



RhAPP

RHEUMATOLOGY ADVANCED
PRACTICE PROVIDERS

Inaugural National Conference

December 3 – 5, 2020

VIRTUAL CONFERENCE



RhAPP

RHEUMATOLOGY ADVANCED
PRACTICE PROVIDERS

Bugs & Drugs

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Disclosures

- No actual or potential conflicts of interest to disclose regarding this presentation

Learning Objectives

- Summarize the value of a local antibiogram
- Recognize potential short falls of antibiotics discussed
- Identify potential alternative antibiotic choices for the infectious processes discussed

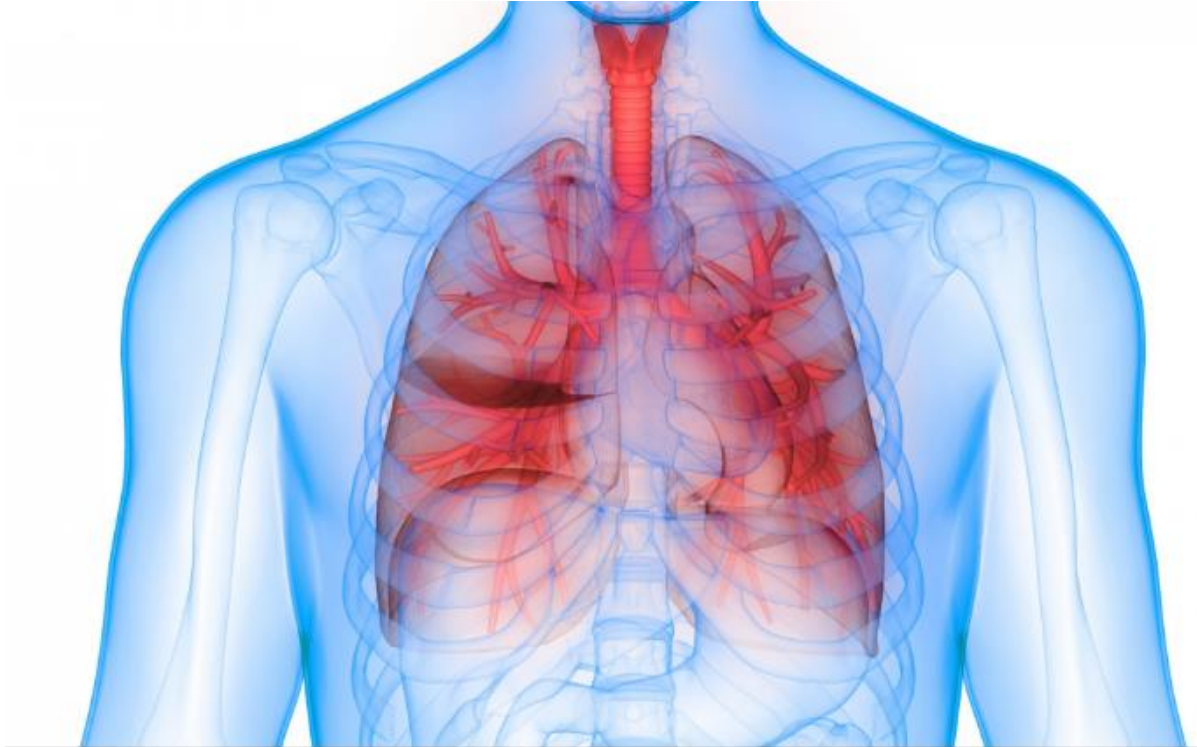
Antibiograms Are Your Friend

- Generally produced as a joint effort by infectious diseases and the microbiology laboratory
- Demonstrate local susceptibility rates of common pathogens to commonly used antibiotics
- Ask about this at your institution
 - Preferably an outpatient specific antibiogram

