CBPP Research: Challenges and progress

CBPP GF-TADS

July 22-25,2024

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ILRI INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE

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ILRI's potential contribution

- Capacity for surveillance and modelling of environmental and societal drivers of CBPP occurrence
- Development and improvement of diagnostics tests and vaccines
- Research on antimicrobial resistance profiles
- Assessment of socio-economic burdens of CBPP and micro and macro—economic benefits of disease control
- Technical support in designing disease control programs
- Technical support in evaluation of disease control strategies
- Technical support in laboratory assays
- Evidence for using in continuous improvement of CBPP programs

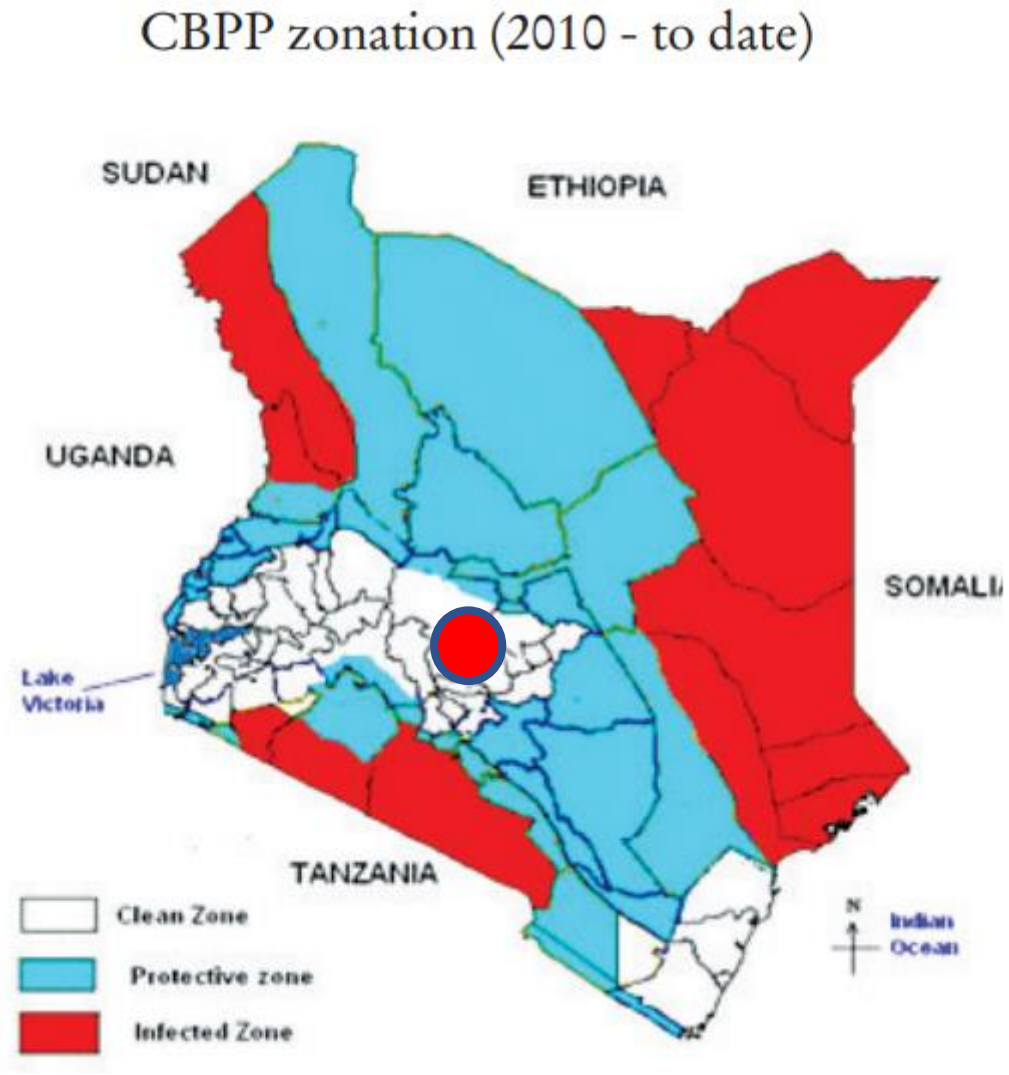
Contagious Bovine Pleuropneumonia: Zoning approach

The control strategy was based on vaccination and animal movement control in three zones:

- **CBPP clean areas "zone I":** surveillance was carried out in all slaughter facilities accompanied by zoosanitary measures at livestock markets, borders check points and stock routes.

- **Recently infected areas "zone II":** disease surveillance and vaccination in the event of a confirmed outbreak. enforced zoosanitary measures.

