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FAO-OIE-AU/IBAR-IAEA
Consultative group on CBPP
Fifth meeting, Rome, 14-16 October 2015

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Acronyms

AHG	Ad Hoc Group
AMR	Antimicrobial resistance
AU	African Union
CBPP	Contagious bovine pleuropneumonia
CCPP	Contagious caprine pleuropneumonia
cELISA	Competitive ELISA
CFT	Compliment fixation test
CIFSRF	Canadian International Food Security Research Fund
CIRAD	Centre de coopération internationale en recherche agronomique pour le développement
CMAEE	Contrôle des maladies animales, exotiques et émergentes
CMC-AH	Crisis Management Centre – Animal Health
CP	Control plan
CVO	Chief Veterinary Officer
DFATD	Department of Foreign Affairs, Trade and Development (Canada)
EAREN	Eastern Africa Region Epidemiology Network
EARLN	Eastern Africa Region Laboratory Network
ELISA	Enzyme linked-immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
FMD	Foot-and-mouth disease
GALVmed	Global Alliance for Livestock Veterinary Medicines
GF-TADs	Global Framework for the progressive control of Transboundary Animal Diseases
GLEWS	Global Early Warning System
HPAI	Highly pathogenic avian influenza
IAEA	International Atomic Energy Agency
IBAR	Interafrican Bureau Animal Resources
ICRC	International Committee of the Red Cross
IDRC	International Development Research Center

IGAD	Intergovernmental Authority on Development
ILRI	International Livestock Research Institute
KALRO	Kenya Agricultural and Livestock Research Organization
KAP	Knowledge, attitudes and practices
Mmm	*Mycoplasma mycoides* subsp. *mycoides*
NGOs	Non-Governmental Organizations
OIE	World Organisation for Animal Health
PACE	Pan-African Programme for Control of Epizootics
PANVAC	Pan African Veterinary Vaccine Centre
PARC	Pan-African Rinderpest Campaign
PCP	Progressive Control Pathway
PoC	Proof of Concept
PPR	Peste des petits ruminants
PVS	Evaluation of Performance of Veterinary Services
QC	Quality Control
RAHN	Regional Animal Health Networks
SADC	Southern African Development Community
SCAD	Commission for Animal Diseases
SDG	Sustainable development goals
SEIR	Susceptible – exposed - infected – recovered
SMP-AH	Standard methods and procedures in animal health
STSD	Surveillance in Trade Sensitive Diseases
TADs	Transboundary Animal Diseases
TREC	Tandem Repeat coupled with Endonuclease Cleavage
UEMOA	West African Economic and Monetary Union
WHO	World Health Organization

Opening remarks

Berhe Tekola
Director Animal Production and Health Division

Distinguished experts and participants, welcome and thank you for taking the time to be with us here in Rome for this important meeting. It gives me a great pleasure to open the 5th Consultative Group meeting on Contagious bovine pleuropneumonia (CBPP) which offers an opportunity for experts to express varied opinions on key issues related to CBPP control dynamics, and identify areas where research would be needed to address gaps in knowledge and technical capacity.

Contagious bovine pleuropneumonia (CBPP) remains one of the major Transboundary Animal Diseases (TADs), most affecting rural livelihood in Africa, despite the fact that it has been eradicated from many parts of the world. It is a serious threat to livestock production in many sub-Saharan African countries and a significant obstacle to livestock development in the continent. This situation requires attention, and coordinated efforts from all stakeholders are definitively needed.

This meeting is both timely and important in reviving the process of the research group consultations on CBPP to advise FAO on the latest developments and tools for CBPP prevention and control. The last consultative group was held in 2006 in Rome, followed by a regional consultation in Senegal in 2013. I am sure that during this period knowledge has accumulated, and that over the next two days, this expert meeting will be a great opportunity to share research results and experience in different topics. We need to be innovative in our approach in the fight against CBPP, and I count on your ideas and insights towards this objective.

As we all know, this consultative process involves the World Organisation for Animal Health (OIE), the African Union - Interafrican Bureau for Animal Resources (AU-IBAR), the Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture and FAO/OIE reference centres, and FAO – as far as resources allow – will continue to support such collaborative consultations with our partners, the international scientific community and donors to promote and support sustainable CBPP control in Africa so as to enhance food security and to improve people's livelihoods on the continent.

Various collaboration and partnership initiatives are ongoing to support global control of peste des petits ruminants (PPR), foot-and-mouth disease (FMD) and highly pathogenic avian influenza (HPAI). This meeting helps to refocus attention on this equally important disease, CBPP, that also requires our concerted efforts. The Food and Agriculture Organization's commitment to the control and eradication of animal diseases, in close collaboration with OIE and regional partners under the umbrella of Global Framework for the progressive control of Transboundary Animal Diseases (GF-TADs), will support this objective.

As you know, FAO´s mission is to eliminate hunger, food insecurity and malnutrition, and promote sustainable development. It is important to note that our work in the fight against TADs that have a negative impact on food security and rural livelihoods, such as CBPP, is in line with this FAO mandate, and well positioned in the FAO strategic framework, and contributes particularly to strategic objective

SO3 (improving rural livelihood) and SO5 (strengthening resilience), with clear targets at global, regional and country levels.

The international community is transitioning from the Millennium Development Goals to the Sustainable Development Goals (SDG) era, which will officially commence on 1 January 2016. The Food and Agriculture Organization, as one the UN leading agencies, will support countries in implementing and monitoring particularly SDG 1 and 2 (namely, "No Poverty" and "Zero Hunger"). These goals encompass a comprehensive vision of food security, including: improved nutrition, promotion of sustainable agriculture and food systems, for achieving zero hunger by 2030. The Organization's core work in the fight against transboundary animal diseases as part of its strategic objectives to help eliminate hunger, food insecurity and malnutrition, and reduce rural poverty is perfectly in line with the global perspective of the SDG. I wish you a very productive and successful meeting. Thank you.

Juan Lubroth
Chief Veterinary Officer, Animal Health Service

Distinguished participants,

We were all excited about the accomplishment of the Declaration of Global Freedom from Rinderpest [mid-2011] and the accolade that it represented for the veterinary profession. We have since embarked using the Progressive Control Pathway strategy for foot-and-mouth disease (FMD) and most recently adapted this to the Peste des petits ruminants (PPR), and the need to continue to join forces with different partner institutions, particularly the World Organisation for Animal Health (OIE), in tackling other high impact diseases.

Contagious bovine pleuropneumonia (CBPP) was highlighted from the very start of EMPRES in 1994 as a major transboundary animal disease (TAD) that requires attention. Attention has oscillated for the last couple of decades. It is of note that this very disease was eradicated from the United States of America at the end of the nineteenth century, and from most of southern Europe in the late twentieth century. It is high time we do the same in Africa this century!!

Three things are needed for the eradication (if we can use this word) of CBPP:

(1) Knowledge of the disease epidemiology;

(2) Having the right tools in place (vaccines and diagnostics), and

(3) Having the political will.

I would say that currently we are not in possession of these, and much less the financial investment required. Contagious bovine pleuropneumonia (CBPP), this silent and devastating killer, is of a transboundary nature and national efforts need to be coordinated at regional level. I think by utilizing what we learned and did with Rinderpest and what we are hoping to achieve with FMD and PPR, this same methodology can be adapted and applied to CBPP control and elimination. Part of the strategy for control of these diseases is the strengthening of veterinary systems and access to animal health care services and this should be part of CBPP control.

The control of CBPP is constrained by several factors including deterioration of the quality of veterinary services, the lack of financial resources for sustainable control, uncontrolled cattle movement or the way meat and markets are handled without the necessary regulatory oversight that we may want to have in place along the production and value chains for surveillance and implementation measures.

I do not need to tell to this distinguished crowd of experts that the tools currently available are insufficient for effective CBPP control and elimination. These are issues that I hope will be discussed during the next two days as they relate to the quality of the vaccines, discriminatory diagnostic tests, the use of antibiotics, and other aspects of CBPP control.

We would like to have a roadmap and an action plan launched with the concerted action at the sub-Saharan Africa level to address gaps in the control of CBPP. There are lessons that we can learn, such as from the risk management pathways, that are already underway for several high impact diseases such as FMD and PPR as I mentioned earlier. Can this approach be a model that we can use for CBPP?

I am sure this consultation will stimulate discussions on the subject of the use of antibiotics in treating CBPP. It may be of interest, but in a few moments I will also be opening another meeting today - on antimicrobial resistance (AMR), where the

World Health Organization (WHO) and OIE are participating. I consider it both relevant and essential that the "Tripartite" (FAO, OIE and WHO) speak with one voice on how best to use antibiotics, how they should be deployed, and what a farmer can really use as tools to be able to stop devastating bacterial infections such as CBPP.

In conclusion, we must critically examine all the available options in the control of CBPP with a view to assisting countries or clusters of countries within the same agro-ecological context in the effective management of the disease, and towards its control and elimination.

Recommendations

INTRODUCTION

Long eliminated in developed countries, contagious bovine pleuropneumonia (CBPP) remains a serious threat to cattle production in the sub-Saharan Africa. Some 26 countries in the continent are affected by the disease which is spreading to countries and areas where it had been previously eliminated or had never been reported. In affected countries, the disease has serious implications for food security and livelihoods caused by mortality, loss of milk production and drastic weight loss in more chronic cases. The impact on agricultural/ crop production and consequential food insecurity is also the result of reduced draught power and use of manure for soil fertility.

The control of CBPP has been constrained by several factors including the deterioration in the quality of veterinary services, lack of financial resources to mount sustained control programmes and uncontrolled cattle movement within and between countries. CBPP control programmes currently suffer from lack of concerted actions and financial support, which have resulted in the gradual spread of the disease throughout much of the African continent.

The continuing spread of CBPP disease throughout Africa and the urgent need to review current knowledge on disease dynamics in the continent prompted FAO together with the World Organisation for Animal Health (OIE), AU-IBAR and the Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture to convene this technical meeting to offer an opportunity for experts to exchange new ideas and technical information on CBPP control, and to advise on the technical feasibility for global eradication of CBPP, bearing in mind that the disease seems to be confined largely to one continent (Africa), and does not have a wildlife reservoir.

The last CBPP consultative group meeting was held in Rome (Italy) in November 2006 with the objective to provide the relevant platform for interactions on the use or not of antibiotics in CBPP disease management, within the context of available technical information on the subject. This consultation was followed by a regional consultation in November 2013 in Dakar (Senegal) in which experts and representatives from 12 infected countries attempted to identify the key elements for a collective strategy for controlling the disease in different epidemiological settings in Africa using the knowledge and experience of affected and at-risk countries.

It was perceived that there was a need to hold a new technical consultation to review current knowledge on disease prevention and control strategies and explore the recent developments in CBPP diagnostics and prophylactic tools since the last consultative group held in Rome in 2006. This could be of use in the design of prevention and management strategies for CBPP outbreaks in Africa, with a view to controlling the disease in infected areas, and even eliminating it in some countries, clusters of countries, sub-regions or possibly production systems, and halting its spread throughout the continent.

OBJECTIVES OF THE MEETING

The main purpose of the 5th technical consultative group was to seek views and stimulate debate on key issues of CBPP control dynamics with a view to elaborating the technical and policy approaches for sustainable progressive control and ultimately,

the eradication of the disease. The meeting was expected to identify areas where research could be intensified to address missing gaps in knowledge and highlight concrete and integrated actions that could lead to the control and eradication of CBPP.

SUMMARY OF THE MEETING RECOMMENDATIONS AND CONCLUSIONS

The Food and Agriculture Organization (FAO) convened the 5th technical meeting on CBPP in close collaboration with OIE, AU-IBAR and the joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture at FAO, Rome from 14 - 16 October 2015, with the participation of 20 CBPP experts in addition to technical staff from FAO, OIE, the Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture and the Global Alliance for Livestock Veterinary Medicines (GALVmed). The representatives of AU-IBAR and AU-PANVAC were connected by Skype.

The programme of the meeting included different sessions with technical presentations on (i) the disease situation including an overview of the global status of CBPP and evolution of its causal agent, the disease situation in Africa and in selected countries (Kenya, Senegal and Zambia), and the OIE standards related to CBPP, (ii) prevention and control strategies, (iii) update on diagnostics and surveillance tools, (iv) update on vaccine developments, and (v) update on the use of antibiotics in CBPP control. These presentations were followed by round table discussions on CBPP dynamics, with a view to defining technical and policy approaches for sustainable progressive control and ultimately eradication of the disease in Africa.

A fundamental question, central in discussions during the meeting, was whether eradication of CBPP is an achievable target given the technical constraints of disease control and socio-economic realities of Africa today.

General Considerations

General and key considerations discussed by the participants are the following:

- CBPP is widely regarded by veterinary policy-makers as a disease of strategic importance that exerts broader impacts on trade, food security, nutrition, and people's livelihoods.
- The disease persists in sub-Saharan Africa, particularly in countries where factors such as cross-border transhumance, weak regional control policies, lack of resources and technical capacity by governments, as well as lack of interest by donors make disease control difficult.
- CBPP control measures such as cattle movement restriction, quarantine and test and slaughter are not applicable within the economic and social reality of many countries in Africa.
- There is a need to develop coherent realistic national and regional strategies for the progressive control of CBPP.
- Specific data, especially at national level on the impact of the disease and the costs/benefits of control programmes are lacking.
- The definition and use of tools, methods and strategies have to be compliant with OIE standards including those related to veterinary services.
- There is a need to reduce the use of antibiotics in farm animals in line with international recommendations to reduce the usage of antimicrobials through better animal husbandry including good-farming practices and application of effective vaccines.

Considering the above points, the participants made the following recommendations and conclusions, which should be read along with the recommendations from the 4th consultative group meeting that are still valid but not always implemented considering different reasons.

