

Diagnostics and their role in evidence-based bacteriology in veterinary practice



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- Speaker's affiliation: School of Veterinary Medicine University College Dublin



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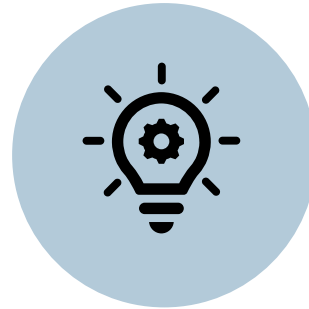
OUTLINE



AMR AND
ONE HEALTH



BACTERIOLOGY IN
VETERINARY PRACTICE



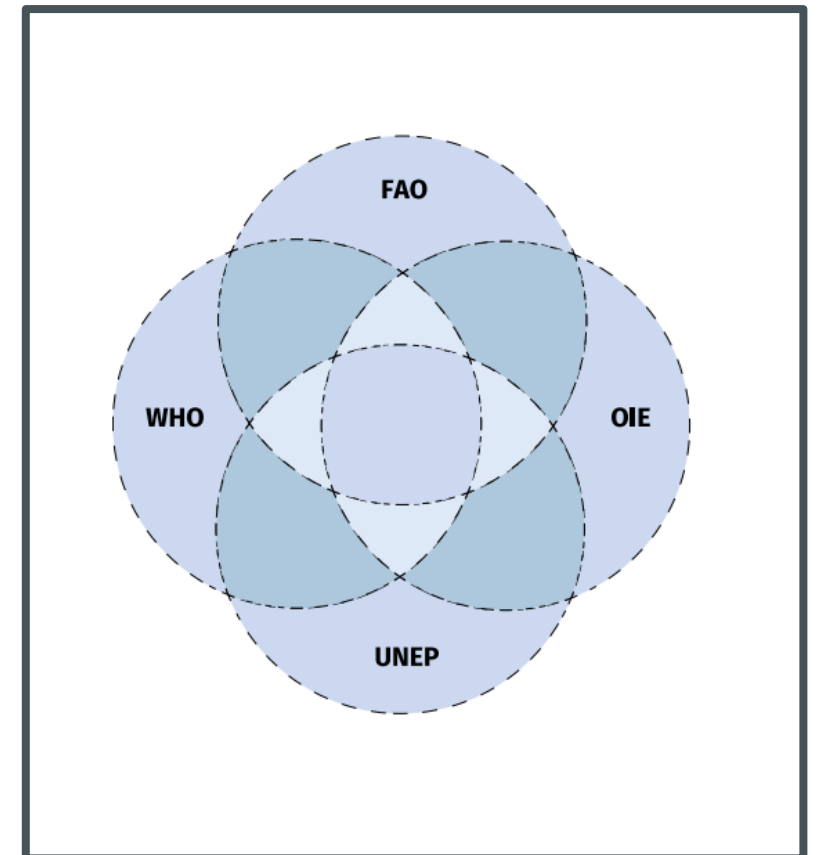
ENOVAT



TAKE HOME
MESSAGES

BACKGROUND

- Antimicrobial resistance (AMR) is a major global threat to humans, animals, plants, food systems
- Addressing AMR requires a **One Health** approach as AMR can impact human, animal, plant and ecosystems health (multisectoral problem)
- In EU, EFSA coordinates the AMR Surveillance Programmes in food-producing animals and EMA analyses data on sales and use of antimicrobials
- Limited information available on AMR in bacteria isolated from companion animals



ONE HEALTH APPROACH TO TACKLE AMR

- AMR bacteria
- AMR genes
- MGEs
- Humans, animals and the environment
- Complex problem



