



# SPRING SUNDAY CE SESSIONS

**ONLINE, INTERACTIVE, IN REAL-TIME**  
Four Sundays, Six CE Credits Each—Take One Sunday or Take Them All

SUNDAY  
March 13, 2022



SUNDAY  
April 3, 2022



SUNDAY  
April 10, 2022



SUNDAY  
April 24, 2022



# Urinary Tract Infections in Small Animals

---

M. Casey Gaunt, DVM, MVetSc, DACVIM (SAIM)

Joe Rubin, DVM, PhD

# Agenda for Today

- Why this topic?
- How to talk about the urinary system
- Categorize UTIs
- Diagnose UTIs
- How to treat UTIs
- Non UTIs
- Factors and diseases that influence UTIs
- Weird and fun variations



# Why Urinary Tract Infections?

- This is a common disease in pets
  - 5%-27% of dogs will get a UTI at some point in their lives
  - 3-19% of cats will get a UTI at some point in their lives
- Treatment of UTIs is among the leading reasons for antimicrobial use in Veterinary Medicine
- Antimicrobial use and Antimicrobial Resistance (AMR)
  - Increasing focus in both Human and Veterinary medicine
  - As a self-governing profession, we have an obligation to ensure we identify and follow best practices
- Sometimes, they are just plain difficult cases to manage!!!



# Urinary Terminology

## Lower Urinary Tract

- Bladder or urethral disease

## Upper Urinary Tract

- Renal or ureteral disease

# Lower Urinary Tract Terminology

## Pollakiuria vs polyuria

- Pollakiuria
  - Small volume
  - Frequent episodes
- Polyuria
  - Large volume
  - Frequency may not change

## Stranguria

- Attempting to produce urine with minimal success
- Continues “trying to pee” after done urinating

## Hematuria vs pigmenturia

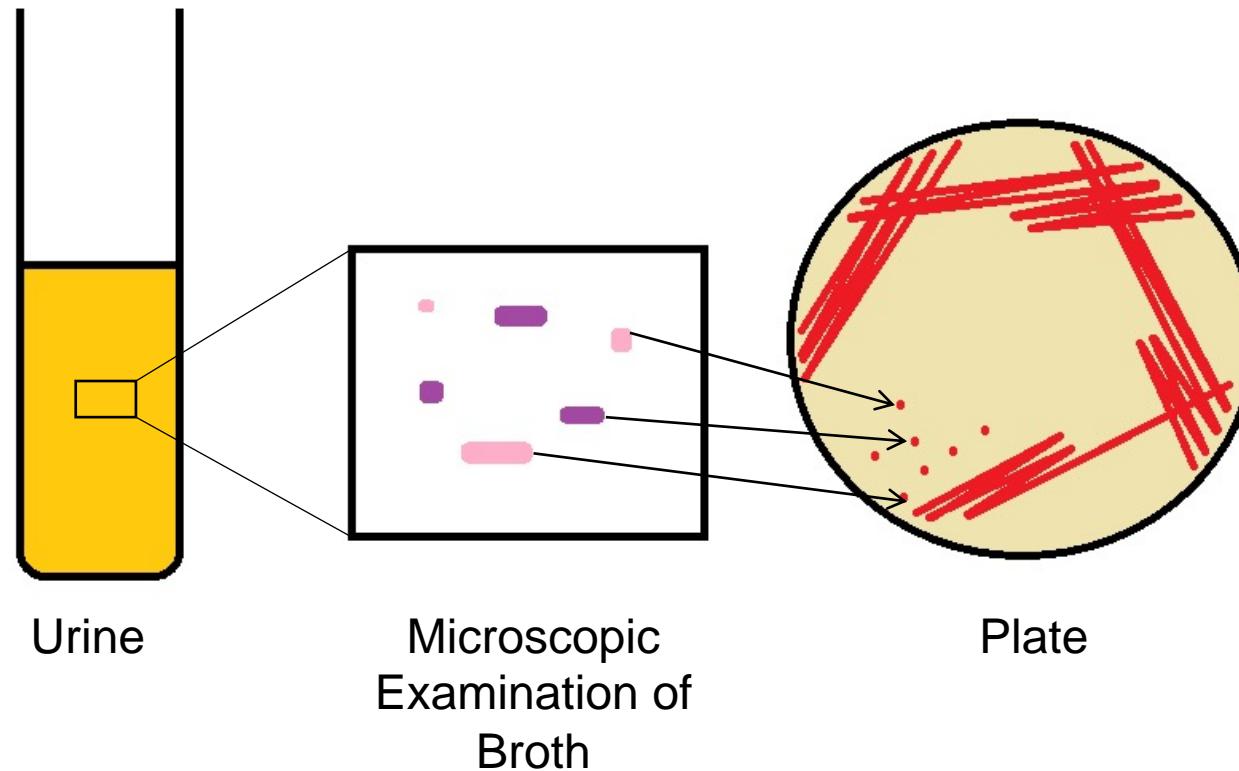
- Hemoglobinuria
  - Secondary to intravascular hemolysis
- Myoglobinuria
  - Secondary to profound muscle injury

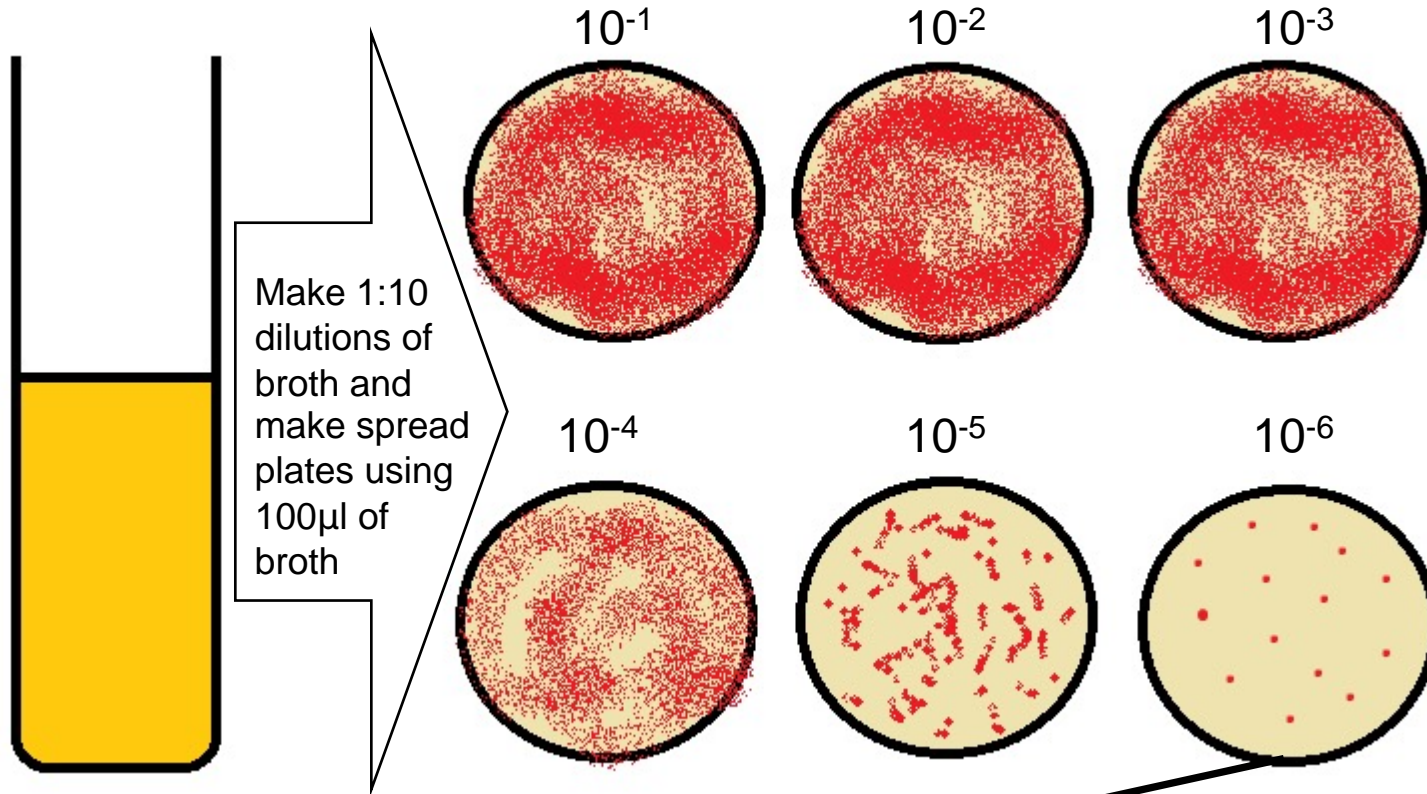
## Dysuria

- Attempting to urinate without producing urine
- Urine stream starts and stops
- Poor urine stream

# What is a UTI?

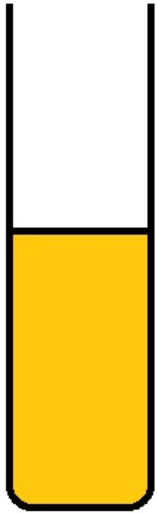
- Microbiologically defined as  $>100,000$  cfu/ml
  - Quantitative (or crudely quantitative) culture required



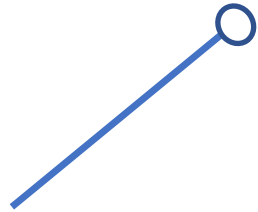


$$(14 \text{ colonies}/0.1 \text{ ml}) / (10^{-6}) = 140 \text{ Million CFU/ml}$$

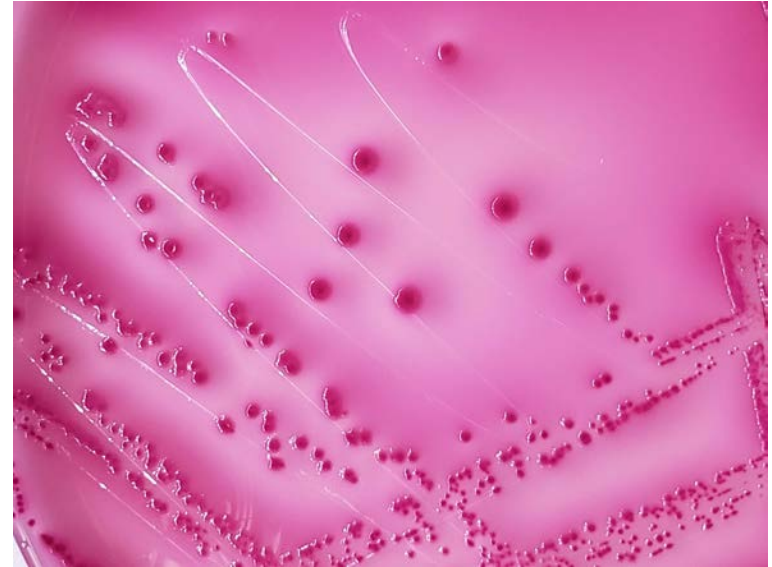




Urine




Calibrated Loop  
1 $\mu$ l

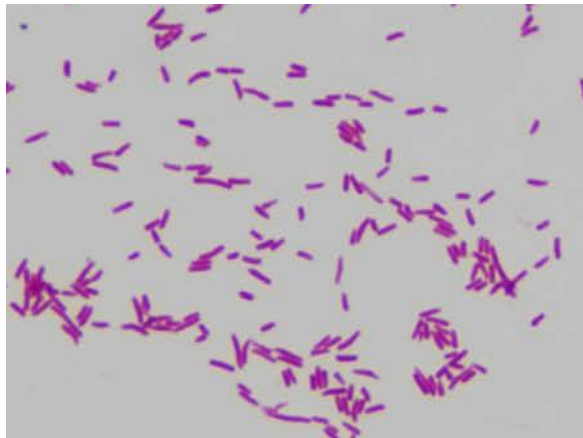


Roughly count colonies  
on plate. If >100 then >  
100,000 CFU/ml

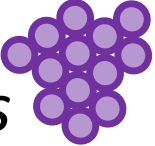
# Most Common Etiologies

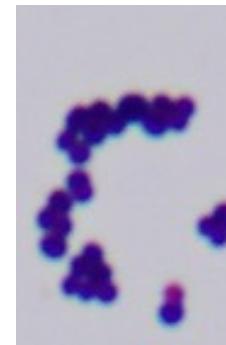
## Gram-negatives

-  *E. coli* (~50%)
- Other Enterobacterales  
(*Klebsiella*, *Proteus*, *Enterobacter*)
- Pseudomonas aeruginosa*

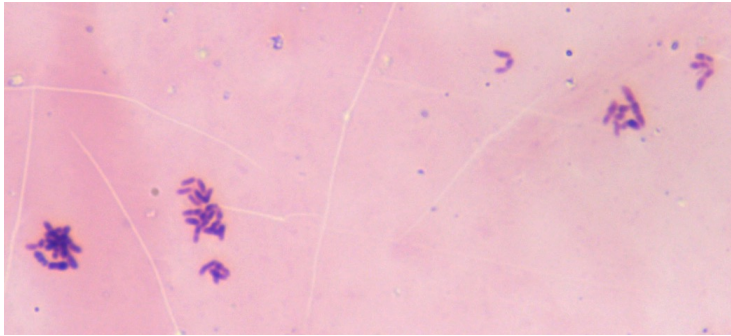


## Gram-positives

- Staphylococcus* 
- Streptococcus* 20-30%
- Enterococcus*



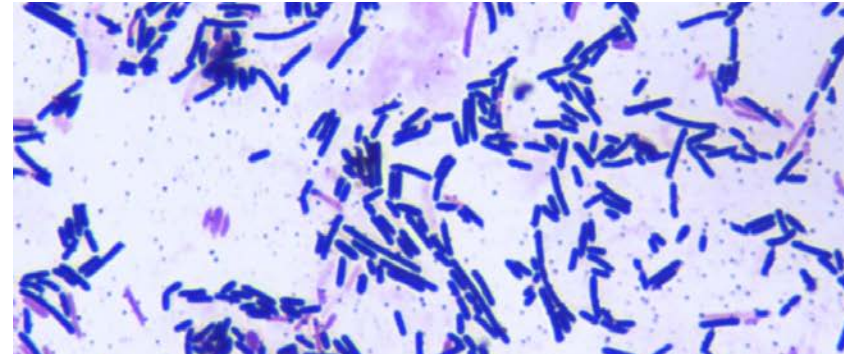
# Other Etiologies



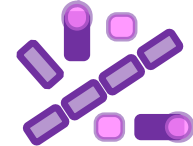
Urease producing  
*Corynebacterium* spp.



Irregular, club shaped, Gram-positive rods in  
“palisades” or “Chinese-letter” formations

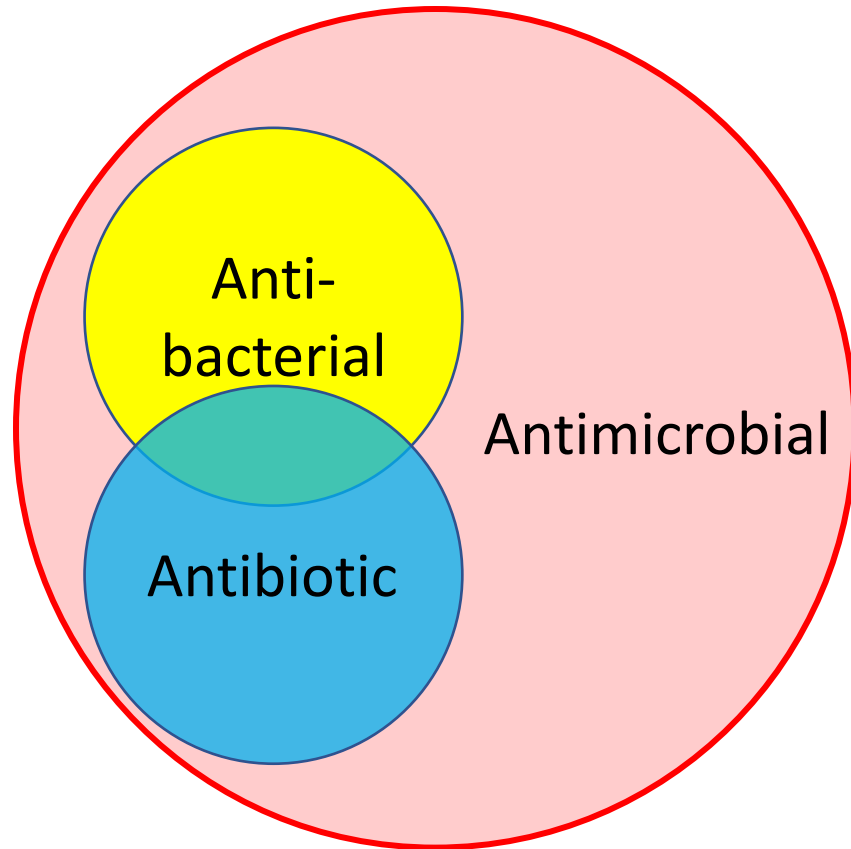


*Clostridium* spp.



Gram-positive rods, +/- spores depending on  
species and handling of culture

# Pharmaceutical Terminology



**Antimicrobial:** a drug which has lethal or inhibitory activity against microorganisms

**Antibacterial:** a drug which has lethal or inhibitory activity against bacteria

**Antibiotic:** a drug which is naturally produced by a microbe which has lethal or inhibitory activity against bacteria

# Additional Urinary Terminology

- Urinary incontinence
  - Unconscious leaking of urine
    - Often noted when sleeping or lying in the owner's lap
- Pyelonephritis
  - Infection of the upper urinary tract (kidneys)
  - Pylectasia
    - Dilation of the renal pelvis
- Prostatitis
  - Infection of the prostate gland in an intact male dog

# ISCAID Guidelines

- International Society for Companion Animal Infectious Diseases
  - Group focused on infectious diseases in companion animals
  - Clinicians and scientists from all over the world
  - Meet every 2 years
    - Alternate between North America and International locations

## Antimicrobial Use Guidelines:

UPDATED URINARY GUIDELINES AVAILABLE FREE BY [CLICKING HERE](#)

GUIDELINES FOR DIAGNOSIS AND THERAPY OF SUPERFICIAL BACTERIAL FOLLICULITIS (PYODERMA) AVAILABLE FREE BY [CLICKING HERE](#)

GUIDELINES FOR DIAGNOSIS AND TREATMENT OF RESPIRATORY TRACT DISEASE AVAILABLE FREE BY [CLICKING HERE](#)

The ISCAID Antimicrobial Guidelines Working Group was established in 2010, and is comprised of clinical microbiologists, pharmacologists, and internal medicine specialists with expertise in infectious disease and antimicrobial use. The goals were 1) to develop guidelines containing recommendations for antimicrobial drug choice and dosing for specific diseases of companion animals, in order to reduce inappropriate use of antimicrobial drugs; 2) to educate of veterinarians about the need for rational and effective antimicrobial drug use; 3) to disseminate the guidelines widely in accessible formats; and 4) to identify areas for further research.