Antibiograms Are Your Friend

GRAM-NEGATIVE ORGANISMS	# Isolates	Amox/Clav	Ampicillin	Amp/Sulb	Aztreonam	Cefazolin (f)	Cefepime	Ceftriaxone	Cefuroxime	Ciprofloxacin (g)	Ertapenem	Gentamicin	Levofloxacin (g)	Meropenem	Nitrofurantoin
Escherichia coli (h)															
ED Systemic	33	93	54	66	90	84	90	90	90	90	100	93	90	100	–
ED Urine (i)	955	89	58	64	95	92	95	95	93	88	100	94	88	100	98
Outpatient Systemic	46	93	58	69	93	76	93	93	91	82	100	91	82	100	–
Outpatient Urine (i)	3,440	89	63	67	94	92	96	95	93	87	99	93	88	100	98
Klebsiella pneumoniae (h)															
ED Urine	96	90	R	78	92	90	92	92	86	91	100	96	95	99	46
Outpatient Urine	570	95	R	84	95	95	96	96	91	96	99	98	97	100	45
Pseudomonas aeruginosa															
ED Urine	36	R	R	R	86	R	94	R	R	80	R	86	77	95	R
Outpatient Systemic	69	R	R	R	89	R	92	R	R	91	R	95	92	97	R
Outpatient Urine	149	R	R	R	90	R	93	R	R	81	R	86	81	100	R

Azithromycin for Community Acquired Pneumonia (CAP)



Azithromycin for CAP

Common pathogens in community acquired pneumonia (CAP)

