Food and Agriculture Organization of the United Nations

SUSTAINABLE DEVELOPMENT GOALS

Use of antibiotics in the control of CBPP: challenges and aspirations

1st meeting of the SGE on CBPP of the GF-TADs for Africa
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MENU

1. **Reminder**

   - What is CBPP

   - Control strategies of CBPP

2. **Antibiotic in CBPP treatment**

   - Historical background

   - Progress made until the present

   - <u>Perspectives/Aspirations</u>:
     - Approach to integrate antibiotics in the control strategies
     - Challenges & limiting factors of antibiotic option in the control strategies

3. **Conclusions**

I. BACKGROUND/REMINDER (5 slides)

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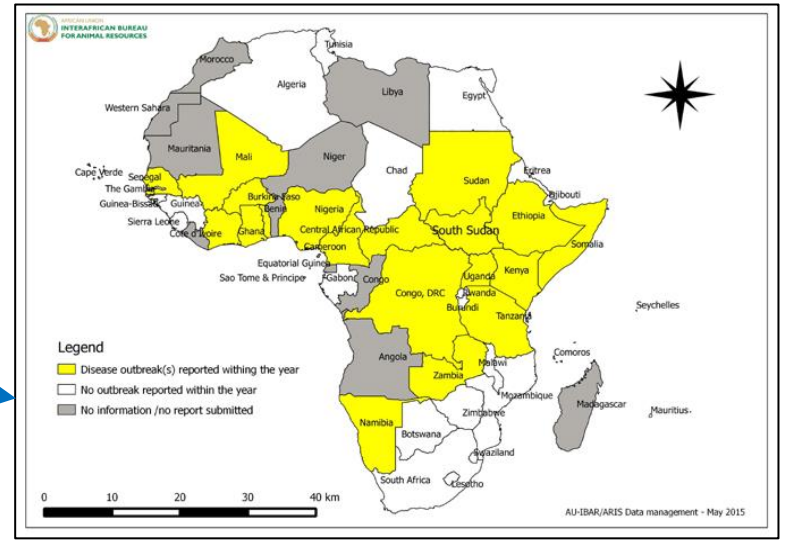
What is CBPP??

- One of the most important diseases in Africa
- Classical animal movement disease
- Huge **economic losses** (45 million Euros/year)??
- Endemic in sub-Saharan Africa



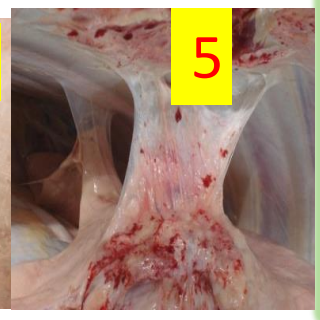
1. Respiratory disease
2. Pleural fluid
3. Hepatization and fibrin of the lungs (unilateral)
4. Marbled appearance of the lungs when cut

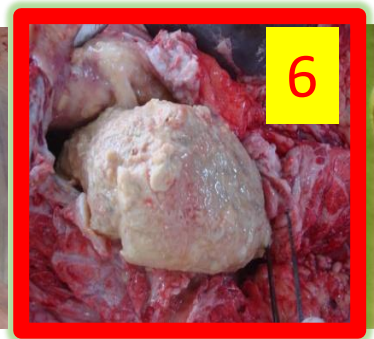
} acute lesions

5. Lung adherence
6. Pulmonary sequestrations

} chronic lesions

7. Caused by *Mmm*





Control strategies of CBPP

1. **Sanitary prophylaxis based on:**
   - Restriction of cattle movement
   - Quarantine
   - Slaughtering and compensation

➢Unfortunately, difficult to achieve in most African countries

2. **Medical prophylaxis based on the vaccination:**
   - live attenuated T1/44 vaccine
   - live attenuated T1/SR vaccine

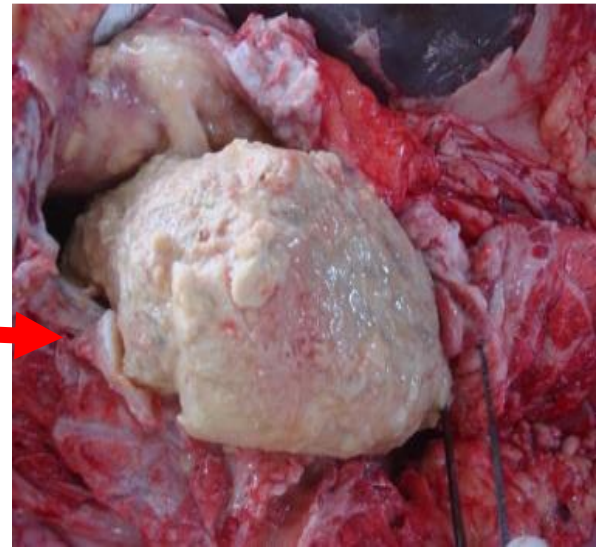
➢To be effective, comprehensive and sustained vaccination campaigns over several years is required. Unfortunately, this has proved very difficult to achieve in most African countries

Question 1: What is the place of antibiotics???