The Veterinary Journal 247 (2019) 8–25



Contents lists available at [ScienceDirect](#)

## The Veterinary Journal

journal homepage: [www.elsevier.com/locate/tvj](http://www.elsevier.com/locate/tvj)



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<sup>a,\*</sup>, Joseph Blondeau<sup>b,c</sup>, Dawn Boothe<sup>d</sup>, Luca G. Guardabassi<sup>e,f</sup>, Nigel Gumley<sup>g</sup>, Mark Papich<sup>h</sup>, Lisbeth Rem Jessen<sup>i</sup>, Michael Lappin<sup>j</sup>, Shelley Rankin<sup>k</sup>, Jodi L. Westropp<sup>l</sup>, Jane Sykes<sup>l</sup>



# Main Categories of UTIs

Sporadic  
Bacterial  
Cystitis

Recurrent  
Bacterial  
Cystitis

Upper Urinary  
Tract  
Infections

Bacterial  
Prostatitis

Subclinical  
Bacteriuria

# Sporadic Bacterial Cystitis

- Replaces the term “uncomplicated” or “simple” UTI
- Bacterial infection of the bladder resulting in inflammation and clinical signs
- Classical signalment:
  - Otherwise healthy neutered male or nonpregnant female dogs
- Fewer than 3 episodes in the previous 12 months
- Generally occur in patients without concurrent/complicating disease
  - But not always



# Cats

- Sporadic cystitis is less common in cats than in dogs
- Often there are underlying conditions contributing
- FIC/FLUTD
  - Interstitial or Idiopathic cystitis
  - <2% are caused by bacterial infection
  - Very common in younger cats



## *Causes of non-obstructive FLUTD*

Non-obstructive idiopathic cystitis	65%
Uroliths	15%
Anatomical defects/neoplasia/other	10%
Behavioural problems	<10%
Bacterial infection	<2%

## *Causes of obstructive FLUTD*

Obstructive idiopathic cystitis	29%
Urethral plug	59%
Uroliths	10%
Uroliths+bacterial infection	2%

**jfms**

NOVARTIS FORT DODGE

PROCEEDINGS OF THE ESFM FELINE CONGRESS, STOCKHOLM,  
SEPTEMBER 2002  
Feline lower urinary tract disease

Danièle A Gunn-Moore\*

# Physical Exam Findings

- Often normal
- Licking/irritation around penis or vulva
- Penile or preputial discharge
  - Is it coming from *inside* the urinary tract?
- Vulva/vaginal mass
- Recessed or hooded vulva
- Rectal Exam
  - Palpate urethra
  - Can feel thickening or stones



Transmissible Venereal Tumour

# Diagnostic Approach to Sporadic Cystitis

- Clinical signs

- Pollakiuria
- Hematuria
- Stranguria/Dysuria
- Urinary incontinence
- Peri-genital licking



- Laboratory Testing

- Urinalysis
- Urine culture and susceptibility profile
  - Required for every case??
  - Not always practical or affordable



# Importance of Urinalysis

Tara L. Piech, DVM, MS\*, Kathryn L. Wycislo, DVM, PhD

Vet Clin Small Anim 49 (2019) 233–245

<https://doi.org/10.1016/j.cvsm.2018.10.005>

Although overlooked by some practitioners, a complete urinalysis is often considered to be the single most important diagnostic test by many veterinary specialists. In addition to the identification of urinary tract disorders, such as bacterial cystitis, protein-losing nephropathy, and transitional cell carcinoma, a urinalysis can aid in the diagnosis of nonurinary tract disorders. Endocrinopathies such as diabetes mellitus and other systemic disorders such as intravascular hemolysis can often be diagnosed through urine evaluation.

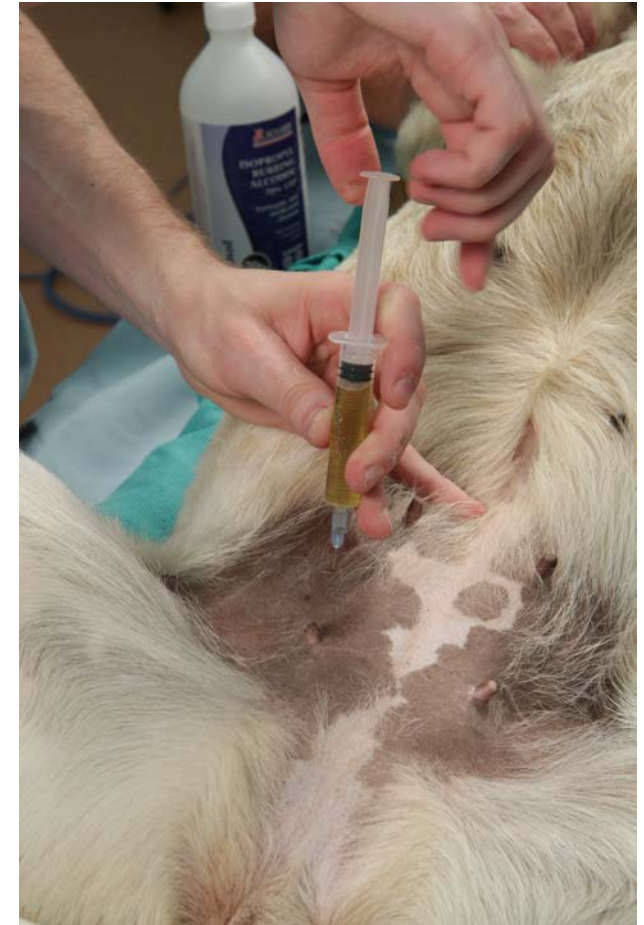


# Urinalysis

- Collection Method
  - Free catch
    - Caught in a clean container
    - Off the floor?
  - Catheter
    - Aseptic technique
    - Traumatic?
  - Cystocentesis
    - Clean stick?
    - Adjacent organs/vessels?
    - Not possible in this patient?

- Colour
  - Concentration
  - Hydration status
  - Hematuria vs Pigmenturia

- Clarity
  - Clear
  - Turbid
  - Flocculant
  - Clots



# Urinalysis

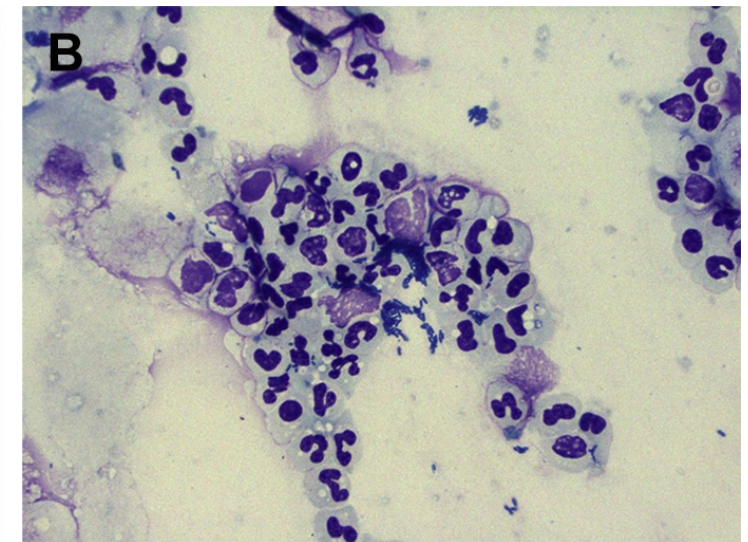
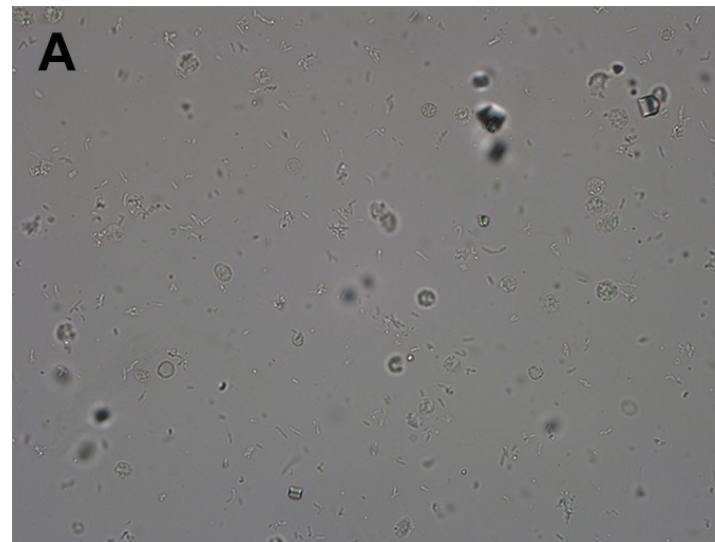
- Urine Specific Gravity
  - Concentrated
    - 1.030 for a dog
    - 1.035 for a cat
  - Isosthenuria
    - 1.008-1.013
  - Hyposthenuria
    - 1.007 or less
  - Is my patient PU/PD?

- pH
  - Alkaline urine degrade RBC & WBC
  - Urease producing bacteria
    - Alkaline urine
  - Diet
- Glucosuria +/- Ketonuria
  - DM or DKA
- Proteinuria
  - Active sediment
  - Concurrent diseases
    - Teeth?
  - Medications
    - Steroids

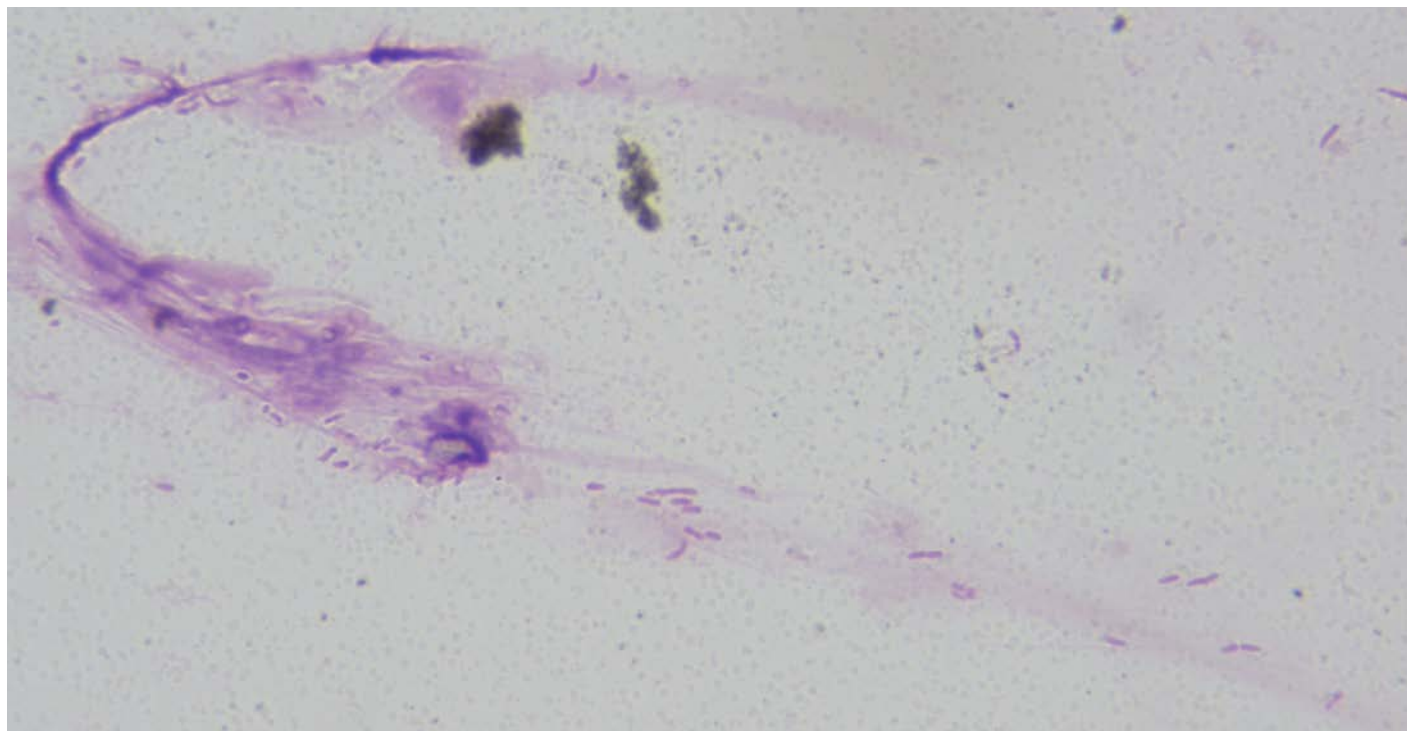
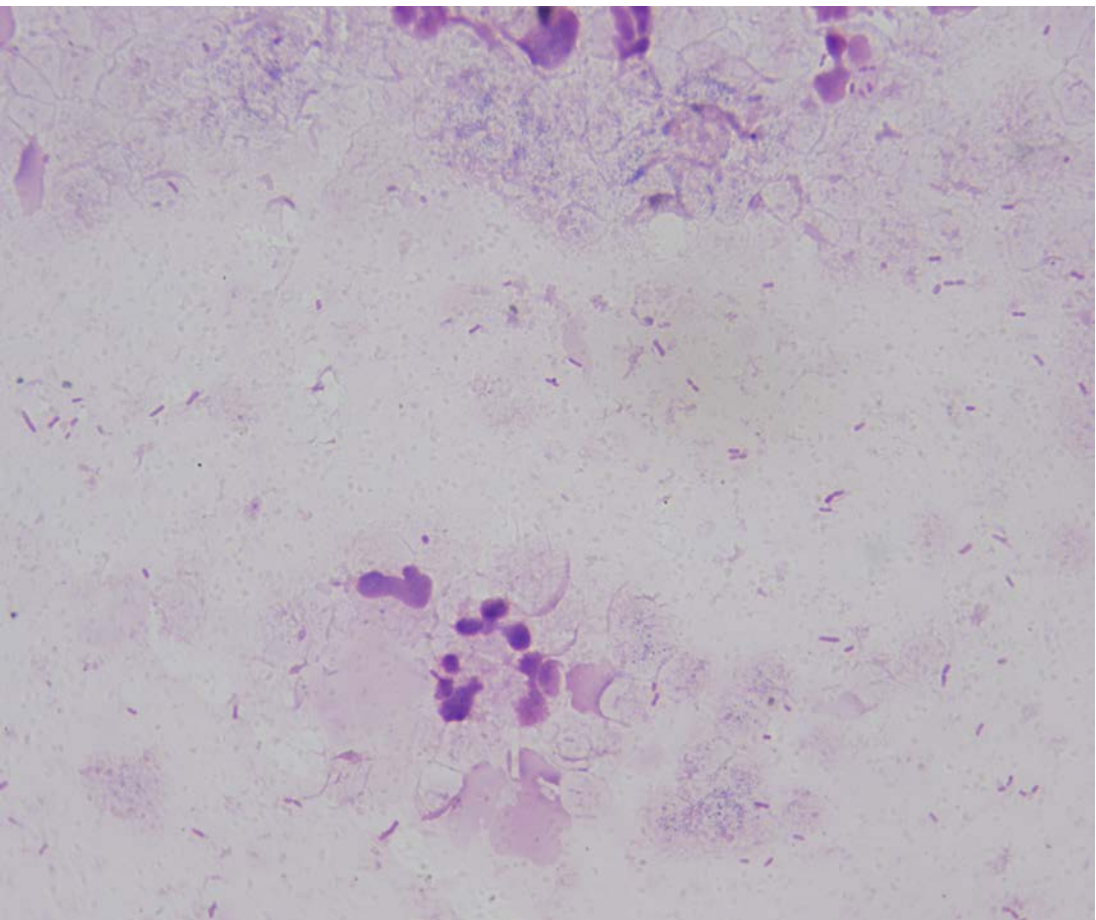


# UA – Sediment Exam

- Hematuria
  - Vs hemoglobinuria/myoglobinuria
- Pyuria
- Bacteriuria
  - Cocci vs rods
  - Gram stain
- Important, but...
  - Doesn't always match culture just one more piece of evidence

