Antimicrobial Use In The Emergency Patient

Steven Epstein, DVM, DACVECC

Professor of Small Animal Emergency and Critical Care

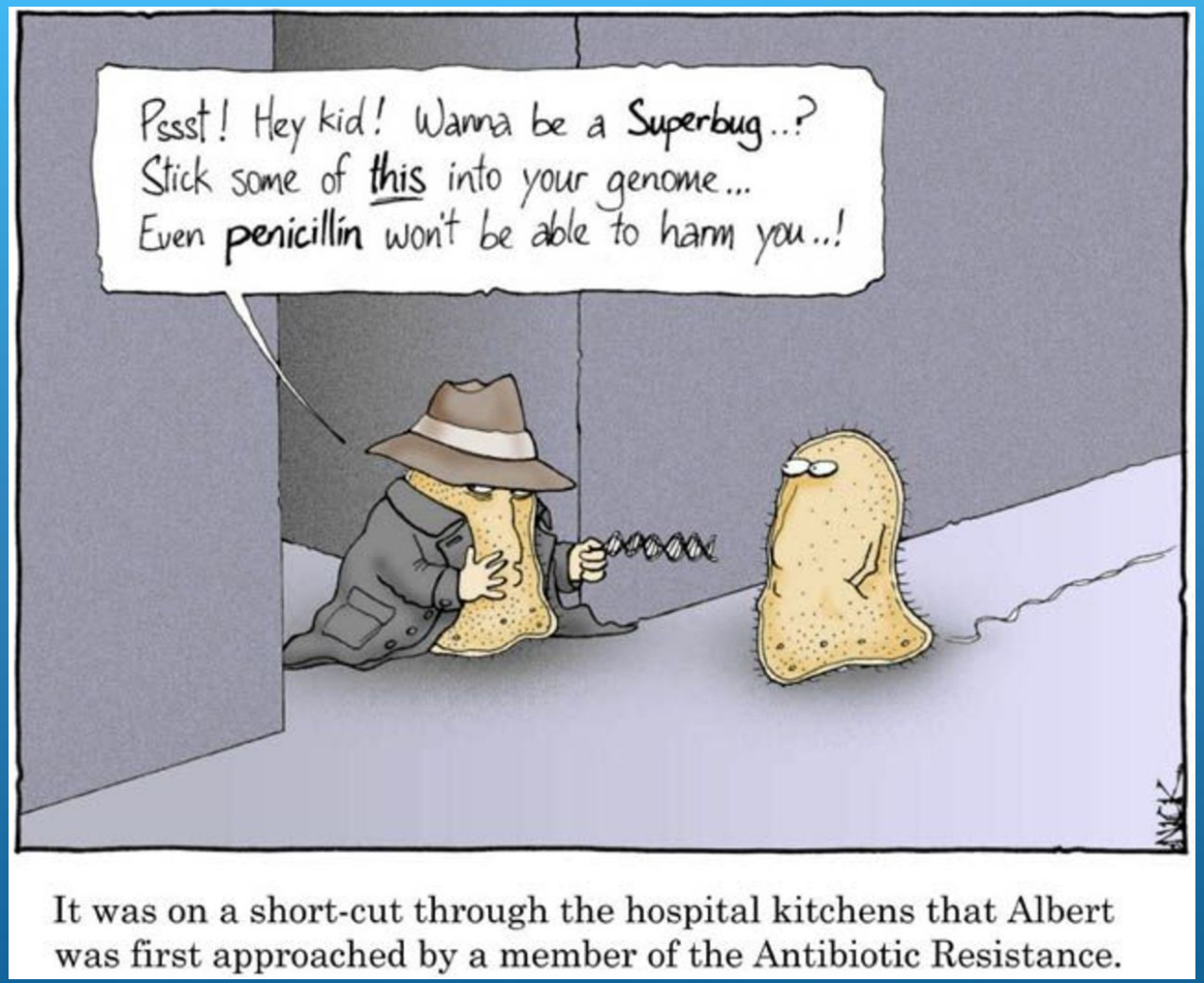
UCDAVIS

VETERINARY MEDICINE

Surgical and Radiological Sciences

Introduction

- Indications
- Timing of initiation
- Empiric choices
- Duration of use
  - Disease examples



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

What is the goal of antimicrobial therapy?