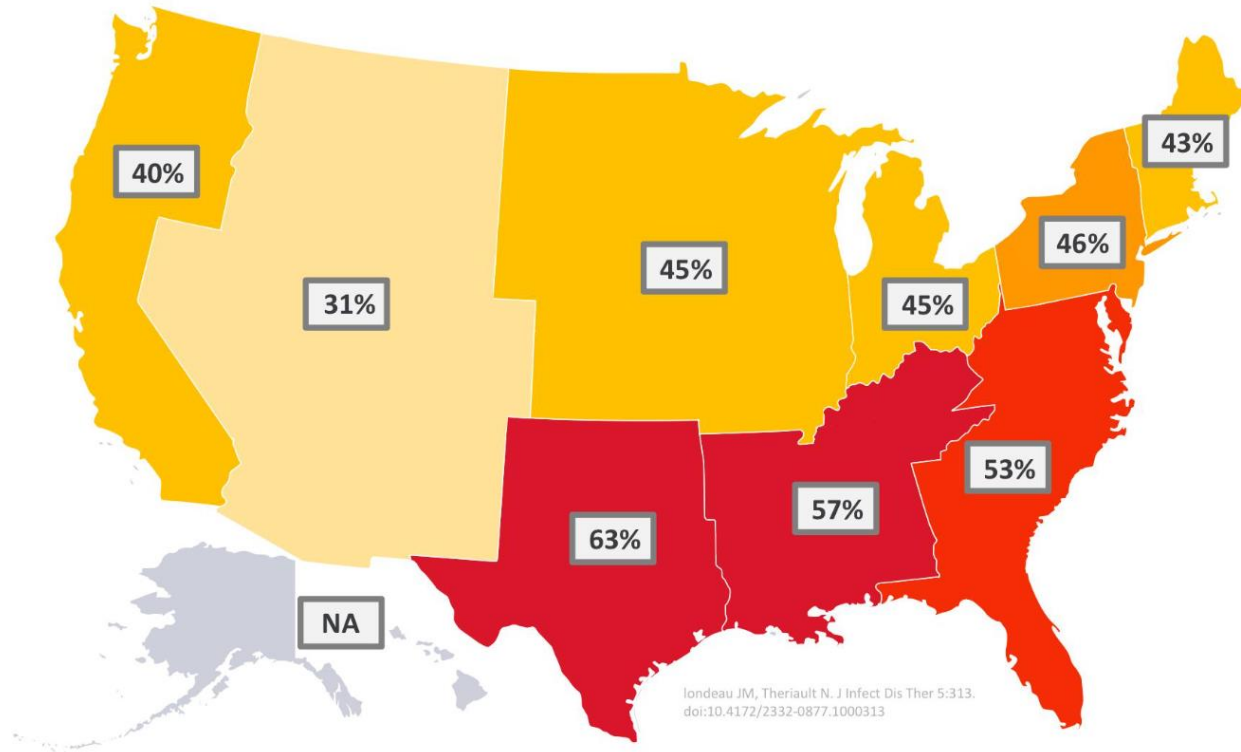
Typicals

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*

Atypicals

- *Mycoplasma pneumoniae*
- *Chlamydia pneumoniae*
- *Legionella spp.*

S. pneumoniae Resistance to Azithromycin



Azithromycin: Alternative for CAP

- Doxycycline
 - Less resistance
 - Same duration
 - Generally well tolerated
 - Avoid taking with foods or medications containing Ca^{2+} , NaHCO_3 , Zn^{2+} , Fe, Mg^{2+} (2 hours before or 6 hours after) to avoid chelation
 - Causes sensitivity to the sun

Sulfamethoxazole/Trimethoprim for Urinary Tract Infection (UTI)



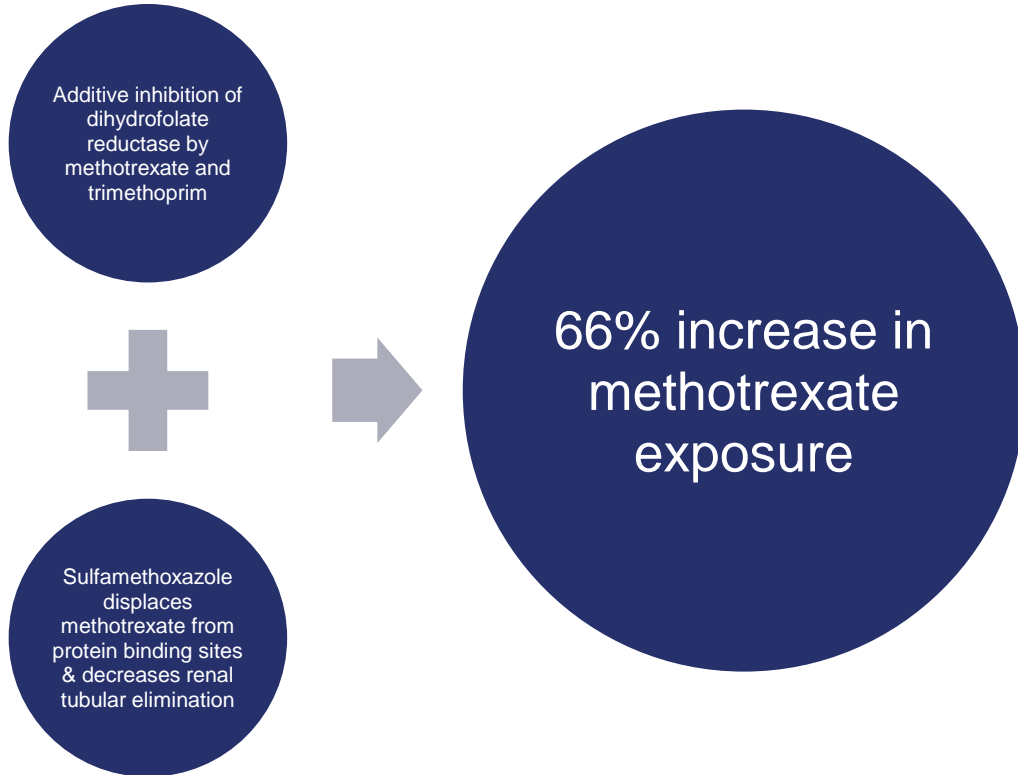
Sulfamethoxazole/Trimethoprim for UTI

Review > Clin Infect Dis 2011 Mar 1;52(5):e103-20. doi: 10.1093/cid/ciq257.