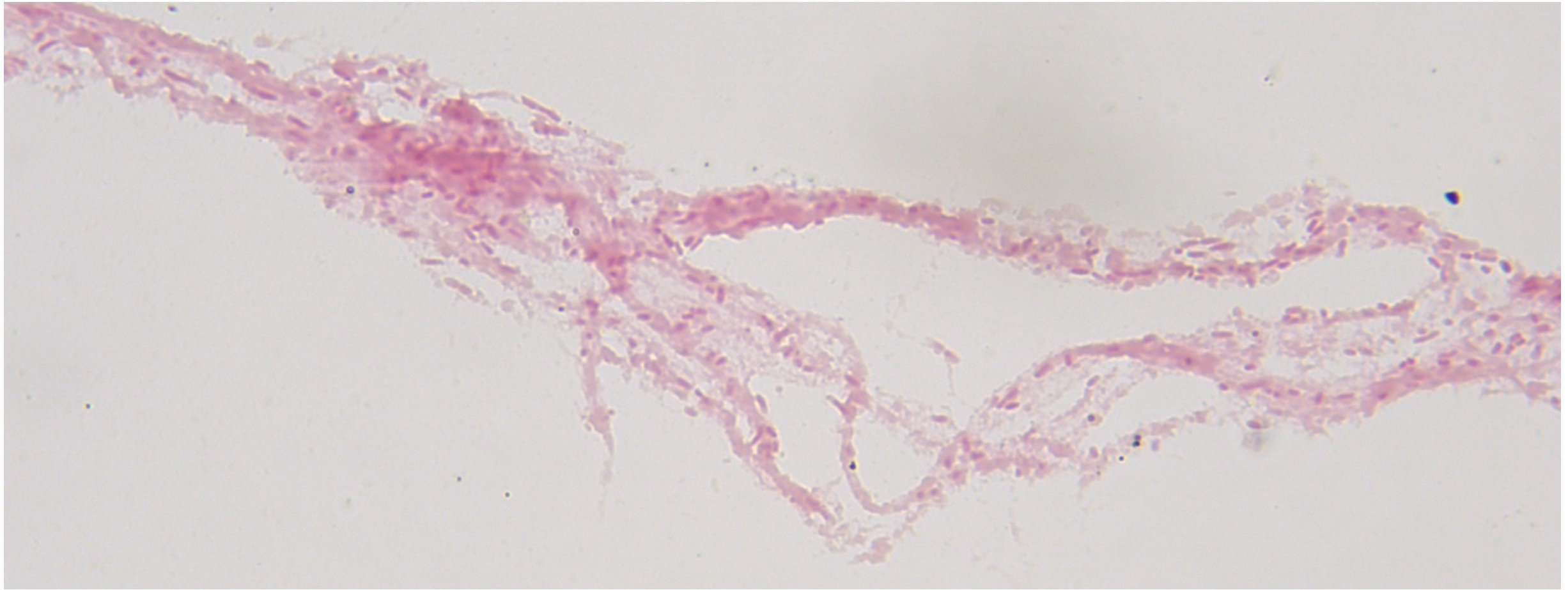


Unstained vs stained – bacteria and neutrophils present



Proteus on cytology - canine urine





Klebsiella seen on cytology from urine

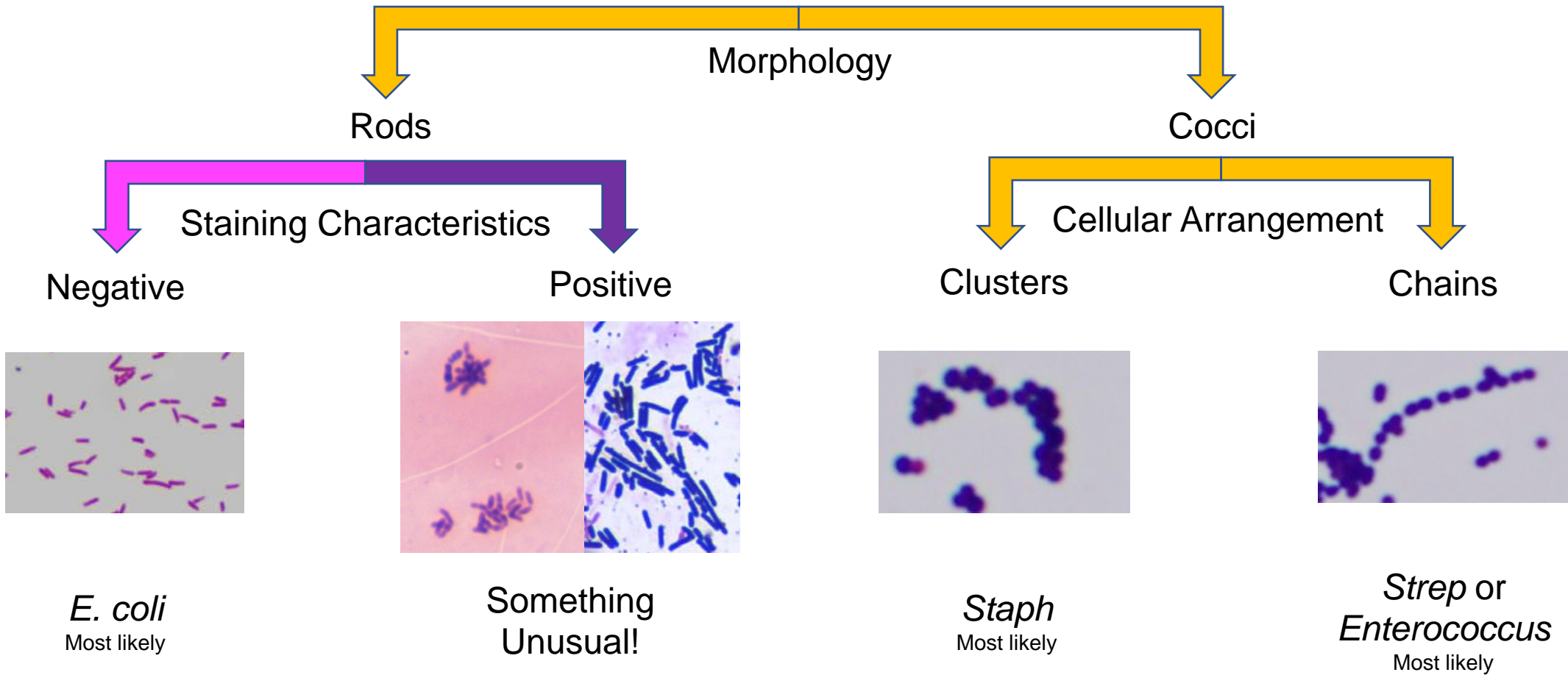
# Gram Stain

- How does this help?
- How to do

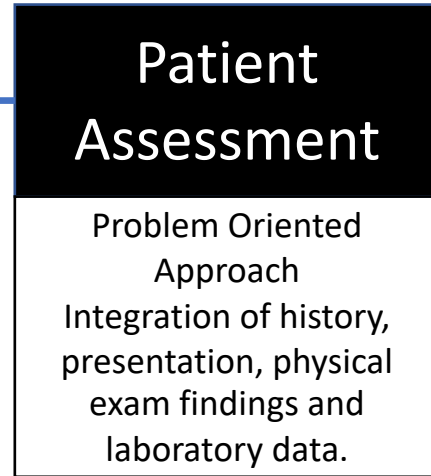
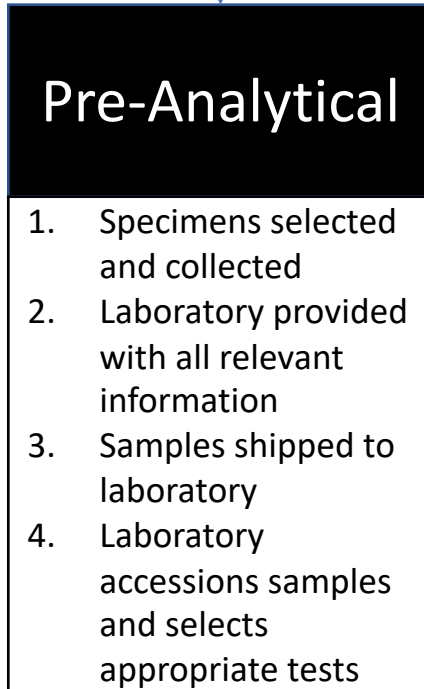


How to do a Gram-Stain

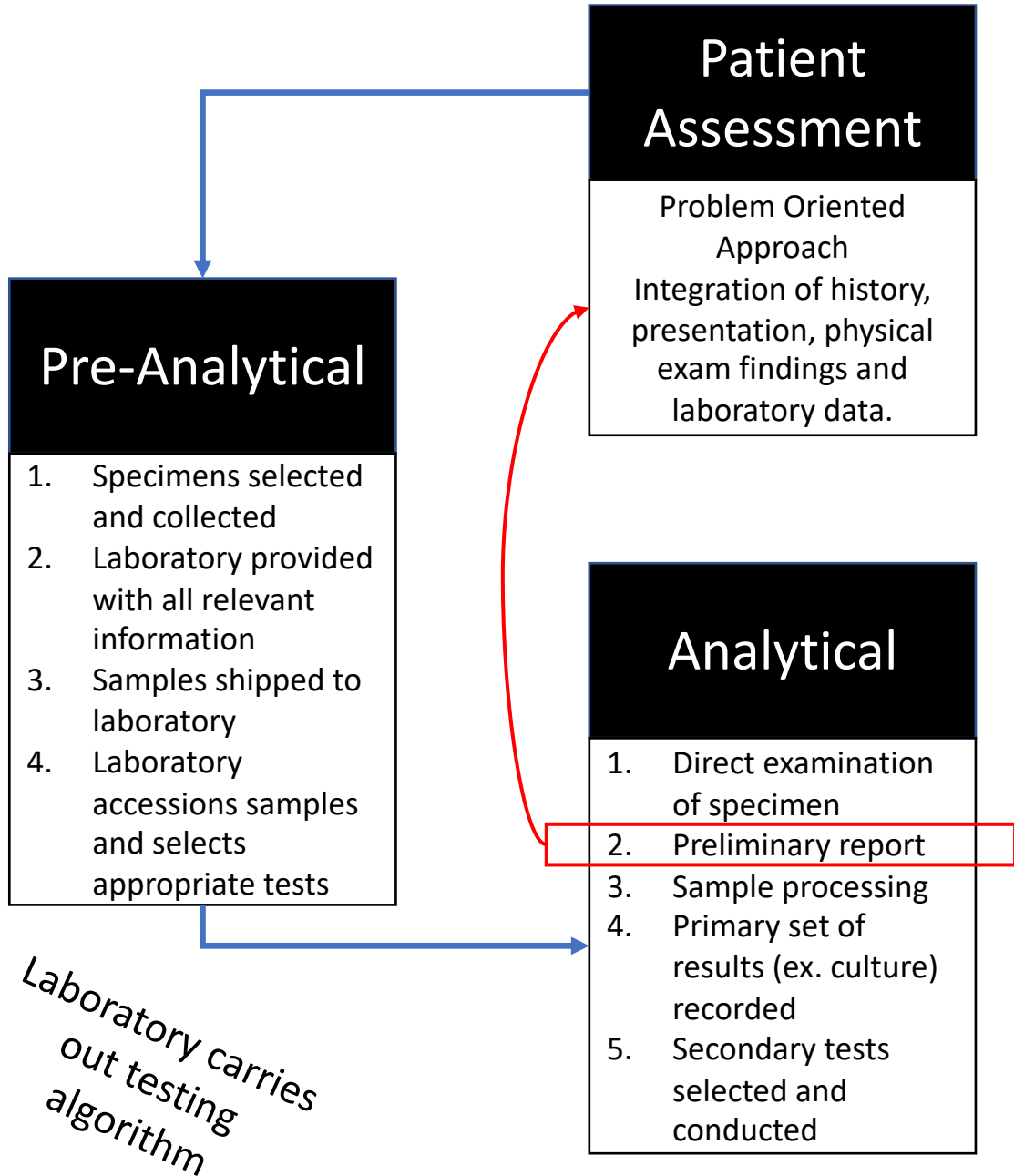
# Gram Stain

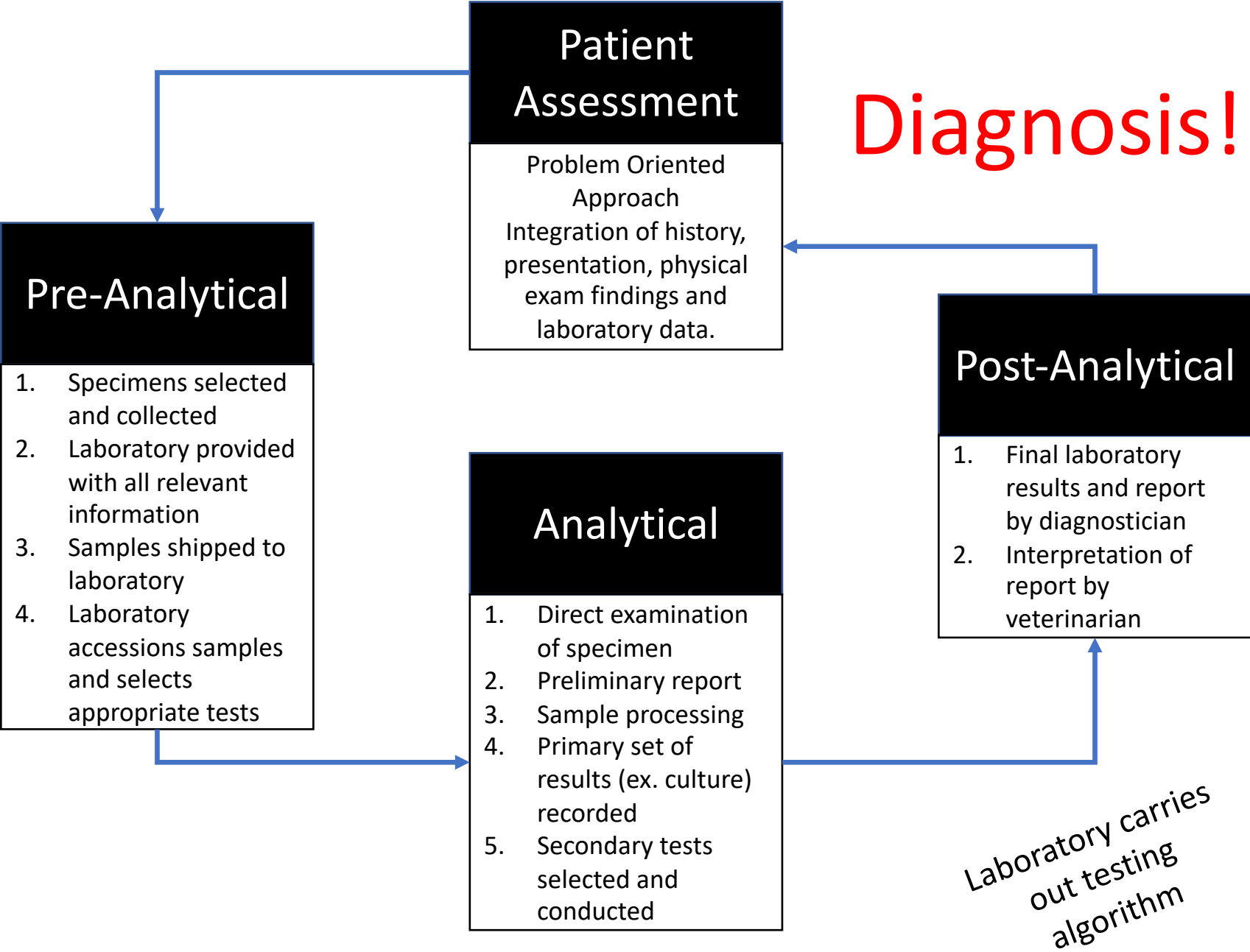


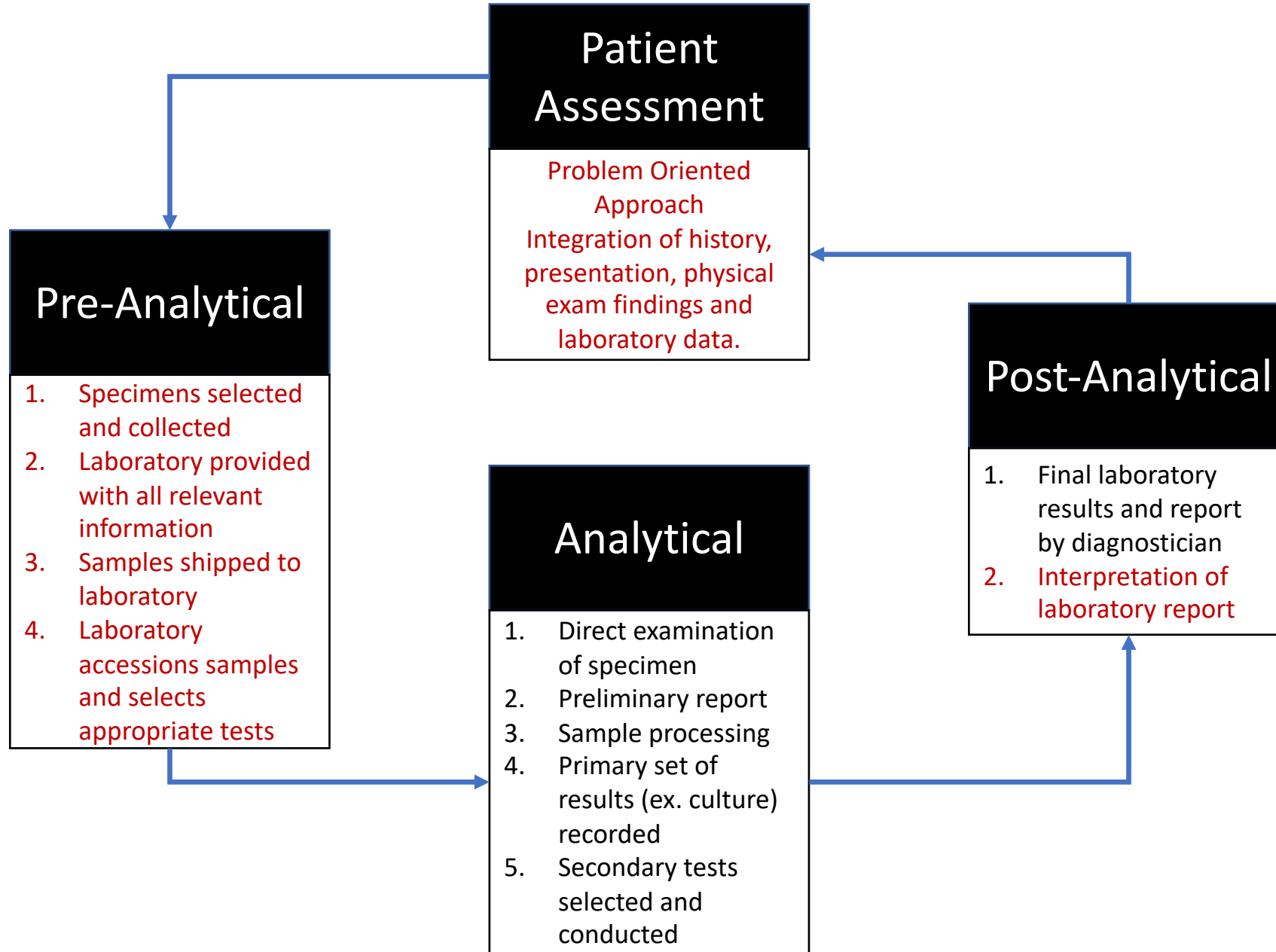
Strategy to  
confirm, rule out  
differentials



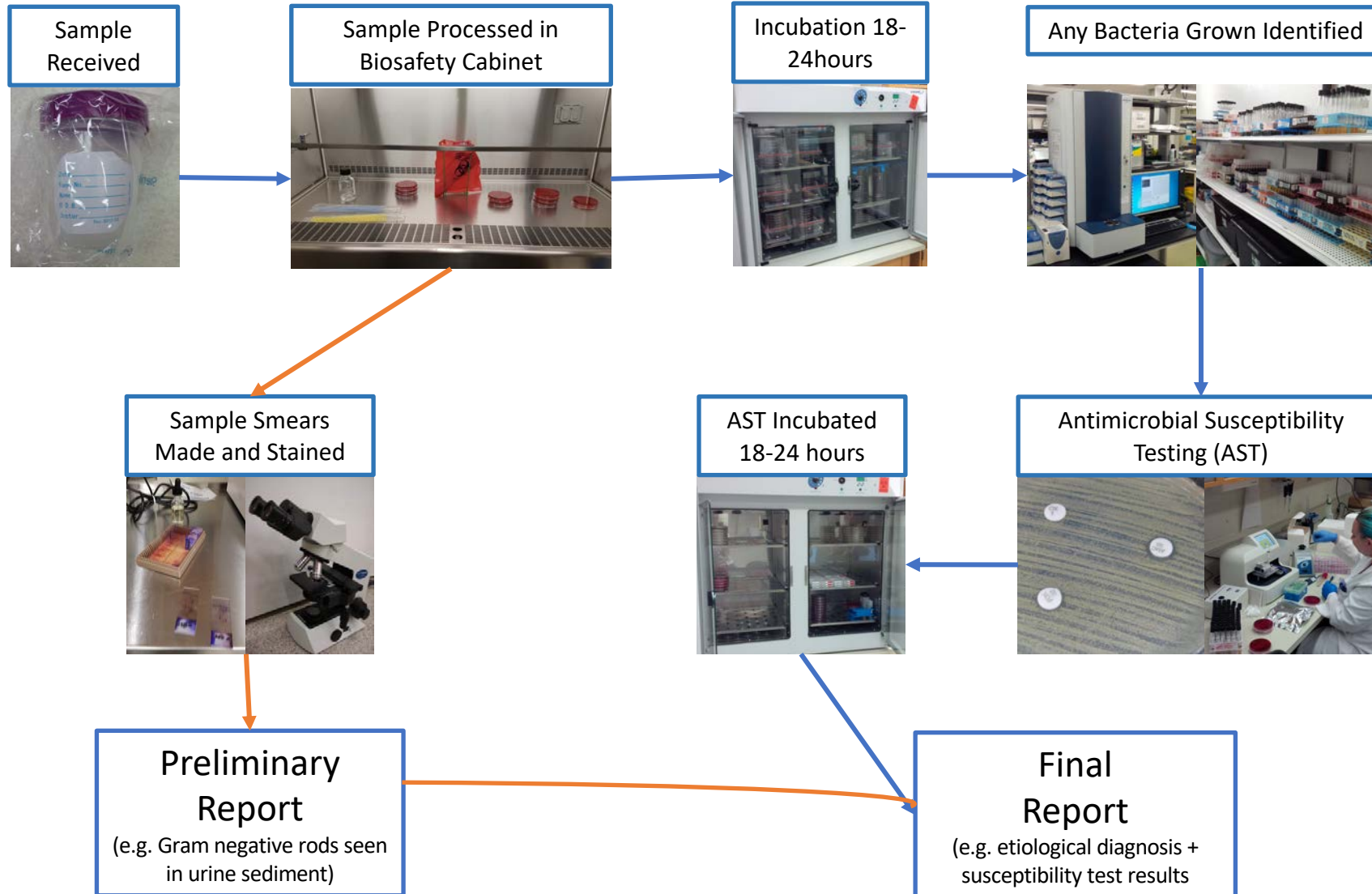
Is an infectious process ongoing?  
List of differentials?