- A. To eradicate bacteria at the site of infection
- B. To reduce the bacterial load at the site of infection to a level where the host immune system can handle it

New Definitions

- Sepsis – Life threatening organ dysfunction caused by dysregulated host response to infection
- Septic Shock – Subset of sepsis in which particularly profound circulatory, cellular and metabolic abnormalities associated with greater risk of mortality

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Surviving Sepsis Guidelines (SSG)

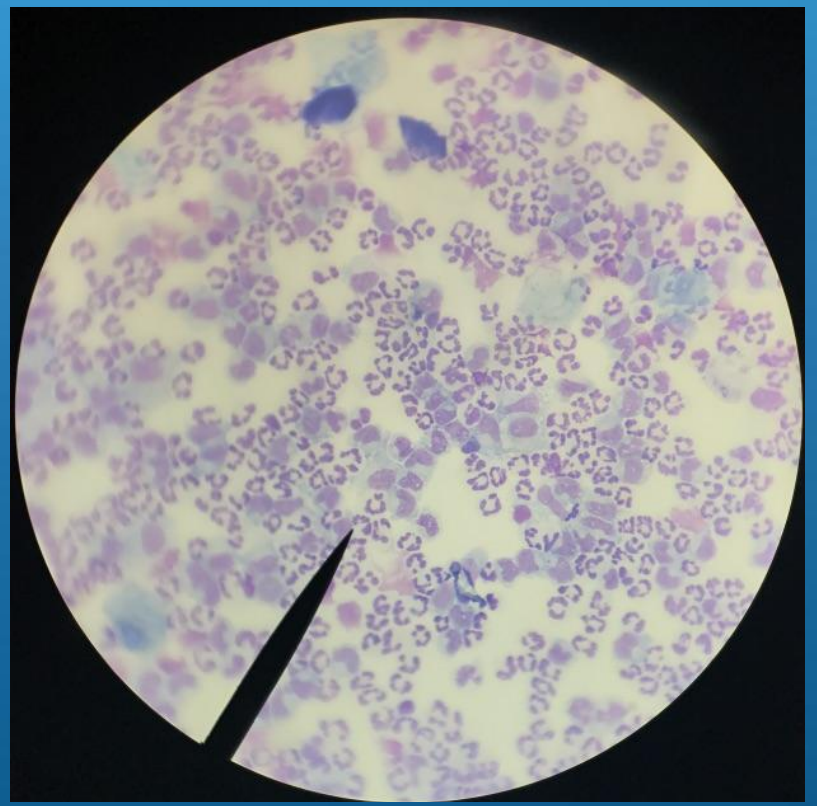
Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

- Recommend a system to be in place for screening patients for sepsis and septic shock

Critical Care Medicine: November 2021 - Volume 49 - Issue 11 - p e1063-e1143
doi: 10.1097/CCM.0000000000005337