CBPP control Strategies

The failure to contain CBPP is largely the result of the lack of a coherent and achievable policy with realistic approaches for coordinated and progressive control. It is therefore a matter of urgency to reconsider the strategic approach to CBPP in the continent and identify improved control strategies that countries can implement effectively. Following a discussion of different CBPP control strategies, the participants agreed on the following recommendations and conclusions:

For an appropriate and sustained CBPP control, there is the need for a strong political commitment that prioritizes CBPP as a major disease to convince governments, regional organizations, international bodies and funding partners to invest in CBPP control as a basis for improving food security, people's livelihoods and general well-being.

Due to several factors hindering CBPP control, global and continental CBPP eradication remains a challenging and distant goal. The strategic approach to CBPP should be based on progressive control through achievable steps towards increased and sustainable disease control. This could make real progress and perhaps achieve elimination in some areas.

There is evidence that antibiotics could play an effective role in CBPP control, especially where they are applied under controlled conditions, essentially to replace slaughter of affected or in-contact animals and as a substitute to the "stamping out" policy. There is an urgent need to conduct pilot studies as proof of concepts that compare control alternatives, and particularly to demonstrate that the combination of vaccination and controlled use of antibiotics can be applied to full effect for CBPP control.

In countries where CBPP remains endemic, an effective vaccination policy is the only realistic method of choice at present for control of the disease, and should be encouraged. Current vaccines, despite their limitations (short duration of immunity and requirement of a cold chain for delivery), can provide sufficient protection if properly deployed, by using the correct dosage and ensuring efficient delivery of the vaccines.

Table 1: Oxytetracyclines therapy of CBPP

Questions	Answers
Can antibiotic therapy (oxytetracycline) clinically cure infected cattle?	Yes
Can antibiotic therapy (oxytetracycline) provide bacteriological cure of the infected animals?	No
Does treatment of infected cattle with oxytetracycline generate or increase the number of chronic carriers?	No
Can Oxytetracycline significantly reduce disease transmission risk?	Yes
Risk of animals with pulmonary sequestra transmitting the disease to susceptible animals	Negligible to low*

**The* risk is difficult to evaluate

Any plan for CBPP control must be phased and flexible enough to be adapted to local epidemiological and socio-economical contexts. It must be viewed at the regional level beyond national borders.

The participants exhorted the Southern African Development Community (SADC) member states to seek as a matter of urgency both internal and external resources, to address the issue of CBPP control in countries north of SADC region, so as to mitigate the risks posed by CBPP incursions in SADC countries. This will support peoples' livelihoods, improve nutritional security and general well-being by avoiding CBPP outbreaks in the sub-region with subsequent devastation of the cattle industry in the region.

Combining control of CBPP with other priority diseases as part of integrated animal health care (multi-disease control approach) should be explored to increase incentives and minimize costs.

It is imperative that different policy initiatives and strategies for CBPP are rationalized by FAO/OIE/IBAR for a single cohesive continental policy on CBPP control/eradication, which other international bodies and nations could buy into.

Finally, the experts concluded that a strong public-private strategy should be implemented at country level. Such a strategy can be a key instrument in the policy balance between the oversight and regulatory role of the State Veterinary Service and the regulated, subcontracted (by the State) operational role of the private veterinary sector.

Antibiotic use

Although the use of antibiotics is theoretically prohibited, they are widely applied in the field for the specific treatment of CBPP, or simply to combat a range of respiratory diseases. Treatment should be presented as a present day reality that, however, offers both opportunities and risks. The primary concern is risk of antibiotic resistance, although this would be greatly mitigated by a structured programme with recommended treatment regimens applied through supervised community animal health programmes or veterinary personnel. The meeting acknowledged and recognized the need to take into account the new Global Action Plan on Antimicrobial Resistance adopted at the WHO General Assembly in May 2015, and the recent standards and recommendations published by the OIE on this subject. Along those lines, the FAO Conference in it 39th session (June 2015) adopted a resolution on AMR calling for support in the implementation of the WHO Global Action Plan, and the strengthening of tripartite collaboration between FAO, OIE and WHO for combatting antimicrobial resistance in the spirit of One Health approach.

There is little information on the clinical efficacy of antibiotic treatments, the emergence of resistant strains and persistence of chronic carriers, and on the role of these carriers in the transmission and spread of the disease. The participants discussed the work done with oxytetracyclines for the treatment of CBPP and summarized the conclusions as follows:

Public-private-community partnership

Contagious bovine pleuropneumonia control programmes can be used as a means to improve veterinary services, especially in respect of private/public sector collaboration. The national public veterinary services should bear policy and overall

strategy responsibility while implementation should involve the private sector, local authorities and non-governmental organizations (NGOs).

Models for public-private-community partnership should be operationalized to ensure effective delivery systems of animal health interventions, particularly vaccination and surveillance activities.

Research

A tremendous amount of research work is being undertaken, notably to improve and develop new vaccines and diagnostics tools. There is an urgent need to validate these tools to incorporate them into updated and more cost-effective strategies.

Smart partnerships between African institutions and those at the research discovery end in either developed countries or international research institutions based in Africa, should be encouraged for research and validation of new tools and strategies.

The main driver of research in new vaccines should be a target of induced protective immunity for at least two years.

More research should continue to develop improved diagnostic tests, especially point-of-care tests. The establishment of improved diagnostic reagents will also rely heavily on the results of immunological studies and genome analyses.

Scientific studies on the efficacy of antibiotics (existing and new generation) including their treatment regimens should be encouraged to provide clear conclusions with regards to their possible use and if this use appears to be appropriate, to allow for the definition of policy guidelines in the regulated treatment and control of CBPP. Special attention must be given to the prevention of antimicrobial resistance in both human and animal pathogens.

It is very difficult to evaluate the losses due to CBPP in many African countries where the disease is enzootic because of the lack of proper reporting and economic evaluation. Evaluation of the real epidemiological situation and economical losses of CBPP is a critical step for developing an effective control programme of CBPP. There is an urgent need to conduct proper cost benefit analyses regarding CBPP control strategies in order to convince stakeholders, governments and their donors of the need for action and to justify the anticipated expenditure required for progressive control of CBPP. Such studies on the cost of control programmes and their expected benefits should investigate all possible strategic options, paying particular attention to the introduction of regulated use of the private sector in sub-contracted operations, such as vaccination.

PART 1

DISEASE SITUATION

Evolutionary history of CBPP and spread during the past 25 years. How did we fail?

François Thiaucourt

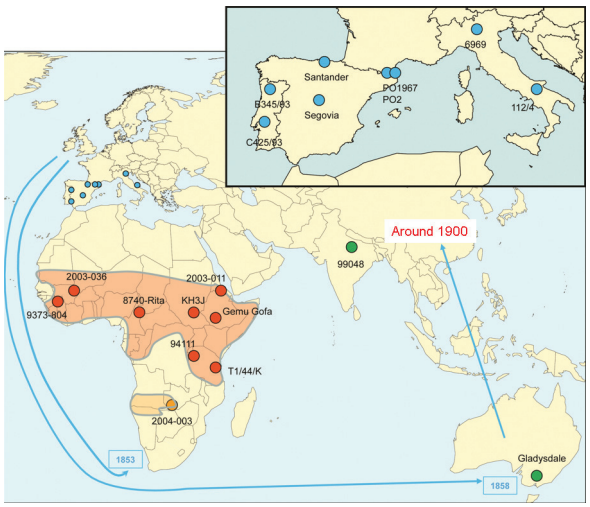
- According to molecular data, CBPP was introduced into sub-Saharan Africa around 1800.
- CBPP was controlled (but not eradicated) thanks to vaccination campaigns organized to eradicate rinderpest (late 1980s).
- Since 1990, CBPP distribution in Africa has been progressively expanding with a single exception: Botswana.
- It is now present in all countries south of the Sahara down to North Namibia, Zambia and South Tanzania.

Historical accounts are not sufficiently precise to determine when and where CBPP emerged. Some statues dating from the Roman times suggest that traditional vaccinations were performed at that time. What we know for sure is that CBPP was prevalent in Europe in 1770 and that it gained a worldwide distribution during the second half of the nineteenth century through the cattle trade. The advent of new generation sequencing techniques as well as Bayesian statistical analysis allowed for the determination of the time of emergence of the common ancestor to all *Mycoplasma mycoides* subsp. *mycoides* (Mmm) strains: around 1700. The ancestor of all African Mmm strains emerged around the 1800s which implies that CBPP was introduced into Africa.

Contagious bovine pleuropneumonia (CBPP) was eliminated from most of the world's continents during the first half of the twentieth century, at a time when no antibiotics or vaccines were available. 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. CBPP gained a wider extension in Africa in the 1990s as it re-invaded countries, such as Botswana, Tanzania and Rwanda, that had eliminated this disease in the past. At the same time, CBPP re-occurred in Southern Europe and the molecular analysis showed that these outbreaks were due to the resurgence of European strains rather than to a new introduction.

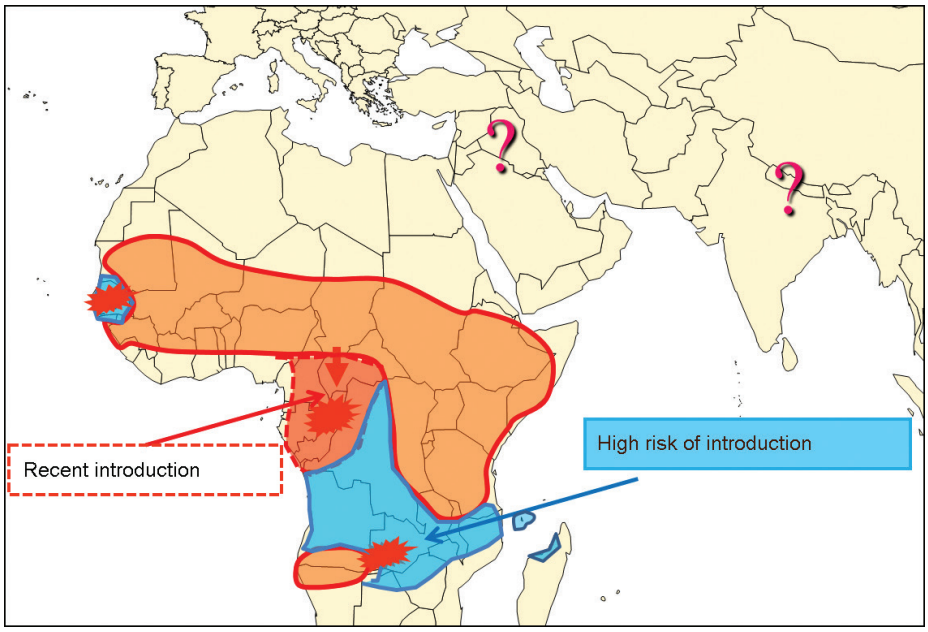
This finding raises the question of how Mmm could have remained unnoticed in-between outbreaks that were notified in 1967, 1982 and 1991. In Africa Botswana was the only country that succeeded in regaining a free status after very strict sanitary measures were applied. In the rest of the continent, CBPP 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 south of the Sahara. The Southern part of the continent is still free thanks to physical barriers

Figure 1
Mmm strain sample used to perform evolutionary analysis of CBPP



Source: V. Dupuv *et al.*, 2012

Figure 2
Actual distribution of CBPP and risks of introduction



that prevent its spread (for example, the Namibian veterinary cordon fence) but the Southern African Development Community (SADC) countries are clearly at risk due to higher meat prices that are an incentive to bring in cattle for slaughter.

The slow but irresistible expansion of CBPP in Africa clearly shows that the strategies that have been put in place to control that disease were either inadequate or not implemented correctly. There is an urgent to analyse the causes of these failures, to take corrective actions and to prevent the further spread of CBPP.

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CBPP Situation in Africa and initiatives supported by AU-IBAR

Ibrahim Gashash Ahmed

- CBPP is endemic in no less than 24 African countries based on the ARIS and OIE reports, although the epidemiological situation and socio-economic impact of the disease in each of the affected countries needs to be assessed properly;
- There is lack of a coordinated approach to the control of CBPP in Africa which is further exacerbated by insufficient production of quality vaccines to control the disease. The available vaccines offer protection for only six months. There is, therefore, a need to emphasize research on the development of new vaccines;
- There is a need for harmonization of CBPP control policies and interventions (including – but not limited to – which vaccines to use, development of SOPs, other preventive and control measures, cost-recovery etc.) in the affected member states;
- AU-IBAR is supporting a pilot project on the establishment of a scientific network of laboratories in Southern African countries (Botswana, Angola, Zambia and Namibia) with a view to improving the scientific relationship among laboratories engaged in CBPP disease diagnosis and control.

INTRODUCTION

Sub-Saharan African livestock production – albeit with very high potential for improving income and livelihood – is, however, hampered by numerous constraints including poor nutrition, lack of lucrative market access and diseases. Among the diseases, the TADs are the ones against which individual farmers often have little ability to control, and which require coordinated, often expensive, preventive and control measures. CBPP is currently the most important transboundary animal disease (TAD) of cattle in Africa, because of its wide range of direct and indirect negative effects - having a significant socio-economic impact on trade, demand and supply, food security and nutrition with estimated economic losses of up to US$2 billion per annum.

EPIDEMIOLOGICAL SITUATION OF CBPP IN AFRICA

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 (refer to the graph and map). The disease is also encroaching on new areas with The 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 ranges between 17-20%.