# Sample Processing... the labs job





# Treatment of Sporadic Cystitis

- Clinical signs are the result of inflammation
  - In humans, good evidence to support treatment with NSAIDs
    - Good choice in dogs
    - Consider carefully in cats
- NSAID for 3-4 days while culture is pending
  - Allows for responsible antimicrobial use
- Must consider underlying illness
  - Eating?
  - Renal disease?
  - Concurrent medications?

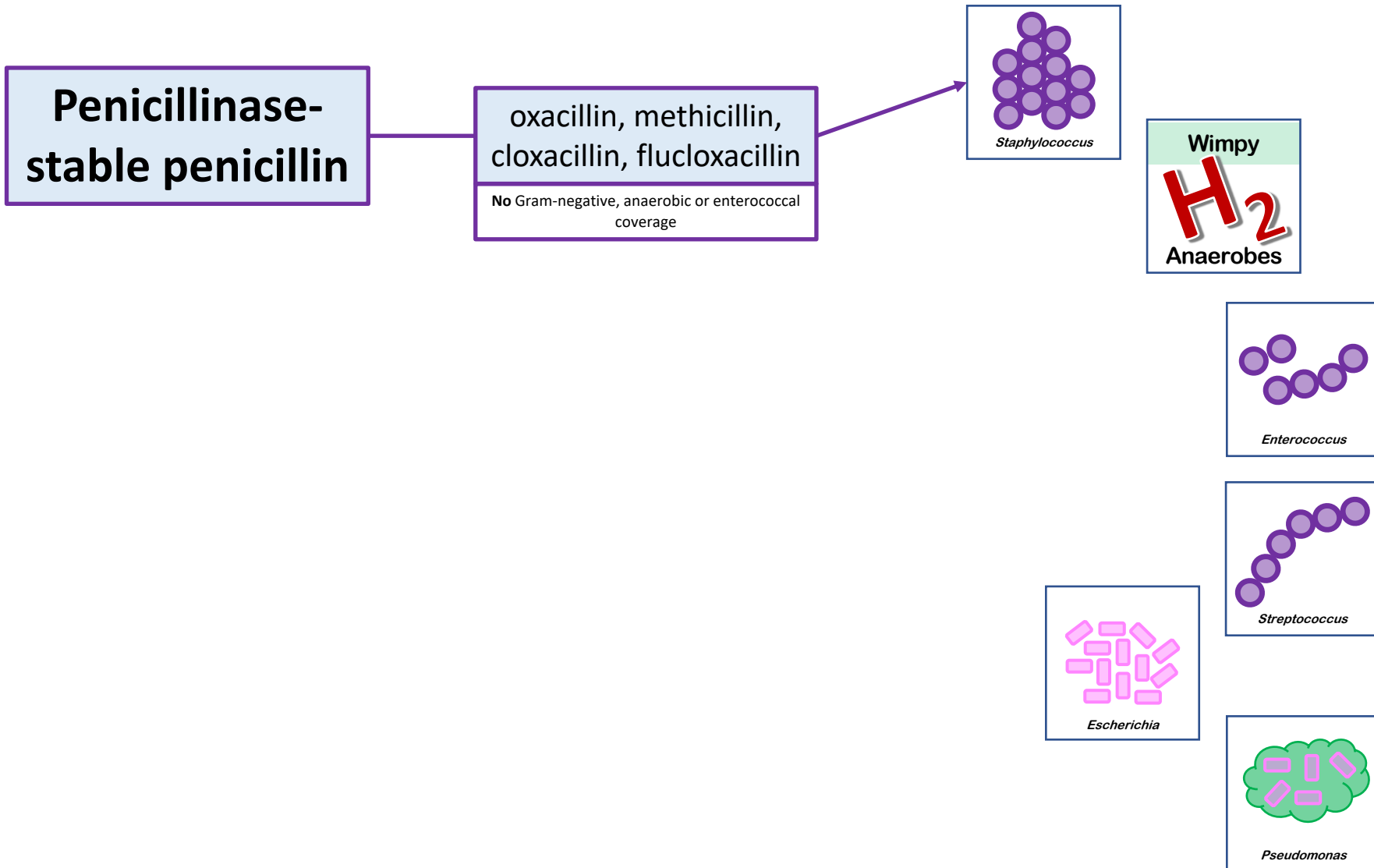


# Empirical and First Line Antimicrobial Therapy

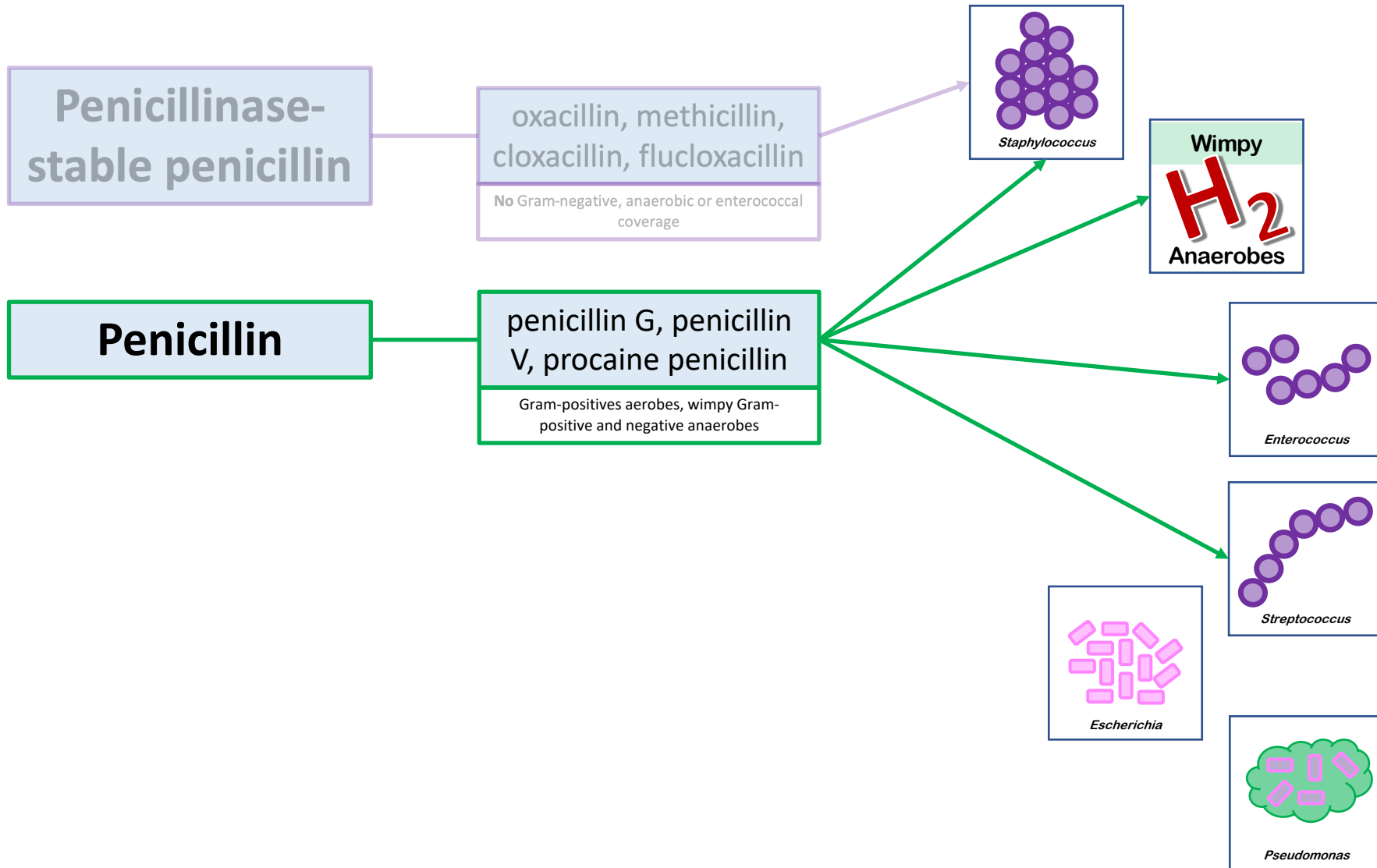
- Often appropriate in sporadic cystitis
- Which drug to choose depends on regional susceptibility patterns
- First Line therapy
  - Amoxicillin is the most appropriate option in dogs and cats
    - Evidence of the need for clavulanic acid is lacking
      - Even in  $\beta$ -lactamase producing bacteria
      - Different rates of excretion?
    - High urinary concentrations
  - Trimethoprim-sulfonamides
    - Possible adverse effects
    - Uncommon with short duration therapy