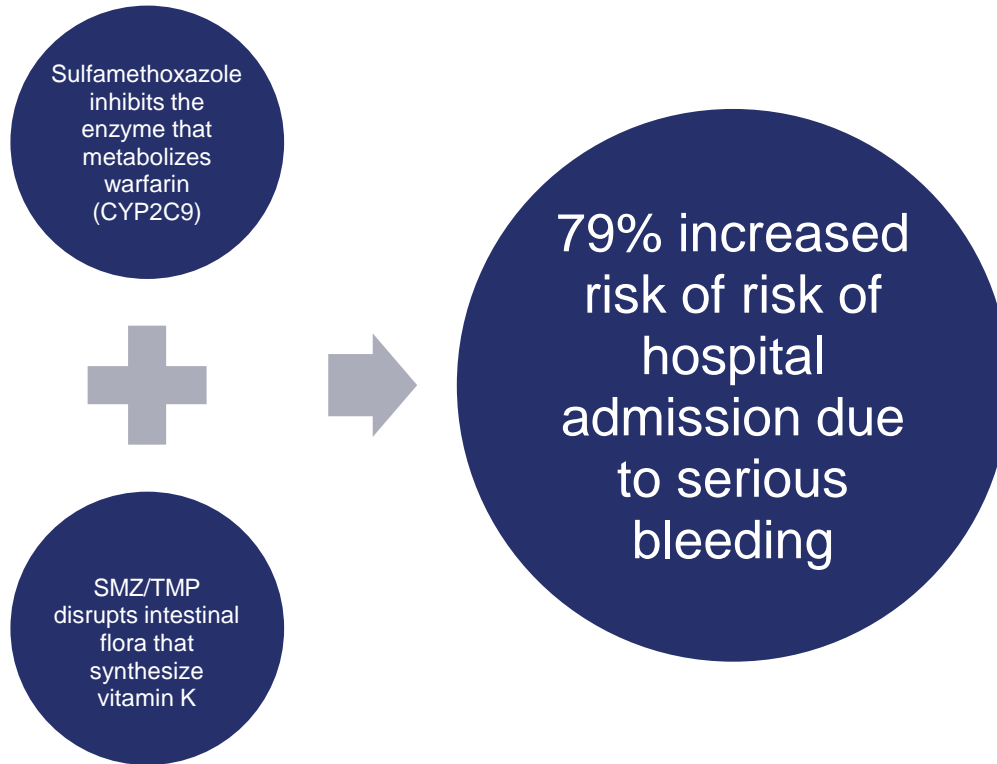
International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases

- IDSA recommends against empiric use when *E.coli* resistance is >10%
- Adverse affects
- Drug-drug interactions

Sulfamethoxazole/Trimethoprim Drug-Drug Interactions of Note: Methotrexate



Sulfamethoxazole/Trimethoprim Drug-Drug Interactions of Note: Warfarin



Sulfamethoxazole/Trimethoprim Drug-Drug Interactions of Note: ACE Inhibitors, ARBs, Spironolactone

Trimethoprim
impairs renal
potassium
excretion

Additive
potassium
sparing effects
w/ ACEi,
ARBS, &
spironolactone

12 times higher risk
of hyperkalemia
then with other
antibiotics

Sulfamethoxazole/Trimethoprim : Alternatives for Lower UTI

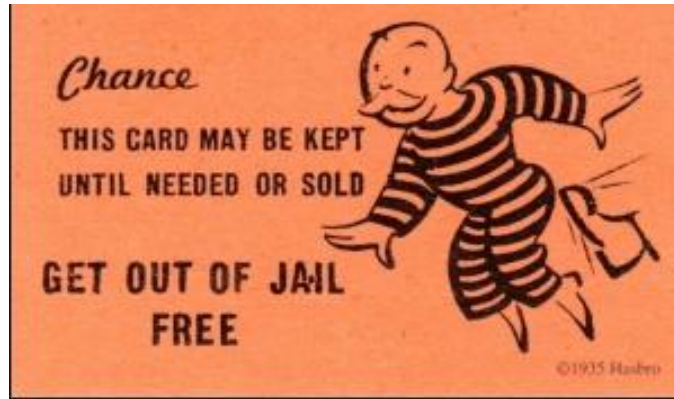
- Nitrofurantoin
 - Extremely low resistance to common urinary pathogens
 - Well tolerated
 - Data for use in patients with creatinine clearance as low as 30 ml/min

