Frequent and Urgent!
Urinary Tract Infection Misconceptions

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Disclosures

The speakers have no relevant disclosures or conflicts of interest.

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Learning Objectives

At the end of this session, participants should be able to:

- Describe the clinical presentation of simple and complicated urinary tract infections and differential etiologies
- Outline urine laboratory testing indications, characteristics, implications, and misconceptions
- Select the most appropriate treatment strategies, including antibiotic selection
- Discuss common UTI misconceptions

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Session Activation

Which antibiotic is NOT considered first-line for empiric treatment of an uncomplicated cystitis in an adult?

a. Nitrofurantoin
b. Trimethoprim-sulfamethoxazole
c. Ciprofloxacin
d. Fosfomycin

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Session Activation

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Session Activation

Which patient with asymptomatic bacteriuria should be treated with antibiotics?

a. 13 year old female in the emergency room with a myofascial back strain
b. 23 year old female at her initial obstetrical visit
c. 67 year old male with type 2 diabetes mellitus
d. 47 year old female with hypertension in clinic for Department of Transportation physical

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Session Activation

Which patient with asymptomatic bacteriuria should be treated with antibiotics?

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b. 23-year-old female at her initial obstetrical visit
c. 67-year-old male with type 2 diabetes mellitus
d. 47-year-old female with hypertension in clinic for DOT physical

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Session Activation

Which bacteria is the most common cause of cystitis?

a. Klebsiella pneumoniae
b. Proteus mirabilis
c. Escherichia coli
d. Staphylococcus saprophyticus

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UTI antibiotic treatment was avoidable at least 39% of the time

CDC - 2014

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The Workup

Presentation, Exam, Labs

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Clinical Symptomology and Presentation

- UTI is a *clinical* diagnosis, not a laboratory one.

- Certain symptoms in combination increase odds of UTI
  - Dysuria + frequency = 50% UTI
  - Dysuria + frequency + NO vaginitis/cervicitis = over 90% UTI and +LR of 24.6
  - Cloudy Urine = 96% specificity for UTI
  - Self-diagnosis = +LR of 4.0

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Stats Time Out

Likelihood Ratio (LR):

- Used to assess the value of performing a diagnostic test
  - "Is this test going to change what I do?"
- Calculated using a ratio of sensitivity to specificity
- Likelihood a given test result would be expected (positive or negative) in patient with target disorder compared to one without

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Clinical Symptomology and Presentation

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  - Cloudy Urine = 96% specificity for UTI
  - Self-diagnosis = +LR of 4.0

Dysuria plus urinary frequency in the absence of symptoms of STI is diagnostic.

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Physical Exam

- Targeted at ruling in/out other diagnoses
  - Pelvic exam
    - Cervical motion tenderness
    - Bleeding
    - Discharge
  - Abdominal Exam
    - CVA tenderness
- Ensure UTI is uncomplicated

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Laboratory Workup

Urine tests NOT REQUIRED for majority of uncomplicated lower UTI (cystitis)

Low Probability	Intermediate Probability	High Probability
Probably Don't Have UTI	Most Useful	Will Treat Regardless

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Laboratory Workup

Possible indications for urine testing of suspected cystitis:

- Immunocompromised patients
- History of
  - Multiple courses of antimicrobial therapy
  - Antibiotic resistance
  - Multiple drug allergies

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Laboratory Workup - Urinalysis

Microscopy slightly more accurate than dipstick

Urine Dipstick	Sensitivity	Specificity
Pyuria OR Nitrites	Good - up to 94%	Poor
Pyuria AND Nitrites	Poor	Strong – near 100%

Urine Microscopy	Finding
WBCs per hpf	> 5

Dipstick Net Result:
Overtreating 47% of UTIs
Undertreating 13% of UTIs

Microscopy Net Result:
Overtreating 44% of UTIs
Undertreating 11% of UTIs

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Laboratory Workup - Urinalysis

Collection Method

- Classic standard – Midstream Catch
- Midstream catch vs. asking patient to urinate into container
  - Little difference on urinalysis; possible insignificant, small effect on culture

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Laboratory Workup - Urinalysis

Epithelial Cells

- Classic "contaminated sample" > 5 epithelial cells
  - Negative effect on ability to obtain reliable culture
  - Effect on dipstick and microscopy not to same degree