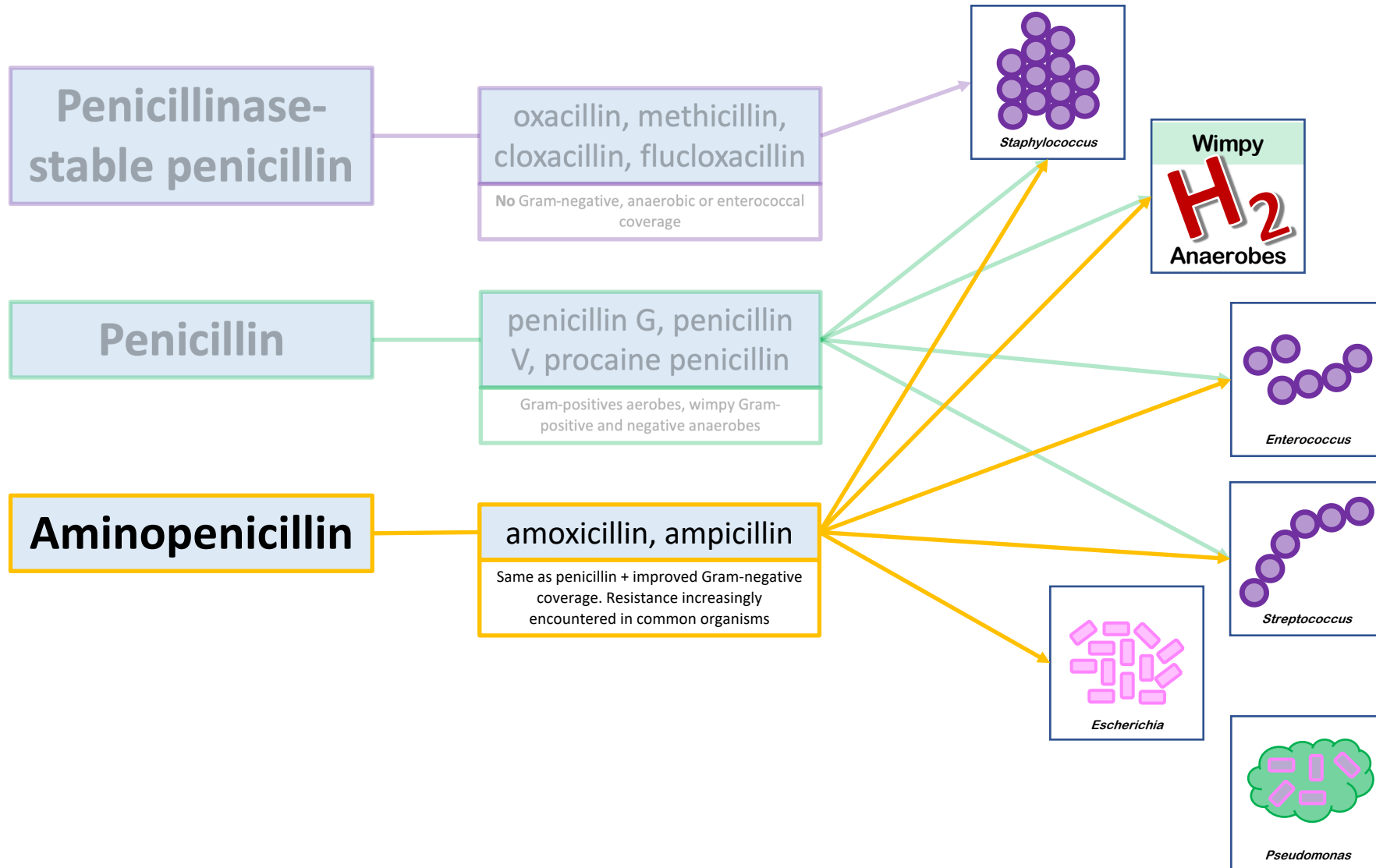
# $\beta$ -lactams - Penicillins



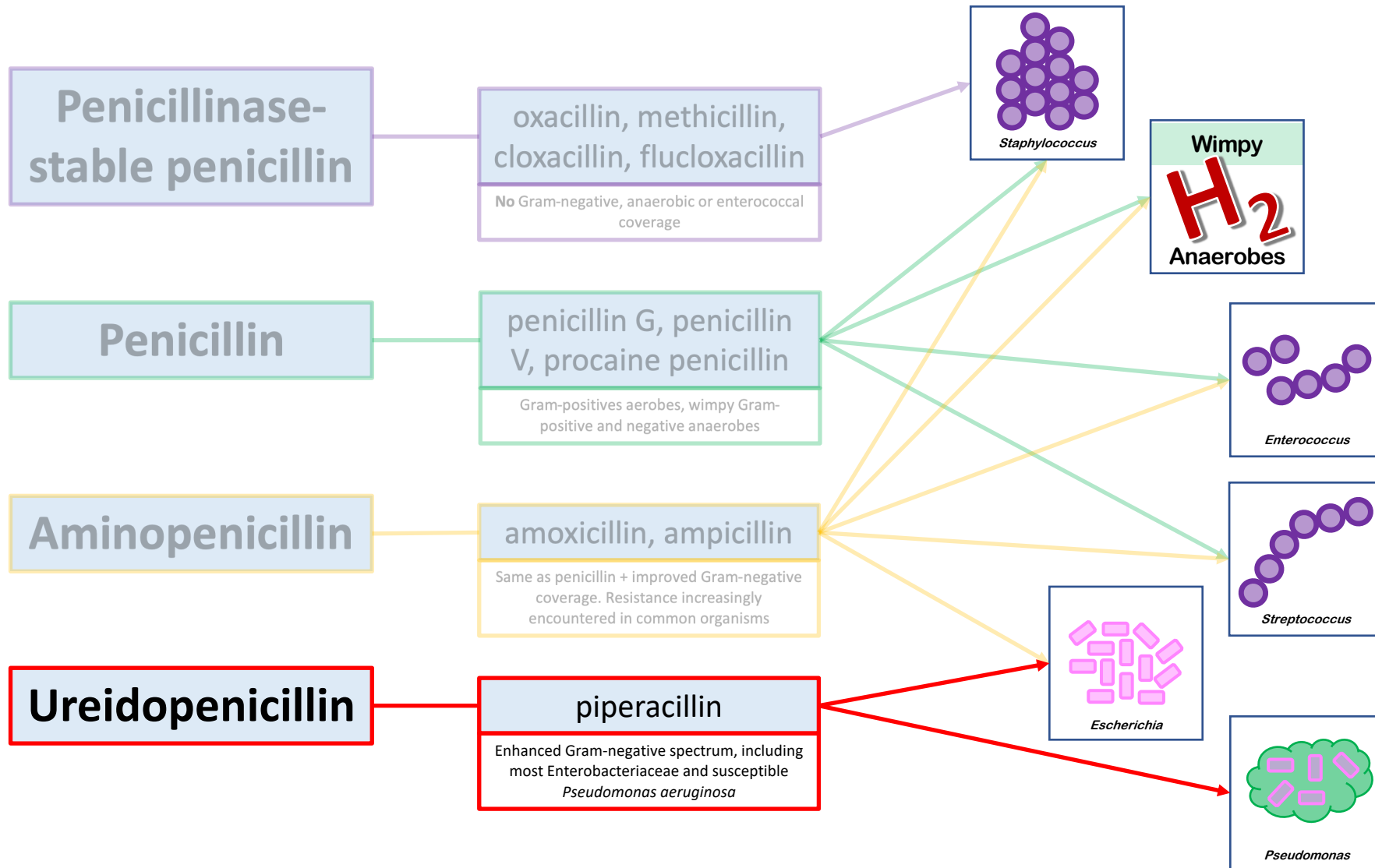
# $\beta$ -lactams - Penicillins



# $\beta$ -lactams - Penicillins



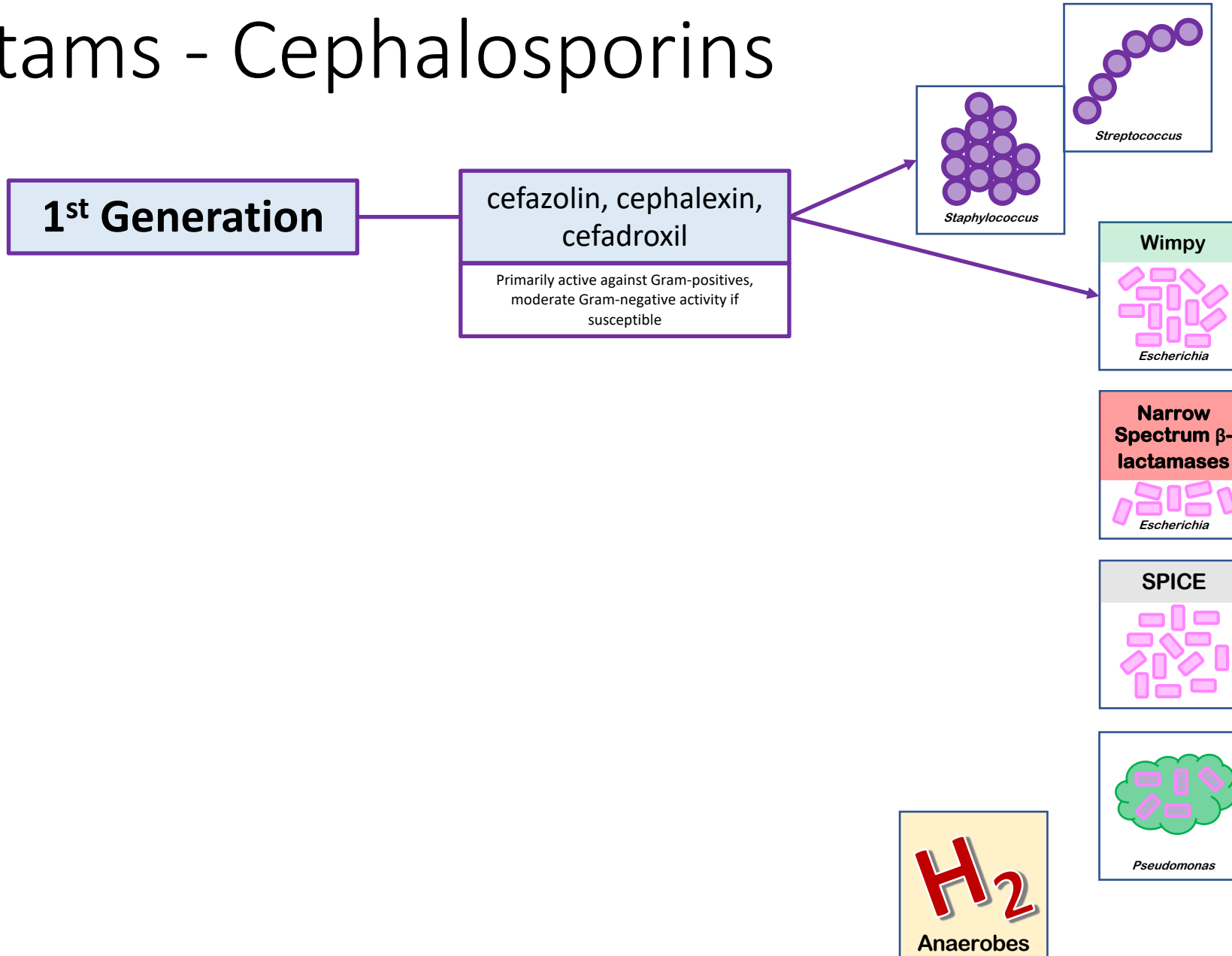
# $\beta$ -lactams - Penicillins



# $\beta$ -lactams - inhibitors

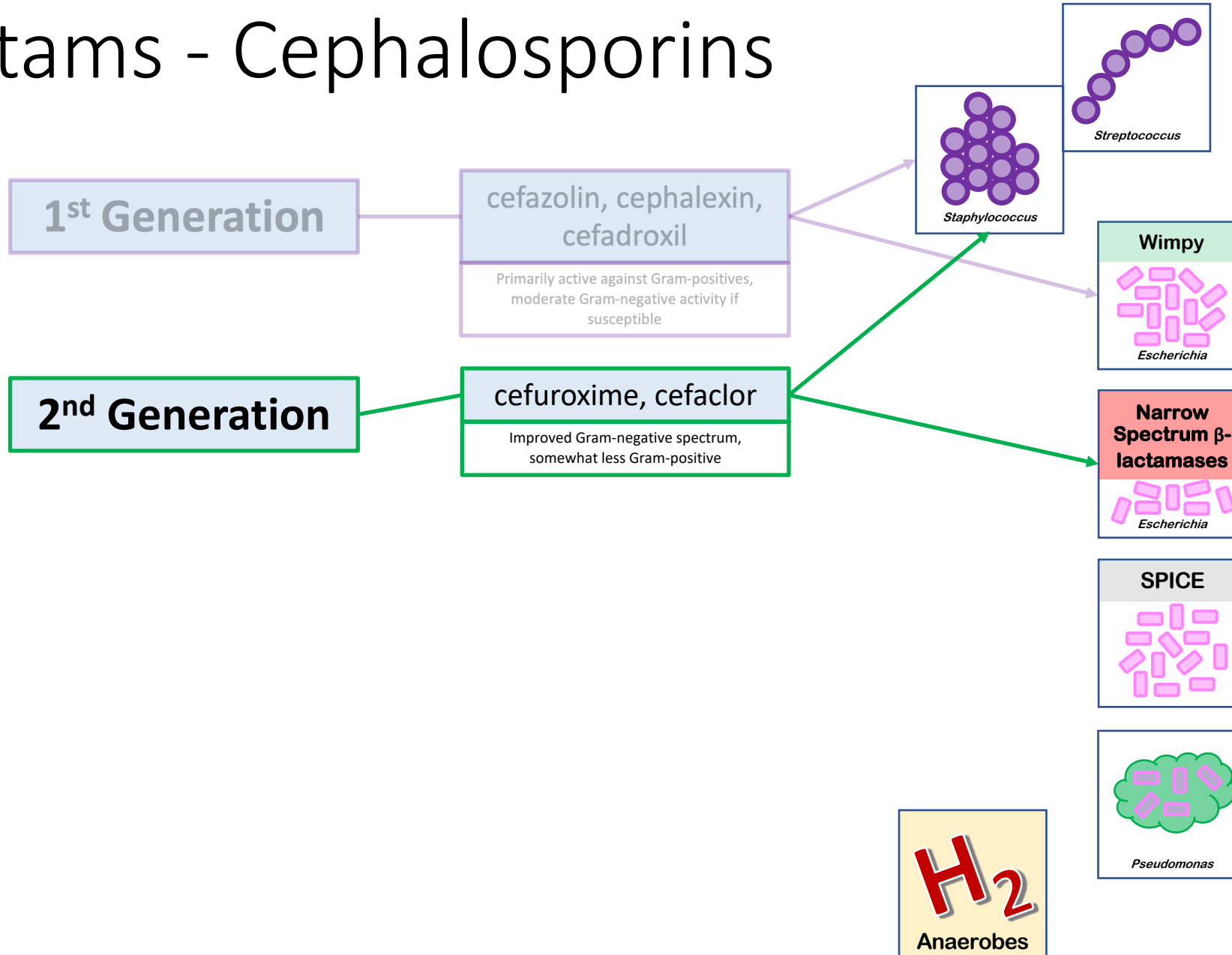
- Currently available  $\beta$ -lactamase inhibitors
  - Clavulanic acid (amoxicillin + clavulanic acid)
  - Sulbactam (ampicillin + sulbactam)
  - Tazobactam (piperacillin + tazobactam)
- Act by irreversibly binding to the serine catalytic site of certain bacterial  $\beta$ -lactamases
  - Only active against Class A enzymes
  - Key point is that NOT ALL  $\beta$ -LACTAMASES can be inhibited

# $\beta$ -lactams - Cephalosporins

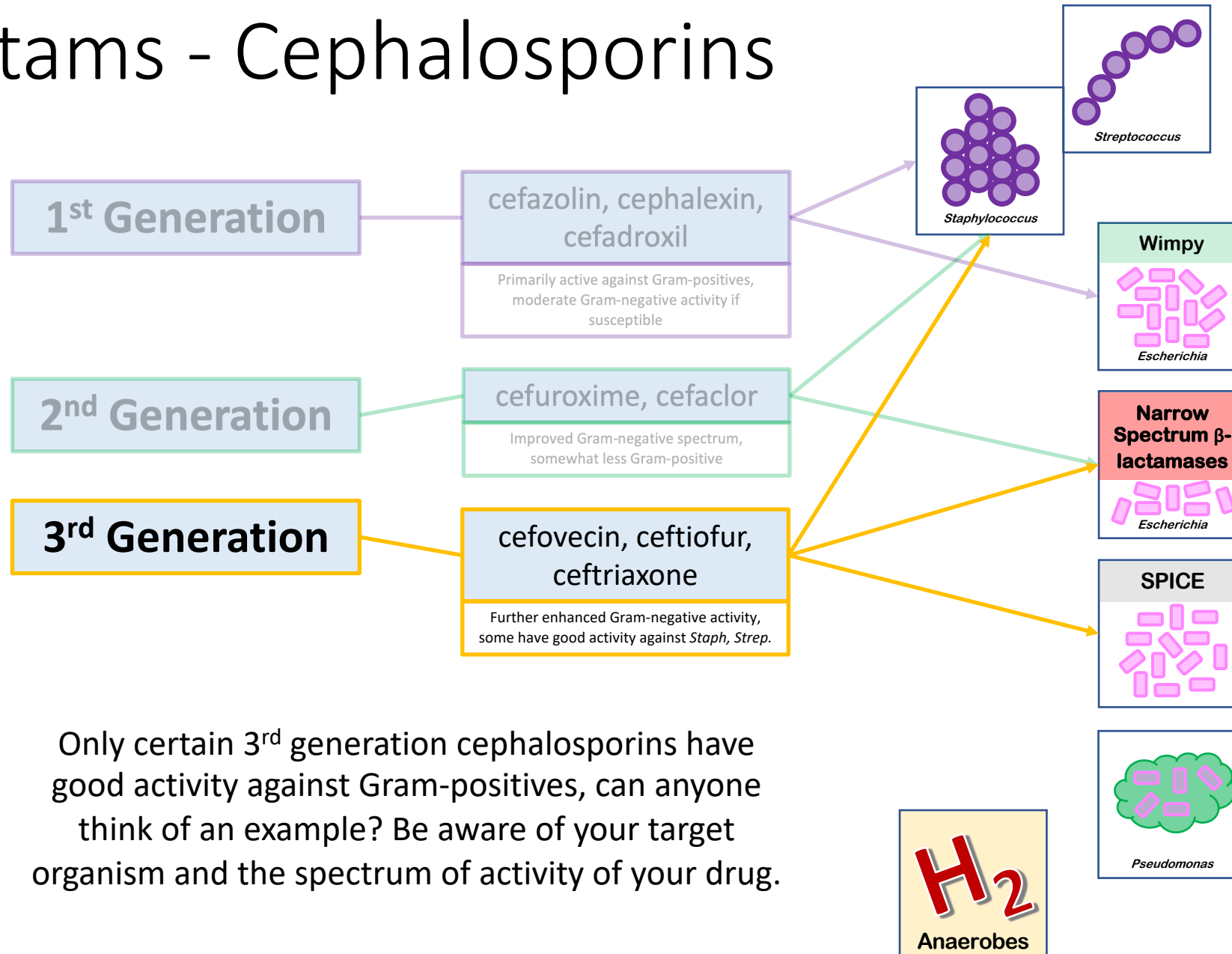




# $\beta$ -lactams - Cephalosporins

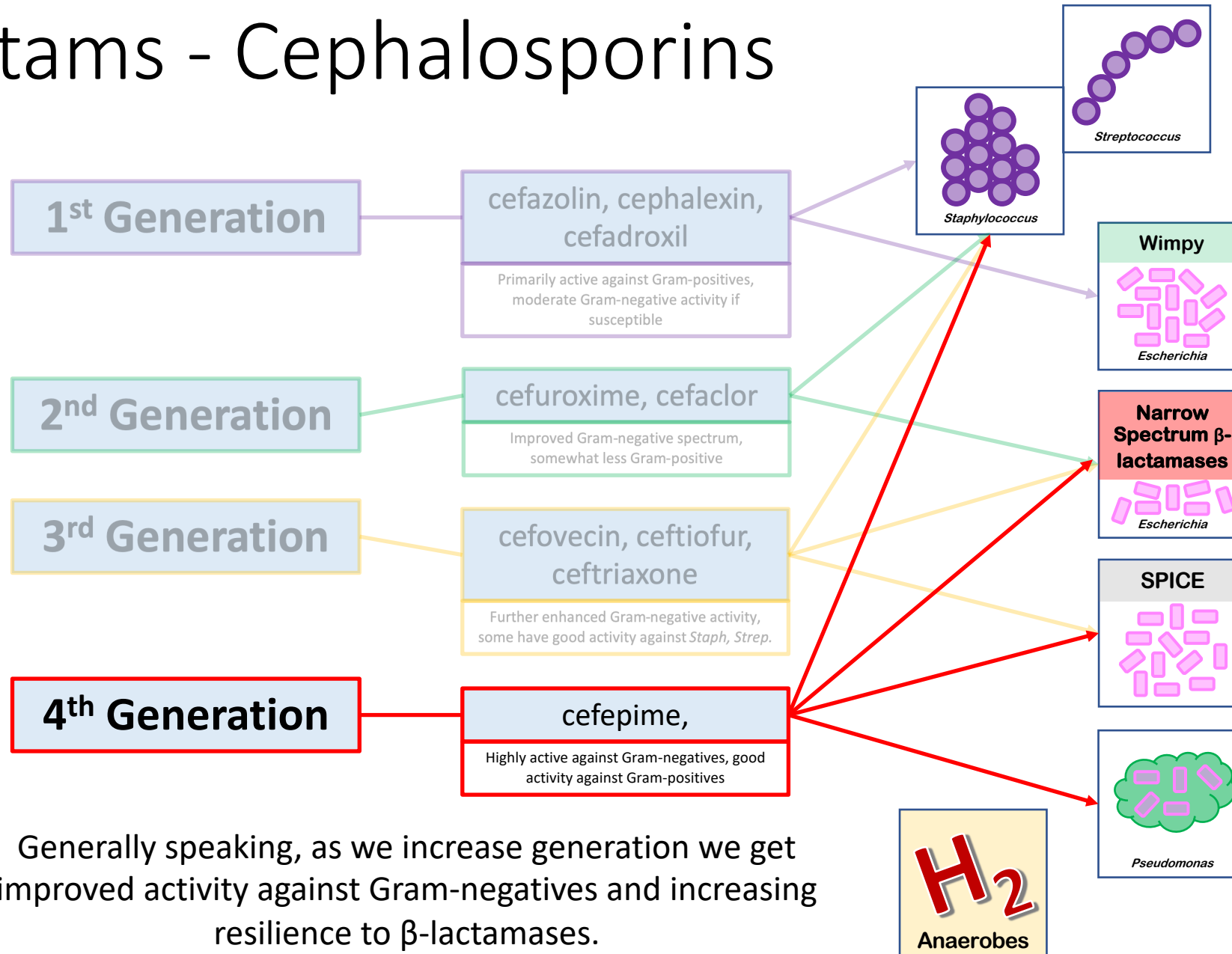


# β-lactams - Cephalosporins



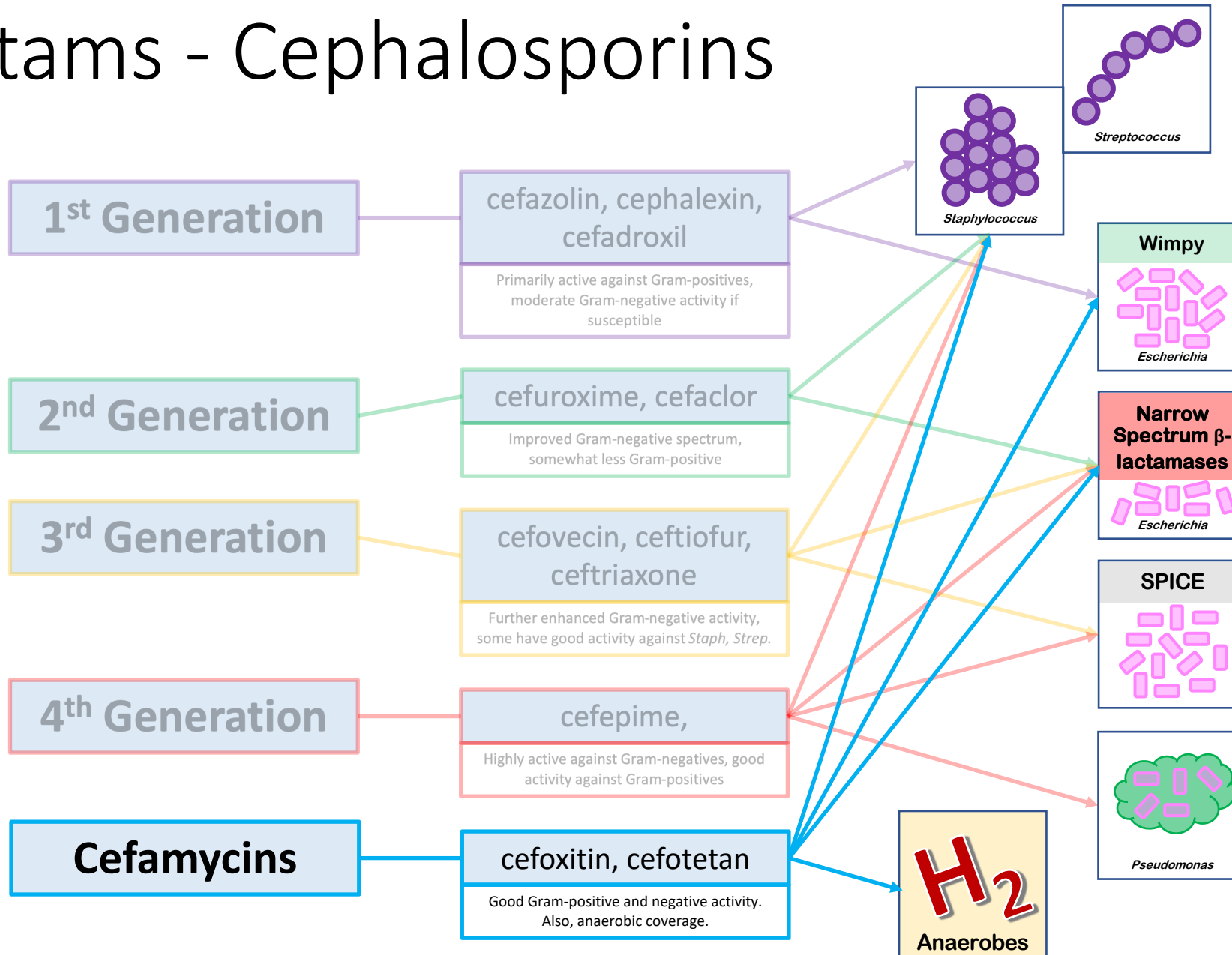
Only certain 3<sup>rd</sup> generation cephalosporins have good activity against Gram-positives, can anyone think of an example? Be aware of your target organism and the spectrum of activity of your drug.