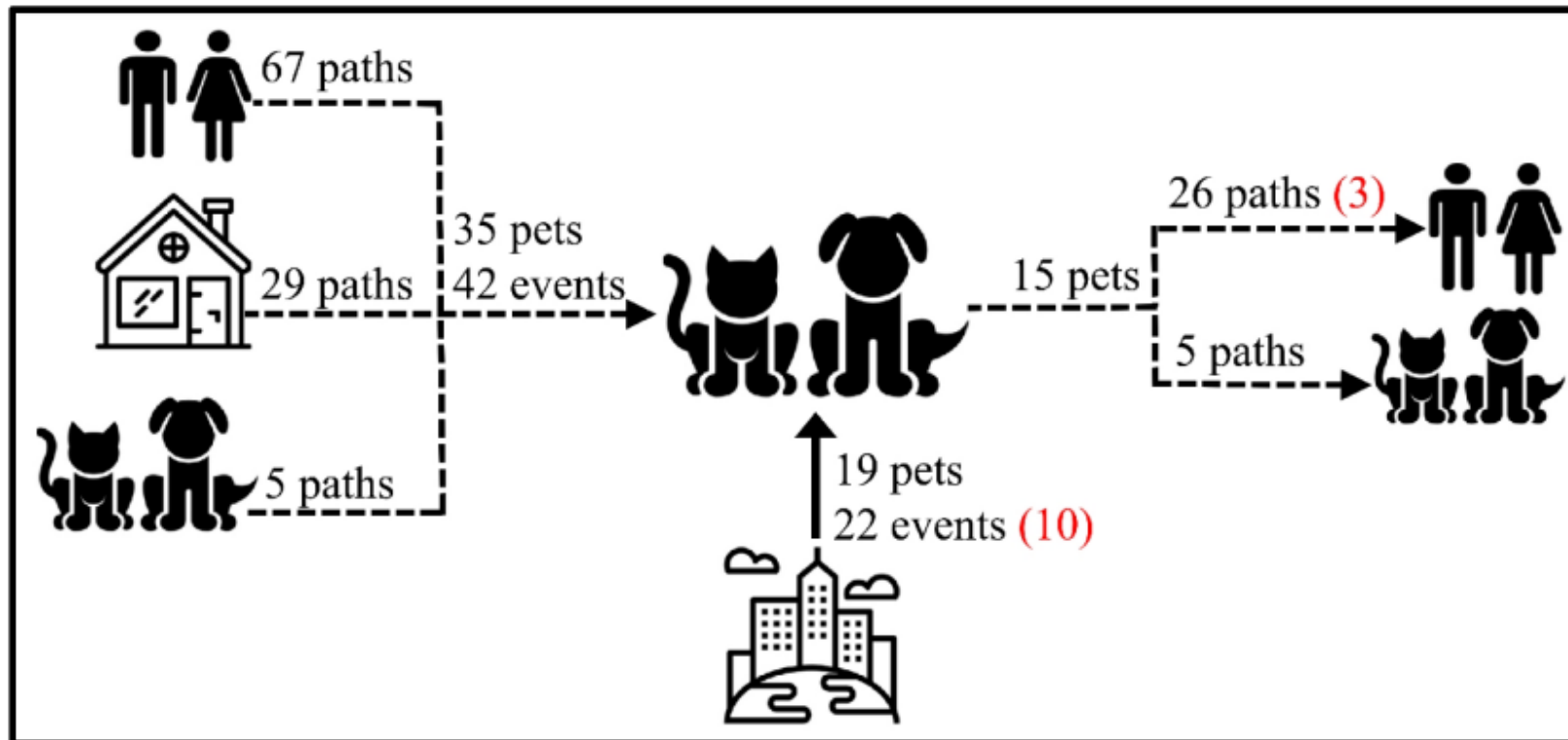
Food and Agriculture Organization
of the United Nations

ANTIMICROBIAL RESISTANCE



MRSA: a zoonosis or reverse zoonosis?

- Longitudinal study in St Louis, Missouri
- 150 CA-MRSA positive children and their households including pets (154 pets in 75 households)
- Pets were rarely the presumptive source of transmission to humans



Categorization of Antimicrobials

WHO Critically Important Antimicrobials (2018)

EMA category A and B of antibiotic classes for veterinary use (2020)

Antimicrobial class		Criterion / Prioritization factor (Yes = ●)				
CRITICALLY IMPORTANT ANTIMICROBIALS		C1	C2	P1	P2	P3
<i>HIGHEST PRIORITY</i>						
Highest Priority	Cephalosporins (3 rd , 4 th and 5 th generation)	●	●	●	●	●
	Glycopeptides	●	●	●	●	●
	Macrolides and ketolides	●	●	●	●	●
	Polymyxins	●	●	●	●	●
	Quinolones	●	●	●	●	●
<i>HIGH PRIORITY</i>						
Critically Important	Aminoglycosides	●	●		●	●
	Ansamycins	●	●	●	●	
	Carbapenems and other penems	●	●	●	●	
	Glycylcyclines	●	●	●		
	Lipopeptides	●	●	●		
	Monobactams	●	●	●		
	Oxazolidinones	●	●	●		
	Penicillins (antipseudomonal)	●	●		●	
	Penicillins (aminopenicillins)	●	●		●	●
	Penicillins (aminopenicillins with β -lactamase inhibitors)	●	●		●	●
	Phosphonic acid derivatives	●	●	●	●	
	Drugs used solely to treat tuberculosis / mycobacterial diseases	●	●	●	●	