Figure 3
CBPP affected countries 2004-2014

CONTROL OPTIONS

Effective control of CBPP is best achieved when the real epidemiological situation and economical losses have been evaluated. Once this is done, control strategies may rely on various tools such as slaughter, movement control, vaccination and antibiotic treatment. Ideally the best control strategy should be a combination of these tools adapted to each local situation to reach the highest cost/benefit ratio. Eradication would be the most cost-effective alternative in a long-term perspective. Available control options being employed by most countries based on their reports to AU-IBAR include: treatment, vaccination, movement control and slaughter, but with no clear policy on compensation.

Table 2: Economic losses caused by CBPP

Year	Countries	Outbreaks	Cases	Losses (Death, Slaughter, Destroyed)
2004	18	314		1985
2005	18	156		570
2006	14	323		2810
2007	13	247	5517	3033
2008	17	355	47405	13928
2009	20	213	15187	2355
2010	24	218	7043	2682
2011	18	304	16836	5137
2012	26	364	223480	19348
2013	22	301	31740	12975
2014	19	294	10569	4232

INITIATIVES SUPPORTED BY AU-IBAR ON CBPP

The AU-IBAR in discharging its mandate of supporting and providing leadership in the development of animal resources in Africa has – over the years – developed and implemented projects and interventions to control animal diseases in the continent, including CBPP. Some of the more recent interventions implemented by AU-IBAR to control CBPP include the following:

VACNADA activities related to CBPP: The Vaccines for the Control of Neglected Animal Diseases in Africa (VACNADA) project was implemented between 2010 and 2013 with the aim of strengthening the capacity of AU-MSs to control selected TADs including CBPP. Under the project, prophylactic and control vaccination was conducted in project countries during which 1.5m cattle were vaccinated in 3 countries. Coordination and harmonization of intervention activities was organized in west and eastern Africa and CBPP diagnostic capability improved in selected laboratories in the continent. In general, CBPP vaccine production capacity was improved in many countries.

The contagious bovine pleuropneumonia (CBPP) **scientific network pilot project:** Within the scope of the "Reinforcing Veterinary Governance in Africa" project (VetGov), a specific intervention aimed at improving scientific relationships amongst the laboratories engaged in disease control in the South African sub-region is being supported. The activity involved harmonization and exchange of data, information and reference materials, joint training programmes, proficiency testing and research on CBPP control by the partners' laboratories: the Botswana National Veterinary Laboratory (BNVL, OIE Reference Laboratory (RL) for CBPP), the Angolan Instituto dos Serviços de Veterinaria (ISV), the Central Veterinary Research Institute, Lusaka, Zambia (CVRI), the Central Veterinary Laboratory, Windhoek, Namibia (CVL), and the partner laboratory, Isituto Zooprofilattico Sperimentale, Teramo, Italy.

SMP-AH – SMP activities related to CBPP in the Horn of Africa (GHOA) countries: Under this project, AU-IBAR has developed the "Standard Methods and Procedures (SMPs) for CBPP" that specify how CBPP is to be controlled and/or eradicated. The SMP is essentially an operational protocol to support regional harmonization and coordination for control of CBPP. Its aim is to create uniformity in TADs detection and control procedures. It outlines the minimum standards, procedures and goals, in line with OIE standards on how to deal with CBPP surveillance, epidemiology, laboratory procedures, and control in the context of the GHoA.

Surveillance for Trade Sensitive Diseases (STSD) project: Within the scope of this project, AU-IBAR has supported a cross sectional survey on major TADs in order to improve understanding on the epidemiological situation and risk factors of selected diseases including CBPP in the MS of the IGAD region.

ISSUES AND THOUGHTS ON CBPP CONTROL IN AFRICA

- The need for in-depth understanding of the epidemiological situation of the disease and risk factors associated with its spread;
- Establishment of economic losses being incurred as a result of CBPP;

- Role of the private sector : while mass vaccination for CBPP – where implemented – is being provided by the public sector, in many countries health care provision especially vaccination services are fairly deregulated and the private sector plays a key role in discharging this function;
- New approaches needed to control CBPP in Africa given the experience with existing control activities. There may be a need to develop a pragmatic progressive control pathway;
- Identify and operationalize interventions that involve a combination of control measures that include:
  1) Achievement of desirable herd immunity threshold through vaccination of appropriate proportion of susceptible animals;
  2) Improve access to high quality vaccine through production of quality assured vaccine, development of thermostable vaccine as well as involvement of private sector in the delivery process;
  3) Improve enforcement of animal disease control regulations (animal movement control);
  4) Put in place an effective surveillance and disease reporting system;
  5) Development of contingency plans including the establishment of response capacity, incident command system and simulation exercises;
  6) Sustainability of a control programme which will hinge primarily on the improvement of animal health delivery system in general.
- Define a clear policy on CBPP in Africa;
- Multi-disease control approach;
- Regional approach;
- Deal with pastoralism;
- Involvement of all stakeholders (farmers, traders, public and private VS, etc.) and strengthening of partnerships between public and private sectors in animal health service delivery.

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AU-IBAR: About VACNADA: http://www.au-ibar.org/vacnada

AU-IBAR current programmes and projects: http://www.au-ibar.org/smp-ah and http://www.au-ibar.org/stsd

CBPP: the worldwide situation The OIE official country status and control programmes

Joseph Domenech

THE CBPP GLOBAL SITUATION

The situation worldwide is regularly updated and published by the World Animal Health Information System of the World Organisation for Animal Health (OIE). The number of endemic countries is increasing. CBPP has spread during the past decade particularly towards Eastern and Southern Africa and it has become a major constraint in many countries in Africa since it can have severe impacts on cattle production (e.g. mortality, loss of milk, weight and draught power) as well as on food security and people's livelihoods.

THE OIE OFFICIAL NATIONAL STATUS

The possibility for a country to submit a dossier to the OIE for the official recognition of a disease-free status (or for the recovery of the free status after occurrence of a CBPP outbreak) for the national territory or for a zone, exists according to the CBPP chapter 11.7 of the OIE Terrestrial Animal Health Code (Terrestrial Code, articles 11.7.3, 11.7.4, 11.7.6, 11.7.16 and 11.7.17). The requesting country presents a questionnaire laid out in the Chapter 1.6 of the Terrestrial Code (article 1.6.7) with all necessary specified requirements. The Scientific Commission for Animal Diseases (SCAD) will assess the recommendations of the CBPP Ad Hoc Group (AHG) and will present them to all OIE Delegates at the annual General Assembly for adoption. All countries with an officially recognized status must submit an annual reconfirmation form.

THE OIE ENDORSED OFFICIAL NATIONAL CONTROL PROGRAMMES

Article 11.7.18 of the terrestrial Code ,which gives the possibility for a country to submit its official CBPP control programme for OIE endorsement, was adopted in May 2014. It is considered a powerful incentive for countries to embark on the implementation of a control plan (CP) with the vision and final objective of eliminating CBPP from the country or the zone. The questionnaire (article 1.6.13) lists all the requested supporting documents to be included in the dossier. The CPs will be adopted by the OIE delegates at the annual General Assembly.

THE ROLES OF THE OIE AND FEY FEATURES REGARDING CBPP CONTROL

The OIE plays an important role in transforming sciences into practice and policy-making through the publication of standards, guidelines and recommendations which will be translated in tools, methods, strategies and policies, laws and regulations. The standards of the Terrestrial Code and the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Terrestrial Manual) are prepared by groups

of internationally recognized experts coming in particular from the OIE Reference Centres. After a consultation process of all member countries, the standards are adopted by a vote of the 180 OIE Delegates at the annual General Assembly. The relevant chapters of the Terrestrial Manual are comprised of horizontal and vertical chapters. Regarding the Terrestrial Code, CBPP is also addressed through horizontal and vertical chapters. The CBPP specific chapter 11.7 contains 18 articles, including one on general provisions and one on safe commodities, 5 articles on criteria for disease status at country, zone or compartment levels, 6 articles on provisions for import of commodities, 3 articles on specific CBPP disease surveillance and an article on OIE endorsement of official national CBPP control programmes. Apart from its standard setting mandate, other roles of OIE related to CBPP control were mentioned, e.g. those on the World Animal Health Information System / Database (WAHIS/WAHID), veterinary education, direct support to member countries and their veterinary services (VS), viz. the OIE Tool for the Evaluation of Performance of Veterinary Services (PVS), Pathway tools, regional vaccine banks…. Several initiatives and activities, mostly carried out in collaboration with other international organizations, particularly with FAO, were also recalled such as the Global Framework for the progressive control of Transboundary Animal Diseases (GF-TADs) initiative, Global Early Warning System (GLEWS), Crisis Management Centre – Animal Health (CMC-AH) or regional networking in epidemiology and laboratory diagnostics. Improving animal health is a global public good and good veterinary governance is needed based on compliance with international standards for the quality of VS.

PART 2

PREVENTION AND CONTROL OF CBPP

CBPP situation in Senegal

Mbargou Lo

- Resurgence of CBPP in Senegal after 34 years of absence.
- Training and sensitization of actors, movement control of animals and emergency vaccination allowed in the control of CBPP in affected regions.
- A regional approach is essential for the control and eradication of CBPP in Africa.

Contagious bovine pleuropneumonia (CBPP) reappeared in November 2012 in Tambacounda Region after an absence that had lasted since 1978. Such a long period of absence of the disease had led the country to stop vaccination in 2005, after four decades of mass vaccination campaigns against CBPP, and had allowed it focus on clinical and serological surveillance of cattle herds at strategically selected sites and abattoirs and slaughter slabs.

1965-1996: Mass vaccination campaign against rinderpest and CBPP.
BISEC (bivalent vaccine)
Vaccination rate: 44-86 %
vaccinated by public service

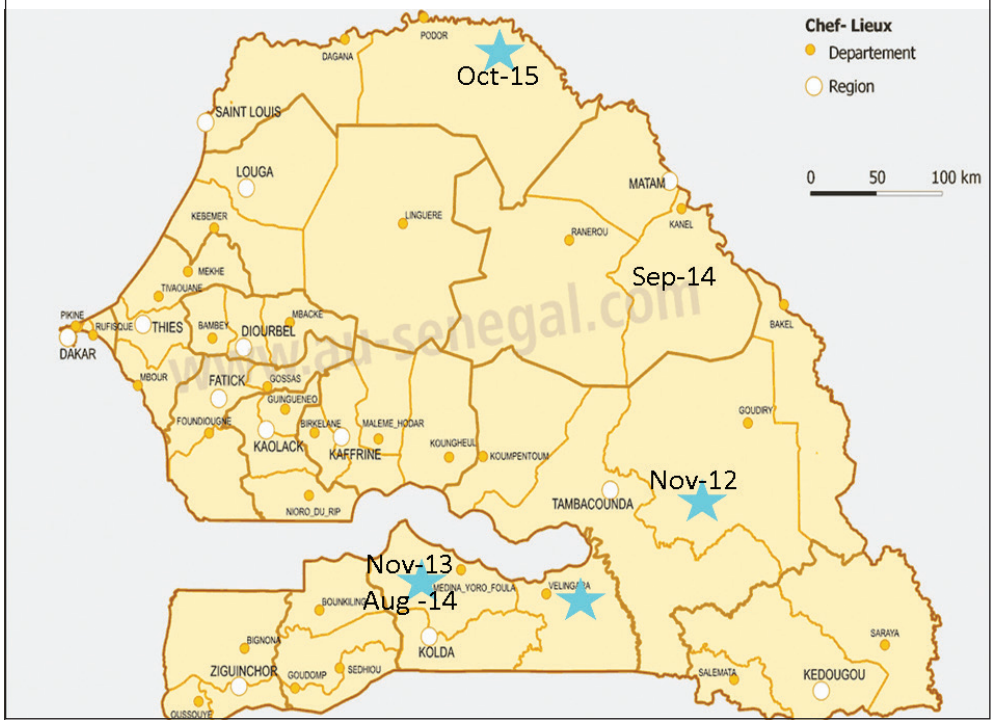
1997-2004: Campaigns of mass vaccination against CBPP
T1/44 vaccine
Vaccination rate: 40-62 %
vaccinated by: 75% by private vets; 25% by public service

October 2005: Ceased vaccination against CBPP
(Disease absent since 1978)

In 2009, Senegal submitted a dossier to the OIE to obtain CBPP-free status. However, the animal identification of an entire cattle population to ensure traceability constitutes a major constraint. Since then, Senegal has monitored CBPP under the national epidemiological surveillance system.

Between 2012 and 2015, a total of five outbreaks were recorded in the regions of Tambacounda, Kolda, Matam and St. Louis. During this period, in a total of 2 442 susceptible cattle population, 334 cattle were reported to be sick, of which 152 died. Under the emergency vaccination campaign, a total of 410 430 cattle were vaccinated in these areas to control the disease. Under the project TCP/SEN/3503 on "l'Assistance pour le contrôle des maladies animales transfrontalières au Sénégal", FAO provided 800 000 doses of T1/44 vaccine to control and prevent disease

Figure 4
Recent outbreaks



outbreaks. In addition, under the national surveillance on disease prevalence, 6 000 sera have been analysed at the National Laboratory for Animal Husbandry and Veterinary Research. The results will help in defining a national vaccination strategy.

At the regional level, a regional programme against this transboundary disease is being developed by the Commission of the West African Economic and Monetary Union (UEMOA). CBPP is a complex transboundary animal disease. The disease is endemic in the sub-region. Its control or eradication requires a regional approach to harmonize and coordinate disease control supported by political will and international assistance.

CBPP situation and control in Zambia and steps towards its eradication

Yona Sinkala

Zambia is surrounded by eight countries, namely: Angola, Botswana, the Democratic Republic of the Congo, the United Republic of Tanzania, Malawi, Mozambique, Namibia and Zimbabwe. The human population is 15 million with 4.2 million of cattle population. Livestock shares 42 percent of the agriculture gross domestic product (GDP)T of 7.9

History

In Zambia, CBPP was first introduced in the Western Province 1914 (eradicated by 1947), re-introduced in 1969 (eliminated in 1972), and re-introduced again in 1997. By 2002, CBPP had spread to the North-Western Province (Zambezi, Chavuma, Kabompo, Mufumbwe and Mwinilunga Districts), northern parts of Zambia (Mbala and Nakonde Districts), and in 2004 it was also recorded in Kazungula District, Southern Province.