# $\beta$ -lactams - Cephalosporins



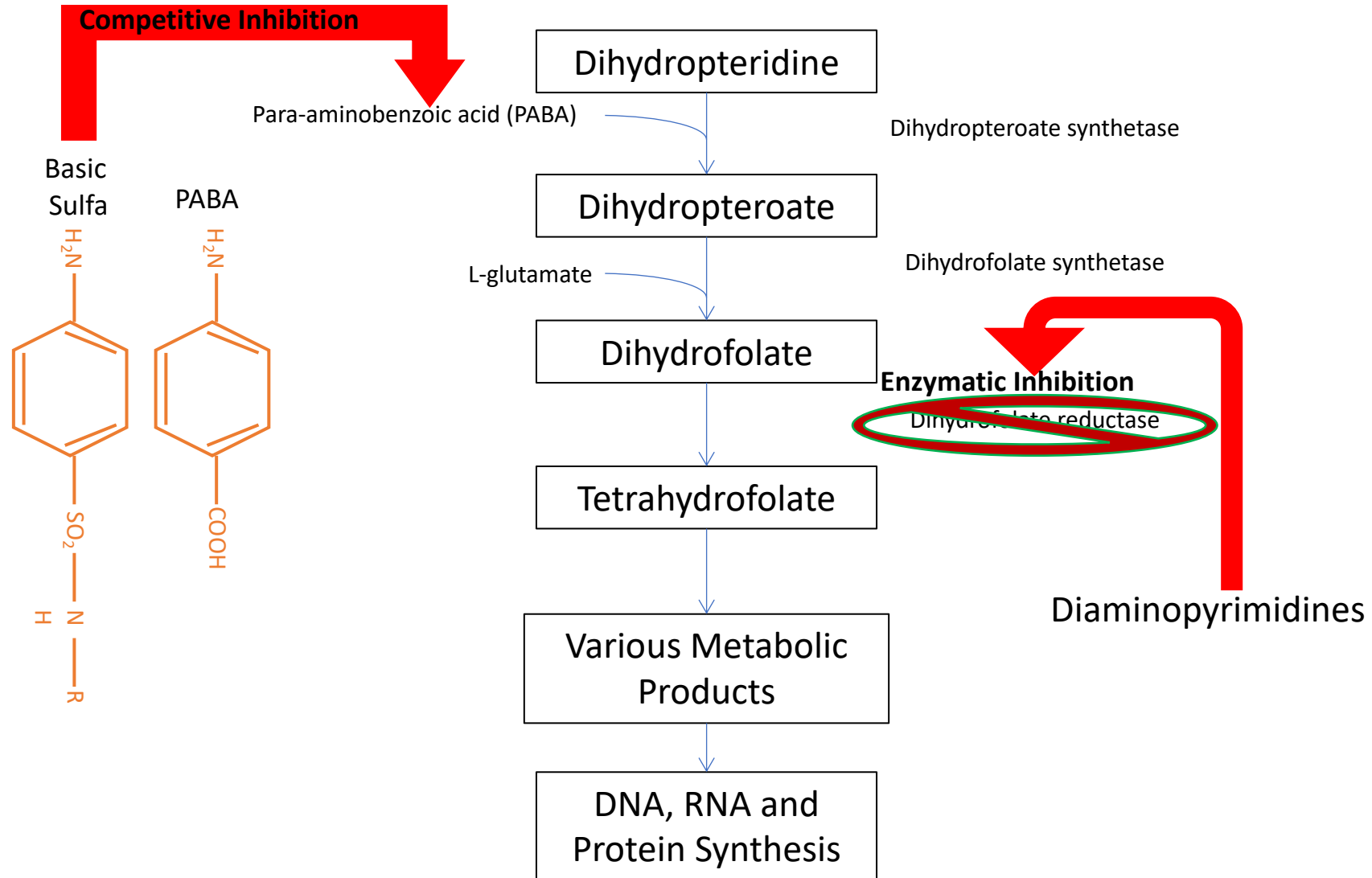
Generally speaking, as we increase generation we get improved activity against Gram-negatives and increasing resilience to  $\beta$ -lactamases.

# β-lactams - Cephalosporins



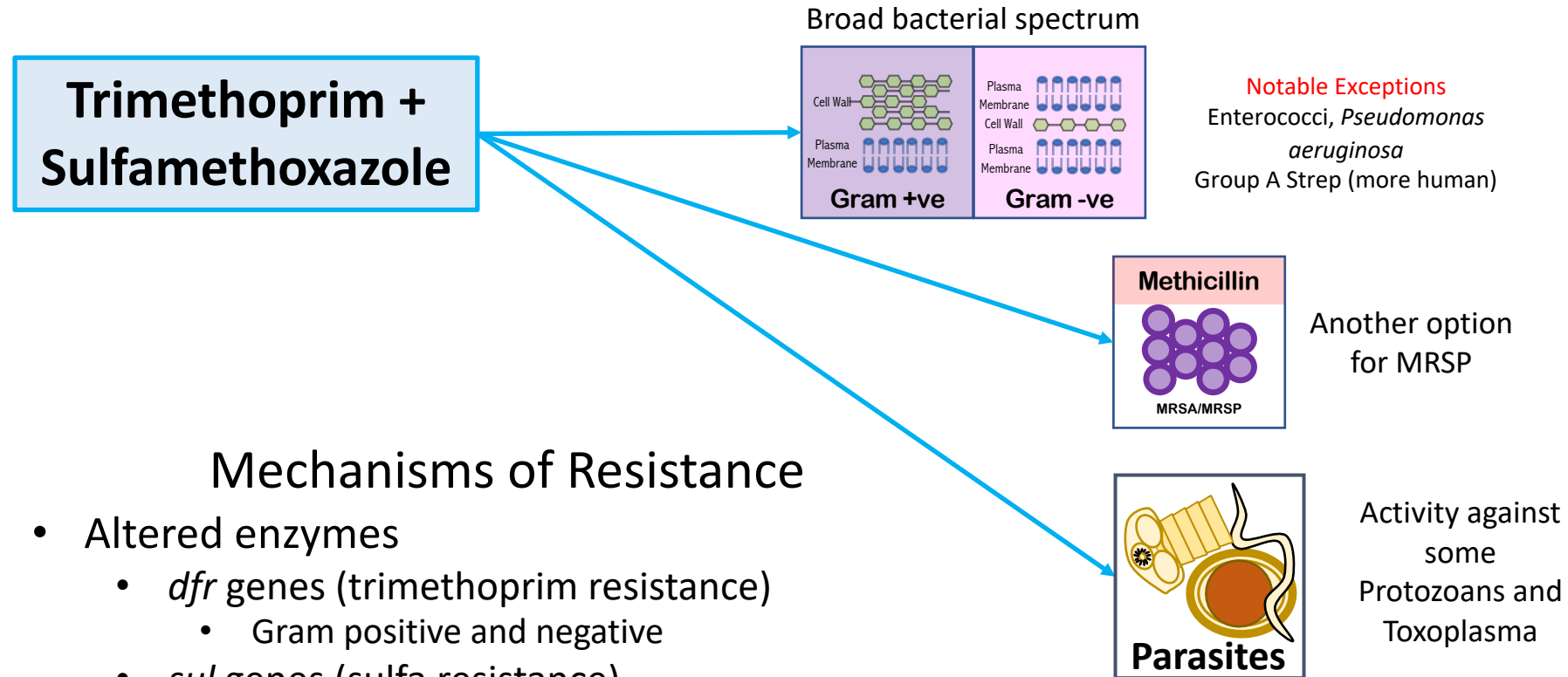
# Folate Synthesis Inhibitors

Bacteristatic



# Folate Synthesis Inhibitors

Oldies but goodies!

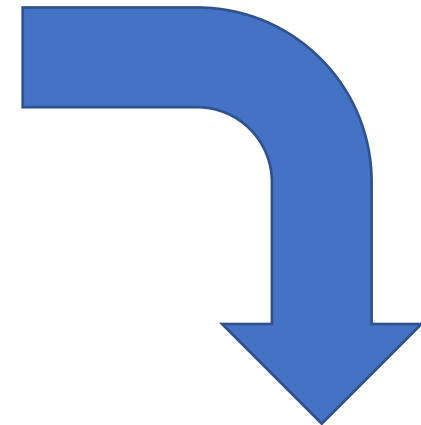


## Mechanisms of Resistance

- Altered enzymes
  - *dfr* genes (trimethoprim resistance)
    - Gram positive and negative
  - *sul* genes (sulfa resistance)
    - Gram negative bacteria
    - Often found in multi-resistant bacteria, linkage to other resistance genes
- Hyper-production of PABA

# Duration of Therapy

- 3-5 days is appropriate for most sporadic cystitis
  - There is sparse literature support in veterinary medicine
  - Previous guidelines recommended 7-10 days
    - Likely still too long



*J.S. Weese et al./The Veterinary Journal 247 (2019) 8–25*

11

**Table 2**

Clinical studies evaluating treatment duration for sporadic bacterial cystitis in dogs.

Study population	Treatments	Results	Reference
Female dogs (n = 38) with lower urinary tract signs	Trimethoprim sulfamethoxazole (15 mg/kg PO every 12 h for 3 days) vs. cephalexin (20 mg/kg PO every 12 h for 10 days)	No difference in clinical cure rates or microbiological cure 3, 4 or >30 days after treatment. Long-term microbiological cure rates were low in both groups	<a href="#">Clare et al. (2014)</a>
Adult otherwise healthy dogs with clinical evidence of cystitis and cystocentesis culture yielding >1000 CFU/mL	Enrofloxacin (18–20 mg/kg PO every 24 h for 3 days) vs. amoxicillin/clavulanic acid (13.75–25 mg/kg PO every 12 h for 14 days)	Enrofloxacin was not inferior (microbiological or clinical cure rates) compared to amoxicillin/clavulanic acid	<a href="#">Westropp et al. (2012)</a>

# Short-course Antibiotic Therapy—Replacing Constantine Units With “Shorter Is Better”

Noah Wald-Dickler<sup>1,2</sup> and Brad Spellberg<sup>1,2</sup>

<sup>1</sup>Los Angeles County and University of Southern California (LAC+USC) Medical Center, and <sup>2</sup>Division of Infectious Diseases, Keck School of Medicine at University of Southern California, Los Angeles

**Table 1. Diseases for Which Short-course Antibiotic Therapy Has Been Found to Be Equally Effective to Longer Traditional Courses of Therapy (With References)**

Diagnosis	Short (d)	Long (d)	Result
Community-acquired pneumonia [6–14]	3 or 5	7, 8, or 10	Equal
Hospital-acquired/ventilator-associated pneumonia [15, 16]	7–8	14–15	Equal
Complicated urinary tract infections/pyelonephritis [17–22]	5 or 7	10 or 14	Equal
Complicated/postoperative intraabdominal infections [23, 24]	4 or 8	10 or 15	Equal
Gram-negative bacteremia [25]	7	14	Equal
Acute exacerbation of chronic bronchitis/chronic obstructive pulmonary disease (meta-analysis of 21 trials [26])	≤5	≥7	Equal
Acute bacterial skin and skin structure infections (cellulitis/major abscess) [27–29]	5–6	10	Equal
Chronic osteomyelitis [30]	42	84	Equal
Empiric neutropenic fever [31]	Afebrile and stable × 72 h	Afebrile and stable × 72 h and with absolute neutrophil count > 500 cells/μL	Equal



# Late-career Physicians Prescribe Longer Courses of Antibiotics

Cesar I. Fernandez-Lazaro,<sup>1,2</sup> Kevin A. Brown,<sup>1,3</sup> Bradley J. Langford,<sup>1</sup> Nick Daneman,<sup>1,4,5</sup> Gary Garber,<sup>1,6</sup> and Kevin L. Schwartz<sup>1,3,7</sup>

<sup>1</sup>Infection Prevention and Control, Public Health Ontario, Toronto, Canada; <sup>2</sup>Department of Biomedical and Diagnostic Sciences, University of Salamanca, Spain; and <sup>3</sup>Dalla Lana School of Public Health, University of Toronto, and <sup>4</sup>Division of Infectious Diseases, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Canada; <sup>5</sup>Institute of Health Policy, Management and Evaluation, University of Toronto, Canada <sup>6</sup>Department of Medicine, Ottawa Hospital Research Institute, Canada; and <sup>7</sup>Department of Medicine, St. Joseph's Health Centre, Toronto, Canada

## CONCLUSIONS

The use of prolonged antibiotic treatments in outpatient settings is common, particularly among those family physicians in late-career stages. Moreover, there is meaningful interphysician variability in the selection of prolonged antibiotic durations, highlighting the need for multifaceted antimicrobial stewardship interventions. Future research should evaluate the optimal community-based interventions to improve prescribing behaviors.

## Duration of Antibiotic Therapy: Shorter Is Better

Vaughn and colleagues' findings add to the considerable body of evidence supporting the antibiotic mantra "shorter is better" (2, 3, 9). The cumulative evidence indicates that each day of antibiotic therapy beyond the first confers a decreasing additional benefit to clinical cure while increasing the burden of harm in the form of adverse effects, superinfections, and selection of antibiotic resistance. The question is, where do those 2 competing trends cross, such that continuing tilts the balance to harm over benefit? For community-acquired pneumonia, the data indicate net harm somewhere around 3 to 5 days of therapy for most patients.

When indicated, the benefits of shorter therapy include:

1. Decreased rate of adverse effects
2. Decreased super-infections
3. Decreased antimicrobial resistance

In a veterinary context, additional benefits conceivably include:

- Increased client compliance
- Decreased cost to client

# What if it doesn't work!?

- Lack of response within 48 hours should trigger additional investigation
  - Is there truly cystitis?
    - Pyuria, hematuria vs pigmenturia
  - Culture if you have not
  - Look for underlying contributing factors if you have not
- DO NOT just empirically select a new antibiotic
  - Does not mean you must immediately escalate to a 2nd or 3<sup>rd</sup> line drug
  - Review your culture results!

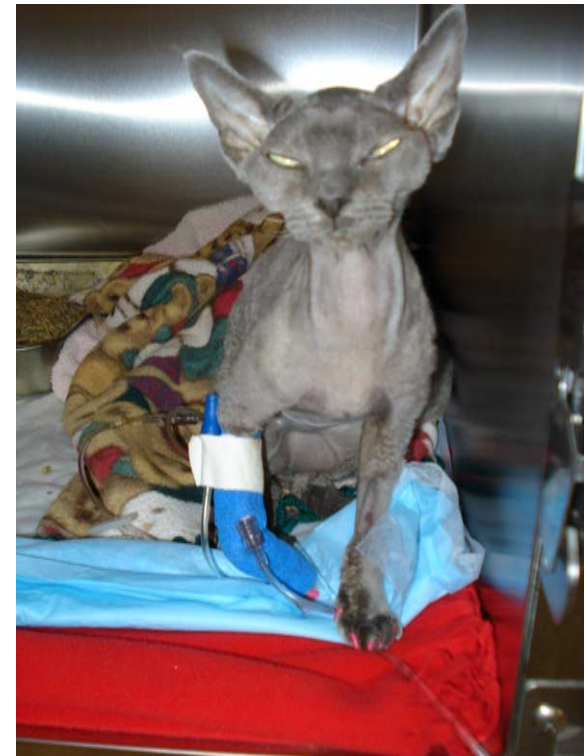
# Second Line Therapy

- Reserved for culture directed therapy
  - Nitrofurantoin
  - 3<sup>rd</sup> generation cephalosporins
  - Fluoroquinolones
- These drugs are effective, but rarely needed in sporadic cystitis
- Fluoroquinolones
  - Use discouraged in humans in sporadic/uncomplicated infections
    - Joint, tendon and nerve damage
  - Young dogs – joint/tendon/cartilage defects
  - Cats – retinal damage



# Special Cases

- Intact Male Dogs
  - If no evidence of concurrent prostatitis, can treat as a sporadic UTI
  - Difficult to determine if prostate is involved
    - AUS
    - Prostatic washing
- Difficult to treat patients
  - Owners can't pill or administer liquid
    - Can't or won't? (does it matter??)
  - May need to choose once daily treatment
  - Injectable options
    - Cefovicin – longer duration of action....





Complications  
of Therapy

# Bladder Infusions

---

- Don't do this. Period.
- Lack of evidence that this works
  - Particularly in sporadic cystitis
- Complications:
  - Trauma from catheter placement
  - Inflammation from the substances
  - Iatrogenic infection
  - Reflux into ureters/upper urinary tract

## **Intravesical instillation of amikacin for treatment of a lower urinary tract infection caused by *Pseudomonas aeruginosa* in a dog**

Ahmira R. Torres, DVM, and Kirsten Cooke, DVM

---

**Case Description**—A 9-year-old neutered male Golden Retriever was evaluated because of recurrent lower urinary tract infection subsequent to placement of a permanent cystostomy tube.

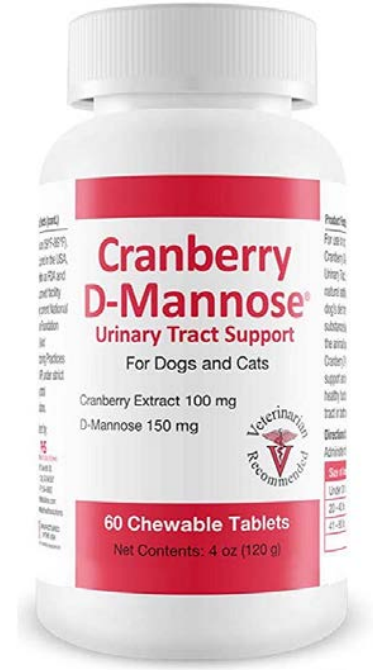
**Clinical Findings**—The dog was clinically normal except for the presence of malodorous urine. Bacteriologic culture of a urine sample obtained by cystocentesis yielded growth of *Pseudomonas aeruginosa*, which was susceptible to amikacin, gentamicin, imipenem-cilastatin, and ticarcillin-clavulanic acid.

**Treatment and Outcome**—The dog was administered amikacin sulfate (15 mg/kg [6.8 mg/lb], SC, q 24 h) for 14 days before treatment was discontinued because of the presence of casts in the urine. The cystostomy tube was replaced, and intravesical instillation of amikacin (15 mg/kg diluted in 30 mL of saline [0.9% NaCl] solution, q 12 h) was initiated. On day 25 of instillation treatment, bacterial culture of a urine sample yielded no growth, urinalysis revealed no casts, and SUN and creatinine concentrations were within reference intervals. On day 27 of instillation treatment, gross hematuria was observed, which resolved following discontinuation of amikacin instillation.

**Clinical Relevance**—In this dog, treatment of a lower urinary tract infection caused by a multidrug-resistant strain of *P aeruginosa* was successfully achieved with intravesical instillation of amikacin. Results of serial serum biochemical analyses remained within reference limits, and urine casts were not identified on urinalyses during the treatment period, which suggested that systemic absorption of amikacin was minimal. Intravesical instillation of antimicrobials may be a viable treatment option for dogs with lower urinary tract infections caused by multidrug-resistant bacteria. (*J Am Vet Med Assoc* 2014;245:809–811)

---

# Adjunctive Therapies



- Cranberry products
  - Extracts, Juices
- D-Mannose
  - Rationale is that it prevents adhesion of some E.coli organisms to the urinary endothelium
    - Not an issue in sporadic disease
- There is no evidence that these have any benefit in sporadic cystitis



# Follow up and Monitoring

---

- No follow up culture is recommended in sporadic cystitis
  - As long as the clinical signs have resolved
- If the patient is doing well, you're done!