A	Aminopenicillins medellinam pivmecillinam	Carbapenems meropenem doripenem	Drugs used solely to treat tuberculosis or other mycobacterial diseases isoniazid ethambutol pyrazinamide ethionamide	Glycopeptides vancomycin	AVOID
	Ketolides telithromycin	Lipopeptides daptomycin		Glycylcyclines tigecycline	
	Monobactams aztreonam	Oxazolidinones linezolid		Phosphonic acid derivatives fosfomycin	
	Rifamycins (except rifaximin) rifampicin	Riminoferazines clofazimine		Pseudomonic acids mupirocin	
	Carboxypenicillin and ureidopenicillin, including combinations with beta lactamase inhibitors piperacillin-tazobactam	Sulfones dapson		Substances newly authorised in human medicine following publication of the AMEG categorisation to be determined	
		Streptogramins pristinamycin virginiamycin			
B	Cephalosporins, 3rd- and 4th-generation, with the exception of combinations with β-lactamase inhibitors cefoperazone cefovecin cefquinome ceftiofur	Polymyxins colistin polymyxin B	Quinolones: fluoroquinolones and other quinolones cinoxacin danofloxacin difloxacin enrofloxacin flumequine ibafloxacin	marbofloxacin norfloxacin orbifloxacin oxolinic acid pradofloxacin	RESTRICT

Carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae*

WHO Critically Important Antimicrobials (2018)

Antimicrobial class		Criterion / Prioritization factor (Yes = ●)				
CRITICALLY IMPORTANT ANTIMICROBIALS		C1	C2	P1	P2	P3
HIGHEST PRIORITY						
Highest Priority	Cephalosporins (3 rd , 4 th and 5 th generation)	●	●	●	●	●
	Glycopeptides	●	●	●	●	●
	Macrolides and ketolides	●	●	●	●	●
	Polymyxins	●	●	●	●	●
	Quinolones	●	●	●	●	●
HIGH PRIORITY						
	Aminoglycosides	●	●	●	●	●
	Ansamycins	●	●	●	●	●
	→ Carbapenems and other penems	●	●	●	●	●
	Glycyclines	●	●	●	●	●
	Lipopeptides	●	●	●	●	●
	Monobactams	●	●	●	●	●
	Oxazolidinones	●	●	●	●	●
	Penicillins (antipseudomonal)	●	●	●	●	●
	Penicillins (aminopenicillins)	●	●	●	●	●
	Penicillins (aminopenicillins with β-lactamase inhibitors)	●	●	●	●	●
	Phosphonic acid derivatives	●	●	●	●	●
	Drugs used solely to treat tuberculosis / mycobacterial diseases	●	●	●	●	●