Bacteria

- Bacteria on microscopy predictive of positive culture
- Not diagnostic of UTI
  - Can be contaminant or asymptomatic bacteriuria

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Laboratory Workup - Urinalysis

Nitrites

- Not produced by:
  - *S. saprophyticus, Pseudomonas, or enterococci*

WBCs

- May be low in neutropenic or leukopenic patients

Pyuria

- May result from:
  - Dehydration, advanced age, AKI, STI, appendicitis, diverticulitis
  - Poor specificity for UTI

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Laboratory Workup – Urine Culture

Indications

- Patient unresponsive to initial antibiotics
- Recurrent UTI
- Suspected pyelonephritis

Urine Culture Result	Rate	Cause
False Positive	5%	Asymptomatic Bacteriuria
False Negative	25%	Antibiotic Use, Diluted Sample

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Laboratory Workup – Sexually Transmitted Infections

Two approaches to STI screening:

- Screen *all* sexually active women <25 years old as per CDC guidelines with vaginal/cervical swabs
- Selectively screen only patients at high risk for STI, who have symptoms consistent with STI, or if UTI symptoms persist for >48hrs after initiating appropriate antibiotics.

Did you know?

A patient performed self vaginal swab is more accurate than provider performed swabs for gonorrhea and chlamydia.

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Imaging

Indications for imaging in patients suspected of pyelonephritis

Consider in those patients suspected of:

- Perinephric abscess, septic nephrolithiasis, or emphysematous pyelonephritis
  - These patients typically present with either severe pain and/or severe sepsis/septic shock
- Those who have not responded to treatment >48-72hrs
- Looking for alternative diagnoses when there's not a high pretest probability

Imaging is *not* routinely required for patients suspected clinically of pyelonephritis.

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Imaging

Imaging in patients suspected of pyelonephritis

Netherlands ED study – Patients with febrile UTI

- If:
  - No history of urolithiasis
  - Urine pH <7.0
  - No renal insufficiency (estimated GFR ≤40)

- U/S or CT findings – 93% NPV
- Urgent urologic disorder – 99% NPV
  - In validation study, imaging findings (89% NPV), urgent urologic disorder (100% NPV)

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Management and Treatment

Uncomplicated UTI - Cystitis

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Uncomplicated UTI Treatment

General Principles

- Narrow spectrum as possible
- Safest side effect profile

Limitations

- Majority of women, up to 73% with cystitis will be symptom free in 3 days with only ibuprofen
- Local antibiotic resistance/antibiogram

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Uncomplicated UTI Treatment

First Line Antibiotics

- SMX/TMP po × 3 days *or*
- Trimethoprim po × 3 days *or*
- Nitrofurantoin po × 5 days *or*
- Cephalexin po x 5 days *or*
- Fosfomycin 3g as a single dose po

Pregnant Patients

- Cephalexin po x 5 days *or*
- Nitrofurantoin in 3rd trimester

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Uncomplicated UTI Treatment

Caveat

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Uncomplicated UTI Treatment

Extended Spectrum Beta-Lactamase producers (ESBL+)

- Produce enzymes that break open beta-lactam ring
- Do NOT rx penicillins nor narrow-spectrum cephalosporins
  - Up to 3rd generation cephalosporin
- Enterobacteriaceae family
  - Gram negative bacteria
    - Ex: E. coli, proteus sp., pseudomonas

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UTI Prevention

Activity Modifications (have not been shown to prevent recurrent UTIs)

No effect shown from:

- Increased water intake
- Direction of wiping
- Voiding post intercourse

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Uncomplicated UTI Treatment

OTCs

- Phenazopyridine (Pyridium): Weak evidence as urinary anesthetic
  - "numb" up the bladder; acidify urine pH
  - Caution: renal impairment
  - Orange urine
- Ibuprofen
  - 3 days

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Uncomplicated UTI Treatment

Supplements

- Calcium
  - MOA: dec urothelial adherence
  - Suppression
  - Low dose- insignificant
  - Higher dose- inc risk of UTI
- D-Mannose
  - MOA: dec urothelial adherence
  - Suppression, treatment
  - E coli only
  - Best outlook for supplements
- Vitamin C
  - MOA: antibacterial, mild urine acidification
  - Treatment
  - Anecdotal for high dose – oral and IV