Questions?

# Recurrent Bacterial Cystitis

## Human Definition

- 3 or more episodes of cystitis in a 12-month period
- 2 or more episode of cystitis in the preceding 6 months

## Cause?

- Recurrence of Relapse of infection
- Persistent infection
- Reinfection
- Sorting through this allows us to be successfully manage these infections

# Recurrent UTI Clinical Signs

## Transurethral cystoscopy in dogs with recurrent urinary tract infections: Retrospective study (2011-2018)

Marie Llido<sup>1</sup> | Catherine Vachon<sup>1</sup> | Melanie Dickinson<sup>2</sup> | Guy Beauchamp<sup>1</sup> | Marilyn Dunn<sup>1</sup>

**TABLE 2** Dog data for the RUTI population divided by sex and neuter status

Dog data	Total females (n = 48)	Intact females (n = 8)	Spayed females (n = 40)	Total males (n = 5)	Intact males (n = 3)	Neutered males (n = 2)	Total
Mean age (years)	3.9	0.8	4.5	1.2	0.7	2	3.6
Clinical signs							53 (100%)
Pollakiuria	32	6	26	4	2	2	36 (70%)
Hematuria	23	2	21	...	...	...	23 (43%)
Dysuria/stranguria	15	1	14	...	...	...	15 (25%)
Urinary incontinence	25	5	20	5	3	2	30 (57%)
Peri-genital licking	21	4	17	2	1	1	23 (43%)

# Recurrent Bacterial Cystitis

- Often associated with an identifiable cause
  - Must find what it is!
  - Repeated treatment with antibiotics is VERY UNLIKELY to solve the problem!

**Table 1**

Comorbidities that should be considered in a dog or cat with bacterial cystitis.

---

Endocrinopathy
Kidney disease
Obesity
Abnormal vulvar conformation
Congenital abnormalities of the urogenital tract (e.g. ectopic ureter, mesonephric duct abnormalities)
Prostatic disease
Bladder tumor
Polypoid cystitis
Urolithiasis
Immunosuppressive therapy
Rectal fistula
Urinary incontinence/retention

---

# Assess Previous Therapy

- Was there a problem with the process?
- Was the right drug used?
  - Review the susceptibility profile
  - Does the drug reach the desired tissue in appropriate concentrations?
- Did the owner give the medications properly?
  - Right duration, interval?
  - In the right way?
    - Fluoroquinolones with dairy?
    - Antibiotics at the same time a sucralfate or a PPI?
    - Pilled them or put it in food?

# The Quest for a Cause

- Step 1 – Initial culture
  - Urine culture from a cystocentesis, preferably ultrasound guided
    - Allows for visualization of bladder pathology
      - Mass lesion or bladder wall changes
      - Uroliths
  - Interpretation:
    - Is it the same pathogen?
      - Recurrent/Relapse infection is likely
    - Is it a different pathogen?
      - Reinfection is likely



# Recurrent Bacterial Cystitis

## Reinfection

- Is there a pathway for bacteria to get in?
  - i.e. ectopic ureters
  - Hooded/recessed vulvas
- Bacteria being delivered to the site?
  - Diarrhea
  - Urinary incontinence
  - Vaginal mass
- Immunosuppression

## Recurrent/Relapse

- Did we clear the organism with the original therapy?
- Is there some place for bacteria to hide?
  - Mass or Inflammatory lesions
  - Urolithiasis
  - Kidneys, Prostate, etc.
- Concurrent disease
  - DM, HAC
- Immunosuppression



# Diagnostic Testing for UTIs

- Physical Exam
  - Febrile or systemically ill?
- Laboratory Testing
  - CBC
  - Biochemistry Panel
  - Urinalysis
  - Culture and susceptibility testing
- Diagnostic Imaging
  - Ultrasound
  - Radiographs
    - +/- contrast
  - CT
- Cystoscopy

# CBC

- Leukogram
  - Systemic inflammation/infection
    - Indicative of more than just lower urinary tract disease?
- Hemogram
  - Anemia - systemic disease?
  - Hemolysis
    - Along with chemistry (total bilirubin), total protein measurement
    - Hematuria vs. hemoglobinuria
- Thrombogram
  - Platelet count
    - Thrombocytopenia – hemorrhage causing hematuria?
    - Prepare for FNA or traumatic catheterization

HEMATOLOGY			
TEST	RESULT		REF. RANGE/UNITS
RBC	6.5		5.4 - 8.7 x10 <sup>12</sup> /L
Hematocrit	0.44		0.38 - 0.57 L/L
Hemoglobin	145		134 - 207 g/L
MCV	67.7		59.0 - 76.0 fL
MCH	22.3		21.9 - 26.1 pg
MCHC	329.5		326.0 - 392.0 g/L
RDW	15.5		10.0 - 19.0
% Reticulocyte	1.5		%
Reticulocytes	97.5		10.0 - 110.0 x10 <sup>3</sup> /uL
Reticulocyte Hemoglobin	27.2		24.5 - 31.8 pg
WBC	16.6		4.9 - 17.6 x10 <sup>9</sup> /L
% Neutrophils	44.9		%
% Lymphocytes	42.8		%
% Monocytes	5.6		%
% Eosinophils	6.5		%
% Basophils	0.2		%
Neutrophils	7.5		2.9 - 12.7 x10 <sup>9</sup> /L
<b>H Lymphocytes</b>	7.1		1.1 - 5.0 x10 <sup>9</sup> /L
Monocytes	0.9		0.0 - 1.2 x10 <sup>9</sup> /L
Eosinophils	1.1		0.0 - 1.5 x10 <sup>9</sup> /L
Basophils	0.0		0.0 - 0.1 x10 <sup>9</sup> /L
Platelets	300		143 - 448 x10 <sup>9</sup> /L
Platelet Comments	Platelet assessment Adequate Mild platelet clumping observed		
CBC Comment	RBC, WBC, and platelet morphology normal		

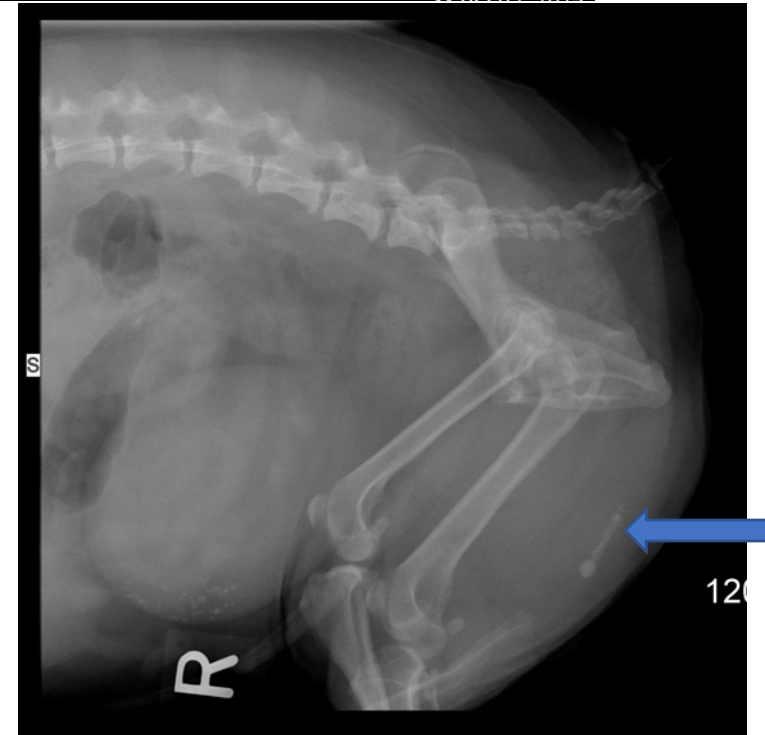
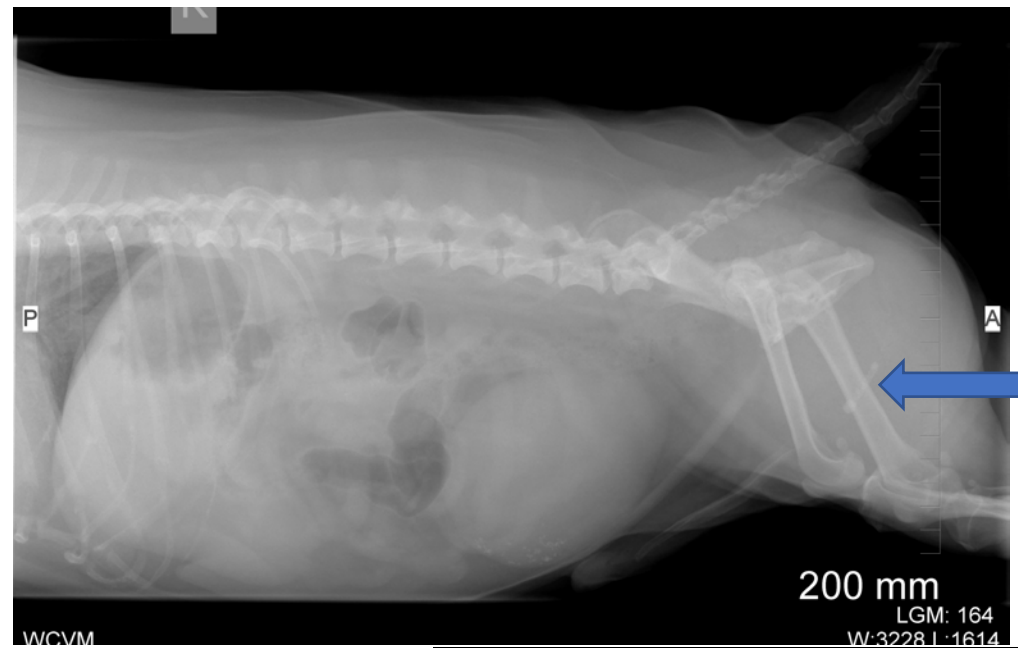
# Biochemistry Profile

- Renal Parameters
  - Identify CKD or raise suspicion of pyelonephritis
- Electrolytes
  - Calcium
- Hepatic Parameters
  - Identify liver disease (ALP, ALT, GGT, Total bilirubin)
  - Pseudofunction tests
    - Albumin, glucose, cholesterol, Total bilirubin
- Endocrine Screening
  - ALP, cholesterol
  - T4 often on many “senior” panels

CHEMISTRY		
TEST	RESULT	REF. RANGE/UNITS
Glucose	5.4	3.5 - 6.3 mmol/L
<b>H IDEXX SDMA<sup>a</sup></b>	<b>17</b>	0 - 14 ug/dL
Creatinine	105	44 - 133 umol/L
Urea (BUN)	8.4	3.2 - 11.0 mmol/L
BUN: Creatinine Ratio	20	
<b>H Phosphorus</b>	<b>2.5</b>	0.8 - 2.0 mmol/L
Calcium	2.7	2.2 - 2.8 mmol/L
Sodium	146	142 - 152 mmol/L
Potassium	4.8	4.0 - 5.4 mmol/L
Na: K Ratio	30	28 - 37
Chloride	110	108 - 119 mmol/L
TCO2 (Bicarbonate)	24	13 - 27 mmol/L
Anion Gap	17	11 - 26 mmol/L
Total Cations	151	mmol/L
Total Anions	134	mmol/L
<b>L Total Protein</b>	<b>54</b>	55 - 75 g/L
Albumin	29	27 - 39 g/L
Globulin	25	24 - 40 g/L
Albumin: Globulin Ratio	1.2	0.7 - 1.5
ALT	24	18 - 121 IU/L
AST	19	16 - 55 IU/L
<b>H ALP</b>	<b>171</b>	5 - 160 IU/L
GGT	5	0 - 13 IU/L
Bilirubin - Total	1.2	0.0 - 5.2 umol/L
Cholesterol	7.2	3.4 - 8.9 mmol/L
Amylase	443	337 - 1469 IU/L
Lipase <sup>b</sup>	62	0 - 250 IU/L
<b>H Creatine Kinase</b>	<b>269</b>	10 - 200 IU/L
Osmolality	294	250 - 310 mmol/kg
Hemolysis Index	Normal	
Icterus Index	Normal	
Lipemia Index	Normal	
ENDOCRINOLOGY		
TEST	RESULT	REF. RANGE/UNITS
Total T4 <sup>c</sup>	44.6	13.0 - 53.0 nmol/L

# Radiographs

- What are you looking for?
  - Radiopaque uroliths
    - Nephroliths, ureteroliths
  - Bladder position
  - Prostatic mineralization
- Positioning
  - Lateral and V/D
  - Legs pulled forward in male dogs
    - Allows unobstructed view of the back of the os penis
- Contrast
  - Radiolucent stones
  - Urethral narrowing
    - Mass lesions
    - Strictures
    - Proliferative urethritis



# Ultrasound

- Assess bladder
  - Wall thickness
  - Debris
  - Ureter placement
- Assess for stones
  - Radio-opaque/radiolucent
- Assess for mass lesions
- Collection of sample
  - If there is a mass, then NO cystocentesis



# Ultrasound

- Upper Urinary Tract
- Ureters

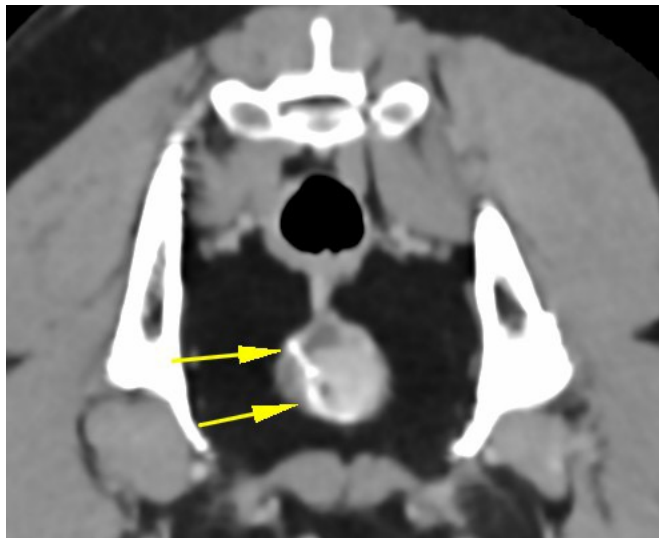
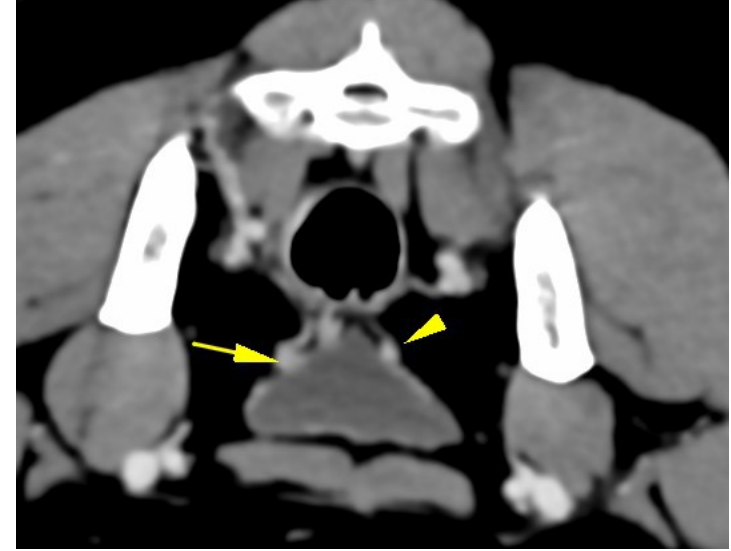
Cystic Right Kidney



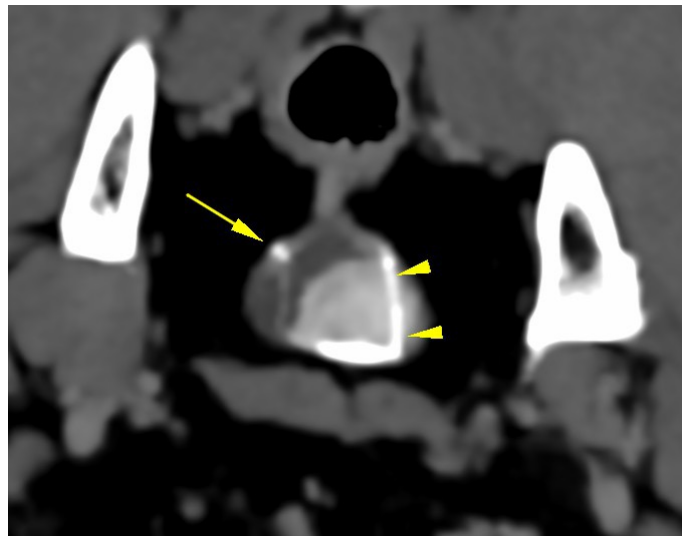
Dilated Right Ureter

# Contrast CT

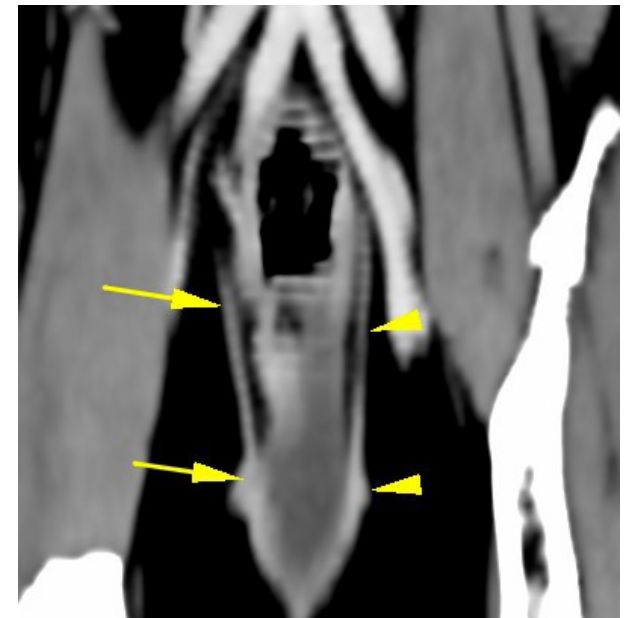
- Complete assessment of the urinary tract
  - Kidneys, ureters, bladder, urethra
  - Prostate, uterus, vagina
  - Regional lymph nodes



note the RIGHT ureteric jet (arrows)



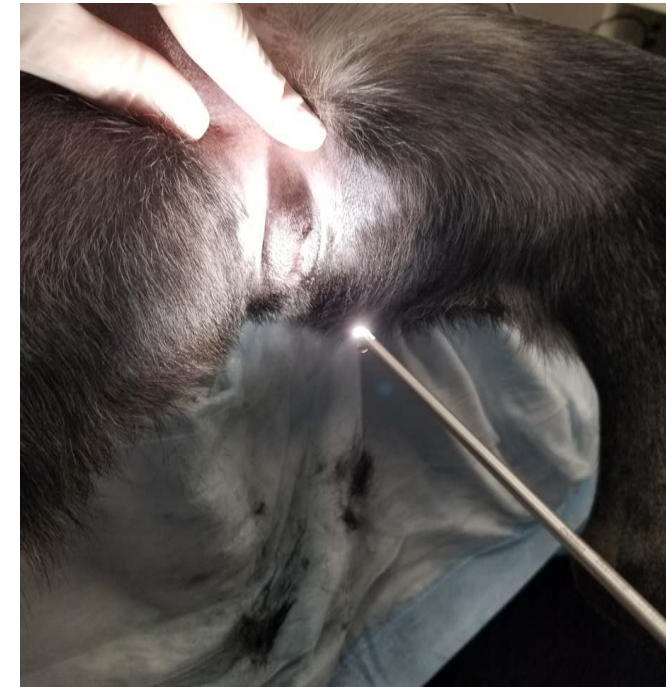
prominent LEFT ureteric jet (arrowheads) and faint RIGHT ureteric jet (arrow).