Indications for Antimicrobials

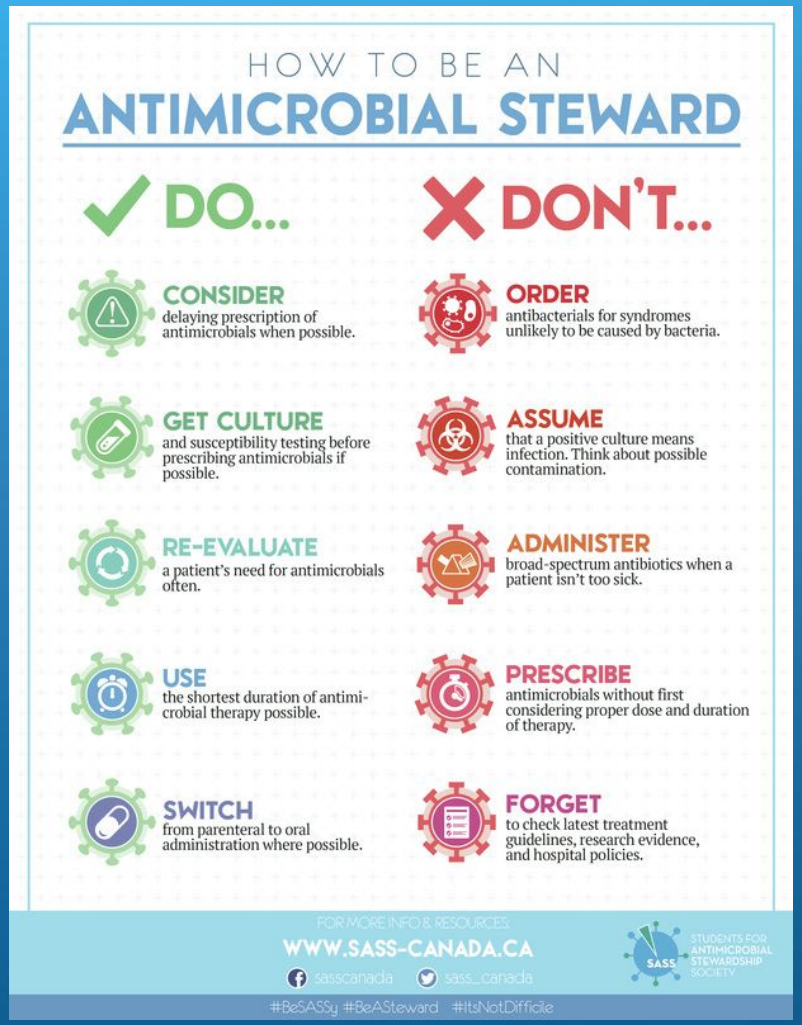
- Known bacterial infection
- Highly suspect bacterial infection
- SIRS vs sepsis?
- Client demands?



To Prescribe or not to Prescribe?

- Balance of
  - Antimicrobial stewardship
  - Increasing morbidity/mortality in patient by withholding

- Level of illness
  - Sepsis/septic shock
  - Stable patient



Timing of Initiation

Possible septic shock or high likelihood of sepsis

- Recommend administration of antimicrobials immediately, ideally within 1 hour of recognition

Strong, *low quality of evidence (Septic shock)*

Strong, *very low quality of evidence (Sepsis without shock)*

Possible sepsis without shock

- Rapid investigation for infection and if concern persists, administer antimicrobials within 3 hours of when sepsis is first recognized

Weak, *very low quality of evidence*

Veterinary Medicine

- Developing a hospital protocol can help ensure rapid administration

Positive impact of an emergency department protocol on time to antimicrobial administration in dogs with septic peritonitis

Journal of Veterinary Emergency and Critical Care **23**(5) 2013, pp 551–556
doi: 10.1111/vec.12092

Empiric Choices

- Escalation vs. De-escalation
  - Level of illness
  - Risk factors for MDR
- What microorganisms do I expect?

Escalation vs. De-escalation

- Escalation – choosing a narrow spectrum empiric antimicrobial based on likely pathogens

- De-escalation – choosing empiric antimicrobial therapy combination that will cover all expected pathogens AND then *reducing spectrum based on culture results*

Varying Illness Level

Risk Factors for Resistance

- Previous antimicrobial use
- Longer duration of hospitalization
- Longer duration in intensive care
- Invasive procedure or surgery
- Mechanical ventilation
- Exposure to other patients/surfaces with resistant pathogens

SSG Empiric Recommendations

- High risk for MDR organisms, suggest using two antimicrobials with gram-negative coverage
  - Suggest against using double gram-negative coverage once the causative pathogen and the susceptibilities are known

Recommendations – Sepsis or Septic Shock

Situation	Antimicrobial drug	Intravenous dosage for Dogs and Cats
Patients with no recent antimicrobial history (30 days) and **community acquired infection**	Ampicillin/sulbactam OR Clindamycin AND Amikacin	50 mg/kg q 6 hr 12 mg/kg q 8 hr 15 mg/kg q 24 hr