Sulfamethoxazole/Trimethoprim : Alternatives for Lower UTI

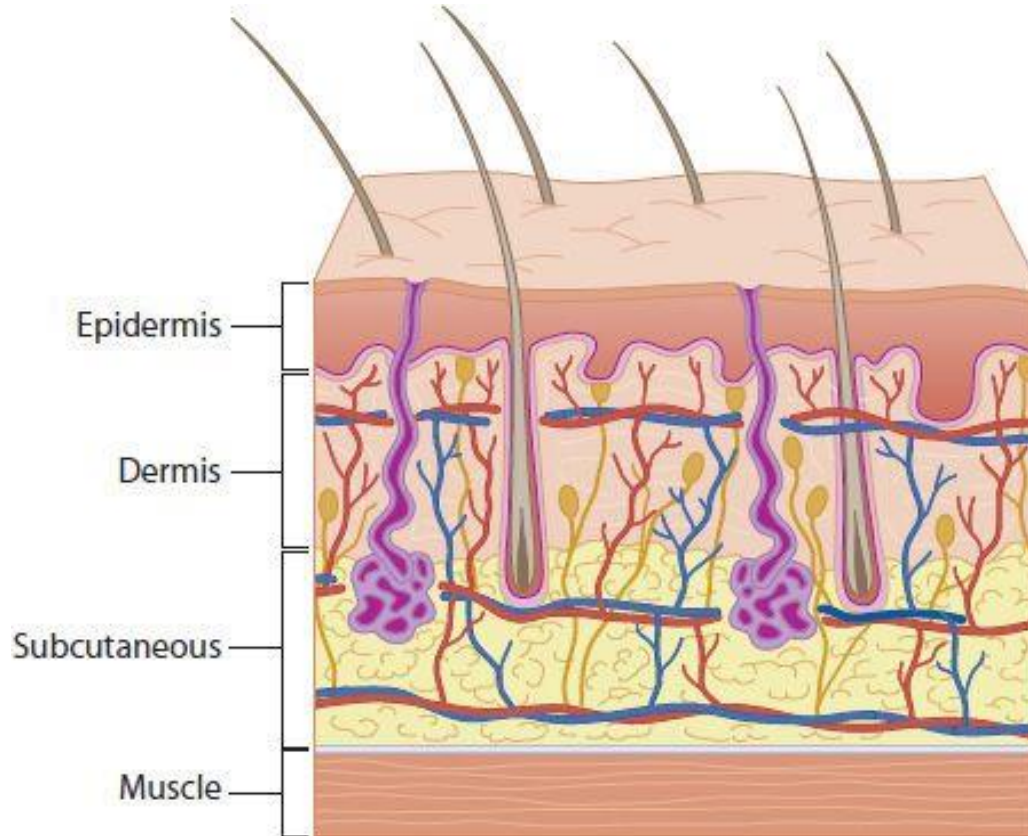
- Cephalexin
 - Generally well tolerated
 - Less resistance for lower cystitis
 - Clinical & Laboratory Standards Institute (CLSI) has higher breakpoints for systemic infections such as pyelonephritis
 - Use caution in this population

Alternatives for Lower UTI

- Fosfomycin
 - Uncomplicated: 3g PO x1
 - Complicated: 3g PO q48h x 3 doses



Clindamycin for Skin and Soft Tissue Infection (SSTI)



