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Recommendations no 7 and 8 of the OIE Global Conference on AMR concerning Autogenous vaccine

6th Cycle Regional Training Seminar for OIE Focal Points for Veterinary Products (Africa),

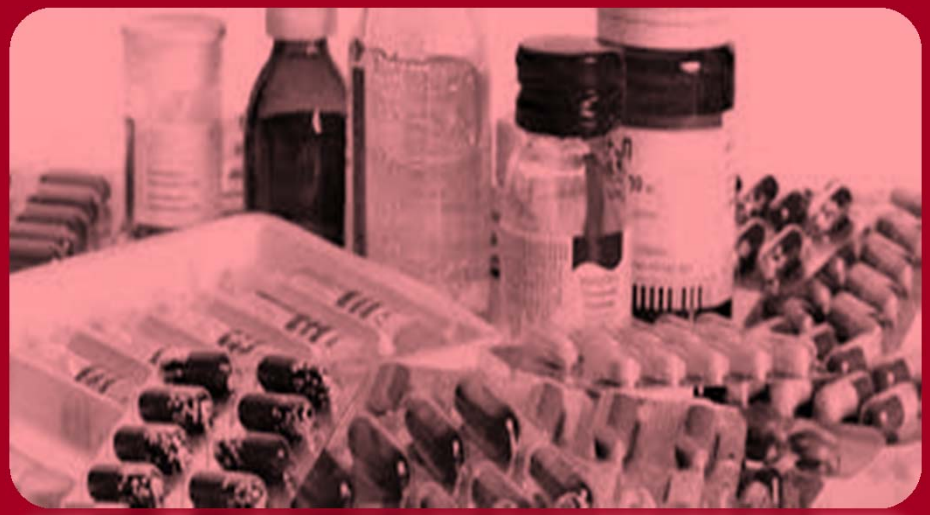
Addis Ababa, Ethiopia

9-11 July 2019

Agenda

- Introduction
- Alternatives to Antibiotics
- Vaccines
- Autogenous Vaccines
- Conclusions

Chapter 1



Introduction

Recommendation no. 7 & 8 of the OIE Global Conference on AMR

encourage research…… on the development of priority vaccines and other alternatives to antimicrobials

develop standards or guidelines related to autogenous vaccines and other alternatives to antimicrobials including guidance for quality, safety and efficacy as tools to reduce the need to use antimicrobials

Chapter 2

Alternatives to Antibiotics

Alternatives to Antibiotics

- increasing public health concern about consequences of increased AMU in livestock production due to;
  - Failure of treatment or prophylaxis
  - Residues of veterinary drugs in food or animals origin
  - Antimicrobial resistance (AMR)

Alternatives to Antimicrobials

urgent need for alternatives to antibiotics

- to prevent economic losses
- improve the growth performance in farm animals
- minimize or eliminate the pathogen load in the livestock and food chain.

Examples of alternatives to antibiotics

- Antimicrobials engineered against multi-resistant pathogens
- Bacteriophage
- Bacteriophage gene products
- Essential oils
- Immune enhancers
- Innate defense molecules
- Naturally occurring antibacterial lytic enzymes
- Organic acids
- Phytochemicals
- Prebiotics
- Probiotics
- Small interfering RNAs
- Therapeutic antibodies
- Vaccines

Chapter 3

Vaccines

Veterinary Vaccines

Veterinary biologics - work by stimulating an animal's immune system to prevent or treat diseases

Effective tools for;

- preventing animal diseases,
- promoting animal health, welfare,
- safe food production and
- preventing animal-to-human transmission of infectious diseases

Veterinary Vaccines

- reduce the need to use antibiotics in animals
- cost-effective medical countermeasure against antimicrobial resistance
- optimally fulfil their potential when used as part of infection prevention and control
- veterinary oversight, good biosecurity and husbandry practices, quality feed, and improved diagnostics ensure targeted treatment for specific pathogen
- ,

OIE ad hoc Group on Prioritisation of Diseases for which Vaccines could reduce Antimicrobial Use in Animals

- Use of multivalent vaccines
- Proposed cattle, chicken, swine and fish diseases where development or improvement of vaccines
- *autogenous vaccines- out of scope due to lack of broad applicability, registration variability and the absence of key efficacy data.

