Rational Use of Antimicrobials in the Emergency Room

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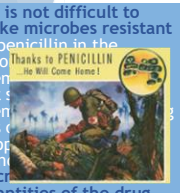
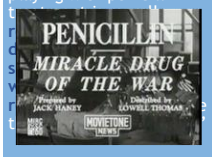
Annual Conference Oct. 2018 - Auburn

History

''It is not difficult to make microbes resistant to penicillin in the labo… then… not s… then… has … happ… …an… micr… quantities of the drug make them resistant''

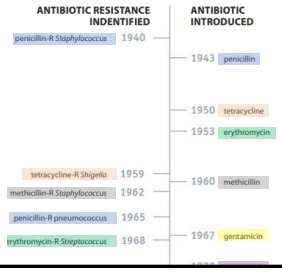


''The thoughtless person playing with penicillin t… r… c… s… v… r… t…

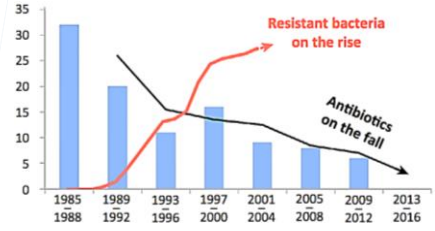


CDC report: ''Antimicrobial resistance threats in the United States'', 2013

Development of Resistance

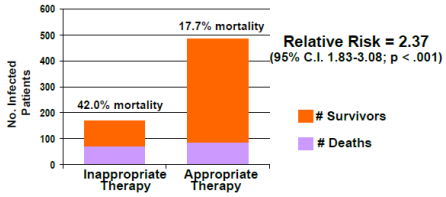


Development of new Antibiotics



Trends In Microbiology. 2014;22(4):165-167.

Impact on inappropriate use of antibiotics in ICU



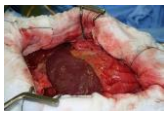
Chest. 1999;115:462-474

Antimicrobial Stewardship Programs

Identify infection

Indications for antibiotics

- Clinical picture
- Fever and leukocytosis ≠ infection
- Cytology, gram stain



NCBI

Retrospective study of fever in dogs: laboratory testing, diagnoses and [J Small Anim Pract. 2006]

Review The diagnostic approach to fever of unknown origin [Compend Contin Educ Vet. 2009]

Fever of unknown origin: discrimination between infectious and non-infect [Eur J Intern Med. 2010]

Diagnostic investigations in 101 dogs with pyrexia of unknown or [J Small Anim Pract. 1998]

Causes, diagnostic signs, and the utility of investigations of fever in dogs. [Can Vet J. 2012]

Identify infection

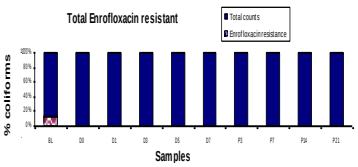
Non-indications for antibiotics

- Feline URI
- Pancreatitis
- Snake bite
- Cat abscess
- Diarrhea
- Mild aspiration pneumonitis
- Prophylaxis in clean surgeries

Identify infection

Impact of Routine Antimicrobial Therapy on Canine fecal *Escherichia coli* Antimicrobial Resistance: A Pilot Study

Dawn M. Boothe, DVM, PhD
DACVIM (Internal Medicine), DACVCP
Nigattra Dehavaiya, DVM, MS, PhD[2]



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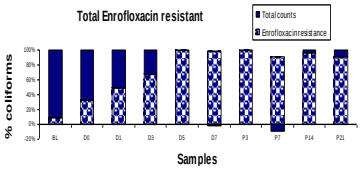


Identify infection

Identify target microbe

Source of infection

Site of infection

Gram stain

Culture

- Before empirical antibiotics
- Should NOT delay the care
- Deep tissue biopsy, cystocentesis, post-lavage effusion, …

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

Identify infection

Identify target microbe

Identify target tissue

Debridement / Control of the source!

No barrier to penetration → water-soluble

Barriers to penetration → lipid-soluble

Sanctuaries → dose X 50-500%

Urine

O2 tension

Purulent material

Identify infection
Identify target microbe
Identify target tissue
Assess host status
Select drug

Previous exposure (< 90 days)

Chronic infection

Immunosuppression

Increased volume of distribution

Clearance

Identify infection
Identify target microbe
Identify target tissue
Assess host status
Select drug

Spectrum of activity (de-escalation for severe sepsis)

Distribution and penetration

Toxicity

Combination (synergy / antagonism)

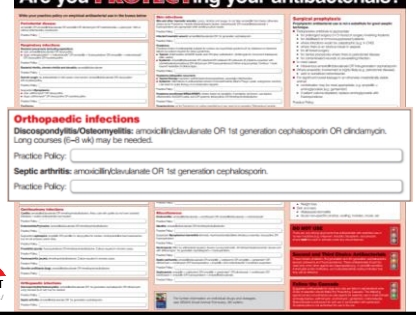
Some potential advantages and disadvantages of using combination empiric therapy versus monotherapy

Advantages	Disadvantages
Broader coverage that includes non-susceptible strains	Possible antagonism
Anti-bacterial synergy	Possible superinfection
Prevents emergence of resistance	May increase resistance
	Increased toxicity
	Increased costs

Crit Care. 2016; 20:133-145.