Clindamycin for SSTI

- *Staphylococcus aureus* resistance
 - Inducible resistance
- Adverse affects
 - Diarrhea
 - *Clostridioides difficile* infection
 - Odds ration 15-20 x placebo

Clindamycin: Alternatives for SSTI

Purulent SSTI

- Trimethoprim/sulfamethoxazole
- Doxycycline

Non-purulent

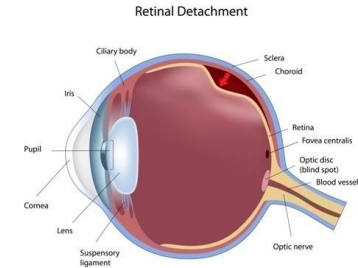
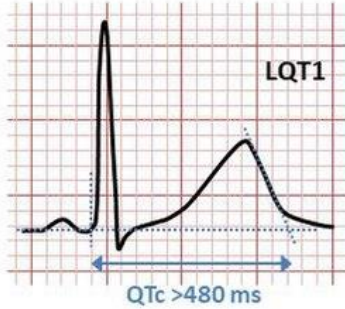
- Dicloxacillin
- Cephalexin

Alternatives for SSTI

- Linezolid
 - Available as a generic which has greatly reduced its price
 - Caution
 - Serotonin syndrome when combined with other pro-serotonergic medications
 - Myelosuppression
 - Associated with therapy ≥ 14 days



Fluoroquinolones Are Not Your Friend



Fluoroquinolones – Adverse Effects

Commonly Known Adverse Effects	Lesser Know Adverse Effects
QT Prolongation	GI Perforation
<i>Clostridioides difficile</i> infections	Aortic aneurism/dissection
Tendinopathy	Retinal detachment
Peripheral neuropathy	Hypo/Hyperglycemia
Black box warnings	Seizures/Psychiatric AEs

Fluoroquinolones: Other Issues

- Increasing resistance
 - Low barrier
- These are the only oral options we have with activity against *Pseudomonas aeruginosa*

Fluoroquinolones: Alternatives

UTI

Nitrofurantoin,
cephalexin

PNA

Doxycycline,
cefuroxime + azithromycin

Sinusitis

Amoxicillin/Clavulanate,
doxycycline

Tools to Bring Home

Urinary Tract Infection: Outpatient Prescribing Recommendations

Uncomplicated Cystitis

	Agent/dosing*	<i>E. coli</i> SUSC. †
1 st line	Nitrofurantoin 100mg BID x 5 days	98%
2 nd line	Cephalexin 500mg BID-TID x 3 – 5 days	92%
Other options	Cefuroxime 250mg BID x 3 – 5 days	93%
	Cefdinir 300mg BID x 3 – 5 days	93%
	SMX/TMP DS 1 tab BID x 3 days	79%
	Cipro 250mg BID x 3 days Levaquin 250 daily x 3 days	88%

* Dosing assumes normal renal function; consult [PseudoQ](#) for renal dose adjustments

† Per 2018 [antibiogram](#).

Complicated Cystitis

	Agent/dosing*	<i>E. coli</i> SUSC. †
1 st line	Nitrofurantoin 100mg BID x 5 days†	98%†
2 nd line	Cephalexin 500mg TID x 7 days	92%
Other options	Cefuroxime 250mg BID x 7 days	93%
	Cefdinir 300mg BID x 7 days	93%
	SMX/TMP DS 1 tab BID x 5-7 days	79%
	Cipro 250mg BID x 5-7 days Levaquin 250mg daily x 5-7 days	88%

* Dosing assumes normal renal function; consult [PseudoQ](#) for renal dose adjustments

† Per 2018 [antibiogram](#). ‡ Avoid use in men

Pyelonephritis

	Agent/dosing*	<i>E. coli</i> SUSC. †
1 st line	Cefuroxime 500mg po BID x 10-14 days	93%
Other options	Cefdinir 300mg BID x 10-14 days	93%
	SMX/TMP DS 1 tab BID x 14 days	79%
	Cephalexin 500mg QID x 10-14 days	84%
	Ciprofloxacin 500mg BID x 7 days Levofloxacin 750mg daily x 5 days	88%