Measures

In the past, CBPP was controlled and eliminated by a combination of movement control, stamping out with/without vaccination.

1915-1947

The first outbreak occurred at a time when the current vaccine had not yet been discovered. Therefore, the main control measures were directed towards breaking the transmission cycle through: 1) restricted movement of cattle from all the areas of Western Province; 2) construction of a cordon line along the border with Angola to curtail incursion of cattle from Angola; 3) mass slaughter and compensation of known infected herds; and 4) branding of cattle in the buffer zone, i.e. an area 10-20 km from the border with Angola.

1969-1973

The second outbreak was due to the movement of refugee cattle from Angola after the removal of the cordon line through a ministerial directive. At this time, a vaccine had been discovered but was not 100 percent protective. The immediate measures to eradicate the disease were: 1) the Vaccination of all the cattle at risk in the defined zone of Western Province; 2) movement ban of live cattle from the Province; 3) reinstallation of the cordon line along the border with Angola; 4) slaughter and compensation of all known infected herds. After eliminating the disease, the following measures were implemented to sustain freedom: a) employment of cordon guards to ensure that no cattle crossed the cordon line from the buffer zone or Angola into Western Province. Personnel was stationed every 10 km along the 540 km; b) branding of all the cattle within the buffer zone with specific government-identified marks; c) vaccination of cattle within the buffer zone annually; d) testing

of cattle within the buffer zone at least twice a year to ensure quick detection of any incursion of the disease.

1997 to date

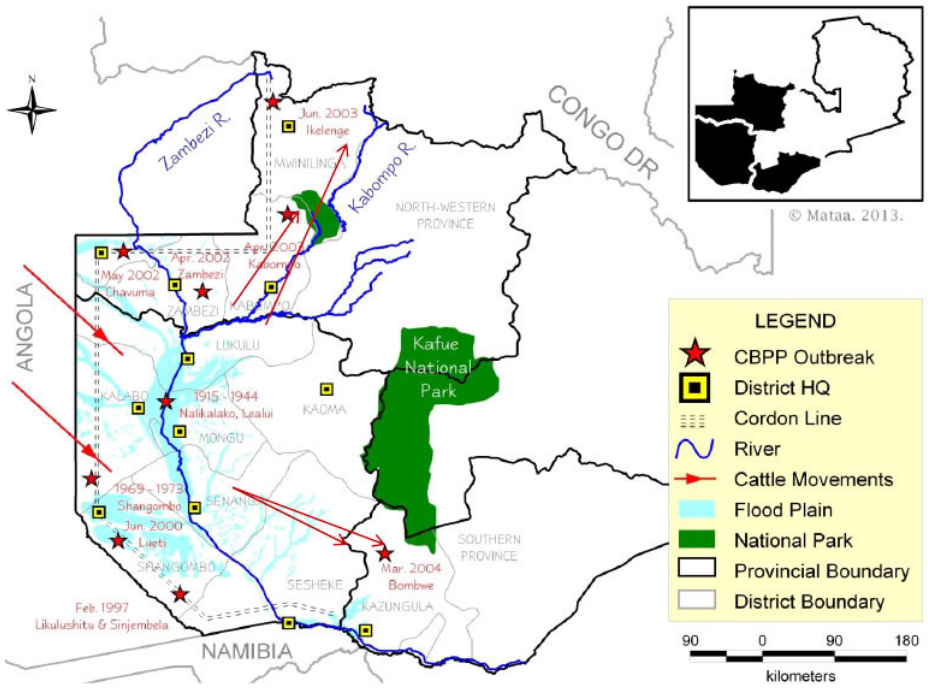
CBPP was initially reported in 1997, in Mombolomoka (Western Province), an area near the border with Angola. The disease was contained in that area for three years through a movement ban. Due to a directive in 2000 to lift the ban by the then minister of agriculture to allow movement of cattle within the province, the disease spread throughout the province. The disease then spread to affect Zambezi and Kabompo by 2002, Kazungula in Southern Province by 2004. Since then, two main risk areas have been identified as CBPP hot spots:

- West/North-western aspects of the country bordering Angola.
- Northern Aspect of the country bordering Tanzania.

Strategy

Zambia's strategy is to eradicate CBPP by removing the source of infection within Zambia through test and slaughter. To achieve this, the following activities must be undertaken: 1) resource mobilization (estimate 12 million USD); 2) stakeholder meetings; 3) sensitisation campaigns; 4) cattle identification; 5) creation of CBPP Zones; 6) serological testing; and 7) slaughter of positive herds.

Figure 5
Historical outbreak areas and cattle movement patterns



CBPP status in Kenya: Is eradication possible?

Kairu-Wanyoike, S.W.

- Status of CBPP in Kenya including zonation, control strategy and methods, stakeholder involvement, reporting, legislation and the pathway to eradication as well as opportunities and challenges.
- Recent research on CBPP in Kenya including knowledge, attitudes and practices (KAP), vaccine studies and impact studies.
- Ongoing activities and the way forward on CBPP in Kenya.

Contagious bovine pleuropneumonia (CBPP) is one of the major diseases affecting cattle in Africa. In Kenya, the disease threatens national food security and the livelihoods of about 1.3 million people. Kenya has 17.5 million cattle. CBPP is found mainly in pastoralist systems and threatens mixed farming and ranching systems (about 10 million cattle). Nearly all of Kenya's neighbours are infected with CBPP and transhumant and trade movement of cattle (Figure 6) from these countries poses an additional risk of CBPP.

The livelihoods of all the actors along the beef/cattle value chain may be impacted on by CBPP. Kenya is zoned into the infected zone, the protection zone and the clean zone (Figure 7) and has a CBPP control strategy. Control methods include government-managed annual preventive vaccination with T1/44 vaccine, with coverage aimed at above 80 percent for three years uninterrupted (infected area) and ring vaccination in the event of an outbreak, as well as movement control and slaughterhouse surveillance with trace-back and trace-forward. Chemotherapy for control of CBPP in Kenya is discouraged until all research results become available. CBPP is notifiable in Kenya and all, including the private sector, are obliged to report the disease.

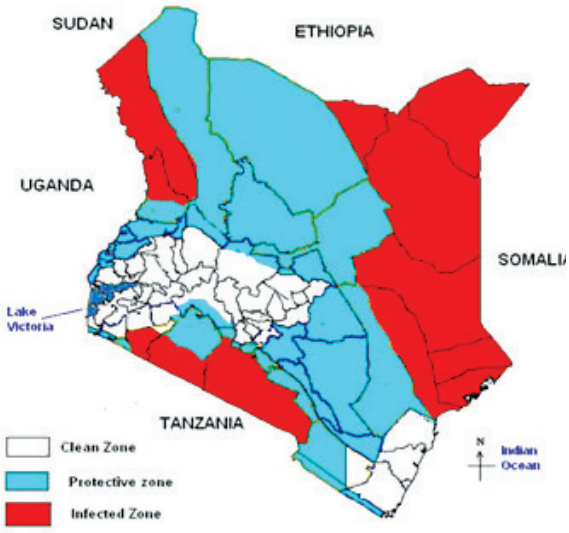
The opportunities in CBPP control include the existence of appropriate legislation, a vaccine, control strategy and contingency plan, considerable stakeholder awareness, past and present control programmes (Pan-African Programme for Control of Epizootics (PACE), creation of disease free zones), cross-border meetings, World Organisation for Animal Health (OIE) evaluation of Performance of Veterinary Services (PVS) evaluation and gap analysis as well as national, regional and international support. The challenges include inadequate political support, human and capital resource, emergency preparedness, information on disease situations, collaboration and coordination, reporting, stakeholder involvement and cooperation, surveillance, laboratory services and diagnostics and movement control; existence of other priority diseases; weak linkages between researchers and implementers. Performance Indicators on control are lacking and so is the link between surveillance and prevention and control. Drought leading to massive movement of cattle, fading institutional memory of methods that have worked before and marginal livestock identification and traceability, as

Figure 6
Movement of cattle marketed

well as absence of regional and international policies on CBPP control are additional challenges.

In the clean zone, CBPP eradication is possible. Indeed, Kenya has in the past applied for recognition of zonal freedom from CBPP to the OIE. However, the major limitations are that livestock identification is marginal and there are no explicit barriers to the other zones. The way forward would be to eradicate CBPP in the clean zone and progress to the protection zone. CBPP can be eradicated in the infected zone in the long term. However, the creation of autonomous county governments (Kenya Constitution, 2010) may assist in achieving this in a shorter period but only if there is adequate collaboration with the national government. To address information gaps, recent research on CBPP in Kenya has been carried out on a modified T1/44 vaccine (Mtui-Malamsha, 2009; Nkando et al., 2008 and 2012; Mulongo, 2013 and 2015), preferences, willingness to pay and demand for vaccine and vaccination (Kairu-Wanyoike et al. 2013 and 2014a) as well as knowledge, attitudes and practices (KAP) in CBPP and CBPP control (Kairu-Wanyoike 2014b; Kairu-Wanyoike submitted a) and estimation of impact of CBPP and its control (Onono et al., 2014; Kairu-Wanyoike et al., submitted) b). Research is ongoing (supported by IDRC/CIFSRF/DFATD) on a new CBPP vaccine and the associated socio-economic (micro-and macro-economic impact of the disease and its control by vaccination along the value chain), as well as policy studies (www.idrc.ca). Other ongoing activities in Kenya include AU-IBAR-led projects (www.au-ibar.org) on surveillance in trade sensitive diseases (STSD) in the Intergovernmental Authority on Development (IGAD) region and standard methods and procedures in animal health (SMP-AH), as well as the FAO-supported Regional Animal Health Networks (RAHN) such as the Eastern African Regional Epidemiology and Laboratory Networks (EAREN and EARLN) which include a CBPP sub-network.

Figure 7
CBPP zonation (2010 - to date)



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CBPP main constraints to efficient control strategies

F. Thiaucourt, L. Manso-Silva

- CBPP has been eradicated from many countries or regions with tools that exist today.
- Failure to control or eradicate CBPP in Africa is the result of the inability to implement a consistent regional control strategy in a long-term perspective.
- Antibiotic treatments are now widely used in the field by cattle owners to mitigate losses due to CBPP. Improper treatments are increasing the antibiotic resistance risk.
- Actual CBPP vaccines are effective when they are applied correctly, however they could certainly be improved if sufficient effort is invested in their development.

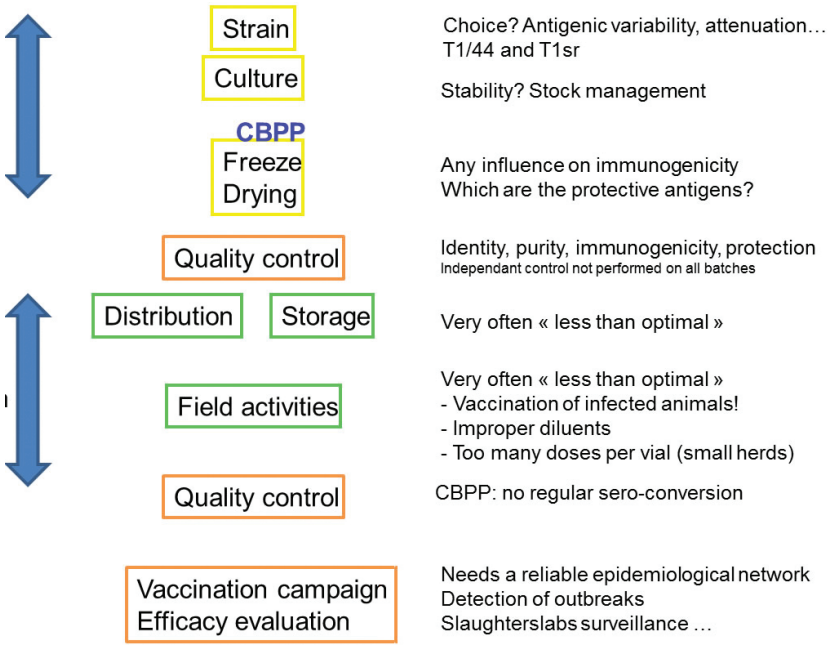
The various steps that are needed to control a disease are almost universal and follow the rules of the Deming wheel that are well known to quality assured establishments: Plan, Do, Check, and Act. These rules also apply to CBPP control.

The planning of activities should start with an evaluation of the epidemiological situation in the country or region, a knowledge absolutely needed to define realistic objectives and a plan to achieve them. There are in fact few reliable and updated data that are available for CBPP in Africa, in terms of prevalence or true economic impact.

CBPP control strategies are based on the use of four different tools: slaughter, animal movement control, vaccination and treatments. Their possible impact can easily be evaluated through classical susceptible – exposed - infected – recovered (SEIR) transmission models that are tailored for CBPP by including a group consisting of chronically infected animals. One interesting point is that these tools can be used in combination with an additive effect. However, in the field, with the exception of few countries, the use of slaughter or strict animal movement control are not implemented. The control of CBPP is therefore most frequently based on the use of vaccines, usually through a state agency, and antibiotic treatments which are delivered through private delivery systems.