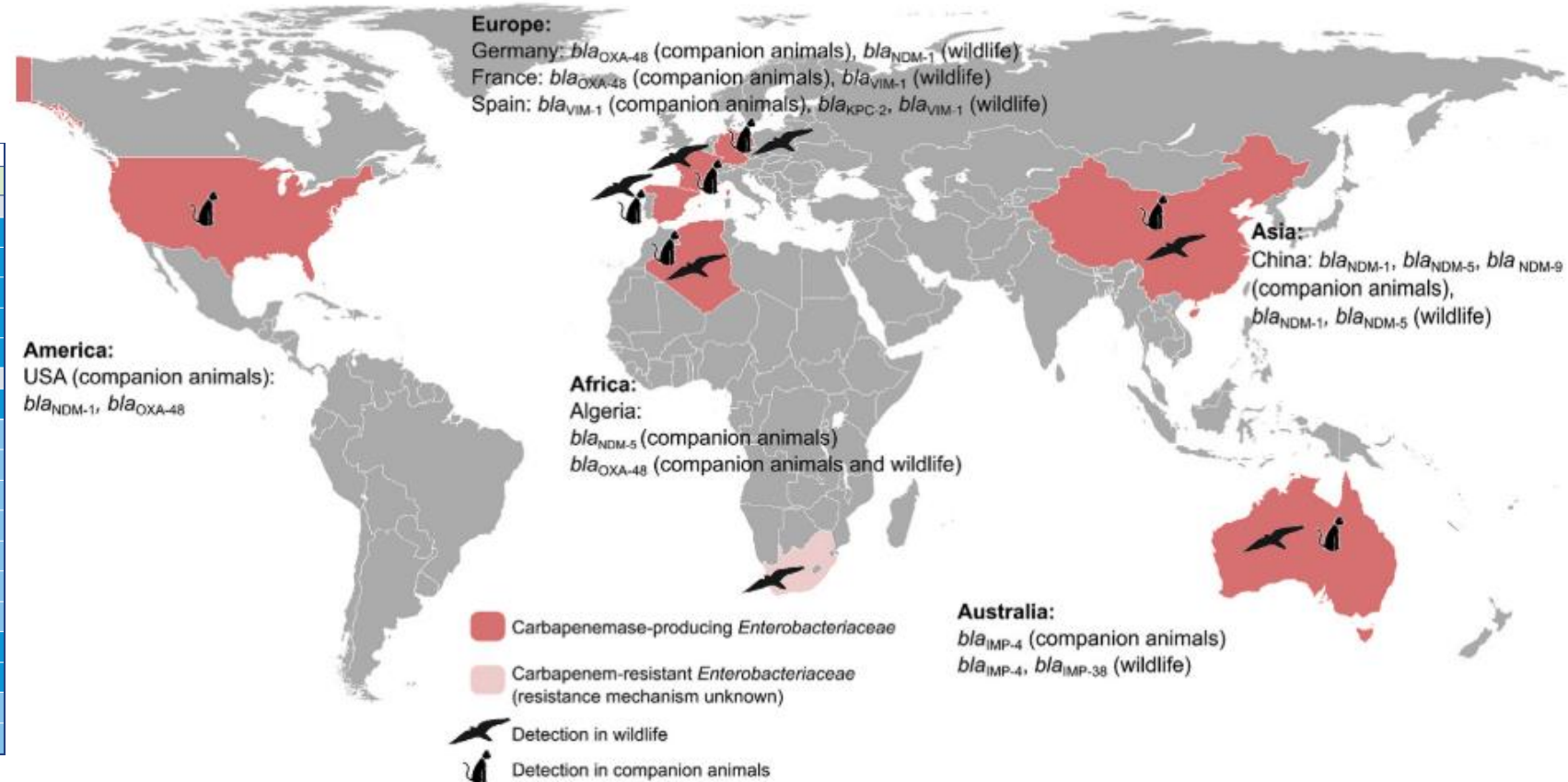


Fig. 3. Global distribution of carbapenem-resistant and carbapenemase-producing *Enterobacteriaceae* in companion animals and wildlife.

Carbapenems not licensed for use in vet practice in EU

Antimicrobial Resistance in Companion Animals: A New Challenge for the One Health Approach in the European Union

Country	Denmark	Finland	France	Germany	Norway	Sweden	Switzerland
Programme	DANMAP	FINRES	RESAPATH	GERM-VET	NORMVET	SWEDRES-SVARM	ANRESIS
Laboratory method	Broth microdilution	Disc diffusion	Disc diffusion	Broth microdilution	Broth microdilution	Broth microdilution	Broth microdilution
AST	CLSI breakpoints	CLSI breakpoints	ECOFFs	CLSI breakpoints	ECOFFs	ECOFFs	CLSI breakpoints
<i>Escherichia coli</i>	✓ (Dogs and cats)	✓ (Dogs and cats)	✓ (Dogs and cats)	✓ (Dogs and cats)	✓ (Dogs and cats)	✓ (Dogs and cats)	✓ (Dogs and cats)
<i>Staphylococcus pseudintemedius</i>	✓ (Dogs and cats)	✓ (Dogs)	✓ (Dogs)	✓ (Dogs)	✓ (Dogs)	✓ (Dogs)	✓ (Dogs)
<i>Staphylococcus aureus</i>		✓ (Dogs)	✓ (Dogs)	✓ (Dogs)			
<i>Staphylococcus canis</i>		✓ (Dogs)					
<i>Staphylococcus schleiferi</i>						✓ (Dogs)	
<i>Staphylococcus felis</i>						✓ (Cats)	

Figure 1. Summary of AMR surveillance programmes in the European Union. AST: ANTIBIOTIC Susceptibility Test; CLSI: Clinical Laboratory Standards Institute. Adapted from [10]. ✓: it indicates the bacteria included in each AMR surveillance program.