* Dosing assumes normal renal function; consult [PseudoQ](#) for renal dose adjustments

† Per 2018 [antibiogram](#); urinary isolates

UTI: Empiric Coverage of Pseudomonas

	Agent/dosing*
Uncomplicated	Ciprofloxacin 250mg BID x 3 days Levofloxacin 250mg daily x 3 days
Complicated	Ciprofloxacin 250mg BID x 5-7 days Levofloxacin 250mg daily x 5-7 days
Pyelonephritis	Ciprofloxacin 500mg BID x 7 days Levofloxacin 750mg daily x 5 days

* Dosing assumes normal renal function; consult [PseudoQ](#) for renal dose adjustments

Pseudomonas spp. risk factors include but not limited to:

- 1.) Urine culture with *Pseudomonas* spp. within 4 weeks
- 2.) Hospitalized within 90 days
- 3.) Reside in nursing home/LTAC
- 4.) Receive hemodialysis
- 5.) Antibiotics or chemotherapy within 30 days

A note about Fluoroquinolones

FQs carry multiple boxed warnings and have been associated with many severe adverse reactions:

Commonly Known Adverse Effects	Lesser Known Adverse Effects
QT prolongation	GI perforation
<i>Clostridium difficile</i> infection	Aortic aneurysm/dissection
Tendinopathy	Retinal detachment
Peripheral neuropathy	Hypo/hyperglycemia
	Seizures

- FQs have a low barrier to resistance.
- Resistance rates to FQs have increased rapidly.
- Ciprofloxacin and levofloxacin are our only oral agents with reliable activity against *Pseudomonas* spp.
- FQs should be reserved for a few clinical scenarios where other antibiotics are not safe or feasible.

Likely Pathogens: Community Acquired UTI

Uncomplicated Cystitis	<ul style="list-style-type: none"> • <i>E. coli</i> (75-95%) • Other Enterobacteriaceae • <i>S. saprophyticus</i>
Complicated Cystitis	<ul style="list-style-type: none"> • <i>E. coli</i> (65%) • <i>Klebsiella</i> spp. (8%) • <i>Pseudomonas</i> spp. (2%) • Gram-positive cocci (10-12%)
Pyelonephritis	<ul style="list-style-type: none"> • <i>E. coli</i> (70-95%) • Other Enterobacteriaceae • <i>S. saprophyticus</i>

Updated 2/2020.

This is intended as a guide for evidence-based decision-making and should not replace clinical judgement.

Tools to Bring Home

Urinary Tract Infection: Outpatient Prescribing Recommendations

Uncomplicated Cystitis

	Agent/dosing*	<i>E. coli</i> susc.†
1 st line		
2 nd line		
Other options		

* Dosing assumes normal renal function; consult [PharmQ](#) for renal dose adjustments
† Per 2018 [acbilograp](#).

Complicated Cystitis

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Pyelonephritis

	Agent/dosing*	<i>E. coli</i> susc.†
1 st line		93%
Other options		

* Dosing assumes normal renal function; consult [PharmQ](#) for renal dose adjustments
† Per 2018 [acbilograp](#), urinary isolates

UTI: Empiric Coverage of *Pseudomonas*

	Agent/dosing*
Uncomplicated	
Complicated	
Pyelonephritis	

* Dosing assumes normal renal function; consult [PharmQ](#) for renal dose adjustments

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Conclusion

- Local antibiograms can help determine which antibiotic therapy is best for empiric therapy
- Azithromycin monotherapy for CAP is unlikely to be the optimal empiric therapy
- Clindamycin for SSTI is unlikely to be the optimal empiric therapy
- Fluoroquinolones carry a long list of adverse effects, are experiencing increased resistance, and should be reserved



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Questions?