The real field efficacy of these various tools is the result of the quality of the tools themselves and the way they are delivered or implemented. In the case of CBPP vaccines, their initial quality can easily be checked and it is also well known that repeated vaccinations of a herd lead to a very high protection rate. However, all batches are not systematically quality controlled, a small proportion of susceptible animals are vaccinated and improper vaccine use in the field result in very low protection rates. Some classes of antibiotics have proved to be efficient in bringing about a clinical cure of CBPP although not allowing for the complete elimination of the mycoplasma infection. However, antibiotic quality controls are usually not performed in Africa and their delivery leaves much to be desired. In fact, the delivery of antibiotics is an important source of income, contrarily to vaccines, which makes them very popular. The huge quantity of antibiotics that are improperly

Figure 8
Vaccine production and field implementation



Source: Thiaucourt & Manso-Silvan, 2012.

delivered in Africa is a real concern for the antibiotic-resistance risk and should be considered a major "one health" issue with antibiotic residues contaminating the human food chain.

Finally, as CBPP prevalence is not regularly updated, it is quite difficult to make an appraisal of the control strategies to identify the shortcomings and correct them before the next round of activity.

History has shown that the elimination or even the eradication of CBPP could be achieved. Research is now offering new and better products that may replace the existing tools. In addition, models can be used to evaluate in silico the possible impact of various strategies. Great efforts will have to be made to ensure that these strategies are correctly applied in the field to ensure an effective CBPP control and reverse the present trend of expansion of CBPP.

Elements of a progressive approach for CBPP control

Ahmed El Idrissi

- The strategic approach to CBPP should be based on progressive control through achievable steps in the progression toward increased and sustainable disease control and elimination from an area or a country.
- There is a need for a coordinated policy for CBPP control with focus on practical and achievable options to ensure sustainability.
- CBPP control programmes could be used as a model on which to base improvement of veterinary services and strengthening of private/public sector collaboration.

Contagious bovine pleuropneumonia (CBPP) remains a huge threat to cattle production in sub-Saharan Africa. The disease persists in 27 countries with negative impacts on production efficiency, livelihoods and food security. Animal movements and livestock trade within and between various countries and regions have been considered as potential risk factors that facilitate the entry and spread of the disease. The persistence of CBPP in sub-Saharan Africa seems to be associated also with a wide range of factors including the lack of regional control policies, inadequate vaccination campaigns, and lack of effective surveillance and reporting, as well as insufficient government resources allocated to CBPP control.

Addressing the challenges of CBPP requires a risk-based strategy for the development and application of the best CBPP control options, as well as their adequacy in different epidemiological contexts. The strategic approach to CBPP should be based on progressive control leading ultimately to elimination of the disease from infected areas and countries.

A framework for progressive control of CBPP should be developed to create motivation for CBPP control and assist countries in developing sustainable national strategies based on a realistic assessment of the disease's impact and of the best control options available. This presentation summarizes the key elements for progressive control of CBPP through achievable steps in the progression towards increased and sustainable disease control, keeping in mind the national needs and wider regional efforts for progressive CBPP control. The components of this pathway are crafted in a such a way as to allow national veterinary authorities to generate reliable data for better understanding of the dynamics of the disease and estimating its impact so as to formulate strategic control and start implementing risk-based control strategies to progressively reduce the impact of the disease in susceptible cattle populations and ultimately, to achieve freedom from disease (Figure 9. Progressive approach for CBPP control).

This approach has taken lessons from the global Rinderpest eradication and the Progressive Control Pathway (PCP) approach developed for foot-and-mouth disease and its implementation through regional roadmaps.

Figure 9
Framework for progressive control of CBPP

The Predicted Impact of CBPP Control Strategies

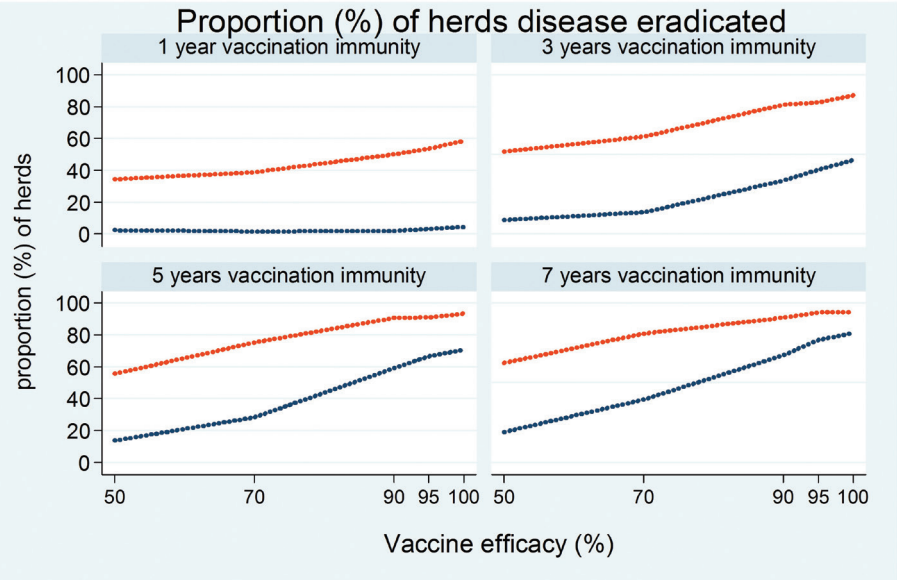
Jeffrey C. Mariner, John McDermott, J.A. Heesterbeek, Gavin Thomson, Wayne Martin

- CBPP is a disease with a long infection cycle and small populations are capable of indefinitely harbouring the disease
- Programs that combine treatment and elimination of animals transmitting CBPP are required to eradicate CBPP
- Vaccines of efficacy approaching 100% and long duration of immunity are required, and antibiotics may be a more socially acceptable approach to elimination of transmission

Pastoral cattle live in highly structured communities characterized by complex contact patterns. The presentation describes a spatially heterogeneous model for the transmission of contagious bovine pleuropneumonia (CBPP) developed specifically for pastoral communities of East Africa. The model is validated against serological data on the prevalence of CBPP infection in several communities of southern Sudan and against livestock owner information on community structure, livestock contact and cattle exchange. The model was built using parameter estimates based on data published in the literature and on observations of livestock owners obtained through participatory research. The basic reproduction number for CBPP in southern Sudan was estimated as ranging from 3.2 to 4.6. The model indicates that the critical community size for the persistence of CBPP falls within the typical herd sizes for pastoral communities in East Africa, suggesting that individual isolated herds are capable of maintaining infection indefinitely.

The model is used to assess the impact of alternative control strategies including mass and elective vaccination programmes, potential treatment regimes and the combination of vaccination and treatment in a single unified strategy. The results indicate that the eradication of CBPP using mass vaccination alone with currently available vaccines or improved vaccines is unlikely to succeed. Given that strict movement control is no longer feasible from a socio-economic perspective, even vaccines with 95 percent efficacy and more than five years duration of immunity are unlikely to eradicate CBPP. On the other hand, elective control programmes based on herd level vaccination, treatment of clinical cases or a combination of both vaccination and treatment enabled individual livestock owners to capture a large benefit in terms of reduced animal-level prevalence and mortality experience. The most promising intervention scenarios were programmes which combined the vaccination of healthy animals with treatment of clinical cases. Given the current widespread ad hoc use of treatment by both livestock owners and veterinarians, establishment of national control strategies based on coordinated vaccination and treatment programmes have the potential to both reduce antibiotic use and improve CBPP control.

Figure 10
The proportion of herds where CBPP will be eradicated as a function ofvaccine efficacy in four scenarios with duration of immunity ranging from 1 to 7 years



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PART 3

CBPP DIAGNOSTICS AND SURVEILLANCE

Serology diagnostic testing sensitivity and specificity based on vaccine trials and field cases

Roger D. Ayling

- Stage of infection affects test sensitivity.
- Which tests are best to use?
- What approaches should we use to develop the best test?

Using the previously described vaccine trial, under those conditions, no one test compliment fixation test (CFT), competitive enzyme linked-immunosorbent assay (cELISA), latex agglutination test (BoviLAT), immunoblot detected the disease at all stages of infection. The sensitivity and specificity calculated from that trial, gave some data that contradicted prior knowledge. However, testing of a negative population in Afghanistan indicated excellent test specificity. Use of different conjugates or mix of conjugates may improve the current tests, facilitating improved detection at different stages of infection.

Photo 1. Contagious bovine pleuropneumonia in lung, showing encapsulated lesion, thickening of the interlobular septa with areas of necrosis

Photo 2. Contagious bovine pleuropneumonia in lung, showing marbling effect in the lung with thickening of the interlobular septa

Development of a novel cocktail ELISA and a lateral flow assay for CBPP

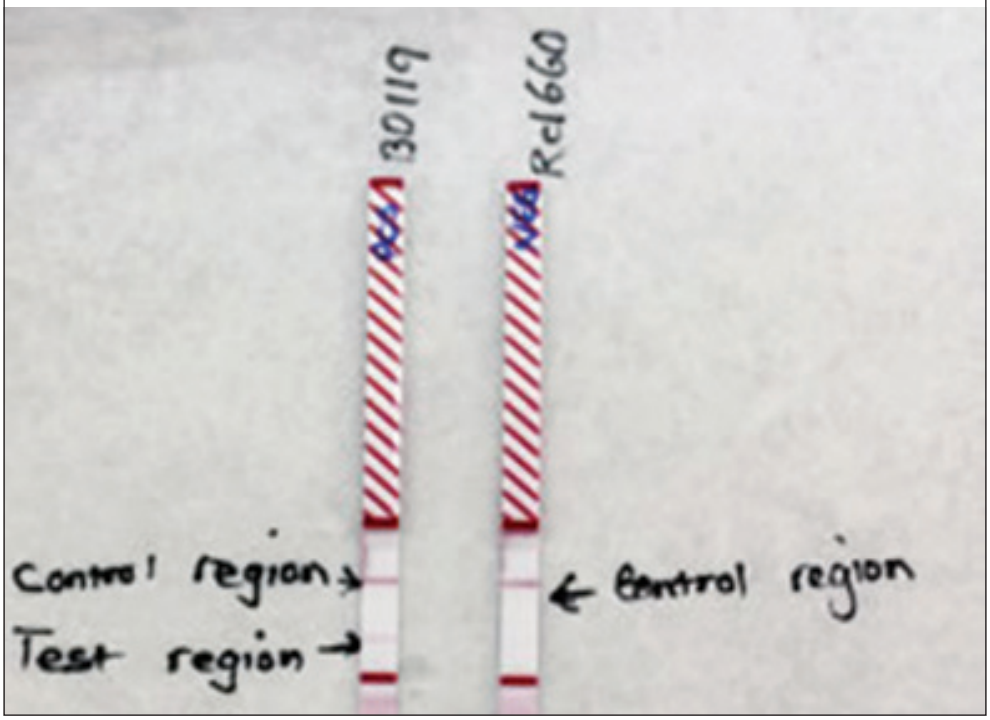
Martin Heller, Nimmo Gicheru, Joerg Jores, Anne Liljander

- Identification of immunogenic proteins.
- Expression and purification of immunogenic proteins -Identification of best immunogens through comparison using well defined experimental and field sera
- Set up of a cocktail enzyme linked-immunosorbent assay (ELISA)
- Proof of principle for a lateral flow assay using a recombinant immunogen.

Scientists from the International Livestock Research Institute (ILRI), and partners developed a new cocktail, ELISA, and a lateral flow rapid test for CBPP, which is based on recombinant *Mycoplasma* proteins. Seventeen immunogenic proteins, selected based on literature reviews and previous laboratory findings, were included in a comprehensive comparison study.

The protein encoding genes were codon optimized for *Escherichia coli* expression, synthesized, expressed and purified by a commercial company to ensure comparable purities. A standardized ELISA protocol was established prior to screening. In the initial screening around 86 well characterized cattle sera were used in order to select the best performing single antigens (n=5). These antigens were subsequently combined in seven cocktails containing two or three proteins, which were then screened against a subset of the sera (n=47) to determine the diagnostic sensitivity and the diagnostic specificity. The three best performing cocktails were further evaluated using one hundred and six additional well characterized sera (experimental and field sera). The final selected cocktail ELISA is easy to produce, generates reproducible results and has a specificity and a sensitivity comparable to the current OIE prescribed serological assays for CBPP diagnosis, i.e. compliment fixation test (CFT) and competitive ELISA (cELISA). Furthermore, we developed a lateral flow rapid test based on one of the strong recombinant proteins from the cocktail ELISA. This field-applicable test was produced by a commercial company and proved to be working in initial tests, thus enabling CBPP diagnosis in <30 minutes. Future ring-trials, evaluating the novel cocktail ELISA and the lateral flow rapid test, should be performed in collaboration with African national laboratories and international bodies such as the World Organisation for Animal Health (OIE), the African Union-Interafrican Bureau for Animal Resources (AU-IBAR) or FAO, to pledge the way for the rollout and subsequent uptake of the assays.

Figure 11
Prototype field applicable lateral flow assay for CBPP produced by Senova GmbH (Weimar, Germany)



CBPP vaccination campaign seromonitoring by c-eLIsa: brief outline of the results of pilot studies in the northern regions of Mali

C.A.K. Sidibe, A. Sery, M. Kone, J. P. Nereyabagabo, F. Mayen, A. Soumano & M. Niang

- Whether c-ELISA could be adapted for CBPP vaccination campaigns seromonitoring despite the limitations of the test.
- Out of 970 vaccinated animals, 507 (51.21 percent) animals seroconverted as compared to only 97 (10 percent) that were positive prior vaccination. This represented an overall increase rate of 41.21 percent.
- Interval of 8-9 weeks post-vaccination was the best time for serum sampling.
- Use of cell phone proved to be very helpful to track the movement of transhumant herds.