THE VETERINARY MEDICINAL PRODUCTS REGULATION

- Regulation (EU) 2019/6 updated the rules on the **authorisation and use of veterinary medicines** in the EU
 - Strengthen EU action to fight AMR through specific measures **ensuring prudent and responsible use of antimicrobials** in animals
 - Reserving certain antimicrobials for the treatment of infections in people



EVIDENCE-BASED PRACTICE

- Challenges:
 - Gaps in scientific knowledge
 - Financial pressure
 - Client compliance
- ✓ Safeguard animal health and welfare, and public health

IN-HOUSE DIAGNOSTICS

Real-time information

Low cost

Target treatment

Avoid empirical therapy

Improved patient outcomes

- Cytology: presence of bacteria in BALs, skin, otitis, urine etc.
- Staining: Gram-negative bacteria?
- Point of care (POC) tests (antigens, antibodies): viral diseases, tick-borne diseases, urinary tract diseases etc. (sensitivity and specificity)
- In the future POC molecular tests may be available for pathogen ID and AMR markers in vet practices.

PYODERMA – STEPS AND PRACTICAL TIPS

- Type of pyoderma (lesion recognition)
- Exclusion of ectoparasites
- In-house cytology to confirm bacterial infection (neutrophils and intracellular bacteria)
- Risk factors for MDR
- Managing owners' expectations



(Nuttall, 2021)

CYTOLOGY

- Simple, quick and cheap
- Techniques: adhesive tape-strips, impression smears, urine sediments, BALs, fine needle aspirates
- Quick stains: Rapi-Diff[®], Diff-Quick[®]
- Infer ID from bacteria appearance and location
- Culture needed for full ID

