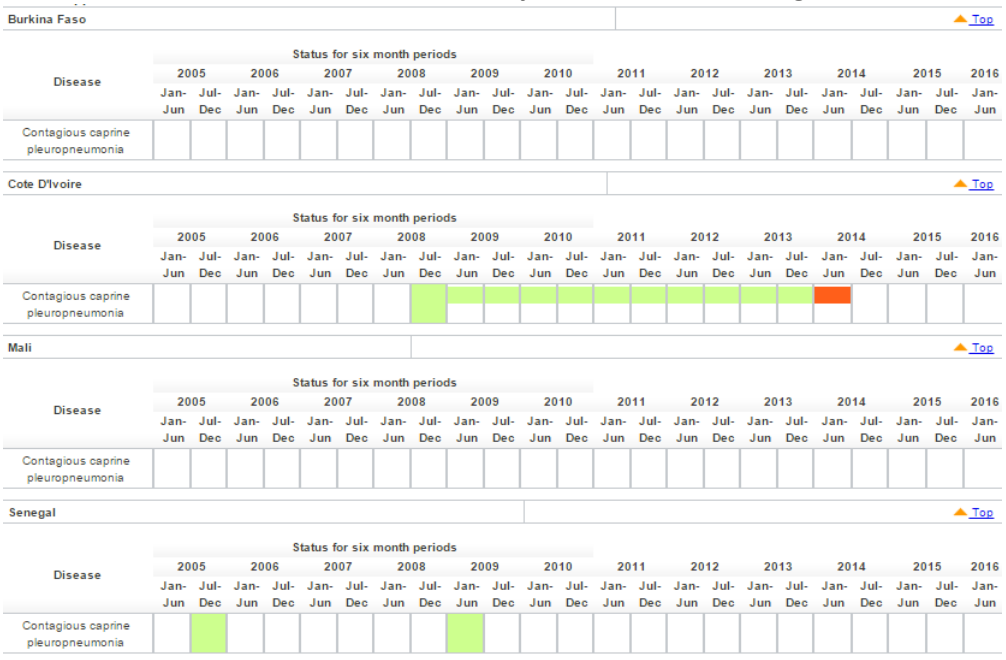
- There is no information available on this disease
- Never reported
- Disease absent
- Disease suspected but not confirmed
- Infection/infestation
- Disease present
- Disease limited to one or more zones
- Infection/infestation limited to one or more zones
- Disease suspected but not confirmed and limited to one or more zones

When different animal health statuses between domestic and wild animal population are provided, the box is split in two: the upper part for domestic animals, and the lower part for wild animals.

CCPP in Asia: Bangladesh, India, Indonesia, Myanmar, Nepal and Vietnam

CCPP in Asia: Bangladesh, India, Indonesia, Myanmar, Nepal and Vietnam

CCPP in Western Africa: Burkina Faso, Ivory Coast, Mali and Senegal



CCPP in Eastern Africa: Ethiopia, Kenya, Rwanda, Tanzania and Uganda

CCPP in Southern Africa: Madagascar, Malawi, Mozambique, South Africa and Zambia