What is the place of antibiotic therapy?

Dismissed from the onset based on prejudgments not scientifically and objectively founded:

- Antibiotic therapy may predispose infected cattle to develop chronic carriers (pulmonary sequestras)
- Chronic carriers spread the disease by reactivation of sequestrated lesions



Note:

1. Formation of sequestra is a natural healing process (defence mechanism of Mmm)
2. Lack of scientific data to substantiate reactivation of sequestrated lesions
3. Existence of scientific data that contest this theory

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Paradox in current CBPP control policies

❖ Antibiotic therapy is officially prohibited, yet:

- Vaccination recommended, but vaccines not authorized and not accessible to farmers
- Antibiotics not recommended, but widely available and accessible to farmers who treat their animals freely

❖ Despite official condemnation, antibiotic treatment is a very common practice in the field

Photo (F. Thiaucourt, CIRAD, Montpellier)

Conclusion: This condemnation is counterproductive, because despite its prohibition, the practice will certainly increase due to the privatization of clinical services and the increasing availability of antibiotics (private pharmaceutical stores).

Question 2: What to do???

What to do now?

Growing initiatives and ideas among the scientific community calling for greater consideration of antimicrobials in CBPP

Instead of blindly condemning the procedure, efforts should be made to integrate antibiotics in CBPP control strategies.

But, there are prerequisites to work on:

- **Assess the effect of treatment on the pathogenesis of the disease**
- Optimize the drug formulation and regiments for use to meet established and accepted control criteria

Note: These requirements are critically important for consideration of antibiotics in CBPP control strategies

Question 3: What was known about antibiotics in CBPP: very old contested issue

II. ANTIBIOTIC IN CBPP TREATMENT

- Historical background (3 slides)

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Antibiotic treatment for CBPP: Very old contested issue

At the 3rd FAO/OIE/OAU Expert Panel meeting on CBPP in Khartoum in 1967 it was reported that "The mass drug or antibiotic treatment of CBPP should be discouraged"

- ✓ Moret P, Balis J, Bachirou SM, (1949). Action de quelques antibiotiques sur le virus péripneumonique de bovin. Bull. Acad. Vét. Fr., 22: 255-257.
- ✓ Mornet, P., Orue, J., Marty, J.P. (1951). Note sur le traitement de la PPCB par la pénicilline la streptomycine et certains dérivés sulfamides. Action comparée au novarsenobenzole. Bull. Acad. Vet. Fr. 24, 213-218.
- ✓ Camara A.H., (1956). Essai de traitement de la PPCB par la Bronchocilline. Rev. Elev. Méd. vét. Pays trop., 9 (4): 351-357.
- ✓ Hyslop, N.S.G., Ford, J. (1957). Therapy of CBPP. Preliminary observations on the treatment of early cases by chlortetracycline. Vet. Rec. 69, 541-543.
- ✓ Orue J, Mémery G (1961). La PPCB. Traitement par le Novarsénobenzol. Conséquences épidémiologiques et prophylactiques. Rev. Elev. Méd. vét. Pays Trop., 14(4): 405-411.
- ✓ Hudson, R., Etheridge, J.R. (1965). CBPP: experiments with the antibiotic tylosin. Aust. vet. J. 41, 130-135.
- ✓ Windsor R.S., and Masiga W.N., (1977). Investigations into the role of carrier animals in the spread of CBPP. Rev. Sci. Tech. Off. Int. Epiz, 23: 224-230.

Antibiotic treatment for CBPP: Very old contested issue

No doubt, since these days and based on these studies, antibiotic therapy was recognized to clinically improve the outcome of the infection.

Question 4: But, what triggered the controversy?

Orue J, Mémery G (1961). La PPCB. Traitement par le Novarsénobenzol. Conséquences épidémiologiques et prophylactiques. Rev. Elev. Méd. vét. Pays Trop., 14(4): 405-411. May have been the source of the controversy.

