



**Antibiotic stewardship – multiple-  
drug resistance - *with the emphasis on  
companion animals***

# Introduction

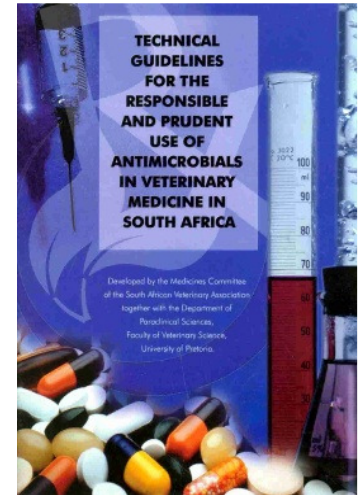
Antimicrobial resistance (AMR) is an emerging problem in companion animals, underpinned by:

Difficult-to-treat infections

Possible pressure to use antimicrobials that are important in human medicine

Potential zoonotic transmission

The extent and importance of AMR in companion animals are not fully understood, in part because of limited surveillance



# Multiple drug resistance – *the basics*



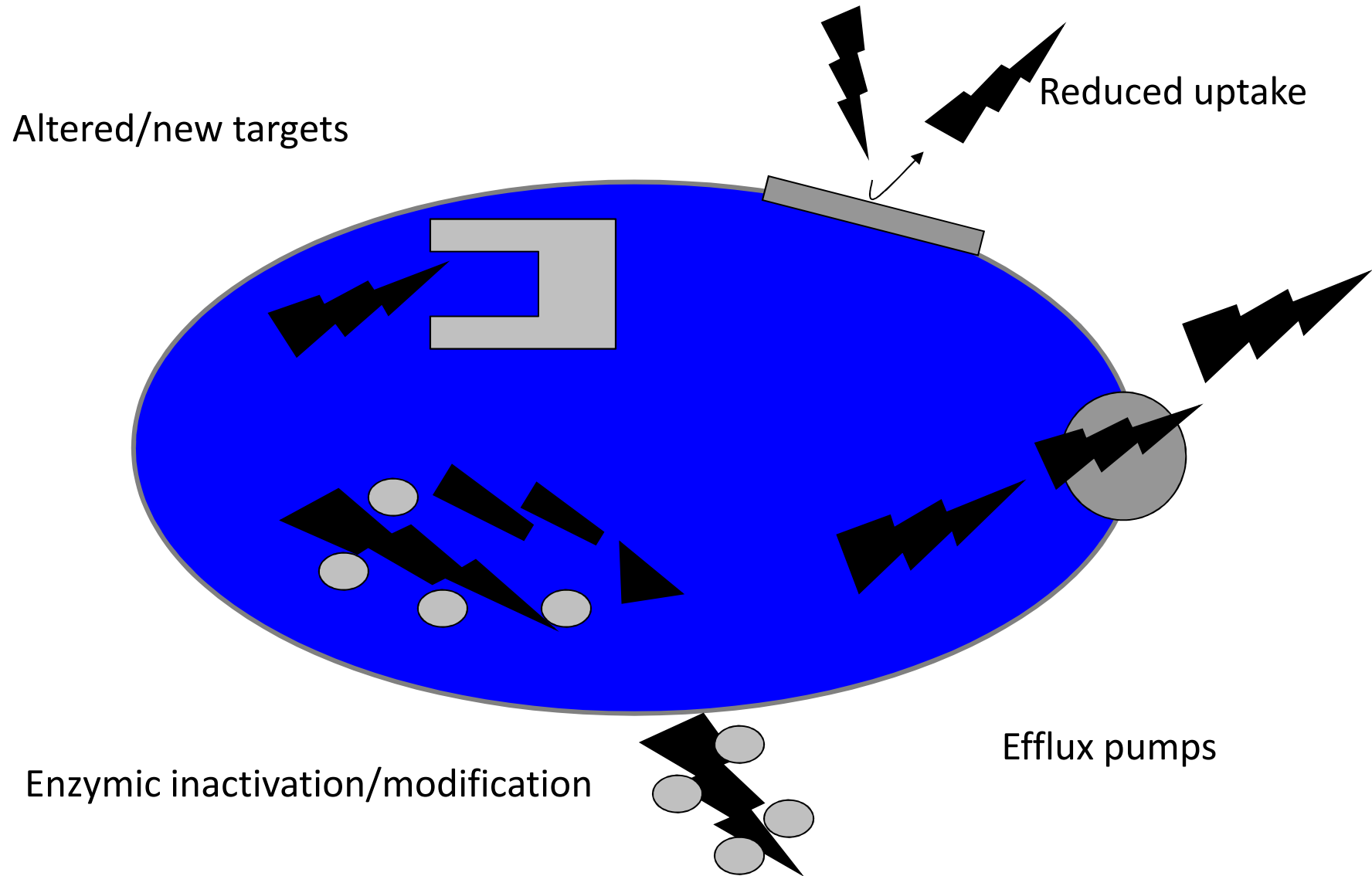
MDR bacteria possess resistance traits against different antibiotics that are structurally diverse with different modes of action