Initial post-contrast series. Note the symmetrical, early enhancement of the ureters and ureteric papillae

# Cystoscopy

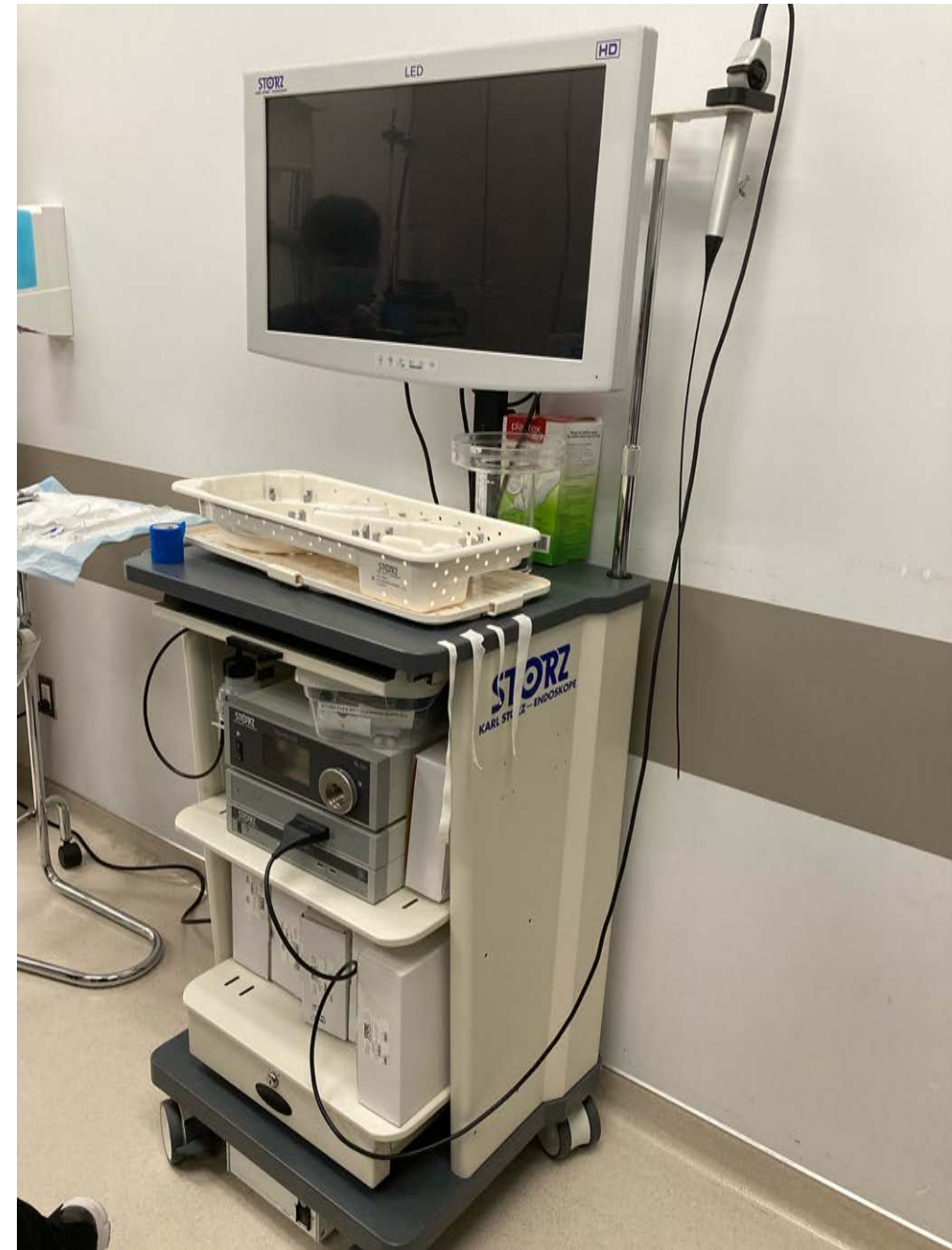
- Minimally invasive option to assess urinary and reproductive tracts
  - Visualize the urethral papilla, urethral mucosa, bladder mucosa
  - Look for ectopic ureters
    - In urethra, vagina, vestibule
  - Look for persistent membranes
  - Look for vaginal masses
- Rigid cystoscopy
  - Female dogs
- Flexible cystoscopy/ureteroscopy
  - Male and Female dogs





# Cystoscopy

- Allows for tissue biopsy
  - Bladder wall histopathology and culture
  - Urethral mass cytology/histopathology
- Stone removal/destruction
  - Basket retrieval
  - Laser lithotripsy
- Laser correction of ectopic ureters
- Interventional procedures
  - Urethral or ureteral stents
  - Balloon dilation of proliferative tissue



# Cystoscopy in dogs with recurrent UTIs

- Mean age at presentation was 3.8 years
  - Majority female dogs (48/53)
    - 40/48 of which were spayed
    - Hooded vulva noted in 33/48
- Transurethral cystoscopy found anomalies in 45/53
  - Mucosal edema (19/53)
  - Vestibulovaginal septal remnant (15/48)
  - Lymphoid follicles (8/53)
  - Short urethra (<7cm) (6/53)
  - Ectopic ureter (5/53)
- Urine culture at the time of cystoscopy positive in 13/49
- Bladder wall edema and ulceration were the most common findings on histopathology (25/39)

Received: 13 September 2019 | Accepted: 30 January 2020  
DOI: 10.1111/jvim.15728

STANDARD ARTICLE

Journal of Veterinary Internal Medicine   
Open Access American College of Veterinary Internal Medicine

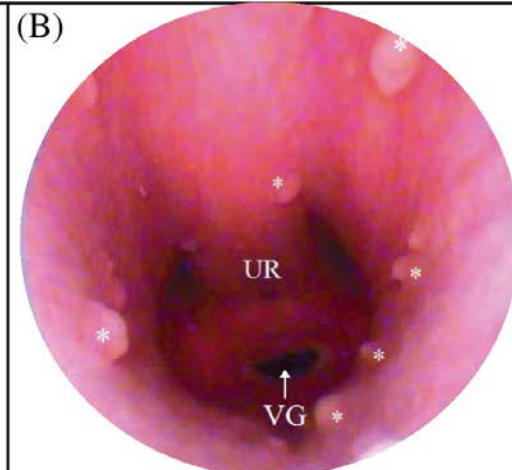
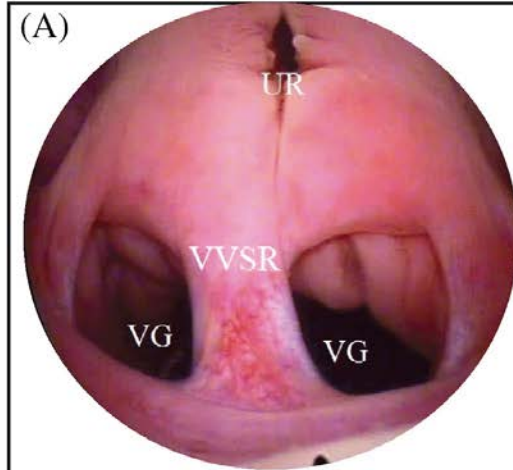
**Transurethral cystoscopy in dogs with recurrent urinary tract infections: Retrospective study (2011-2018)**

Marie Llido<sup>1</sup> | Catherine Vachon<sup>1</sup> | Melanie Dickinson<sup>2</sup> | Guy Beauchamp<sup>1</sup> | Marilyn Dunn<sup>1</sup>

# Transurethral cystoscopy in dogs with recurrent urinary tract infections: Retrospective study (2011-2018)

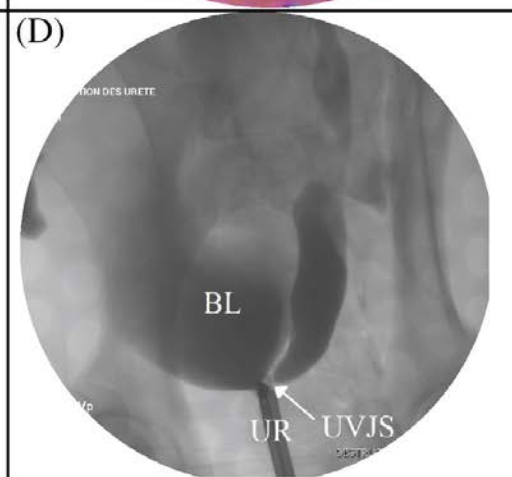
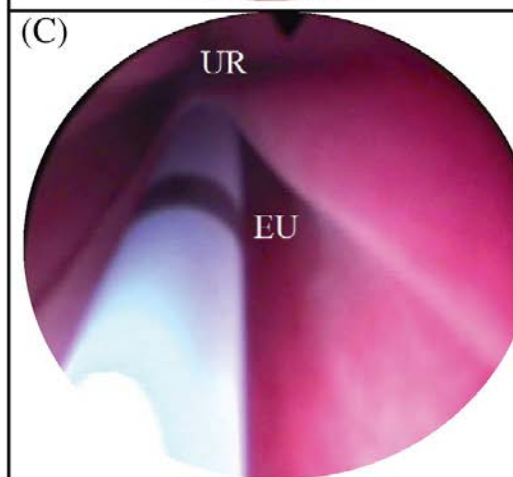
Marie Llido<sup>1</sup> | Catherine Vachon<sup>1</sup> | Melanie Dickinson<sup>2</sup> | Guy Beauchamp<sup>1</sup> | Marilyn Dunn<sup>1</sup>

Vestibulovaginal septal remnant



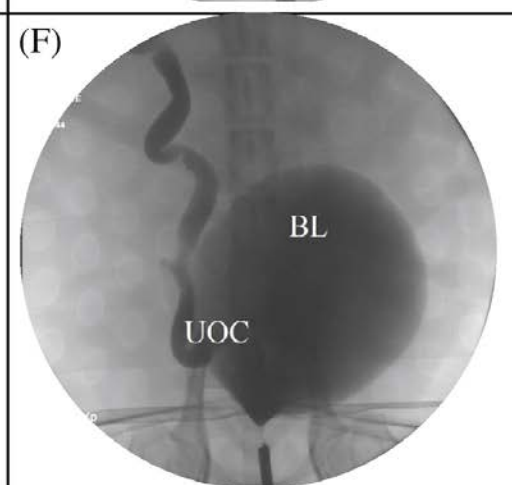
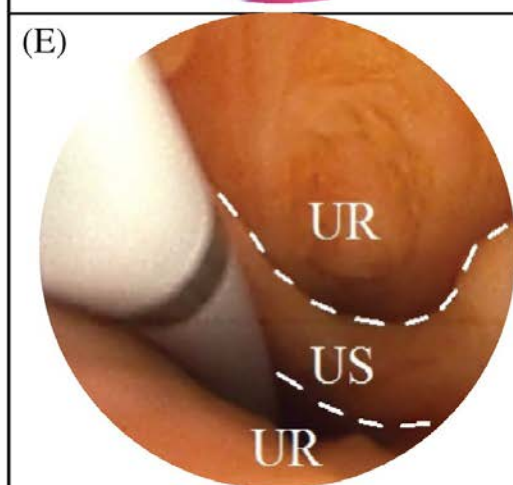
Lymphoid follicles

Ectopic Ureter with catheter in place for laser ablation



Ureterovesicular stenosis

Urethral septum



Ureterocele – dilation of the ureter due to distal obstruction

# Recurrent Cystitis - Treatment

- Objective of treatment of the UTI:
  - Resolution of clinical signs
  - Minimal risk of adverse effects of treatment
    - Both to the patient and to AMR
- Previous recommendation was 4 weeks of treatment
  - Probably not appropriate, as all infections are not the same
    - UTI secondary to urolithiasis that has been resolved likely only needs 3-5 days of treatment, just like sporadic cystitis
    - A bladder tumour, or polypoid cystitis will likely require longer duration therapy
- Most Important: Treat the underlying disease!
  - Fix this and the UTIs will likely also go away

# 3 Culture Approach

- Culture 1
  - At the time of diagnosis to direct selection of appropriate antimicrobial
- Culture 2
  - While ON antimicrobial therapy (5-7 days into treatment)
    - Tells us that the therapy is working
    - Drug is appropriate, the owner is giving it, it is getting to the site, etc..
- Culture 3
  - 5-7 days AFTER completion of antibiotics
    - A tool to establish relapse, re-infection or persistent infection
    - If clinical signs are resolved, then we move to the subclinical bacteriuria section later

# What to do first

- While the culture is pending:
  - Remember Sporadic Cystitis!
    - NSAID therapy (if appropriate)
      - This option is limited in sick patients (especially cats)
    - Empirical antimicrobial therapy
      - Amoxicillin, TMS
- Once the culture and susceptibility profile are back:
  - If your empiric drug is appropriate, continue with therapy
  - If not, consider your patient:
    - Is the patient better?
    - Clinical signs persist?

# When Things Don't Work Out as Expected

Possible Reasons for Disagreement Between Test Results and Clinical Outcome		
Factor	Positive Outcomes	Negative Outcomes
Patient/Disease Factors	Pharmacokinetic	High urine drug concentrations Failure of drugs to penetrate sequestered sites (ex. CNS) Drug interactions decreasing absorption or increasing elimination
	Pharmacodynamic	Failure of aminoglycosides in acidic or anaerobic environments Failure of folate synthesis inhibitors in purulent environments (excessive PABA in environment)
	Disease/pathology	No infection Self-limiting infection Predisposing disease or underlying pathology such as atopy, diabetes or neoplasia Indwelling medical device
	Therapeutic	Utilization of localized therapy, high concentrations overcoming low level resistance Off label use (dose, dosing frequency, route of administration) Off label use (dose, dosing frequency, route of administration) Poor owner compliance
Organism/Test Factors	Resistance	Development of resistance in vivo
	Organism lifestyle	Biofilm formation Intracellular infections
	Organism Identification	Mis-identified organism False positive culture Mis-identified organism Mixed infection
	Antimicrobial Susceptibility Test	Incorrectly performed or reported test Inducible resistance Incorrectly performed or reported test

# The hard part – How long to treat?

- Long-term therapy not automatically warranted in all recurrent cases
  - Even with co-morbidities (even DM!)
  - Particularly true if this is re-infection
  - 3-5 days of treatment can be considered
- Persistent or relapsing infections
  - 7-14 days likely to be more appropriate
  - Many factors to consider:
    - Bladder wall invasion, mass lesions, polypoid change – all may require longer treatment
      - Intracellular infection requires a drug that will penetrate into the cell...
- Consider how long it will take to control the inciting cause...



# Recurrent Cystitis – Follow Up

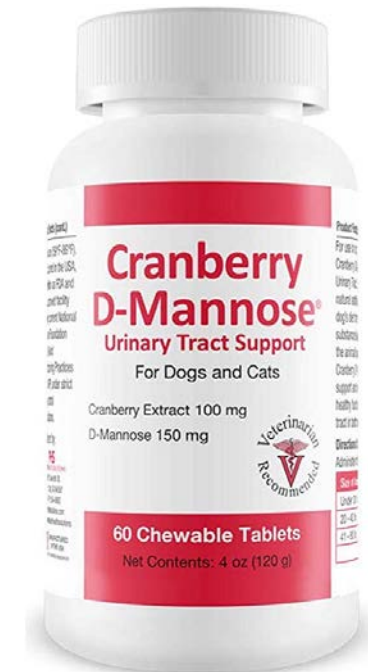
- If you treat for 3-5 days:
  - Culture during treatment is NOT recommended
  - Nor is culture after therapy is complete
- With longer duration (7-14+ days) treatment:
  - Culture at 5-7 days is reasonable
    - Positive culture needs evaluation
      - Compliance?
      - Right drug for the location?
- 5-7 days AFTER therapy is complete
  - If clinical signs are resolved, then urine culture can help determine presence of subclinical bacteriuria

# Prevention – Antibiotics?

- Prophylactic antimicrobial administration?
  - Some benefit in women, but also an increase in AMR
  - Anecdotal evidence of nightly Nitrofurantoin in dogs
    - Limited evidence
    - Side effects of the drugs?
    - Antimicrobial resistance?
- Pulse dose therapy
  - Night-time treatment in dogs
    - Have antimicrobial in urine during the longest period of bladder retention
- Prophylactic administration not recommended in dogs and cats

# Supplements

- Cranberry extract, cranberry juice
  - Type A proanthocyanidins
    - *In vivo* inhibits *E.coli* P fimbriae adherence to uroepithelium
  - Info in humans mixed
    - May help reduce UTI in healthy women
  - Dogs – *VERY* limited data
    - May have helped in 6 dogs with recurrent UTIs
    - In 94 dogs with IVDD had no effect
- D-mannose
  - Prevents adhesion of *E. coli* to uroepithelium
    - Blocks adherence of fimbriae H on type 1 pili of *E. coli*
  - Promising results in people, no evidence in dogs yet



# Other preventative options

- Probiotics
  - In women with UTIs, the vaginal microbiome is quite different from women who do not have a UTI
    - “Normalizing” this with probiotics has shown promise in managing chronic UTIs
  - No such support in dogs
    - Limited study, but what info there is doesn’t look as good as in people
- Biotherapeutic products
  - Asymptomatic strains of *E. coli*
  - Promising experimental data, but not ready as a treatment yet
- Vaccines
- Intravesicular or oral glycosaminoglycans

# Methenamine

- Converted to formaldehyde in low pH
  - With the goal of killing the bacteria directly
  - How effective conversion to active form is unclear
- No evidence of efficacy or safety in dogs and cats
- Humans
  - May be effective in some populations with recurrent cystitis
- Not recommended in dogs and cats at this time



Questions?

---