Despite the opposing publication of: Windsor and Masiga (1977). Investigations into the role of carrier animals in the spread of CBPP. Rev. Sci. Tech. Off. Int. Epiz, 23: 224-230.

Debates: frequently asked questions include:

1. Does antibiotic therapy clinically cure CBPP infected cattle?
2. Does antibiotic therapy bacteriologically cure infected CBPP cattle?
3. Does treatment of infected cattle can generate chronic carriers (sequestra)?
4. Do chronic carriers (animals with sequestrations) disseminate the disease?
5. Does treated cattle transmit the disease?

❖ More recently, the problem of AMR comes in.

Question 5: Why the sudden renewed interest in this taboo issue??

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Meetings/Conferences calling for greater consideration of antimicrobials in CBPP

Vaccination failure has led to calls for greater consideration of antibiotics in CBPP control:

Recently, to stimulate in-depth discussions of what for many years had been a taboo subject, P. Roeder, M. Rweyemamu and W. Amafu (Retired from FAO) initiated debates on the issue thru several forums.

FAO/IBAR joint meeting in Arusha, Tanzania, in 1995 was the starting point

Then, followed several similar consultative forums:

- FAO-EMPRES, 2001 "Electronic Forum on CBPP"
- FOA-OIE-AU/IAR-IAEA, Rome, 2003 "Towards sustainable CBPP control programs for Africa"
- FOA-OIE-AU/IAR-IAEA, Rome, 2006 "CBPP control: antibiotics to the rescue?"
- GALVmed, Nairobi, 2012 "Responsible and prudent use of antibiotics in the control of CBPP"
- FOA-OIE-AU/IAR-IAEA, Rome, 2015 "Can CBPP be eradicated?: the use of antibiotics in its control"

Question 6: Do we have data evidence to move forward??

II. ANTIBIOTIC IN CBPP TREATMENT

- Recent progress made (3 slides)

Antibiotic therapy for CBPP: recent progress made

FAO-OIE-AU/IBAR-IAEA: Conclusions of the CBPP advisory group (FAO Rome 2015) indicated the following.

1. Based on animal experiments: KARI-Kenya/ILRI, 2003; LANAVET-Cameroon, 2003; CVL-Namibia; 2006; **LCV-Mali, 2006/2010;** ILRI-Kenya, 2014

Questions	Answers
1. Can antibiotic therapy (oxytetracycline) clinically cure infected cattle?	Yes
2. Does oxytetracycline treatment of infected cattle generate or increase the number of chronic carriers (sequestras)?	No
3. Can oxytetracycline treatment significantly reduce the risk of disease transmission?	Yes
4. Can antibiotic therapy (oxytetracycline) provide complete bacteriological cure of animals with sequestra?	No*
5. Is there a risk that animals carrying sequestra lungs transmit the disease to susceptible animals?	Negligible to low**
*Recovery of Mmm in some sequestra; **The risk is difficult to assess	

Antibiotic therapy for CBPP: recent progress made

These results are supported by other recent similar experimental trials conducted in some African research institutions using different molecules:

- **Third-generation macrolides** such as tulathromycin and gamithromycin (GALVmed) in CVRI-Zambia, 2019 and VSRI-Kenya/ILRI, 2022

- **Oxytetracycline** in VSRI-Kenya, 2022

Antibiotic therapy for CBPP: recent progress made

2. Based on the various modeling studies:

Control by annual vaccination with current vaccines is technically possible, but eradication is not possible.

- It appears that current vaccination campaigns serve only to limit clinical disease to reasonable proportions rather than to eradicate infection.

- With current vaccines, it is unlikely, even with mass vaccination campaigns over several years, to achieve eradication unless other strategies, such as antibiotic therapy, are also associated.

An alternative approach to CBPP control/eradication is needed:
Antibiotic therapy option

Question 7: How to go about the antibiotic option?

II. ANTIBIOTIC IN CBPP TREATMENT

- **Perspectives:** approach to integrate antibiotics in the control strategies (4 slides)

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Approach to integrated antibiotic in CBPP control strategies

As a reminder:

- Three main classes of antibiotics are effective against mycoplasmas (tetracyclines, fluoroquinolones and macrolides)
- Existence of recently approved 3rd generation macrolides (tulathromycin, gamithromycin, etc.) which can be administered less frequently and for a shorter duration.
- **Two commonly discussed approaches based on the modeling work of Jeff Mariner:**

1. Elective/optional strategies:

Determined by the livestock keepers: it is a question of integrating the vaccination of healthy animals with the treatment of sick animals to improve the condition of the animals for slaughter;

Public good vs private good: should CBPP be considered a private good?