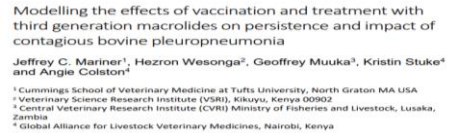
- **Endemic areas "zone III":** the strategy was intensive vaccination and zoo-sanitary control measures.



Contagious Bovine Pleuropneumonia: Reality

- **Diagnosis:** took up to 3 months for a section of herd
- **Livestock death:** 400
- **Movement control**: None
- **Control policy**: Unclear

Background



For vaccines to be a truly “stand-alone” intervention, high levels of efficacy >90% and longer duration of immunity will be required.

The results indicate that intervention programs based on systematic detection and treatment of suspect cases with oxytetracyclines or third generation macrolides can result in the elimination of CBPP from defined endemic populations within a period of six months.

A second option identified was programs that promote treatment of clinical cases and vaccination of the contact population at risk. These targeted treatment and vaccination approaches have the potential to eliminate infection in time frames of two to three years.

In the future, pilot control programs based on public-private-community-partnerships should be implemented at the community level that address both the technical strategy and the institutional and socio-economic challenges and opportunities for control.

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Modelling and testing integrated CBPP disease control for adoption by governments, WOAH and FAO

- Identify critical parameters for building a practical and feasible CBPP disease control model in an endemic area
- Model and pilot a combination of treatment, vaccination and quarantine for control of CBPP
- Expand geography of model to demonstrate feasibility of new method
- Develop written protocols and guidelines for integrated CBPP control
- Present new protocols and guidelines to the WOAH General Assembly for inclusion in scientific manuals and the Terrestrial Code for adoption.

Objective:

- To develop, model and test an integrated CBPP disease control program for endemic areas.
- To present for adoption to WOAH, FAO and regional partners new guidelines and protocols for CBPP control in Africa.

Funding: BMGF & IDRC

Partnership:

1. **Lead: ILRI, Kenya – (Musa Mulongo, Bernard Bett, Elise Schieck)**
2. GALVMed (Edinburgh, UK)
3. University of Cambridge, Vet. Med & Epidemiology
4. Tufts University, Boston, USA
5. KALRO
6. Directorate of Veterinary Services, Kenya

Recent observations on use of Tulathromycin and oxytetracylines in the treatment of contagious bovine pleuropneumonia in Kenya)

Authors

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Overview

01 introduction

02 Drugs used

03 Ranches Followed

05 Results

06 Outcomes

07 Recommendations

Introduction

•Contagious Bovine Pleuropneumonia (CBPP) is a severe lung disease of cattle, caused by Mycoplasma mycoides subspecies mycoides (Mmm).

•Without intervention, mortality can reach 100% in naïve herds during outbreaks

•Kenya has places which have not had CBPP since the 1970s. But now effects of climate change have seen movement to more distant grazing areas, introducing CBPP in places it had not been observed for long.

Introduction cont..

- **This makes traditional control recommendations of slaughter of infected animals and prophylactic mass vaccinations less effective, requiring a better approach in previously clean areas.**
- **In these non-endemic areas, effective action for control follows conclusive diagnosis, which may take up to 30 days**
- **By then, the disease has spread to almost the entire herd and farmers resort to antimicrobials**

Introduction cont..

- Not recommended because of the perception that they induce formation of lung sequestrate
- Farmers know that antimicrobials have a positive effect on progression of the disease. They use first because:
- Differential diagnosis for clinical signs of CBPP
- East Coast Fever,
- Pasteurellosis (Shipping fever)
- Any condition with fever and labored breathing (trypanosomosis)

Drugs used

- We followed several ranches in Kenya for outcomes on treatment and vaccination. Most used:
  - Oxytetracyclines (Yaya et al., 2003: Niang et al., 2010; Otina et al., 2020) as the first line of response
  - On confirmation of CBPP they used Tylosin (Windsor and Masiga, 1976)
- Whereas some other countries have reported use of : Danofloxacin (Huebschle et al., 2006) a flouroquinolone, Mycoplasmacidal/Bactericidal
- In Kenya, Tulathromycin (Muuka et al., 2019), a 2nd generation macrolide was tried on one of the ranches.