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Uncomplicated UTI Treatment

Supplements

- Methionine
  - MOA: urine acidification, dec urothelial adherence
  - Suppression
  - Small studies, uncontrolled
  - S/e - inc homocysteinemia levels
- Probiotic
  - MOA: Competitive exclusion of other organisms
  - Suppression, treatment
  - Conflicting studies
    - Different strains for different body flora
- Cranberry
  - MOA: dec urothelial adherence, acidify urine, hippuric acid --> antibacterial
  - Suppression
  - Insignificant findings
  - Comorbid considerations

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Uncomplicated UTI Treatment

Supplements

- Downfalls
  - Poor studies/minimal studies
  - Lack of regulation
  - Unknown s/e
  - Unknown therapeutic doses

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Complicated UTIs

Criteria

Those urinary tract infections that involve:

- The upper urinary tract (pyelonephritis, nephrolithiasis, hydronephrosis, etc.)
- Anatomic problem (outflow obstruction, urolithiasis, urinary catheter, etc.)
- Male gender (always culture)
- Complicated by systemic disease (DM, leukopenia, etc.)
- Systemic manifestations (urosepsis)

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Complicated UTIs

Treatment Approaches - Outpatient Pyelonephritis

- Fluoroquinolones
  - Ciprofloxacin 500 mg PO BID for 7d **or**
  - Levofloxacin 750 mg PO daily for 5d
- If fluoroquinolone resistance is thought to be >10%:
  - B-lactams (Amoxicillin/Clavulanic acid (e.g. Clavulan or Augmentin) 875 mg PO q12hr for 14d) **or**
  - Cephalexin 500mg PO q6h for 14d

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Complicated UTIs

Treatment Approaches - Inpatient Pyelonephritis

- Ciprofloxacin 400 mg IV q12h for 10-14d **or**
- Levofloxacin 750 mg IV q24h for 5d
- If fluoroquinolone resistance is thought to be >10%:
  - 3rd generation cephalosporin (ceftriaxone 1 g IV q24h **or** cefepime 1 g IV q12h **or** cefotaxime 1-2 g IV q8h **or** ceftazidime 2 g IV q8h) **or**
  - Ampicillin 1-2 g IV q6h **plus** gentamicin IV 1.5 mg/kg q8h

Pyelonephritis with Septic Shock

- Coverage should include *enterococcus* as well as *E.coli*
- Ampicillin 1-2 g IV q6h **plus** gentamicin IV 1.5 mg/kg q8h **or**
- Vancomycin 1g IV **plus** gentamicin IV 1.5 mg/kg q8h

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Asymptomatic Bacteriuria

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Asymptomatic Bacteriuria

<u>Treatment Indications/Approaches</u>

- Patients prior to a urologic procedure
- Pregnant women
- Patients with recent kidney transplant

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Asymptomatic Bacteriuria

Reasons for not treating

- Benign
- Usually no treatment benefit
- Antibiotic adverse effects

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Asymptomatic Bacteriuria

Prior to urologic procedures

- IDSA recommendation:
  - Strong recommendation; moderate quality evidence
    - Avoidance of post-op sepsis
    - ABS is a major risk factor for febrile UTI
    - Risk dependent on invasiveness of procedure
- What's next?
  - Antibiotic duration
  - Optimal antibiotic choice

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Asymptomatic Bacteriuria

Pregnant Women

- IDSA recommendation:
  - strong recommendation; moderate quality evidence
    - Reduction of pyelonephritis
    - Preterm labor
    - Dec low birth weight
- Culture of urine at first OB visit
- What's next?
  - Low risk female? No treatment?
  - Repeat cultures?
    - Insufficient evidence

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Asymptomatic Bacteriuria

Recent kidney transplant

- IDSA recommendation:
  - <1 month: insufficient evidence
    - Prevent pyelonephritis
    - Decrease graft rejection
  - >1 month: no treatment; strong recommendation; high quality evidence

- What's next?
  - <1 month vs <3 months
    - Efficacy of screening < 1 month
  - Only select patients/ high risk