Recommendations – Sepsis or Septic Shock

Situation	Antimicrobial drug	Intravenous dosage for Dogs and Cats
Patients with no recent antimicrobial history (30 days) and community acquired infection	Ampicillin/sulbactam OR Clindamycin AND Amikacin	50 mg/kg q 6 hr 12 mg/kg q 8 hr 15 mg/kg q 24 hr
Patients with no recent antimicrobial history (30 days) and **community acquired infection with renal disease**	Ampicillin/sulbactam OR Clindamycin AND Enrofloxacin	50 mg/kg q 8 hr 12 mg/kg q 8 hr Dogs: 15 mg/kg first dose then 10 mg/kg q 24 hr Cats: 5 mg/kg q 24 hr

Recommendations – Sepsis or Septic Shock

Situation	Antimicrobial drug	Intravenous dosage for Dogs and Cats
Patients with **recent antimicrobial use, or hospital acquired infection**	Third generation cephalosporin with anti-*Pseudomonas* activity. Cefotaxime Ceftazidime	 30 mg/kg q 6 hr 30 mg/kg q 6 hr

Recommendations – Sepsis or Septic Shock

Situation	Antimicrobial drug	Intravenous dosage for Dogs and Cats
Patients that developed new onset or worsening severe sepsis/septic shock while on a third generation cephalosporin AND/OR has risk factors for methicillin resistant staphylococcus or MDR enterococcus	Meropenem AND/OR Vancomycin	12 mg/kg q 8 hr 15 mg/kg q 8 hr

Antibiogram

	Amikacin	Amoxicillin/ Clavulanate	Ampicillin	Cefazolin	Chloramphenicol	Clindamycin	Doxycycline	Enrofloxacin	Gentamicin	Imipenem	Methicillin	Penicillin	Ticarcillin/ Clavulanate	Trimethoprim/ Sulfamethoxazole	Amoxi/Clav and Enrofloxacin
All Organisms (n=4106)															
Gram Positive (n=2298)															
Non-ß hemolytic *Streptococcus* (n=107)															
Corynebacterium spp. (n=163)															
Enterococcus spp. (n=408)															
Enterococcus faecalis (n=256)															
Enterococcus faecium (n=104)															
Staphylococcus spp. (n=1584)															
Gram Negative (n=1797)															
All Enteric organisms (n=1269)															
E. coli (n=941)															
Pasteurella spp. (n=159)															
Proteus spp. (n=140)															
Pseudomonas aeruginosa (n=225)															
By Source															
Blood (n=60)															
Dermatologic (skin, ears) (n=1464)															
Ocular (n=99)															
Bone and Joint (n=86)															
Abdominal (n=72)															
Respiratory (n=231)															
Soft Tissue (n=519)															
Urinary (n=1363)															

The information needs to be considered in light of selection of the most appropriate drug for the bacteria cultured, and in light of the anatomic site (i.e., drug penetration) and patient factors.
This should not be used as a substitute for culture and susceptibility testing.
Green>70% susceptibility, Yellow 40-70%, Red <40%, Blue= insufficient/not applicable data, and Black=intrinsic resistance

