Contagious Bovine Pleuropneumonia
Summary

Introduction

This is a summary of an analysis undertaken by a DISCONTOOLS group of experts on contagious bovine pleuropneumonia (CBPP) in 2023. The group reviewed the current knowledge on the disease, considered the existing control tools, identified gaps in the availability and quality of these tools and determined the research necessary to develop new or improved tools. Full details of the analysis can be downloaded from the website here.

Disease profile

CBPP is a severe respiratory disease of cattle, caused by the bacterium *Mycoplasma mycoides* subsp. *mycoides* (*Mmm*). CBPP has a classical transboundary nature: it can spread through populations of live animals across international borders causing considerable economic and societal harm. For these reasons, it is included in the list of notifiable diseases of the World Organisation for Animal Health (WOAH). In the EU context, CBPP is additionally subject to an emergency health response plan, requiring immediate eradication measures to be implemented as soon as it is detected.

CBPP affects zebu and taurine cattle and there is no known wild species reservoir. The disease is transmitted directly from infected to susceptible animals by the airborne route. *Mmm* is very sensitive to physical, chemical, and biological factors and does not persist in the environment, so the possibility of indirect transmission through fomites or animal products can be practically excluded. However, chronic carriers may act as reservoirs, as well as young animals and small ruminants, which can harbour the agent for long periods. These potential reservoirs cannot be easily detected, which may facilitate the spread of the disease, though this has not been demonstrated experimentally.

Molecular dating analyses showed that CBPP originated only around 300 years ago, most likely in Europe. During the 19th century, the disease was exported to other continents, including Africa. CBPP was successfully eradicated from the USA, Australia, and Europe, mainly by applying drastic stamping-out policies. In Africa, Botswana and most of Namibia have managed to eradicate the disease, while Zambia and the region of Namibia that remains infected have put in place official eradication programmes. However, CBPP remains endemic in sub-Saharan Africa, where it inflicts severe losses, posing a threat to food security and compromising peoples' livelihoods and wellbeing.

Risk

Although its precise distribution, incidence and impact have not been established, CBPP is widespread in sub-Saharan Africa. It also appears to be present in the Middle East and other parts of Asia, although the situation in these regions is unclear. The disease has been eradicated in other parts of the World, including Europe, where the last outbreaks were reported in 1999. The most recent European outbreaks were shown to be most likely due to a resurgence of the disease, and not to a re-introduction from Africa, though a potential reservoir was not identified. The mechanisms of persistence and transmission from chronic carriers (via the reactivation of sequestered lung lesions) or alternative reservoirs, sites and transmission routes need to be investigated.

CBPP has been spreading in Africa over the last 30 years and both climate change and increased insecurity are contributing to a deterioration of the situation in the continent. The inability to enforce the control of animal movements and the limited implementation of vaccination campaigns using suboptimal vaccines, coupled to almost inexistent diagnosis, traceability and reporting systems, and to the impossibility to implement slaughter policies

to eliminate infected herds, all contribute to the persistence and further spread of the disease in Africa.

Data on transboundary animal movements in Africa are rarely collected and livestock movement monitoring and control is very difficult due to lack of animal identification systems in most countries. Furthermore, restriction of animal movements in regions that practise extensive nomadic and transhumant livestock herding is extremely complicated. Efforts should be made towards collecting, centralising and harmonising livestock mobility, disease prevalence, and socioeconomic impact data at different temporal and spatial scales, in order to identify areas at risk and support the implementation of control strategies. Trade data collected by commercial and trade platforms must be explored to give a representation of the temporal patterns of animal movements to assess the risk of introduction into Europe, notably via the Middle East.

Diagnostics

Since CBPP lesions are highly evocative, abattoir surveillance and post-mortem investigations of lung lesions are of paramount importance for diagnosis and constitute the basis for disease surveillance in CBPP-free countries. Molecular diagnostic assays may be used for the rapid confirmation of CBPP suspicions, while serology is used for animal testing before trade.