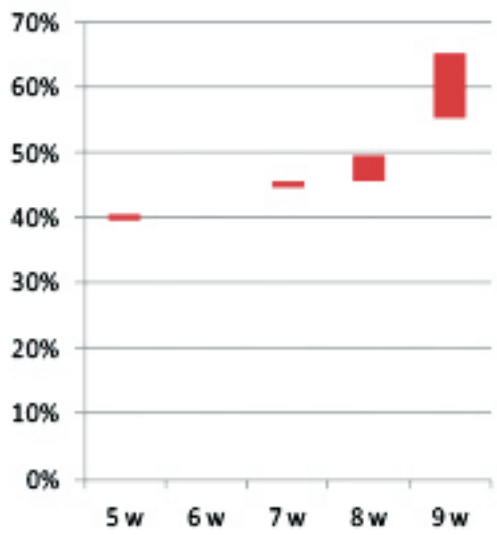
Cattle husbandry plays an important role in the economy of many tropical African countries, including Mali, especially in nomadic areas. Therefore, improving cattle production in these countries is a major objective of the national veterinary services. To achieve this objective, the control of animal diseases, such as contagious bovine pleuropneumonia (CBPP) is a necessary requirement.

Contagious bovine pleuropneumonia (CBPP) is an important infectious disease of cattle that is caused by *Mycoplasma mycoides* subsp. *mycoides* (Mmm). Now that the Rinderpest has been eradicated in Africa, CBPP remains the most important disease in tropical Africa causing great economic losses. Due to socio-cultural and economic reasons, applications of sanitary measures for its control appear not to be feasible in most African countries. For these reasons, at this point in time, the only realistic way of controlling CBPP is by massive and repeated vaccination campaigns. However, the major constraints of such campaigns include the lack of tools for monitoring antibody responses following vaccination.

The competitive enzyme linked-immunosorbent assay (c-ELISA) is currently used for the diagnosis of CBPP. However, it is generally accepted that, like any other serological test, c-ELISA cannot differentiate between post-vaccination antibodies and infectious ones. Nonetheless, it is also accepted that the antibodies induced by T1 vaccines are not detectable by the c-ELISA for more than three months after animals have been vaccinated against CBPP. Hence, with a carefully designed sampling framework, we hypothesize that, at least within the vaccinated herds, it is possible to observe an increased proportion of post-vaccination positive animals compared to that of pre-vaccination.

Since 2012, the northern regions of Mali (Mopti, Tombouctu and Gao) have been under armed conflict. To assist the populations, the International Committee of the

Figure 12
Rate of seroconversion by post-vaccination week



Red Cross Delegation of Mali (ICRC) has been organizing regular annual vaccination campaigns against major animal diseases including CBPP in these regions. The main objective of the present pilot studies was to monitor antibodies levels against Mmm by c-ELISA in herds vaccinated against CBPP, taking into account the limitations of the test.

The study area consisted of four sites selected purposively in each region. Forty-eight (48) herds were also purposively selected in each site. Within each herd 20 animals were randomly selected, giving a total of 960 animals. Selected animals were marked with indelible ink for easy identification. Immediately prior to vaccination, animals were bled for serum sample collection and later after vaccination (5 to 9 weeks post-vaccination).

A total of 1922 sera samples were collected throughout the study area. Preliminary results showed an overall animal positive rate of 10.11 percent (97/970) before vaccination against that of 51.21 percent (507/952) positive animals after vaccination, thus an increase rate of 41.10 percent positive animals. On the basis of these results, it seems that c-ELISA can be adapted for CBPP vaccination campaigns seromonitoring.

Acknowledgement

This study was financed by the International Committee of the Red Cross-Delegation of Mali (ICRC).

Figure 13
Proportion of positive animals (before and after vaccination) by Region

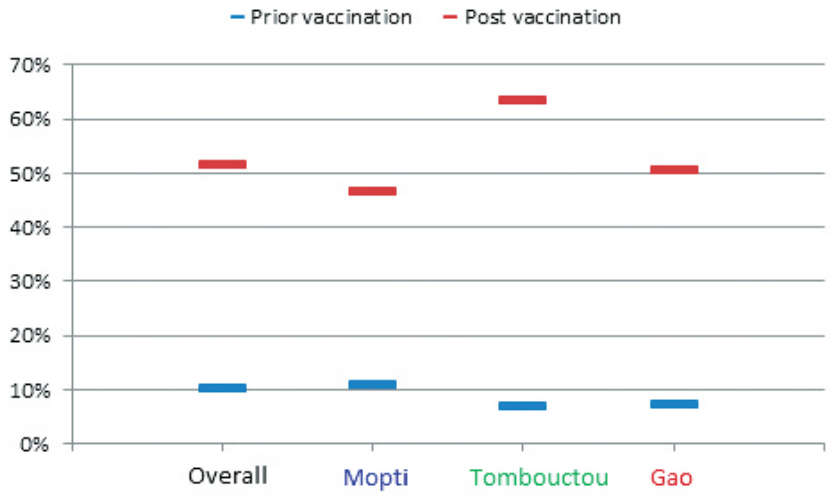
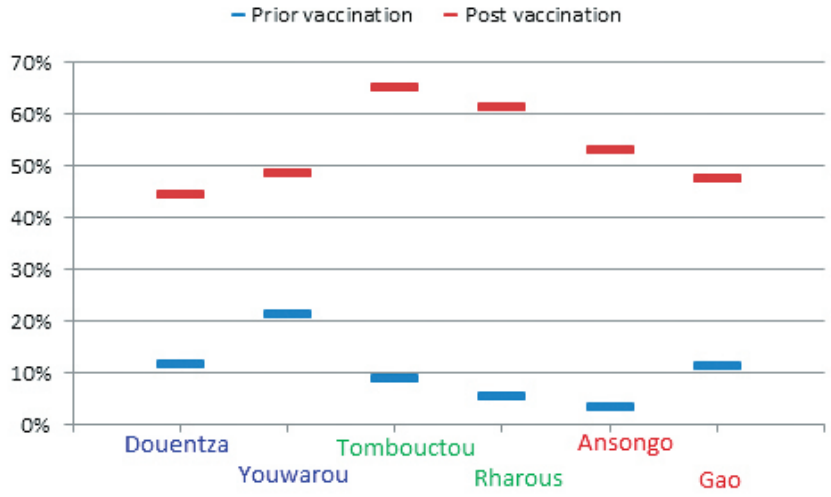


Figure 14
Proportion of positive animals (before and after vaccination) by Circle (Prefecture)The colour of circle names represent region: Mopti (blue), Tombouctou (green), Gao (red)



Mathematical modelling of the transmission dynamics of CBPP for improved vaccines and diagnostic assays

Amos Sematimba, Jorg Jores, Jeffrey C. Mariner

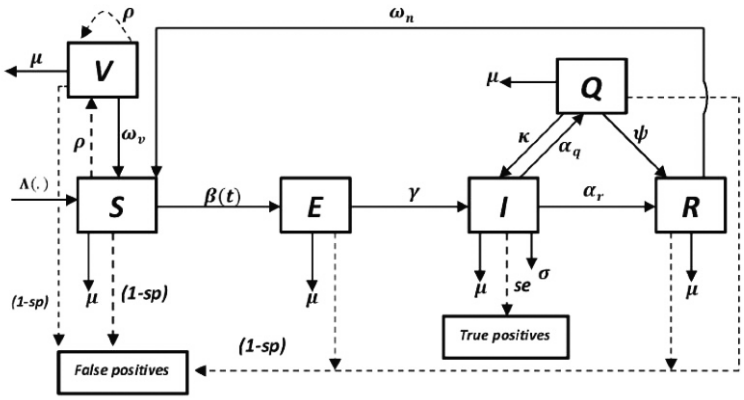
- Small populations, in the order of 100 head of cattle, are able to sustain the transmission of CBPP for indefinite periods and movement control and removal of animals transmitting CBPP (stamping out or treatment) are the most powerful tools for the control of CBPP.
- Vaccination in the absence of movement control or removal of transmitting animals is unlikely to eradicate CBPP, and combined interventions are needed.
- Treatment is the most common control practice utilized today and rationalization of the treatment through research and extension would increase its impact and reduce the risk of the development of antibiotic resistance.

Contagious bovine pleuropneumonia (CBPP) is a cattle disease that has hampered the development of the livestock sector in sub-Saharan Africa through costs associated with trade restrictions, decreased productivity, mortality and disease control. Currently, vaccination with a live vaccine strain is the recommended control measure against CBPP although unofficial use of antimicrobials is more widely practised in the field. Early isolation of infected cattle via accurate diagnosis of the disease is an alternative measure being modelled here.

Modelling techniques are used to assess the potential impact of isolation of infected cattle via improved tests on CBPP dynamics. A herd-level stochastic epidemiological model explicitly incorporating test sensitivity and specificity is developed. Waning of vaccine-induced immunity is implemented using the method of steps and the force of infection is seasonal due to the seasonality in contact pattern. Interventions by annual vaccination, annual screening and isolation, and annual vaccination coupled with annual screening and isolation are implemented in a stepwise manner and their effectiveness compared by running 10 000 simulations per intervention over a ten-year period.

The model predicts that increasing vaccination coverage and vaccine protection duration to 90% and >18 months respectively would clear CBPP at herd level in a few years, if herds are fully isolated from all other contacts (complete biosecurity). Annually vaccinating 37.5 percent of the susceptibles with a vaccine that protects for two years, coupled with screening and isolation or elimination of 75 percent of the infectious animals, performed better than annually vaccinating 90 percent with a vaccine that protects for 8 months and also better than annually screening 95 percent with an improved test that is 95 percent sensitive and 98 percent specific.

Figure 15
Diagram of the heterogeneous CBPP model illustrating the relationship between the 6 states modelled and the parameters governing state transitions



We conclude that regular screening and elimination (quarantine, slaughter or treatment) of infected animals from the herd using improved tests will play a significant role in minimizing the CBPP burden, especially in the current situation where improved vaccines are yet to be developed.

PART 4

CBPP VACCINES DEVELOPMENT

Comparison of novel and conventional vaccines against CBPP using contact challenge

Roger D. Ayling

- Antigen concentration and which adjuvant?
- Challenge Model: in - contact; or direct challenge - a challenge for licensing new vaccines.
- Pathology scoring - usually based on lung lesions. Is pleural fluid, or pericardial fluid part of the immune response or disease?
- Are we using the information / clues we have to help future vaccine design?

Based on a successful experiment carried out in Namibia (full details in manuscript) and subsequent discussions with other experts, the following questions have been raised and discussed. 10-11 year old cattle were intubated to serve as a source of challenge for 3 year old cattle.

What is the optimum age of cattle for testing vaccines and should challenges be by intubation or in-contact?

- For licensing purposes, a known challenge by intubation may be preferable, but does not simulate natural exposure to infection
- The challenge strain used in this study was "Matapi" which caused disease in the intubated and in-contact challenge control cattle. However, what is the best challenge strain to use and should this be consistent in all trials?
- This study had an in-contact ration of 1 to 2.5, which is a much higher contact ratio than the calculated R0 value. What is the optimum in-contact ratio to use?
- The group size in this experiment was 5 animals per group, which gave valuable data, but what is the required size of groups to produce good data for vaccine licensing?
- This novel vaccine experiment used an arbitrary antigen concentration of 1mg/ml, but what is the optimum antigen concentration?
- The adjuvant used was Emulsigen and Rehydragel-LV, but which adjuvant would help stimulate a protective immune response?
- The vaccine was given as a single dose of 1ml subcutaneously, is that a reasonable volume and site for vaccination?
- The time between vaccination and being placed in contact with the challenge animals was 36 days, is that a suitable time gap?
- The length of the trial was 18 weeks, which gave good pathology results, but could it have been shorter and did the unprotected in-contacts then serve as additional challenge?
- The pathology - scoring systems, is biased to lung lesions. Should pleural fluid, pericardial fluid, enlarged lymph nodes and presence of Mmm have more weight?

Photo 3. Cattle in vaccine trial in Namibia

OVERALL VACCINE TRIAL COMMENTS

Using washed cells (Triton for example), and possibly grown as a biofilm, may be effective. (A more thorough washing of cells may have worked). A better, cheaper (3R's) vaccine / animal model is needed. Not titrating out antigens or testing different adjuvants could result in vaccine candidates being missed.

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Setting up of a caprine *Mycoplasma mycoides* infection model and testing of a genome edited mutant strain for its virulence

E. Schieck, A. Liljander, P. Ssajjakambwe, S. Vashee & J. Jores

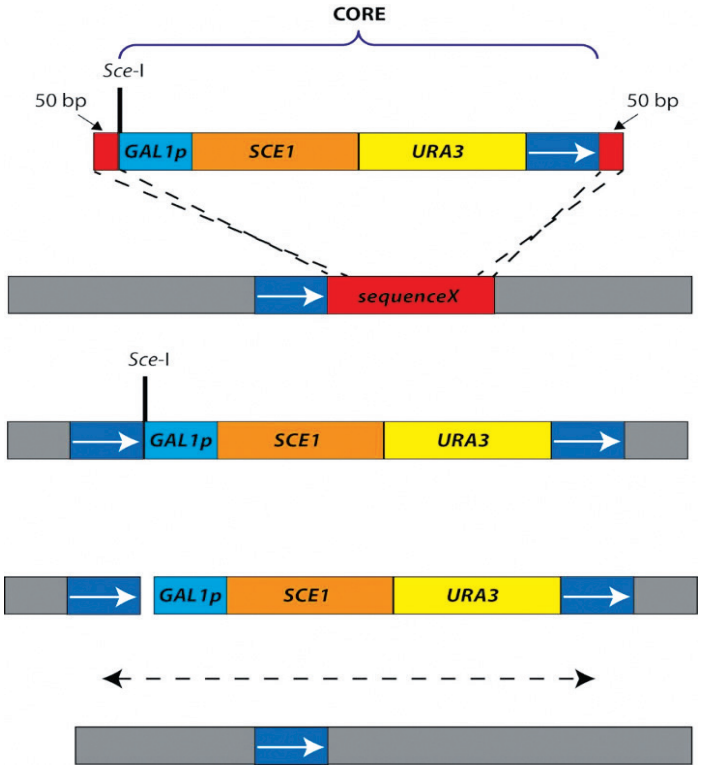
- Setting up of a caprine infection model
- Site-directed mutagenesis of *Mycoplasma mycoides* subsp. capri for proof of principle of an attenuated vaccine strain

Members of the '*Mycoplasma mycoides* cluster' cause diseases such as contagious bovine and caprine pleuropneumonia in small and large ruminants. The advent of genome transplantation and genome editing using an intermediary yeast host enabled the targeted mutagenesis in the goat pathogen *Mycoplasma mycoides subsp. capri.* Better understanding of mycoplasma pathogenicity mechanisms and virulence traits is beneficial for the development of rational vaccines to better protect livestock.