Table 1: Pathogens/diseases which entail high and medium use of antimicrobial agents and for which vaccines would significantly reduce the need for antibiotic use in cattle

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
Respiratory	*Mannheimia haemolytica* (Bovine Respiratory Disease Complex, BRD)	High	Yes	• Timely delivery (time of vaccination in relation to natural challenge) • Onset of immunity (one dose versus two doses) • Differences in serotype • Potential lack of cross-protection • Leukotoxoid content in some vaccines is not controlled	High
	Pasteurella multocida (BRD)	High	Yes	• Timely delivery • Marginal efficacy • Potential lack of cross-protection	High
	Mycoplasma mycoides subsp. mycoides small colony (Contagious Bovine Pleuropneumonia, CBPP)	High	Yes	• Marginal efficacy • Short duration of immunity • Safety (live vaccine with residual virulence) • Access limited to official control programmes	High
	Histophilus somni (BRD)	High	Yes	• Timely delivery • Adverse reactions when used in large combinations • Basic research needed on epidemiology and pathogenesis	Medium
	Bovine Virus Diarrhoea Virus (BRD)	High	Yes	• Timely delivery • Maternal antibody interference • Not all vaccines protect against Type 1 and Type 2, and Hobi-like viruses	Medium
	Mycoplasma bovis (BRD)	Medium	Yes	• Timely delivery • Limited efficacy • Vaccine not available in all countries • More research needed on epidemiology and pathogenesis • Lack of challenge model • Co-infections	High

Mastitis	*Streptococcus agalactiae*	High	Yes	• Marginal efficacy • Strain variation • Lack of cross-protection • Multiple doses needed for efficacy	High
	Streptococcus uberis	High	Yes	• Marginal efficacy • Strain variation • Lack of cross-protection • Multiple doses needed for efficacy	High
	Coagulase negative *Staphylococci*	High	Yes	• Marginal efficacy • Strain variation • Lack of cross-protection • Multiple doses needed for efficacy	High
	Staphylococcus aureus	High	Yes	• Marginal efficacy • Strain variation • Lack of cross-protection • Multiple doses needed for efficacy	High
Systemic	*Pasteurella multocida* (haemorrhagic septicaemia)	High	Yes	• Satisfactory vaccines, but issues with availability	Low
	Leptospira spp.	Medium	Yes	• Limited efficacy, due to regional differences in serovars	Medium
	Bacillus anthracis (anthrax)	Medium	Yes	• Effective vaccines available	Low
Reproductive	*Trueperella pyogenes*	High	No	• No vaccine labelled for metritis	High
	Fusobacterium spp.	High	No	• No vaccine labelled for metritis	High
	Escherichia coli	High	No	• No vaccine labelled for metritis	High
Cutaneous	*Dermatophilus congolensis* (rain scald)	Medium	No	• Lack of a challenge model • Difficult to grow the pathogen for vaccine production	Medium

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
Lameness (interdigital and digital dermatitis)	*Fusobacterium necrophorum*	High	Yes	• Cost prohibitive • Limited efficacy • Limited availability	High
Enteric	*Fusobacterium necrophorum*	High	Yes	• No products labelled for this application. When used off-label, limited efficacy for enteric diseases/acidosis/liver abscess	High
	Salmonella enterica subsp. enterica	High	Yes	• Predominant serotypes (e.g. Typhimurium, Dublin) vary between geographic regions • Lack of cross-protection between serotypes • In dairy calves, exposure precedes onset of active immunity following vaccination • Limited availability	Medium
	Enterotoxigenic *Escherichia coli*	High	Yes	• Effective vaccines available for predominant strains	Low
	Rotavirus	High	Yes	• Reasonable efficacy of vaccine • Limited geographic availability	Low
	Helminth enteric parasites	Medium	No	• Need research in vaccine technology for multi-cellular parasites	High
	Cryptosporidium parvum	Medium	No	• Research and development investment needed	Medium
	Mycobacterium avium subspecies paratuberculosis (Johne's disease)	Medium	Yes	• Existing vaccines have safety and performance issues (including potential cross reactions on TB test) • Require new vaccine technologies • Need DIVA vaccine • User safety • Injection site reactions from experimental vaccines • Limited distribution	Medium
	Eimeria spp.	Medium	No	• Research and development investment needed	Medium
	Bovine coronavirus	Medium	Yes	• Satisfactory efficacy of vaccines • Limited geographic availability	Low