Livestock keepers can adopt a private/individual management of the disease, allowing them to treat clinical cases in a well-framed strategy through authorized agents.

Approach to integrated antibiotics in CBPP control strategies

2. Targeted use of antibiotics to reduce shedding (when culling not possible)

This involves regularly vaccinating cattle while treating sick animals and, if possible, isolating individual animals when they develop clinical disease.

In this way, the benefits of vaccination (increase in high levels of herd immunity) and treatment (possibility of saving animals that might have died) would work synergistically to reduce losses.

In both cases, by reducing the duration of the clinical phase, the excretion/transmission, the incidence and the mortality of CBPP, antibiotic treatments could bring "a plus" in the control strategy of the disease

Question 8: How to implement such strategies??

Implementation suggestions

Implementing such strategies would require to:

1. Develop a profile of the antibiotic(s) to be used;

2. Conduct pilot studies as part of a "**proof of concept**" to demonstrate that CBPP can be controlled by combining vaccination with rational and regulated use of antibiotics;

3. Involve livestock owners to understand their coping mechanisms:

   - Collection of traditional knowledge, attitudes, perceptions and practices to generate information for use during sensitization exercises

   - Collection and analysis of the expertise of herders on the use of antibiotics

4. Have adequate distribution systems especially for remote areas

5. Clarify the risks of antibiotic resistance

Proposal of a "proof of concept"

- Define an area (hot spot)
- Vaccinate all healthy animals (100%)
- Treat all outbreaks (sick animals)
- Follow up regularly

Hopefully, results may provide additional solid science-based evidence needed for the amendment of WAHO Terrestrial Animal Health Code in the control of CBPP, which could provide another tool in the progressive control of the disease

Question 9: What are the key practical challenges???

II. ANTIBIOTIC IN CBPP TREATMENT

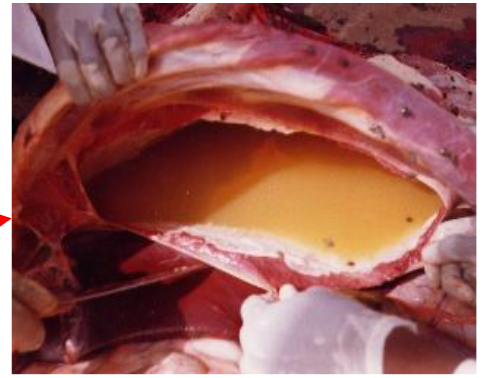
- **Challenges/limiting factors** of antibiotic option in the control strategies (1 slide)

Antibiotic therapy option: Challenges/limiting factors

The use of antibiotics in treatment of CBPP may have some practical implications especially in pastoral areas where CBPP occurs in an endemic status.

Hence, integrated strategies must be carefully designed and properly implemented in consideration of the following parameters:

1. Antibiotic use in Africa is 'sub-optimal'
- Product quality is generally not tested
- Storage conditions are not controlled
- Administration protocols are not optimized
- Regulatory gap/unregulated use



2. Practical implications
- Timing to treat clinical cases as CBPP is insidious in nature
- Under-dosing due to wide range of concentrations may delay early diagnosis of the disease
- Untreated infected animals would pose a serious risk to the treated animals once the antibiotic effect had waned
- Waiting times are not respected (**AMR**)

Antibiotics cannot replace vaccination. Alone do not provide control/eradication

III. Conclusions

1. **Eradication of CBPP in the near future will be difficult with existing policies which are:**
   - Inappropriate in the current African context;
   - Not properly implemented.

Hence, must be thoroughly reviewed to **rationally** include the antibiotic option.

2. **As of today:** enough base line data available to help move forward

3. **Need a "proof of concept"** to demonstrate that CBPP can be controlled by combining vaccination with rational and regulated use of antibiotics.

4. **CBPP victims of antibiotic therapy as:**
   - Most treatments are probably not specifically aimed at CBPP. It is simply a common practice in the field to fight against a series of pathologies
   - Formation of sequestras is part of the normal healing process
   - **Role of small ruminants in the epidemiology of CBPP??**

Note:
- Rational use of antibiotics can reduce the number of antibiotic treatments, hence reduce AMR
- Research on formulations and treatment regimens deserves the same level of attention and investment as that on vaccine development

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Thank You