ILRI scientists and its partners aimed to **1)** establish a caprine infection model and **2)** test a mutant strain lacking genes reported to encode candidate virulence traits *in vivo*.

We established a caprine infection model using the American outbreak strain GM12. Goats were infected intratracheally using one billion bacteria per animal. Animals showed clinical signs of disease two days after infection and had to be euthanized within a week post-infection for ethical reasons. We generated a GM12 mutant strain, which lacked five chromosomal regions encoding potential virulence traits and compromising a total of 68 full-length genes using genome transplantation and genome editing via the Tandem Repeat coupled with Endonuclease Cleavage (TREC) method. We then compared the mutant strain to the parental wild-type strain with respect to its ability to cause disease. As expected, the mutant strain showed significantly reduced virulence. This is the first report in *Mycoplasma* of targeted mutagenesis of genes encoding potential virulence traits, subsequently confirmed to be true virulence traits in an *in vivo* model using an autologous host. In a next step we will test the ability of the genome edited strains/ mutant strains to elicit a protective immune response. This work will foster the development of a rational vaccine for CBPP and other against other diseases caused by *Mycoplasmas*.

Figure 16
Cartoon displaying the Tandem Repeat coupled with Endonuclease Cleavage (Noskov et al., 2009, NAR) method, which has been used to delete potential virulence genes



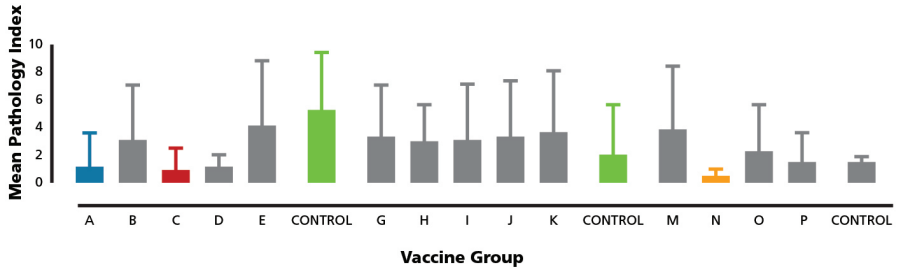
Developing of a subunit vaccine for CBPP in Africa

Jose Perez-Casal, Tracy Prysliak, Teresa Maina, Yeyun Wang, Hugh Townsend, Emil Berberov, Volker Gerdts, Isabel Nkando, Anne Liljander, Joerg Jores, JanNaessens, Reuben Soi, Hezron Wesonga, & Andrew Potter

- Current CBPP vaccines are based on inactivated and live-attenuated strains of *Mycoplasma mycoides* subsp. *mycoides* (Mmm). They do not provide long-term immunity, may cause lesions on vaccinated animals and are not thermo-stable.
- A vaccine based on recombinant Mmm proteins may be beneficial since it would be more stable, could be produced at lower cost, may be combined with other vaccines, and has DIVA potential.
- We used a reverse vaccinology approach to identify potential protective antigens and showed protection of challenged animals after vaccination with some Mmm recombinant proteins. The recombinant vaccine is being tested for safety and duration of immunity.

Contagious bovine pleuropneumonia (CBPP) caused by *Mycoplasma mycoides* subsp. *mycoides* (Mmm) is a devastating respiratory disease of cattle in sub-Saharan countries resulting in significant economic losses to producers due to mortality, treatment and restrictions in trade with other countries. Current vaccines are based on killed Mmm or on live attenuated vaccines such as T1/SR and T1/44. These latter vaccines can reduce the severity of the disease; however, they provide short-time protection and in some cases have mild to severe site reactions and are not thermo-stable. Thus, new vaccines are needed to overcome these disadvantages. We focused on the development of recombinant vaccines since they are more stable, cheaper to produce and they can be used to distinguish vaccinated from naturally infected animals.

Figure 17
Pathology scores



We used a reverse vaccinology approach where the Mmm genome is mined for putative antigens. Using this non-bias approach we selected those proteins that are surface-exposed, including potential adhesins, and have a high probability of stimulating immune responses. We identified 66 antigens and these proteins were formulated with a conventional adjuvant and the oligonucleotide CpG2007. Vaccinated animals were challenged with a suspension of the Mmm Afade strain and monitored for 30 days after the challenge.

We found that animals in two groups showed significantly fewer lung lesions and lung pathology scores; one of these groups was also negative for Mmm in the lungs. An additional group showed reduced lung lesions and pathology scores and was also negative for Mmm. The proteins used to vaccinate the animals of these groups were fused to a truncated form of the M. haemolytica leukotoxin, which is a good carrier. The proteins are currently being produced on a large scale, and they will be tested in vaccination trials for safety and duration of immunity.

Mycoplasma. mycoides subsp. *mycoides* surface antigens and immune deficiency in vaccinated animals

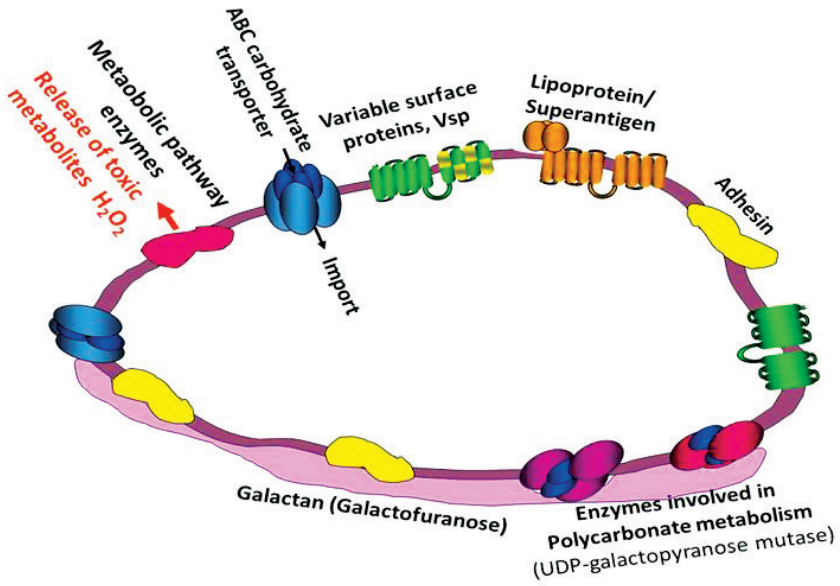
Joachim Frey

- Vaccines against CBPP made from inactivated whole *M. mycoides* subsp. *mycoides* confer no protection but rather increase cattle susceptibility to disease, while life vaccines give relatively low protection.
- Experience from other bacterial pathogens reveals that certain effector proteins completely shut down the host's alert system to recognize infection and to induce immune defence. Such types of antigens, when in vaccines, prevent from inducing protective immunity.
- Design of novel, stable and efficient vaccines against CBPP requires the engineering of *M. mycoides* subsp. *mycoides* deleting such effectors by the use of a gene transplantation technique.

Contagious bovine pleuropneumonia (CBPP) caused by *Mycoplasma mycoides* subsp. *mycoides* is emerging and spreading to most sub-Saharan African countries (Amanfu, 2009). In contrast to Rinderpest, control or eradication of CBPP in Africa using live vaccines was unsuccessful, although vaccines have been applied over many decades. This is mainly due to the fact that the current vaccine strain T1/44, an empirically attenuated strain whose molecular bases of attenuation is unknown, only confers partial short-term protection and provokes side effects due to residual virulence (Thiaucourt *et al*., 2004). Combating *M. mycoides* subsp. *mycoides* with antimicrobials or a combination of antimicrobials and vaccines must be regarded as irresponsible from the point of view of public health, biosafety and ethics because of the tremendous emergence and spread of antibiotic resistant pathogens that represent a major treat to global health (Prescott, 2014; WHO, 2015). Hence, a strong effort to develop a novel, efficient and safe vaccine against CBPP that confers long-lasting immunity is essential for any new strategy to eradicate CBPP from the African continent.

Several attempts to develop new vaccines against CBPP based on inactivated full bacteria or extracts of *M. mycoides* subsp. *mycoides* have failed. New basic knowledge on molecular mechanisms of host::pathogen interactions revealed that *M. mycoides* subsp. *mycoides* is undermining the cattle's immune system, probably due to a particular host adaptation of this pathogen during evolution. Hence, recent data show *M. mycoides* subsp. *mycoides* has adapted central epitopes of virulence factors to the host's own antigens and hence cannot produce neutralizing antibodies (Mulongo *et al*., 2013). Moreover, cattle infected with *M. mycoides* subsp. *mycoides* revealed significant down-regulation of major factors involved in immune defence, such as pro-inflam-

Figure 18
Mycoplasma mycoides subsp. *mycoides* surface antigens.
The determination of the functions of the various surface antigens of *M. mycoides* subsp. *mycoides*, in particular regarding their role in stimulation respectively depression of the host's immune responses will be of principal importance in development of novel and efficient vaccines against CBPP



matory factors, thus causing temporary and local immune suppression that enables the pathogen to proliferate (Rodrigues *et al*., 2015). Knowledge from other bacterial pathogens reveals that specific proteins are able to directly shut down the host's pro-inflammatory warning signals to recognize infection and induce immune defence. Such factors directly hamper vaccination as they do not allow for the mounting an efficient immunization (Figure 1). Finally, *M. mycoides* subsp. *mycoides* expresses certain antigens, in particular lipoproteins, that due to their super-antigen like structures exacerbate the disease in individuals that produce antibodies against these proteins (Mulungo *et al*., 2015). In many bacteria and most probably also in Mycoplasma species, these factors counteract the expected immune-protection of potential live-, inactivated – and subunit – vaccines and must be avoided in new generation vaccine design.

Design of novel, efficient and stable vaccines against CBPP urgently needs an input in profound research on host→pathogen interactions, specifically on the role of interference of particular antigens on the immune response of infected and immunized animals, in order to be able to engineer novel vaccines with the help of gene transplantation techniques (Schieck *et al*., 2015) or expression of single proteins (Perez-Casal, 2015). Based on solid scientific data, a final development of novel vaccines and vaccine formulations will then be possible in a concerted way taking into account climatic, geographic and social factors influencing the efficacy of vaccination campaigns.

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CBPP vaccine:how to improve the efficacy

Hermann Unger

- There is no information regarding IgA build up after standard vaccination. Has it been elicited?
- Is IgA protective against infection?
- As most CBPP vaccines suffer a loss in viability of ~ 2 logs in the production process, there is massive dead antigen compared to the live organisms. As protection against infection is presumably cellular response based, the existing vaccine and its manufacturing process are not able to deliver a product similar to that of the historic original product. Perhaps the addition of a viral immune inducer and improvements in the production process and a re-evaluation of the necessary dose can make the difference (parapox or canarypox).

Vaccinating cattle with the traditional T1/44 derived vaccines does not deliver the protection level needed to be helpful in a control or eradication programme. The reasons for this have long been known:

- Low content of live mycoplasmas in the vaccine (max 10 percent)
- Insufficient understanding of the protective mechanisms towards *Mmm*
- Only anecdotal information on the reduction of CBPP during Pan-African Rinderpest Campaign (PARC), to name but a few. For instance, it is not known whether T1/44 induces a mucosal immunity (Immunoglobulin A) which might be important as it is found in all infected animals which are apparently protected later on.

If the anecdotal information is correct, a viral immune induction in parallel to the T1/44 strain-based immunisation could stimulate a more effective immune response. As morbilliviruses should no longer be applied to cattle; pox viruses may prove useful immune inducers. For instance, Modified Vaccinia Ankara vaccine was shown to stimulate the CD4+ T cell system in cattle and canary and capripox viruses are also considered useful. Along the same lines, it would be beneficial to perform a diagnostic test which could pinpoint (or be correlated with) protection, in order to remove the biggest obstacle in the control campaign: knowing which percentage of a cattle population is protected.

It is therefore proposed to:

- Evaluate the IgA immune response to the T1/44 strain-based vaccine – is IgA immune protective?
- Evaluate a better formulation of the T1/44 based vaccine for lyophilisation to reduce the loss of titre;
- Evaluate the immune response differences between traditional applications and together with a viral immune inducer;
- Expand the search for defining protection parameters against CBPP.

If these topics can be addressed in the context of a national technical cooperation project (IAEA) on controlling CBPP and contagious caprine pleuropneumonia (CCPP) in Senegal, we might gain important missing knowledge to help in controlling CBPP.