Decision Making for Antibiotic Duration

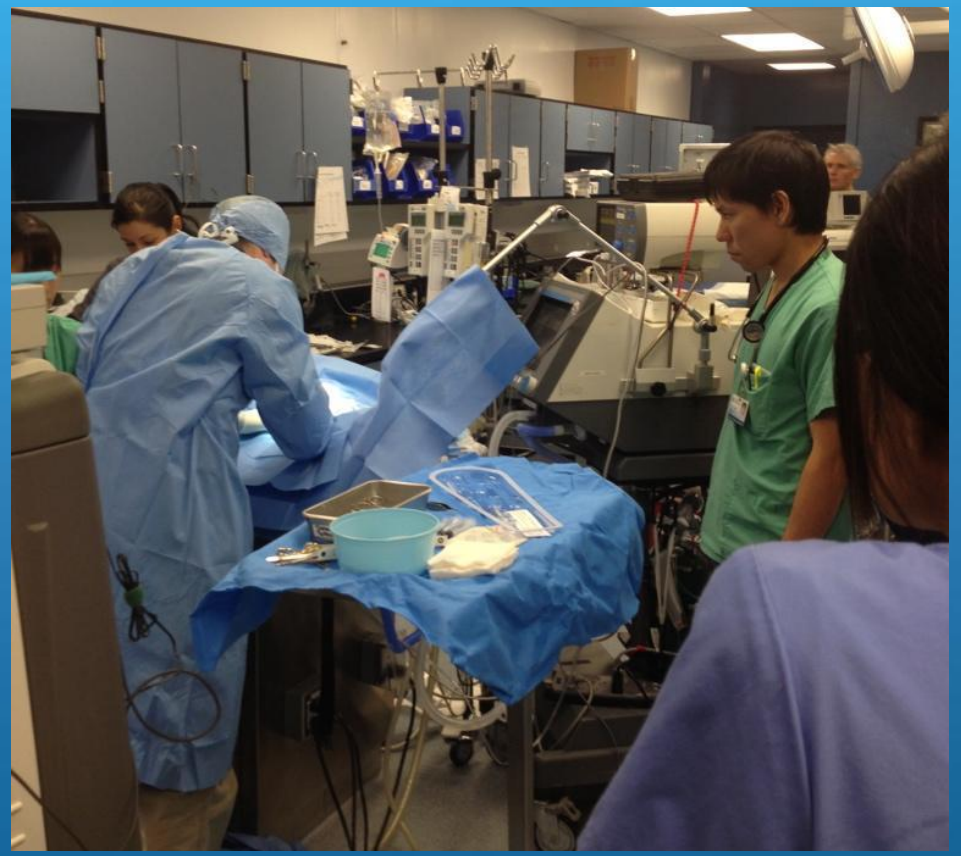
- Can source control be achieved?
- What is the immune status of the patient?
- What is the severity of the disease process?

Source Control

- Physical measures undertaken to eliminate a source of infection or to control ongoing contamination
  - Lancing and draining of abscess
  - Exploratory laparotomy
  - Thoracostomy tube

Lack of Source Control

- Pneumonia
- Pyelonephritis
- CNS infections

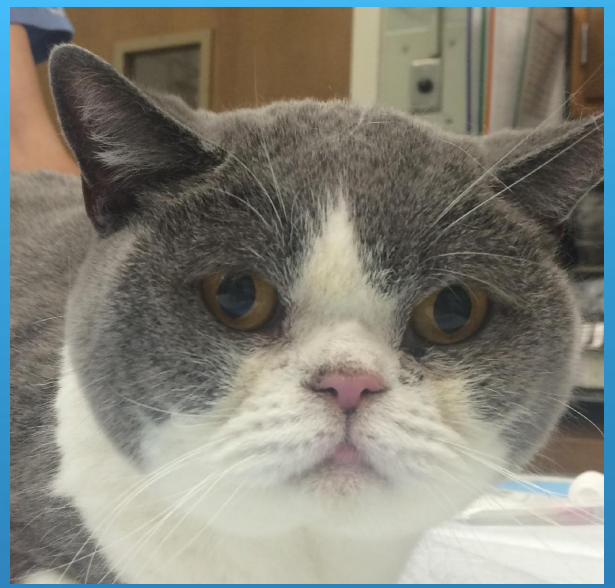


Immunocompetent?

- Lack of an immunosuppressive disease
  - Diabetes mellitus
  - Cushing's
  - Neoplasia
  - Neutropenia
  - Chemotherapy

Disease Severity

- No systemic signs
- Fever
- Sepsis
- Septic shock



Classification of UTI

International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats

J. Scott Weese[a,*], Joseph Blondeau[b,c], Dawn Boothe[d], Luca G. Guardabassi[e,f], Nigel Gumley[g], Mark Papich[h], Lisbeth Rem Jessen[i], Michael Lappin[j], Shelley Rankin[k], Jodi L. Westropp[l], Jane Sykes[l]

- Sporadic
  - a bacterial infection of the bladder with compatible lower urinary tract signs
- Diagnosis
  - LUT clinical signs with bacteriuria
  - +/- Pyuria, hematuria