Resistance traits are not naturally eliminated from or reversed in bacteria

It leads to sequential, cumulative acquisition of resistance traits

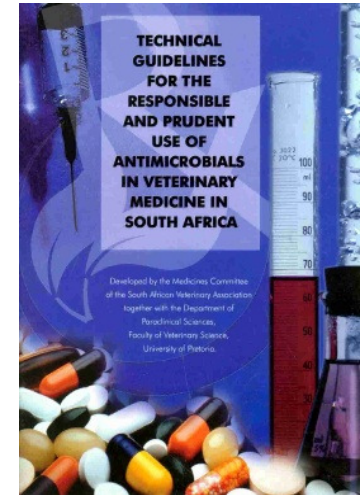
MDR bacteria may use various resistance traits, e.g. multiple-drug resistance efflux pumps

# Mechanisms of resistance





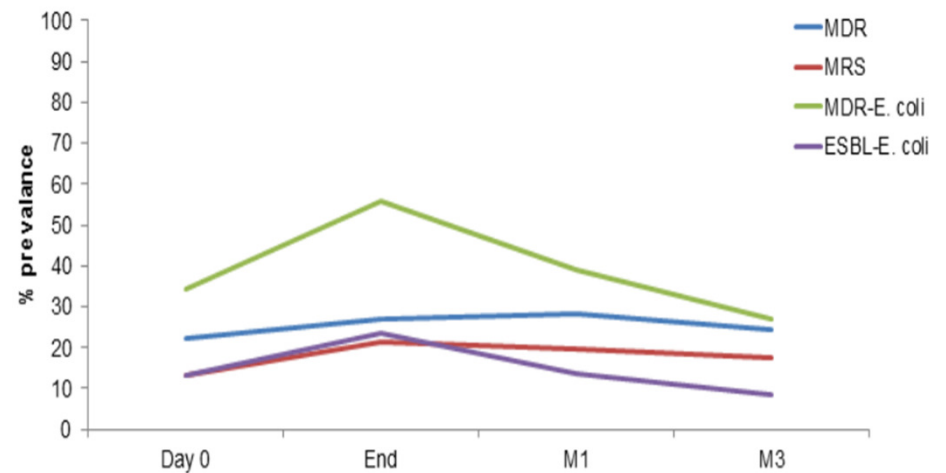
# Will any antibiotic use contribute to antibiotic resistance?



Is it high doses of the antibiotic that drives resistance or low or sub-therapeutic doses?

The WVA recommended approach for the use of antibiotics: antibiotics used for treatment should be used as long as needed but for the shortest duration, and at the appropriate dose and dosage intervals

Effects of antibiotics on resistance



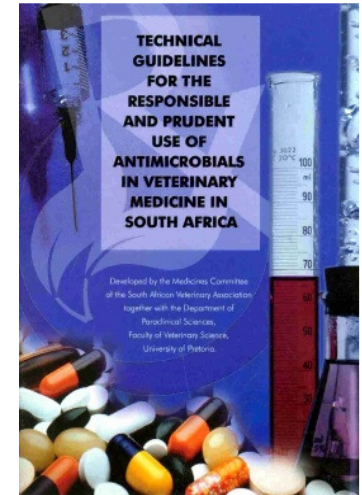
# The influence of dose and duration of treatment

A low dose for a longer period can select for, and drive resistance

A high dose for a short period can also select for or drive resistance but less so than the former