In endemic regions, clinical and abattoir investigations are rarely conducted, the isolation and molecular detection of the CBPP agent are even more infrequently performed and the disease is hardly ever reported. Both the complement fixation test (CFT) and competition ELISA (cELISA) are used for surveillance and prevalence studies, though due to their limited sensitivity they can only be interpreted at herd level and availability of commercial products is currently an important issue. Inexpensive tests, easy to operate at the pen-side may be useful for disease confirmation in remote regions, far from diagnostic laboratories.

Market studies are needed to assess the demand and affordability of new diagnostics and the involvement of manufacturing companies is required to target and optimise the development of inventions into successful commercial products. Serological and direct molecular assays must be validated by international standards and inter-laboratory assays, and reference materials and qualified sample panels are needed for these validations.

Vaccines

In Africa, CBPP control is mainly based on vaccination campaigns organised by the national veterinary services, using live, attenuated freeze-dried vaccine strains T1/44 and T1sr. The stability of these vaccines is an issue, while the efficacy and duration of immunity are limited. Logistical, financial and political constraints greatly limit access to vaccines, as well as their quality. Furthermore, occasional post-vaccinal reactions occur with T1/44, which limit the acceptance of vaccination.

The development of effective inactivated and subunit vaccines that are affordable, safe, and thermostable and may be combined for use as multi-valent products would greatly promote the implementation of vaccination, while the use of a DIVA strategy would facilitate the application of new combined control strategies including therapeutical and sanitary measures, thus accelerating outbreak resolution and disease eradication. However, the production of new generation vaccines will require investments for modernization of production plants and the current legal framework may represent an issue for registration of vaccines derived from modern bioengineering or gene editing technologies, falling under the GMO category.

In the meantime, the current formulation may be improved to increase vaccine stability after reconstitution, while the use of adjuvants must be explored to improve the potency. Quality control requirements must also be reviewed to guarantee products with adequate efficacy.

Pharmaceuticals

Currently in Africa, cattle owners often resort to antimicrobial treatments to reduce disease damage and mortality rates. These treatments are applied with little antibiotic stewardship, which can lead to low efficiency and undesired side effects in both cattle and human populations and can promote the development of AMR, though this has not been assessed in regards to CBPP.

Recent studies have shown that treating sick animals with antibiotics can greatly reduce the transmission to healthy contacts. Besides, since vaccination alone cannot lead to disease eradication, combined strategies including the controlled use of antibiotic treatments should be assessed. However, currently no official strategies include the use of antimicrobials. A policy change towards a rational use of antibiotics, coupled to a surveillance of AMR acquisition by *Mmm* strains may lead to the implementation of improved therapeutic regimens. For that purpose, standardised protocols to determine the *in vitro* sensitivity of *Mmm* strains to currently used antimicrobials are urgently needed to determine epidemiological cut-off values and clinical breakpoints and to assess the emergence of resistant *Mmm* strains in the field.

Knowledge

CBPP has been studied for many years, but there are still significant areas of uncertainty, especially in relation to the pathogenesis and host immune response, as well as the epidemiology of the disease and its impact. Research is needed to fill these gaps, which are closely linked to the research requirements to develop more effective tools and strategies for the control of the disease.

Extensive comparative “omics” analyses conducted on a large sample of strains representing the temporal and spatial diversity of *Mmm* and other members of the “Mycoplasma mycoides” cluster are needed to determine representative pan and core genomes at different levels. These will facillitate the development of diagnostic and genotyping tools, as well as the identification of the molecular basis of virulence attenuation, and acquisition of AMR. A clear understanding of pathogenicity and protection mechanisms is needed, including how the host environment affects the regulation of *Mmm* virulence genes, as well as how *Mmm* affects the regulation of host genes. More comprehensive multi-actor *in vitro* models, as well as improved *in vivo* models should be explored for the study of host-pathogen interactions and the assessment of control tools such as vaccines and treatments.

Conclusions

Significant research contributions are still needed to promote and facilitate the control of CBPP. Mechanisms involved in pathogenicity and persistence of infection (reservoirs), as well as those leading to immunity and protection, deserve further investigation. The search towards the development of new diagnostic tools with high sensitivity and specificity, including pen-side tests for rapid screening in the field, should be continued, as well as the the development of safer, stable and more effective vaccines, including DIVA and multi-valent strategies. With sufficient financial, scientific and political support, CBPP can be eradicated.