Key syndrome / Disease	Primary pathogen(s)	Antimicrobial Use [High, Medium, Low]	Commercial vaccine exists* [Yes/No]	Major constraints to use of vaccine / vaccine development	Vaccine Research Priority [High, Medium, Low]
Vector-borne	*Anaplasma marginale*	High	Yes	• Vaccine production based on live animal infection • Limited availability • Difficult administration • Adequate efficacy	High
	Ehrlichia ruminantium (heartwater)	High	Yes	• Low production capacity • Lack of strain specificity • Vaccine production based on live animal infection • Limited availability • Difficult administration • Adequate efficacy	High
	Trypanosoma spp.	High	No	• Antigenic variation for African Animal Trypanosomosis (AAT)	High
	Bluetongue virus	Medium	Yes	• Strain specific vaccine • Partial cross-protection • Potential reversion to virulence for live attenuated vaccines • Caution for use in pregnant animals	High
	Babesia spp.	Medium	Yes	• Vaccines not available for all species • Low production capacity • Vaccine production based on live animal • Limited availability • Difficult administration • Adequate efficacy	Medium
	Theileria parva	Medium	Yes	• Infection and treatment method (ITM) vaccine • Adequate efficacy • Difficult administration • Residual virulence • Limited availability • Cost	Medium
	Theileria annulata	Medium	Yes	• Cold chain required • Low production capacity • Limited availability	Medium
	Ticks	Medium	Yes	• Limited species coverage • Vaccine only available in limited countries	Medium

Table 1: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use in chickens

Key syndrome	Primary pathogen(s) (disease)	Antibiotic use	Commercial* vaccine exists	Major constraints to use of vaccine / vaccine development	Vaccine research priority
Systemic (Broilers)	*Escherichia coli* *(Yolk sac infection, airsacculitis, cellulitis)*	High	Yes	• Omphalitis: secondary bacterial infection – not a disease one can immunize against • Strain coverage limited • Airsacculitis, cellulitis: vaccines available, e.g. live aerosol vaccine. However, Serotype coverage limited and field efficay variable	High
	Infectious Bursal Disease virus *(secondary bacterial infections)*	Medium	Yes	• Issues with vaccine application • Short window of opportunity to vaccinate • Maternal antibody interference	Medium
Systemic (Breeders, Layers)	*Escherichia coli* *(airsacculitis, cellulitis, salpingitis and peritonitis)*	High	Yes	• Strain coverage limited	High
Enteric (Broilers, Breeders, and Layers)	*Clostridium perfringens,* type A (necrotic enteritis)	High	Yes	• Toxoid vaccine for layers providing only short-lasting passive immunity • Research needed to achieve active immunity. • Improved and/or more convenient (mass vaccination) vaccine needed for broilers	High
	Coccidiosis (secondary bacterial infections)	High	Yes	• Lack of cross-protection • Strains must be matched to infectious agent • Current vaccines are not attenuated and can produce low dose infection • Sub-unit vaccines have not been successful	High
	Infectious Bronchitis virus *(secondary bacterial infections)*	Medium	Yes	• Issues with strain matching and strain coverage • High mutation rate of virus	Medium