Table 3: Inherent parameters and efficacy of vaccines related to the current CBPP vaccine

Safety	safe	some risk	some risk
Virulance	none	might revert	has side effects
Shedding	none	might be shed	might be shed
Immuno suppression	rare	might induce (LSD)	not really known
Side effects	rare	at least fever...	often H202 induction
-100% protection	often requires more than one dose	single dose often enough	only 60% protection
Ab response	yes	yes	yes, to a certain degree
Cellular response	rare	yes	to some extent
Memory development	rare	yes, often	none
Duration	up to 1 year	many years	not even 6 months

Killed vaccine *Attenuated* vaccine *CBPP* T1 vaccine

Quality control of CBPP vaccines in Africa: the role of AU-PANVAC

Nick Nwankpa, Charles Bodjo, Ethel Chitsungo

- Between 2010 and 2015, the African Union- Pan African Veterinary Vaccine Centre (AU-PANVAC) certified 113 batches of CBPP vaccines representing about 169.5 million doses.
- There is a gross inconsistency in the number of countries producing CBPP vaccines and the quantity produced is irregular and inadequate.
- The quality of CBPP vaccines produced on the continent improved generally over the years but a few laboratories still have problems with downstream contamination.

Contagious bovine pleuropneumonia (CBPP) is an infectious and highly contagious cattle disease caused by Mmm. Eradication was achieved in most parts of the world by early diagnosis, slaughter and movement control but in Africa today, especially in endemic areas, vaccination is considered the preferred method of control. Two strains of CBPP vaccines are used at present in Africa; CBPP Strain T1/44, a mild strain isolated in 1951 by Sheriff and Piercy in Tanzania, passaged 44 times in chicken eggs and producing vaccinal reactions in cattle, while strain T1/SR is the Streptomycin resistant variant, sufficiently attenuated not to produce post-vaccinal reactions but considered to be less immunogenic than T1 /44. In 1996, a CBPP reference seed strain, designated T1/44/2 (batch PAN-002), was prepared by PANVAC and the French Agricultural Research Centre for International Development (CIRAD). This seed is in the repository of AU-PANVAC and still being distributed to vaccine-producing laboratories in Africa. Presently, CBPP vaccine strain T1/44 is widely used in most parts of Africa with the exception of some few countries that still use the T1/SR. AU-PANVAC is the African Union Organization mandated to provide international independent quality control of all veterinary vaccines produced or imported into Africa. PANVAC was established in 1986 to certify all vaccines used for the Rinderpest eradication campaign in Africa. Its institutionalization under the African Union in 2004 was in recognition of its contribution to the eradication of Rinderpest and its potential in the eradication of other animal diseases. Between 2010 and 2015, AU-PANVAC certified 113 batches of CBPP vaccines representing about 169.5 million doses (Figure 19). Even though the number of vaccines certified may not accurately represent production values on the continent, this figure is quite low compared to what is required for effective vaccination coverage and the yearly production quantities are irregular. The quality of CBPP vaccines produced on the continent has generally improved over the years but a few laboratories still have problems with downstream contamination.

In order to improve the current CBPP vaccine situation, there is a need to strengthen the capacity of facilities for the production of good quality vaccines and develop a framework for increasing the quantity of vaccines produced; harmonize vaccine production

Figure 19
Vaccine batches certified by AU-PANVAC

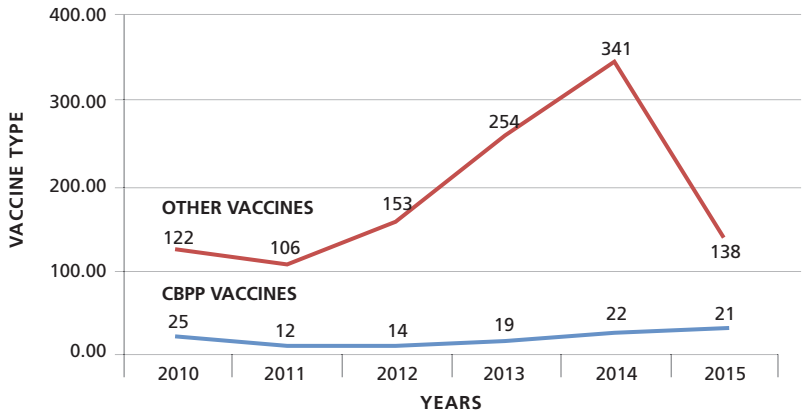

Table 4: CBPP vaccine batches certified by AU-PANVAC

Countries prod. CBPP	2010	2011	2012	2013	2014	2015	TOTAL
Cameroun	7	1	3	4	1	6	22
Nigeria	2	1	2		1		6
Niger	-	-	-	1	-	-	1
Mali	-	-	5	-	-	-	5
Chad	-	-	-	-	-	-	-
Senegal		3		3	3	4	13
Sudan	-	-	-	-	-	-	-
Ethiopia	15	6	2	7	16	9	55
Kenya	-	1	-	1	1	-	3
Botswana	1	-	2	3	-	2	8
TOTAL	**25**	**12**	**14**	**19**	**22**	**21**	**113**

techniques and adopt a single type of vaccine for use on the continent to ensure effective monitoring; develop a system for effective vaccination coverage in the various regions of the continent; develop a framework for public-private partnership in the control of CBPP on the continent and a continental CBPP control strategy with the use of existing vaccines pending the development of new vaccines or vaccine formulations.

AU-PANVAC for its part will provide CBPP vaccine seed to all production facilities in Africa; quality control certification for CBPP vaccines used in eradication campaigns; training in CBPP vaccine production; support capacity of vaccine-producing laboratories for internal quality qontrol of CBPP vaccines; and support diagnostic laboratories in the provision of basic diagnostic reagents for CBPP diagnosis and surveillance. Lastly, AU-PANVAC will continue to strengthen its capacity in order to meet the increasing challenges of animal disease control and eradication on the African continent.

PART 5

THE USE OF ANTIBIOTICS IN CBPP CONTROL

Recommendations of GALVmed Technical Meeting: prudent use of antimicrobials in treatment and control of CBPP in Africa, Nairobi 2012

Angela Colston

- Evaluation of both efficacy and safety of new antimicrobials, and more specifically third generation macrolides in comparison with conventional antimicrobials, in the treatment and control of CBPP is needed.
- Evaluation of the utility of the new generation antimicrobials in integrated programmes for the control of CBPP, including use with current vaccines is supported by new epidemiological modelling.
- The expert group acknowledged the need to support quality assurance of medicinal products, as well as education and training in appropriate use of antimicrobials.

CBPP control has proved extremely difficult given the limitations of available vaccines. Antimicrobials were not approved for CBPP, but despite this, some antimicrobials (principally oxytetracycline) were widely and sometimes inappropriately used against CBPP and other cattle diseases. Existing antimicrobials are often of very variable quality. Two recent developments prompted a re-evaluation of certain specific antimicrobials in the treatment and control of CBPP. Firstly, detailed epidemiological modelling indicates that an antimicrobial of proven high efficacy against CBPP, used in conjunction with current vaccines, would be highly effective in control of CBPP, much more than either vaccine or antimicrobial use alone. Secondly, the novel third generation macrolide antimicrobials (adopted widely in the European Union/United States of America during the last five years for treatment of bacterial and mycoplasma (non-CBPP) respiratory diseases in cattle) have the potential to be highly effective in the treatment of CBPP. Recent scientific data on antibacterial use and CBPP were reviewed by a group of experts and the recommendations of the 2012 Technical Meeting were:

1. Demonstrate Proof of Concept (PoC) for Efficacy of Novel Antimicrobials. Initiate controlled infection studies to demonstrate PoC for efficacy of one or more antimicrobial products compared to conventional antimicrobials. If successful, initiate pilot field studies, using epidemiological modelling data, with or without vaccination. Both regulatory and evaluation of integrated control strategies.
2. Global Alliance for Livestock Veterinary Medicines (GALVmed) to lead a subgroup to define the field studies related to integrated vaccination and treatment strategies. Studies underpinned by good quality standards and partners from Animal Health Industry, experts and international organizations.

3. Develop a Strategic Action Plan for the follow up of these recommendations, including advocacy and implementation. Lead by Global Framework for the progressive control of Transboundary Animal Diseases (GF-TADs)/FAO/ World Organisation for Animal Health (OIE)/ African Union - Interafrican Bureau for Animal Resources (AU-IBAR).
4. Undertake a risk assessment on the use of antimicrobials for CBPP for both human and veterinary pathogens, and other safety matters.
5. Research and related priorities for CBPP (including the social and institutional aspects of service delivery, Public Private Partnerships and the Community) to look at medium- to long-term strategic studies to resolve antibiotic use issues. Importance of maintaining and expanding support for quality control of antimicrobials, and education and training in the prudent use of antimicrobials. Novel, promising vaccines candidates, which are preferably more effective and safer than the current vaccines, require prioritised support and evaluation.

The use of antibiotics in the control of CBPP: an update

William Amanfu

- Key recommendations of CBPP consultative meeting (Rome, November 2006).
- Major outcome of a GALVmed conference on potential use of antibiotics for CBPP. (Nairobi, January 2012).
- The way forward.

In November 2006, the Animal Health Service of the Food and Agriculture Organization of the United Nations, organized a consultative group meeting under the theme CBPP Control: Antibiotics to the Rescue? This meeting was very well attended by the FAO, OIE AU-IBAR and the IAEA and some members of the scientific community with recognized expertise in the prevention and control of contagious bovine pleuropneumonia (CBPP). Major conclusions from this consultation in 2006 were:

- Within the context of the development of new and potent mycoplasmacidal drugs and other chemotherapeutic agents, it is important to revisit the issue of the use of chemotherapeutic agents in CBPP prevention and control because it is a fact of life that farmers are using antibiotics in the field to treat CBPP.
- There is the need for private sector/institutional partnerships in research and development efforts towards medium- to long-term strategic studies to resolve the issue of antibiotic use in CBPP prevention and control.
- Expert opinion of pastoralists in the use of antibiotics in the field must be collated and analysed to link up with structured scientific studies in the laboratory and in the field.

The presentation highlighted the extent to which the recommendations of the 2006 Consultative meeting had been addressed. The potential use of antibiotics in CBPP control was taken up by GALVmed which organized a meeting in London in February 2011, under the technical auspices of the Milken Institute of the United States of America. A major conclusion of this meeting was that whilst there was every justification for the control of CBPP from the point of view of food and nutritional security and improvements in peoples' livelihoods, there was a serious paucity of data to amply support concerted efforts in CBPP control. That notwithstanding, GALVmed organized a meeting in Nairobi, Kenya in January 2012, to evaluate the prudent use of antibiotics in the prevention and control of CBPP. Outcomes from this meeting and some information on what GALVmed is doing with the proof of concept on the use of antibiotics in the prevention and control of CBPP, were presented. Recent declarations by the OIE, the WHO and other statutory bodies on the use of antimicrobial agents in animal production, were also presented at this meeting.

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Photo 4. Cattle severely affected by CBPP. Note the emaciation and distended head

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Photo 5. Lungs of cattle affected by CBPP, cut to show consolidation, areas of grey and red hepatization

Effect of antibiotic treatment on the pathogenesis of CBPP: results of experimental studies with long acting oxytetracycline revisited

Mamadou NIANG

- To assess the efficacy of long-acting oxytetracycline to treat CBPP-infected cattle and define its potential role in the formation of sequestra, as well to determine the potential risk of transmission of the disease from CBPP-infected cattle treated with the molecule.
- Long-acting toxyetracycline treatment had a positive effect on the clinical course of CBPP since all the treated animals recovered completely.
- CBPP-infected animals and those treated with long-acting oxytetracycline do not transmit the disease to susceptible animals.
- Formation of pulmonary sequestra in the majority of CBPP untreated animals, but no evident sequestra in treated animals, except in one animal.
- Thus, CBPP treatment with long-acting-oxytetracycline does not increase the number of carriers.

Contagious bovine pleuropneumonia (CBPP) is an infectious disease of cattle, caused by *Mycoplasma mycoides* subsp. *Mycoides* (Mmm) and represents a serious threat to cattle production. It is nowadays a priority disease in Africa and is currently the subject of various control strategies through either a policy of rigorous restriction of cattle movement, slaughter and compensation (in the developed countries) or massive and repeated vaccination campaigns (in the majority of African countries). In spite of these vast vaccination campaigns in African countries, the disease persists and poses the problem of an immediate alternative solution of control. The use of antibiotic treatment as an alternative option in the control of the disease has always been discouraged based on the perception that treatment of infected animals with antibiotics compromised the control of the disease by generating a large number of carrier animals, which can play an important part in the dissemination of the disease. However, illegal treatment of the disease with antibiotics by livestock owners and even by veterinary auxiliaries is a frequent event in African countries. Indeed, such an illegal practice, despite official condemnation, will surely increase as the privatization of clinical services and the availability of antibiotics increase (photo). In addition, this perception is still not corroborated with relevant scientific information, and is currently the subject of polemics in the scientific community. To fill this gap, limited experimental trials were recently conducted in some African research institutions, including the Central Veterinary Laboratory of Mali,

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Photo 6. Selling veterinary drugs in a local market

with the main objective of evaluating the ability of long-acting oxytetracycline to clinically and bacteriologically cure CBPP infected cattle, and to define its potential role in the formation of pulmonary sequestra in CBPP-infected cattle, as well as to determine the risk of transmission of the disease from treated animals. The objective of the present communication was to revisit the results obtained from these experimental studies in order to provide some answers to the controversy on the CBPP antibiotic treatment issue. Thus, according to the clinical, post-mortem and laboratory findings, it is evident that antibiotic therapy, especially oxytetracycline, which is the most commonly used molecule in Africa:

- can clinically cure CBPP infected cattle;
- cannot provide bacteriological cure of the CBPP infected animals;
- does not generate or increase the number of chronic carriers (sequestra formation);
- can significantly reduce CBPP transmission risk.

In addition, the risk of animals with pulmonary sequestra to transmit the disease to susceptible animals is limited; however, it is difficult to objectively evaluate this fact at this point in time.

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