Sporadic Bacterial Cystitis

- Disease of Female and Male Castrate
  - Male intact, assume bacterial prostatitis
- Anatomic or functional abnormalities may be present
- Comorbidities allowed
  - Endocrinopathies, IVDD, etc.
- Treatment Duration: 3-5 days
  - Empiric amoxicillin or TMS

Feline Urinary Antibiogram

		% Susceptibility								
		Amik	A/C	Ampi	Cefaz	Chlor	Enro	Marb	TMS	MDR
Bacteria	All bacteria (442)	72	72	62	49	86	61	59	75	19
	Enterobacterales (250)	98	68	57	69	92	93	94	96	13
	E. coli (hemolytic) (183)	97	77	66	73	94	99	99	99	8
	E. coli (non-hemolytic) (45)	100	36	24	69	91	76	76	89	26
	Staphylococcus (48)	96	67	42	73	81	79	53	70	29
	Enterococcus faecalis (90)	-	100	99	-	83	-	-	80	24
	Enterococcus faecium (17)	-	24	2	-	94	-	-	38	56

Evidence in Small Animals

J Vet Intern Med 2012;26:506–512

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

J.L. Westropp, J.E. Sykes, S. Irom, J.B. Daniels, A. Smith, D. Keil, T. Settje, Y. Wang, and D.J. Chew

- 3 days ~20mg/kg enrofloxacin vs amoxicillin/clavulanic acid for 14 d
- No difference in cure rates

J Vet Intern Med 2014;28:818–826

Short- and Long-Term Cure Rates of Short-Duration Trimethoprim-Sulfamethoxazole Treatment in Female Dogs with Uncomplicated Bacterial Cystitis

S. Clare, F.A. Hartmann, M. Jooss, E. Bachar, Y.Y. Wong, L.A. Trepanier, and K.R. Viviano

- 3 days TMS vs 10 days cephalexin
- No difference in cure rates
  - Microbial or clinical

Recurrent Bacterial Cystitis

- Three or more episodes of clinical bacterial cystitis in the preceding 12 months
- Two or more episodes in the preceding 6 months
- Workup is indicated for underlying cause
- Urine C&S and wait for results vs empiric???
  - Dependent on severity
  - Consider NSAIDS if waiting

Treatment duration

- Previous guidelines 4 weeks
- Short (3 – 5 days) durations should be considered
- Longer courses (7 – 14 days duration) may be needed

- Reculture 5-7 days post cessation if deciding relapse, re-infection, vs persistent infection