* does not cover autogenous vaccines

Table 2: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use in swine

Key syndrome	Primary pathogen(s) (disease)	Antibiotic use	Commercial* vaccine exists	Major constraints to use of vaccine / vaccine development	Vaccine research priority
Systemic (respiratory)	*Streptococcus suis*	High	Yes	• Strain coverage too narrow • Lack of cross-protection • Poor immunogenicity due to being a capsule based vaccine	High
	Haemophilus parasuis	Medium	Yes	• Serotype specific with variable cross-protection • Maternal antibody interference	Medium
Respiratory	*Pasteurella multocida (for pneumonic disease)*	High	No	• No vaccine with approved label claim for pneumonia (There is a vaccine for atrophic rhinitis)	High
	Mycoplasma hyopneumoniae	High	Yes	• Does not completely prevent lung lesions • Animals continue to shed pathogen • Diagnostics not always accurately done	Low
	Actinobacillus pleuropneumoniae	High	Yes	• Limited coverage • Good immunity only if serotype specific • Sub-unit vaccine which affords cross-protection	High
	Porcine Reproductive and Respiratory Syndrome virus (secondary bacterial infections)	High	Yes	• Strain coverage limited • High virus mutation rate • Modest cross-protection • Vaccine evasion	High
	Swine Influenza Virus (secondary bacterial infections)	High	Yes	• Strain matching • Vaccine-associated enhanced respiratory disease (VAERD) • Lack of cross-protection • Efficacy in piglets limited	High
Enteric – neonatal	*Escherichia coli*	High for the syndrome, Low for *E. coli*	Yes	• Maternal vaccine provides effective lactogenic immunity • Coverage of enterotoxigenic *E. coli* may occasionally need to be updated	Low
Enteric (weaners/finishers)	*Escherichia coli*	High	Yes	• Maternal antibody interference • Short window for induction of immunity	High
	Lawsonia intracellularis	High	Yes	• Other pathogens in the syndrome (*Brachyspira*) not included • Antibiotic-free window for vaccination required (live attenuated oral vaccine)	Low (see also *Brachyspira*)
	Brachyspira spp *B. hyodysenteriae,* *B. pilosicoli*	Medium-high	No	• Low current research investment as changes in husbandry largely eliminated the disease • Technical barriers to vaccine development	High
	Rotaviruses (secondary bacterial infections)	High	Yes	• Reasons limiting wider adoption unknown	High

Table 3: Infections for which new or improved vaccines would significantly reduce the need for antibiotic use in fish

Key syndrome or disease	Primary pathogen(s)	Antibiotic use	Commercial* vaccine exists	Major constraints to use of vaccine / vaccine development	Vaccine research priority
Freshwater cyprinids					
Systemic bacterioses	*Aeromonas hydrophila* and other species	High	No	• Disease is caused by a wide range of serotypes	High
Dermal bacterioses / red spot disease	*Pseudomonas* spp.	High	No	• Disease is caused by a range of species and wide range of strains and serotypes	High
Columnaris	*Flavobacterium columnare*	Medium	Yes	• Limited uptake by some countries for unknown reasons	Low
Freshwater cichlids					
Systemic/dermal bacterioses	*Aeromonas hydrophila* and other species	Medium	No	• Disease is caused by a range of species and wide range of strains and serotypes	Medium (not low because of projected increase in production)
	Streptococcus inae, S. agalactiae	Medium	Yes	• Industry awareness of need is low (first vaccine only became recently available)	Medium
Freshwater salmonids					
Systemic bacterioses	*Aeromonas salmonicida, Yersinia rukerii, Flavobacterium psychrophilum, Vibrio anguillarum*	Medium	Yes (multivalent, injectable)	• cost of vaccine is high relative to harvest value	Low
Marine salmonids					
Salmon Rickettsia Syndrome	*Piscirickettsia salmonis*	Medium	Yes	• Multivalent vaccine which provides low protection for *P. salmonis* compared to other pathogens included in the vaccine.	Unknown because the recent introduction of an oral monovalent vaccine booster may improve the level of protection
Other marine fish					
Systemic / dermal bacterioses	*Vibrio* spp., *Photobacterium* spp.	Medium	Yes	• Disease is caused by a wide range of serotypes • Industry awareness is low in some countries	High
	Streptococcus spp.	Medium	Yes	• Disease is caused by a wide range of serotypes • Industry awareness is low in some countries	High
Catfish					
Systemic	*Edwardsiella ictaluri, E. tarda*	Medium	Yes (for Channel catfish)	• Vaccines are not available for African catfish (an important farmed species) • Vaccines have very recently become available for Tra catfish and yet to be adopted by the industry	High (for African catfish)
Systemic	*Aeromonas hydrophila* and other species	Medium	No	• Disease is caused by a wide range of serotypes	High