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Elderly Patients

Clinical situations

- ASB
  - Healthy geriatric population
    - No screening/treatment
  - Community-dwelling geriatric population w/ functional impairment
    - IDSA recommendation:
      - No screening/treatment
      - strong recommendation; low quality evidence
  - LTC- dwelling geriatric population w/ functional impairment
    - IDSA recommendation:
      - No screening/treatment
      - strong recommendation; moderate quality evidence
  - Patients with long term indwelling catheters
    - IDSA recommendation:
      - No screening/treatment
      - strong recommendation; low quality evidence

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Elderly Patients

Clinical situations

- ASB
  - Geriatric population w/ functional and/or cognitive impairment and delirium w/o local GU s/s nor systemic signs of infection
    - IDSA recommendation:
      - No screening/treatment
      - strong recommendation; very low quality evidence
  - Geriatric population w/ functional and/or cognitive impairment and fall w/o local GU s/s nor systemic signs of infection
    - IDSA recommendation:
      - No screening/treatment
      - strong recommendation; very low quality evidence
- Geriatric population w/ bacteremia and fever + systematic signs of sepsis without other gross source
  - TREAT!

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Elderly Patients

Rationale

- Low/moderate quality evidence for no benefit vs high quality evidence for harm
- Limited reduction of death or sepsis
- Avoidance of adverse outcomes
  - Inc risk of C. diff infection
  - Inc risk of antibacterial resistance
  - Drug s/e

Limitations

- Objective criteria for symptomatic UTI

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Elderly Patients

Treatment Indications

- Geriatric population w/ bacteremia and fever + systematic signs of sepsis without other gross source
  - TREAT!
- Geriatric population with UTI symptoms
  - TREAT!

Approaches

- Talk to the staff
  - Actual s/s
  - Nursing expectations
- Set up protocols

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Antimicrobial Stewardship

- Measure antibiotic prescribing
- Improve antibiotic prescribing
- Minimize misdiagnosis for overuse OR delay diagnosis leading to underuse
- Right drug, right dose, right duration

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Uncomplicated UTI Treatment

First Line Antibiotics

- SMX/TMP po × 3 days *or*
- Trimethoprim po × 3 days *or*
- Nitrofurantoin po × 5 days *or*
- Cephalexin po x 5 days *or*
- Fosfomycin 3g as a single dose po

Pregnant Patients

- Cephalexin po x 5 days *or*
- Nitrofurantoin in 3rd trimester

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Antimicrobial Stewardship

Bacterial Resistance

- Roughly 2.8 million infections yearly
  - Roughly 35,000 deaths
- Almost 224,000 cases of C. diff
  - 2017- 12,800 died

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Antimicrobial Stewardship

Antibiograms - IDSA Guidelines

Lower UTI: choose an antibiotic that is estimated to be at least 80% effective

Upper UTI: choose an antibiotic that is estimated to be at least 90% effective.

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PANHANDLE BACTERIAL ISOLATES January 2019 - December 2019	GENERIC NAME	# Isolates	Amoxicillin-clavulanate	Ampicillin	Ampicillin/sulbactam	Piperacillin/tazobactam	Oxacillin	Penicillin G	Cefazolin[b]	Cefotaxime (meningeal)	Cefotaxime (other)	Ceftazidime	Ceftriaxone (meningeal)	Ceftriaxone (other)	Cefepime	Ciprofloxacin[c,e]	Levofloxacin[c,e]	Gentamicin	Gentamicin High Level	Tobramycin	Imipenem	Cladamycin	Erythromycin	Linezolid	Nitrofurantoin[b]	Tetracycline	Trimethoprim/sulfamethox.	Vancomycin
Gram-negative																											
Acinetobacter baumannii complex		3*			100	100			0			100		33	100	100	100	100		100	100					100	
Citrobacter freundii complex		40	0			89			0			90		88	98	97	97	95		97	100				90		65	
Enterobacter aerogenes		33	0			70			0			85		88	97	88	91	97		97	100				6		94	
Enterobacter cloacae complex		79	0			71			0			74		74	95	96	97	97		97	100				42		89	
Escherichia coli		1058	81	56	63	96			92			95		95	95	79	79	92		93	100				95		77	
Klebsiella oxytoca		69	99	0	65	99			81			100		99	100	99	97	100		100	100				87		94	
Klebsiella pneumoniae		245	95	0	86	97			93			95		96	96	97	96	96		96	100				46		90	
Morganella morganii		18*	0	0	11	72			0			77		100	100	81	81	84		100	95				0		67	
Proteus mirabilis		166	100	73	89	100			89			92		92	92	56	60	90		93	91				0		60	
Pseudomonas aeruginosa		146				100			0			92			91	89	80	92		98	90							
Serratia marcescens		18*	0						0			89		89	89	100	100	100		82					0		89	
Stenotrophomonas maltophilia		13*															100										77	
Gram-positive																											
Enterococcus sp.		201		94				91								66d	66d		75					96	90	18		91e
Staphylococcus aureus		355					61d	18								66	67	100				74	47	100	100	95	99	100
Staphylococcus epidermidis		111					30	8								62	62	88				63	42	100	99	81	54	100
Staphylococcus saprophyticus		7*					43	0								100	100	100				57	43	100	100	86	100	100
Streptococcus agalactiae (Group B)		85		100				100			100						95					6		100		21		100
Streptococcus pneumoniae		12*						67		75	92		75	100			100					83	42	100		92	75	100
Streptococcus pyogenes (Group A)		21*		100				100			86			86			100					71	81	100		86		100