Results from Ranch of focus

- Preceded by a trial replicated in Kenya and Zambia using Tulathromycin and Gamithromycin, the efficacy was above 80%

- On a ranch in Kenya holding approximately 6,000 head of Boran cattle (valued at approx.US$ 712 each) that experienced a CBPP outbreak

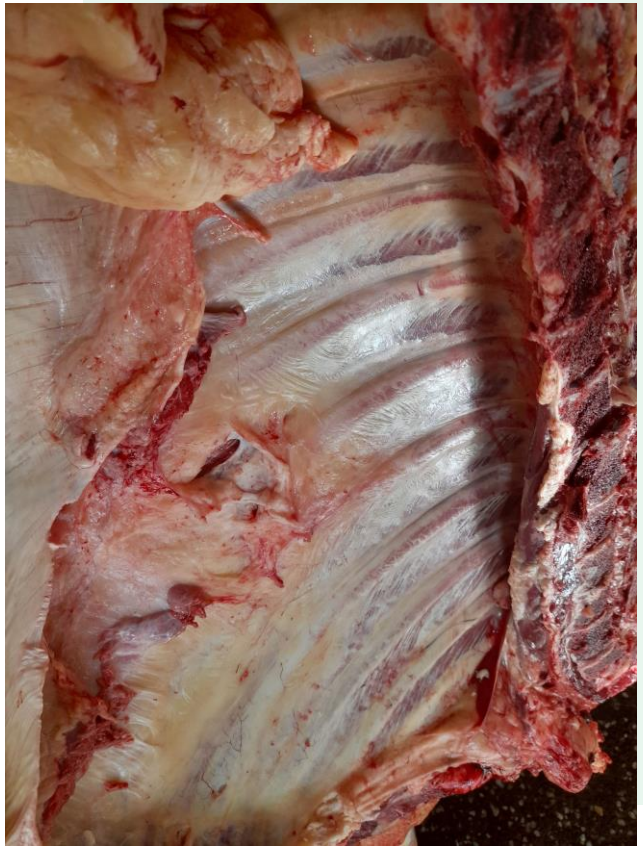
- All cattle on the ranch were administered with tulathromycin in Dec 2022

- Treatment was followed by vaccination[14] 21 days later using live T1 44 strain of *Mmm*

- Booster vaccination in June 2023 (6 months later) to raise efficacy (according to Wesonga and Francois, (2010)

Outcomes

- Treatment with Oxytetracycline alone or followed by Tylosin reduced severity of the disease but new cases as well as relapses were observed



- **No new cases of CBPP were observed in herds treated with Tulathromycin**

- Whereas animals treated on other ranches show evidence of chronic CBPP in carcasses (fibrous adhesions), follow up on slaughtered animals treated with tulathromycin did not show evidence of lung lesions (acute or chronic)

Recommendation

- Apply recommendations of the 3rd meeting of the FAO-OIE-AU/IBAR-IAEA Consultative Group on CBPP(Rome 12–14 Nov 2003):
    - *Mass vaccination and antibiotic treatment for 5 years in enzootic zones*
- Whereas the recommendation then was to sell treated animals when they recover, it appears that the use of new generation macrolides eliminates the need for that recommendation. However, this still requires collection of more supporting data

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Kenya Agricultural & Livestock Research Organization

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Thank You

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Report of CBPP expert Workshop on measurement of efficacy in Clinical Trials

Frankfurt April 9-10, 2024

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Meeting Objectives

- To update and document guidelines for experimental and field efficacy parameters for CBPP

- To develop consensus on most appropriate scoring system for interpretation of CBPP vaccine or pharmaceutical efficacy

General Observations

- Meeting should not replace company claims for new vaccines or treatment as these are specific and should be subjected to normal regulatory rigor

- The usefulness of the scoring system must correspond to the situation:
  - *Controlled trials*
  - *Field trials*
  - *Surveillance*
  - *Presence of absence of trained pathologists*

- Pros and cons of composite scores – what are the alternatives?
  - *Cons: Obscures information*
  - *Pro: A conclusion is made, weighted scoring system*

Recommendations:

- Protection against Disease
  - Mortality
  - Respiratory Signs (Coughing; dysnpea; effort; nasal discharge; auscultation)
  - Post-mortem lesions
  - Immune response- CFT or ELISA
  - Fever
  - % Weight loss
  - Lethargy/Inappetence
  - Isolation of pathogen from lesions
  - Biomarker of disease outcome (current gap)
- Protection against Transmission
  - Above criteria AND
  - Seroconversion of naïve contact animals
  - Measure of shedding
  - Immune response

Recommended Indicators of CBPP Disease

- ***Severe dyspnea (standard)***
- ***More than 3 consecutive days of >40.5 C fever or more than 4 consecutive days > 39.5C or below <36C(standard)***
- ***Prostration of animal (standard)***
- ***% weight loss (standard)***
- ***Pulse-Ox <90% (optional)***

Thank you……

United States Department of Agriculture

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Canada

STAR-IDAZ International Research Consortium on Animal Health