MICROBIOLOGY DIAGNOSTIC LABORATORIES – CONVENTIONAL METHODS

Target treatment

Avoid empirical therapy

Improved patient outcomes

Culture and Antibiotic Susceptibility Testing Workflow

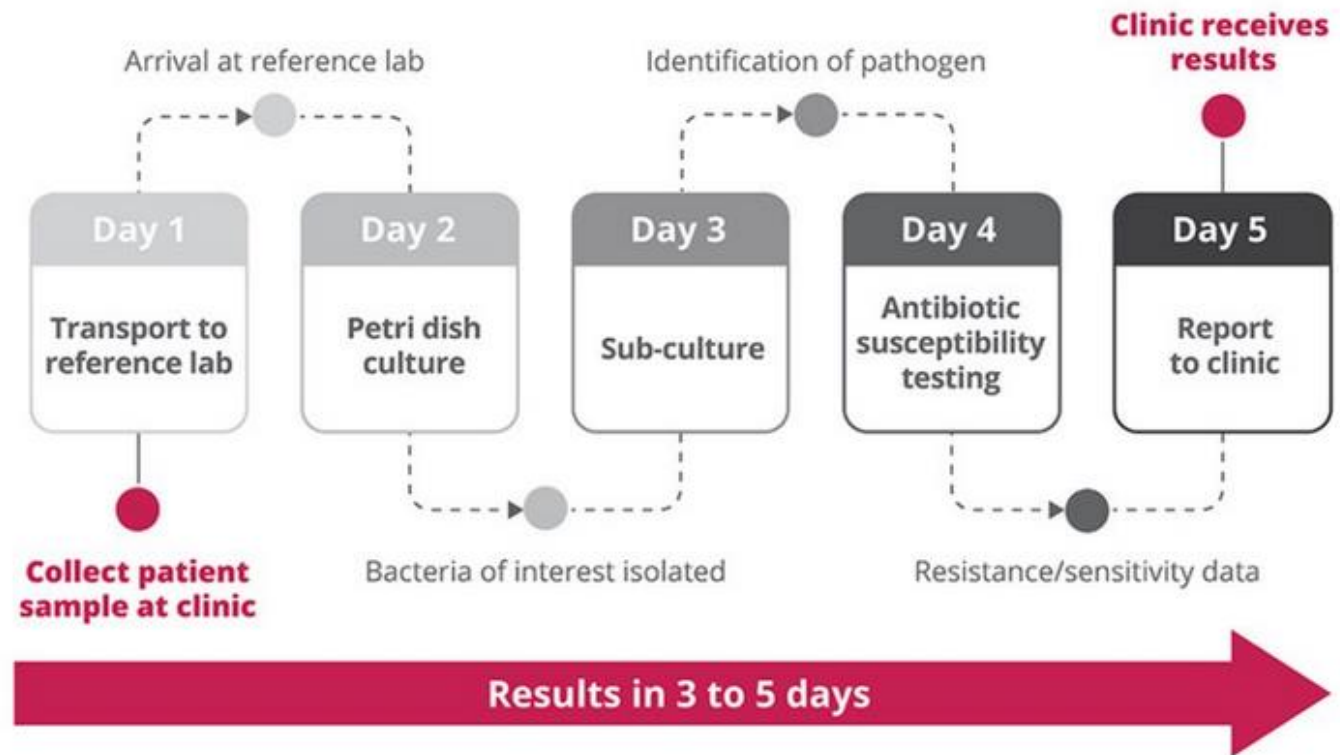


Figure 1. Reference laboratory C&ST simplified workflow.

MICROBIOLOGY DIAGNOSTIC LABORATORIES – NEW TECHNOLOGIES

Rapid result

Expensive equipment

Target treatment

Avoid empirical therapy

Improved patient outcomes

- **Molecular methods:**
 - PCR and qPCR
 - Peptide nucleic acid fluorescent in situ hybridization (FISH) technologies
 - Loop-mediated isothermal assays (LAMP)
- **Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry**
- **MBT Sepsityper®**
- **Future (NGS):**
 - Whole genome sequencing
 - Metagenomics (Nanopore MinION)



CULTURE AND AST ARE NECESSARY

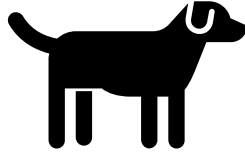
- Life-threatening infections
- Deep/complex infections
- Inconsistency between clinical signs and cytology
- Rod bacteria
- If empirical treatment fails
- If resistance is more likely

WHEN START TREATMENT?

- After cytology and/or culture (and AST) are available (if possible)
- Topical AMs, AI drugs and analgesics can be used to treat clinical signs
- Choice of AMs based on clinical presentation, history, previous AMU and cytology
- If systemic treatment needed select 1st line/tier antimicrobials
- Treatment should be de-escalated to the lowest tier/most narrow spectrum drug that is appropriate (antimicrobial stewardship)

Chlorhexidine baths 2-3 times/week can be as effective as systemic amoxicillin- clavulanate bid.

EVIDENCE-BASED PRACTICE



- In-house testing and diagnostic laboratories facilitate evidence-based treatments and reduce empirical treatments
- Evidence-based treatments reduce the inappropriate use of antimicrobials
- Adequate antimicrobial use reduces the emergence and spread of AMR mechanisms
- Adequate AMU safeguards antimicrobials for humans and animals
- Antimicrobial stewardship is key to promote animal health and welfare, and protect public health

HOW CAN WE
IMPROVE OUR
PRESCRIBING
PRACTICES AND
PROVIDE BETTER
CARE TO OUR
PATIENTS WHILE
PROTECTING PUBLIC
HEALTH?





- European Network for Optimization of Veterinary Antimicrobial Treatment (ENOVAT) is a COST Action (CA18217) funded by the EU.
- Aims to **optimise veterinary antimicrobial use** with special emphasis on the development of **animal and disease specific treatment guidelines**, and refinement of **microbiological diagnostic procedures**. Combined with diverse educational activities, the Action will contribute to build a larger critical mass of **experts in veterinary antimicrobial stewardship throughout Europe**.
- End date: 14/11/2023



ENOVAT
European Network for Optimization of
Veterinary Antimicrobial Treatment

Who are we?

The ENOVAT consortium

Total: 256
participants
from 45
countries

 COST
Countries

 Near
Neighbour
Countries



International
Partner countries:

- Australia
- Canada
- S. Africa
- St Kitts & Nevis
- USA

(Peter Damborg)

Who are we?



ENOVAT

European Network for Optimization of
Veterinary Antimicrobial Treatment

Areas of expertise

Optimizing Veterinary Antimicrobial Treatment

The action has built a network of experts for veterinary microbiological diagnostics, antimicrobial stewardship and treatment guidelines throughout Europe.