Blank cells = insufficient data or drug was not tested

*Organisms with <30 isolates should be interpreted with caution, as small numbers may bias the group susceptibilities.

**Fluoroquinolones values for some Enterobacteriaceae species are not accurate due to current software capabilities discrepant to CLSI guidelines.

Penicillins
Cephalosporins
Carbapenems
Fluoroquinolones
Aminoglycosides

[a] Citrobacter freundii, Enterobacter sp., P. aeruginosa and Serratia sp. have inducible beta-lactamase. Resistance to beta-lactams may arise on therapy.

[b] Indicated in urinary tract infections only.

[c] Penicillin or ceftriaxone may be effective in patients with pneumonia (without meningitis) caused by S. pneumoniae with intermediate susceptiblity.

[d] Methicillin resistance for all S. aureus isolates was 38%.

[e] Vancomycin resistance for all Enterococcus sp. was 8%.

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Antimicrobial Stewardship

CDC Urine Culture Recommendations

- Only specific antibiotics will show up on culture for specific bacteria
  - Restricting antibiotic choices

Role of Fluoroquinolones and Emerging Resistance

- "Good, ole, go-to"
  - Over-use
  - Inappropriate use
- Not first-line

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Antimicrobial Stewardship

Role of Fluoroquinolones and Emerging Resistance

- "Black Box Warnings"
  - Tendonitis
  - Tendon rupture
  - Peripheral neuropathy
  - CNS effects; delirium, myasthenia gravis exac, etc
- Other side effects
  - QT prolongation
  - Hyper/hypoglycemia
  - others

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Case Study #1

- 83 y/o male lives in LTC
- PMH: CAD, HTN, DMII, dementia, neurogenic bladder- indwelling cath
- Meds: Lisinopril, metformin, ASA, cephalexin (daily), PRNs
- S/s: "His bag is turning purple." "He usually becomes septic overnight when this happens." "It's always pseudomonas."
- Vitals: stable/unremarkable
- P/E: unremarkable

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Case Study #1

Work up or not work up?

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Case Study #1

	Providencia rettgeri 50,000-100,000 cfu/ml	
Drug	MIC Interp	MIC Dilutn
Ampicillin	R	>=32
Ampicillin/Sulbac	R	>=32
Cefazolin	R	>=64
Cefepime	S	<=1
Ceftazidime	S	<=1
Ceftriaxone	S	<=1
Cephalexin	R	
Gentamicin	S	<=1
Nitrofurantoin	R	256
Pip/Taz	S	<=4
Tobramycin	S	<=1
Trimeth/Sulfa	S	<=20

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Case Study #2

	E. coli >100,000 cfu/ml	
Drug	MIC Interp	MIC Dilutn
Amoxicillin/Clavulanate	R	>=32
Ampicillin	R	>=32
Ampicillin/Sulbactam	I	16
Cefazolin	R	>=64
Cefepime	S	<=1
Ceftazidime	S	<=1
Ceftriaxone	S	<=1
Cephalexin	R	
Gentamycin	S	<=1
Nitrofurantoin	S	<=16
Piperacillin/Tazobactam	S	<=4
Tobramycin	S	<=1
Trimethoprim/Sulfa	S	<=20