Identify infection
Identify target microbe
Identify target tissue
Assess host status
Select drug

Are you PROTECTing your antibacterials?



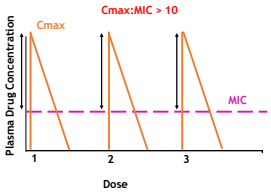
PROTECT

https://www.bsava.com/Portals/0/resources/documents/Protect%20poster_2017.pdf

Identify infection
Identify target microbe
Identify target tissue
Assess host status
Select drug
Design dosing regimen

Time-dependent / Concentration dependent

Minimum Inhibitory Concentration (MIC)



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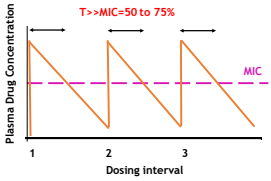

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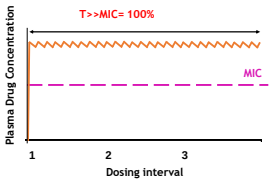

Identify infection
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Identify target tissue
Assess host status
Select drug
Design dosing regimen

Culture and susceptibility			
Antibiotics	MIC		
Amikacin	≤2	S	>32
Amoxi-Clav	≤8	S	< 1
Ampicillin	≥0.5	R	
Carbenicillin	≥512	R	
Cephalothin	8	I	2.5
Ceftiofur	≤1	S	NA
Chloramph	≥32	R	
Ciprofloxacin	≤0.5	S	>5
Enrofloxacin	≤0.25	S	<17
Gentamicin	≤0.5	S	<56
Nitrofurantoin	≤32	S	NA
Piperacillin	≥256	R	
Tetracycline	≤1	S	<7
Ticarcillin	≥256	R	
Tobramycin	≤0.5	S	NA
Trim-Sulfa	10	S	6.7

Table 2. Selected Pharmacokinetic Data for Antimicrobials

Drug	HL	Dose	Route	Cmax
	hr	mg/kg		mcg/ml
Amikacin (C)	1	20	IV	65
Amoxicillin (T)	1	12.5	PO	4.5-6
Amoxi-clav (T)	1-1.5	12.5	PO	4.5-6
Ampicillin (T)+A29	0.5-1.5	30	PO	10
Cefotaxime	0.8	50	IV,IM	41
Cefpodoxime	5.6	5	PO	8.2
Ceftazidime (T)[bcd]	0.82	30	SC	42
Cephalexin (T)[bd]	1.3-2.5	20	PO	20
Chloramphenicol (T)	1.2-2.7	20	PO	23
Ciprofloxacin (C)	5.3	20	PO	2.8
Doxycycline (T)	4.6	2.5	PO	3
Enrofloxacin (C)	4.1	20	PO	4.2
Gentamicin (C)	1	10	IV	28
Imipenem/cilastin (T)	1	5	IM	13
Marbofloxacin (C)	11	2	PO	1.4
Orbifloxacin (C)	5	2.5	PO	2
Sulfadimethoxine (T)	13	55	PO	67
Tetracycline (T)	10	13.75	IV	7
Ticarcillin (T)	1	40	IV	80
Ticar -clav (T)	1	40	IV	80

C=concentration dependent
T=time dependent

Identify infection
Identify target microbe
Identify target tissue
Assess host status
Select drug
Design dosing regimen

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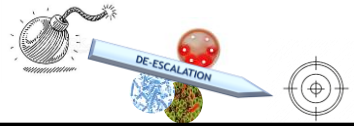
Identify infection
Identify target microbe
Identify target tissue
Assess host status
Select drug
Design dosing regimen
De-escalate

De-Escalation

- Sever sepsis, septic shock
- 1. Broad spectrum pending culture → 2. Narrow spectrum
- Lower mortality in humans
- Does not increase MDR



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Design dosing regimen
De-escalate

Duration – When do we stop?

- Re-evaluate within 48-72 hours (Antibiotic Timeout)
- 7-10 days?
- Until resolution of the clinical signs?
- Until negative culture?
- Prolonged therapy = resistance

Evaluation of the Efficacy and Safety of High Dose Short Duration Enrofloxacin Treatment Regimen for Uncomplicated Urinary Tract Infections in Dogs

A. Westropp, JE. Sykes, S Irom, JB Daniels, A Smith, D Kell, T Settje, Y Wang, and DJ Chew

USE HIGH DOSES AND SHORT DURATION

Conclusion

Microbiology guides therapy
Indications should be evidence based
Narrowest spectrum required
Dosage appropriate
Minimize duration of therapy
Ensure monotherapy in most cases

Useful links

BASVA PROTECT:
https://www.bsava.com/Resources/Veterinary-resources/PROTECT

The Antimicrobial Reference Guide to Effective Treatment:
https://target.naccvp.com/?e=9736acda32cbd1c0932969eb79d4cd8ez23

Centers for Disease Control and Prevention:
https://www.cdc.gov/antibiotic-use/index.html

Federation of European Companion Animal Veterinary Associations:
https://www.fecava.org/en/policies-actions/guidlines

Additional references

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