WG1

Mapping microbiological
diagnostics and treatment
guidelines

WG2

European strain
database

WG3

Clinical
breakpoints

WG4

Antimicrobial treatment
guidelines

WG5

Dissemination



NETWORK

Stay connected



VETERINARY

Antimicrobial stewardship



DIAGNOSTICS

Strain database, clinical
breakpoints



TREATMENT

Treatment guidelines





Mains Objectives:

- **Review and evaluate the methodology and interpretive criteria** used by veterinary diagnostic laboratories across Europe for pathogen identification and AST
- Map and compare the availability, structure, and evidence base of **veterinary antimicrobial treatment guidelines** in Europe

Surveys:

- Veterinary microbiology laboratories (closed)
- **Companion animal clinicians**

Companion animal clinicians (thank you!)

- Survey on treatment guidelines in Europe (published)
- Survey to capture **perceptions, needs and desires of European clinicians regarding practical treatment guidelines** (need your support)















antibiotics

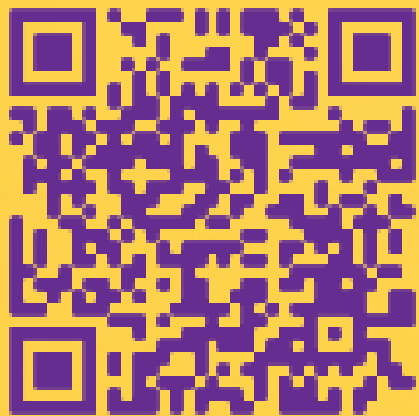


Article

Overview and Evaluation of Existing Guidelines for Rational Antimicrobial Use in Small-Animal Veterinary Practice in Europe

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and Lisbeth Rem Jessen ¹⁵

ENOVAT SURVEY



CALLING ALL VETS

Max needs your help!



WG2 and WG3



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European Network for Optimization of
Veterinary Antimicrobial Treatment

Mains Objectives:

WG2

- Create a European strain database (linked with already existing databases)
- New MALDI TOF MS interpretative criteria for ≥ 20 veterinary pathogens
- ECOFFs uploaded on the EUCAST website for ≥ 5 drug/pathogen combinations

WG3

- Create a list of important clinical breakpoints (CBPs)
- Establish CBPs (data availability and relevance)



Mains Objectives:

- Draft a standard for veterinary practice guidelines
- Write high quality, **species and disease specific, veterinary practice guidelines** in a structured and transparent process (GRADE approach)
- Promote the **transformation of ENOVAT guidelines into national/ local guidelines**



8 drafting groups working on veterinary practice guidelines including:

- Surgical prophylaxis in companion animals (cats and dogs)

<https://enovat.eu/link-1d-veterinary-practice-guidelines-for-surgical-prophylaxis/>

- Acute diarrhea in dogs

<https://enovat.eu/link-1-wg4/>

- Canine pyoderma (ISCAID)





Mains Objectives:

- Disseminate workshops, training schools, short term scientific missions (STSM)
- Disseminate results and recommendations

How can I join?



ENOVAT
European Network for Optimization of
Veterinary Antimicrobial Treatment

- Check <https://enovat.eu/>
- Check <https://www.cost.eu/actions/CA18217/>
- Inform Dr Peter Damborg (chair) of your interest
- Apply to join Working Groups of interest
- Follow ENOVAT on Social Media
- Check our newsletter
- Join training schools etc.
- Read the Project Description MoU





TAKE HOME MESSAGES



DIAGNOSTICS



- In-house testing and/or microbiology diagnostic labs
 - Only some tests can be performed in-house
 - Selection of diagnostic labs
- Promote evidence-based prescription
- Appropriate use of antimicrobials
- Implement antimicrobial stewardship
- Reduce the emergence and spread of AMR
- Promote optimal patient care

PROMOTE RESPONSIBLE USE OF ANTIMICROBIALS



- Prescription
- Administration
- Disposal
- Ecosystem
- Responsibility (patients, public health, planetary health)

PROMOTE ONE HEALTH



- Education of clients/general public
- Education of policy makers
- Training of clinicians/staff
- Collaboration between clinicians and diagnostic labs
- Protect animal and human health

ENOVAT SURVEY



CALLING ALL VETS

Max needs your help!





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ENOVAT Antimicrobial Use Guidelines Survey

Please share this survey as widely as you can among
veterinary practitioners



or

<https://30yw.short.gy/ENOVAT>



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- All my collaborators