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Case Study #2

- 10 y/o female w/ cc: fever
- PMH: seasonal allergies
- Meds: Monteleukast, antihistamine
- S/S: fever (up to 101.1 F), fatigue, NO URI s/s
- Vitals: stable/unremarkable
- P/E: ABD: mild suprapubic tenderness, othwese exam WNL
- UA: dark yellow, slightly cloudy, SG- 1.020, nit +, leuk – small
  - Culture ordered
- Treatment: cephalexin --> nitrofurantoin

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Case Study #3

	E. coli 50,000-100,000 cfu/ml	
Drug	MIC Interp	MIC Dilutn
Amox/Clauv	I	16
Amp/Sulbactam	R	>=32
Ampicillin	R	>=32
Cefazolin	R	>=64
Ceftazidime	R	<=1
Ceftriaxone	R	>=64
Ciprofloxacin	R	>=4
ESBL	POSITIVE	POSITIVE
Gentamycin	R	>=16
Imipenem	S	<=0.25
Levofloxacin	R	>=8
Nitrofurantoin	S	32
Pip/Tazobactam	S	8
Trimeth/sulfa	S	<=20
Tobramycin	R	>=16

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Case Study #3

- 5 y/o female w/ cc: dysuria
- PMH: seasonal allergies, developmental delay per drug in utero
- Meds: Monteleukast, antihistamine, OTC decongestants
- S/S: dysuria, vulva irritation/pruritis
- Vitals: stable/unremarkable
- P/E: mild vulvar erythema, othwese exam WNL

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Case Study #4

- 56 y/o male cc: pre-op H & P for urologic procedure
- PMH: OSA, peripheral nerve d/o, neurogenic bladder- indwelling cath
- Meds: baclofen, gabapentin, oxy/APAP, ropinirole
- S/S: None
- Vitals: stable/unremarkable
- P/E: status quo for patient
- UA: Not needed
  - Culture ordered
- Treatment: per Urology

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Case Study #4

	E. coli >100,000 cfu/ml		Strep agalactiaciae (Group B strep) 50,000-100,000 cfu/ml	
Drug	MIC Interp	MIC Dilutn	MIC Interp	MIC Dilutn
Ampicillin	S	<=2	S	<=0.15
Cefazolin	S	<=4	S	
Cephalexin	S			
Clindamycin			R	4
Levofloxacin	R	2		
Gentamycin	S	<=1		
Nitrofurantoin	S	<=16		
Penicillin			S	<=0.12
Tetracycline			R	>=16
Tobramycin	S	<=1		
Trimeth/Sulfa	S	<=20		
Vancomycin			S	<=0.5

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Case Study #5

- 67 y/o female cc: " I have a bladder infection"
- PMH: HTN, GERD, Fe def anemia, HAs, OAB
- Meds: oral estrogen, HCTZ, verapamil, triptan, H2 blocker, oxybutynin
  - PRN cipro before/after sexual encounter
- S/S: dysuria
- Vitals: stable/unremarkable
- P/E: Overall WNL, +/- suprapubic pain
- UA: positive
  - Culture ordered
- Treatment: cephalexin

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Case Study #5

	E. coli >100,000 cfu/ml	
Drug	MIC Interp	MIC Dilutn
~~Amox/Clauv~~	~~S~~	~~4~~
~~Amp/Sulbactam~~	~~I~~	~~16~~
~~Ampicillin~~	~~R~~	~~>=32~~
Cefazolin	S	<=4
Ceftazidime	S	<=1
Cefriaxone	S	<=1
~~Ciprofloxacin~~	~~R~~	~~>=4~~
ESBL	NEGATIVE	NEGATIVE
~~Gentamycin~~	~~R~~	~~>=16~~
Imipenem	S	<=0.25
~~Levofloxacin~~	~~R~~	~~>=8~~
~~Nitrofurantoin~~	~~S~~	~~<=16~~
Pip/Tazobactam	S	<=4
~~Trimeth/sulfa~~	~~R~~	~~>=320~~
Tobramycin	I	8

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