Pyelonephritis

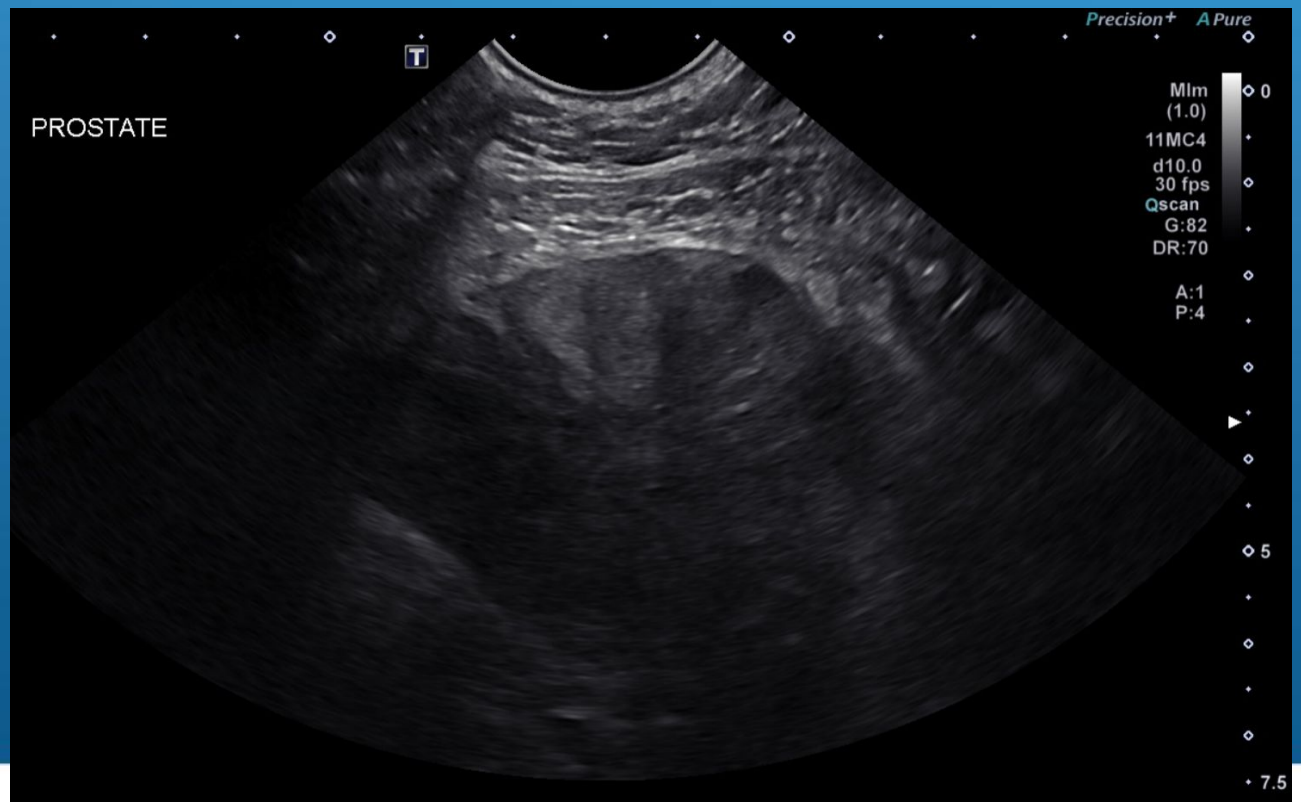
- Infection of the renal parenchyma
- Urine C&S recommended
  - Interpret with serum not urine breakpoints
- Historically 4-6 weeks
- Recommend 10-14 days (no veterinary evidence)
  - Empiric fluoroquinolone or 3rd gen cephalosporin allowed

Human evidence – Pyelonephritis

- Multiple studies document 4-5 days treatment as effective as 10-14 days
- Cochrane review: oral vs intravenous then oral no difference in outcome

Bacterial Prostatitis

- Assumed in every Intact male dog with UTI
- Ultrasound recommended to confirm



Prostatitis treatment

- Antimicrobial with good penetration
  - Fluoroquinolone, clindamycin, macrolides, TMS???
- Duration:
  - Chronic prostatitis: 4 - 6 weeks
  - Acute and responding: “consider shorter”

Subclinical bacteriuria

- Presence of bacteria without evidence of urinary disease
  - No LUT signs or pyuria
  - Enterococcus common
- 59% of bacteriuria in recent feline study
- Treatment duration = 0 Days

Pneumonia

- Recommendations in SA:
- Treat for 2 weeks
- Treat for 2 weeks beyond radiographic resolution
- Treat for 4-6 weeks

Treating Pneumonia

- Humans

Population/Syndrome	RCT/Systemic Review (Data Extracted From)	Shorter Duration	Longer Duration	Outcomes
Pneumonia	Capellier 2012 (301)	8 days	15 days	No difference
	Chastre 2003 (301, 302)	8 days	15 days	No difference
	El Moussaoui 2006 (302)	3 days	8 days	No difference
	Fekih Hassen 2009 (301–303)	7 days	10 days	No difference
	File 2007 (302, 303)	5 days	7 days	No difference
	Kollef 2012 (302, 303)	7 days	10 days	No difference
	Leophonte 2002 (302, 303)	5 days	10 days	No difference
	Medina 2007 (301)	8 days	12 days	No difference
	Siegel 1999 (302, 303)	7 days	10 days	No difference
	Tellier 2004 (302, 303)	5 days	7 days	No difference

Human Pneumonia

- VAP (RCT) – 8 day vs. 15 day course
  - No difference in mortality or recurrent infections

- 2nd RCT: change in hospital protocols reduced mean antibiotic duration from 14.8 to 8.6 days with no increase in mortality