Chapter 4

Autogenous Vaccines

Autogenous Vaccines

Definition

- immunological VMP manufactured for the purpose of producing active immunity from pathogenic organisms obtained from an animal or animals from the same herd that have been inactivated and used for the treatment of this animal or of animals from this herd".

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Autogenous Vaccines

- provide solution where licensed commercial vaccines are not available.
- useful addition to licensed vaccines in animal disease control and in maintaining animal health.
- additional prophylactic tool to avoid occurrence of diseases which require antibiotic treatment.

Autogenous Vaccines

- demanded by practising veterinarians and by animal owners
- widely used in Central European Countries. (the Netherlands, the Czech Republic, Hungary, Thailand, Slovak Republic)
- usually regulated by individual countries

Autogenous Vaccines

Major risks

- transmission of TSE agents (prions) or other viral, bacterial and/or fungal contaminants

Harmonised regulation for the preparation, manufacture, control, storage, transport and monitoring of autogenous vaccines for veterinary use in accordance with good practice is required to ensure compliance and conformity to quality, safety and efficacy standards

Autogenous Vaccines Development

Veterinarian takes a sample, from a sick animal or during an autopsy

Sample sent to a diagnostic laboratory for culture

Pathogenic agent is isolated, identified and serotyped

Veterinarian then orders the manufacture of an autogenous vaccine from the isolated strain

Inactivated non-toxic AV produced is supplied to the veterinarian who issues it to client

Chapter 5

Conclusions

Conclusion

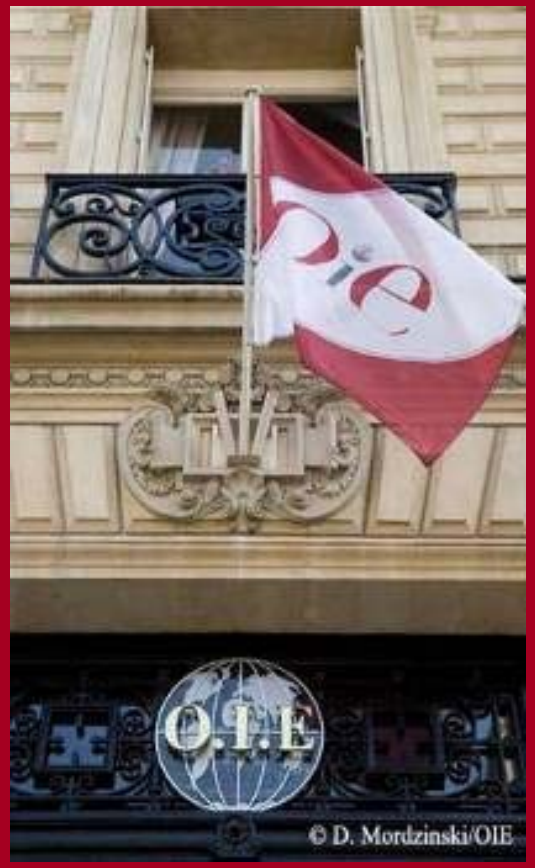
- Judicious use of drugs, vaccines and other veterinary products controls threats to animal health and welfare
- coordinated regulation for the manufacture, control and use of autogenous vaccines and alternatives to antibiotics are a necessary challenge

Conclusion

Regulation and licensing of alternatives to antibiotics for food producing animals will require collaboration between;

- regulatory agencies
- veterinary product companies and
- feed-additive sectors
- academia
- and other stakeholders on regulatory pathways for compliance with standards for quality, safety and efficacy

Thank you for your attention



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