Resistance is also driven by treatment for too short a period

# “Superbugs”



Most pathogenic bacteria possess some resistance traits

Bacteria that are extremely drug resistant, in other words resistant to many or most of the available antibiotics have become known as superbugs, especially in non-scientific publications

Although superbugs also exist among bacteria that mainly affect animals, they are more prevalent among bacteria that affect human beings

In spite of the fact that superbugs in the animal world is less common, bacteria with significant resistance to several antibiotics (multi-resistance) are found in animal infections including companion animals

# Main MDR bacteria in companion animals



Include both pathogens and commensals, e.g. staphylococci, enterococci, *Pseudomonas aeruginosa*, *Escherichia coli* and *Salmonella*

Two groups of bacteria with significant resistance traits that are regularly isolated from dogs are:

Methicillin resistant *Staphylococcus aureus* (MRSA) and *S. pseudintermedius* (MRSP) strains

Extended spectrum beta lactamase (ESBL)-producing strains



## **Applying definitions for multidrug resistance, extensive drug resistance and pandrug resistance to clinically significant livestock and companion animal bacterial pathogens**

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MDR - bacteria that are non-susceptible to at least one antimicrobial agent in three or more antimicrobial classes

EDR - non-susceptibility to at least one antimicrobial agent in all but two or fewer antimicrobial classes

PDR - non-susceptibility to all agents in all antimicrobial classes

These definitions allow for distinction of drug resistance at the more clinically significant levels of XDR and PDR

Allows veterinary practitioners to more accurately assess therapeutic options against bacteria that display highly resistant phenotypes

# Inclusion and exclusion criteria for veterinary use



Does not include bacteria with intrinsic resistance, e.g.

*E. coli* to penicillin

Aerobes to metronidazole

*Streptococcus* to aminoglycosides

Based on ***species-specific clinical break-points***

The definitions therefore currently only apply to:

Bovine and porcine respiratory tract infections

Skin and soft tissue infections in companion animals

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**Table 1.** Applying definitions for MDR, XDR and PDR to antimicrobial agents and veterinary bacterial pathogens from livestock and companion animal diseases

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Animal disease and bacterial species	MDR	XDR	PDR
BRD: <i>M. haemolytica</i> , <i>P. multocida</i> , <i>H. somni</i>	not susceptible to at least one agent in at least three antimicrobial classes	not susceptible to at least one agent in all but one or two antimicrobial classes	not susceptible to all agents in all antimicrobial classes
SRD: <i>A. pleuropneumoniae</i> , <i>P. multocida</i> , <i>S. suis</i>			
Canine SSTIs: <i>Staphylococcus</i> spp., <i>Streptococcus</i> spp.			

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# MDR, XDR and PDR in companion animals

## Otitis externa

The infections are always secondary

There are primary causes  
perpetuating factors  
predisposing factors

The clinical signs of atopic dermatitis often mimics that of external ear infection with the result that atopic dogs have for years received recurring treatment that included antibiotics

The collateral damage that occurred is that wherever dog owners have access to modern veterinary care, a number of highly resistant bacteria have emerged that cause difficult to treat ear infections and include multi-resistant *Pseudomonas*, *Staphylococcus*, *Streptococcus*, *Enterococcus* and *Escherichia* species

## **Public health risk of antimicrobial resistance transfer from companion animals**

MRSA can be passed between pet animals (dogs, cats and horses) and owners with the possibility for zoonotic infections

Veterinary staff and veterinary practitioners are at a higher risk of colonization with MRSA than the general population



# Transmission of resistant bacteria and resistance genes from pets to humans



## More examples

Exposure to puppies can introduce resistant *Campylobacter* spp. infections to humans

Companion animal facilities may serve as foci of transmission for salmonellae between animals and humans if adequate control measures are not followed

Major foodborne zoonotic bacteria such as *Salmonella* and *Campylobacter* do not constitute a significant hazard in respect of antimicrobial resistance emerging from companion animals

# Reduction in the use of antibiotics in companion animals

## Consider withholding antibiotic treatment for:

Uncomplicated sterilization surgeries

Clean surgical procedures of short duration

Sterile feline lower urinary tract disease (feline idiopathic cystitis)

Uncomplicated feline upper respiratory tract disease

Canine infectious tracheobronchitis – mostly self-limiting