Human Pneumonia

- Surviving Sepsis Campaign
- Suggest treatment for nosocomial pneumonia limited to 7 days
  - Recognize there is a group needing longer having poor clinical response

Veterinary Guidelines

Antimicrobial use Guidelines for Treatment of Respiratory Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases

- Treat for 10 –14 days and re-evaluate. Then decisions to extend treatment should be based on clinical, hematological, and radiographic findings

J Vet Intern Med 2017;31:279–294

Recent Evidence

Antimicrobial discontinuation in dogs with acute aspiration pneumonia based on clinical improvement and normalization of C-reactive protein concentration

- 12 dogs treated for 7 days with no short term relapse noted

J Vet Intern Med. 2022;36:1082–1088.

Recent Evidence cont…

Serial evaluation of thoracic radiographs and acute phase proteins in dogs with pneumonia

- Majority of dogs CRP normalized by day 7
  - Repeated in separate study
- 12/17 dogs had 7 days antimicrobials with no relapse
  - 2 had documented normal thoracic radiographs

J Vet Intern Med. 2022;36:1430–1443.

No Antimicrobials?

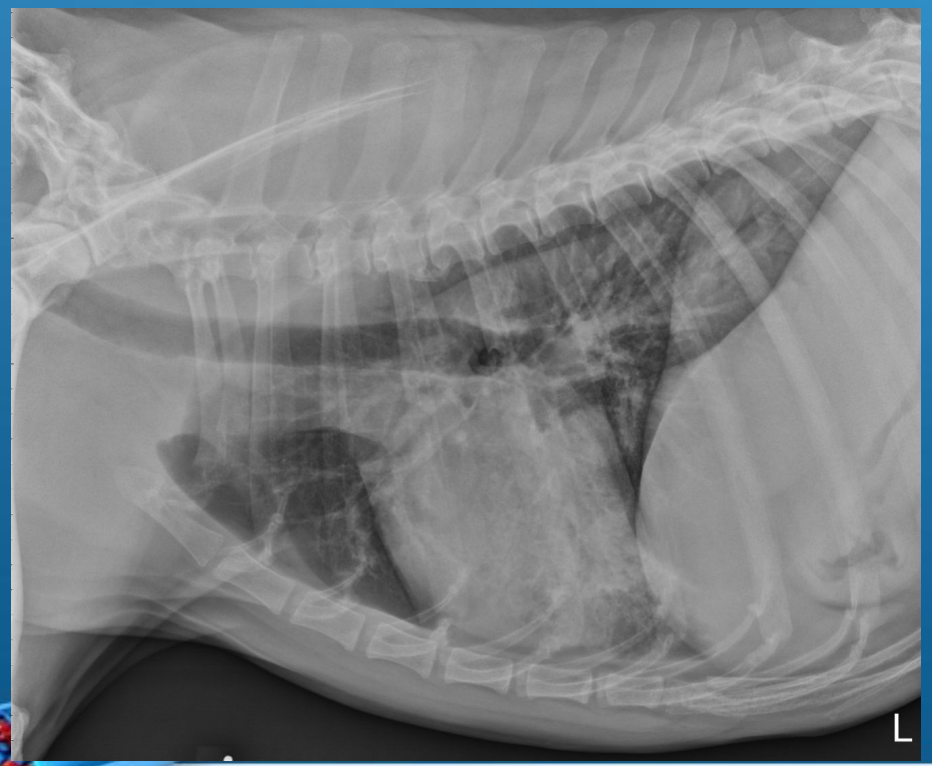
Successful management of aspiration pneumopathy without antimicrobial agents: 14 dogs (2014-2021)

- 6 dogs where oxygen therapy was clinically indicated
- Resolved clinical signs in 12-36 hours

Journal of Small Animal Practice (2021) **62**, 1108–1113
DOI: 10.1111/jsap.13409

Summary - Pneumonia

- If systemically healthy consider withholding
- If clinically sick treat for 7 days



Summary

- In patients with Sepsis in the ER:
  - Give antimicrobials early
    - Stop if non-infectious disease documented
  - Tailor therapy to the patient
  - Use them for as short duration as possible

Questions?