



CENTER FOR
STEWARDSHIP
IN MEDICINE

Antibiotic GUIDE

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The University of Washington Center for Stewardship in Medicine (UW CSiM) empowers antimicrobial stewardship teams by providing education, mentoring, community building, and resource sharing. By combining the resources available in our urban academic setting with the expertise of rural health providers, antimicrobial stewardship program implementation has been accelerated throughout the region with far reaching benefits to our community.

UW CSiM created the CSiM Antibiotic Guide to provide clinicians with a tool to guide prescribing based on local antibiotic resistance data and expert opinion. The guide has been vetted and updated by antibiotic stewards of participating rural and critical hospitals. General treatment principles and guidance are relevant to antimicrobial stewardship teams regardless of geography. Specific antibiotic recommendations are based upon bacterial resistance patterns seen in the Pacific Northwest region of the United States but may be applicable to sites outside of the region depending on local microbiology. Antibiotics listed should be compared to local bacterial resistance trends found in your antibiogram to determine applicability.

These guidelines are intended to support clinical decision-making but should not replace individual patient assessment or provider judgment. We encourage clinical discretion and welcome any feedback to improve these guidelines for future iterations. For more information, please login to the UW CSiM website at www.uwcsim.org. Your username is on the cover of this guide.

Enter the username at the top right of the UW CSiM homepage, please see the image below for detail.



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ANTIMICROBIAL STEWARDSHIP: GENERAL PRINCIPLES AND APPROACHES

The Agency for Healthcare Research and Quality (AHRQ) identifies 4 key moments of decision-making for antimicrobial prescribing. This easy to remember approach can be used in most clinical settings and is outlined below.

CONSIDER THE FOUR MOMENTS OF ANTIBIOTIC DECISION MAKING

MOMENT 1: The Diagnosis

“Does this patient have an infection that requires antibiotics?”

Isolated changes in clinical status, lab values or vital signs ALONE should not trigger initiation of antibiotics. This is the time to pause and consider infectious and alternative non-infectious causes. Delirium in the elderly, aspiration pneumonitis, atelectasis, congestive heart failure, venous stasis, emboli, asymptomatic bacteriuria and/or pyuria are common examples of non-infectious conditions that are frequently treated with antibiotics unnecessarily.

MOMENT 2: Initial Steps

“Have I obtained appropriate cultures before starting antibiotics?”

“What empiric antibiotic therapy should I initiate?”

“How do I ensure timely administration of appropriate empiric antibiotic therapy?”

Many community acquired infections can be treated empirically using local or regional guidelines tuned to surveillance microbiology data (i.e. antibiograms). Complicated, high-risk cases, recurrent infections, or patients at risk for drug resistant infections are most likely to benefit from reliable and timely microbiology. A standardized or institutional approach to treating common infections minimizes the delay to appropriate therapy.

NOTE *Procedures for optimal culture ordering, collection and reporting are detailed in the Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology. The UW TASP guide does highlight some organism and syndrome-specific notes pertinent to empiric antimicrobial selection.*

MOMENT 3: Modification/De-escalation

“A day or more has passed. Can I stop antibiotics?”

“Can I narrow therapy?”

“Can I change from intravenous to oral therapy?”

Performing a regular antibiotic time-out for every patient on antibiotics with review of available microbiological data is the standard of care. Documentation in the medical record should include the anti-infective regimen, indication, the day of treatment, reasoning behind continuation or modification to regimen, plan for narrowing or transitioning to oral, and anticipated total duration. “The antibiotic time out” is best achieved through input by those involved in the prescribing, dispensing, administration and monitoring of antibiotics and hospital/clinic wide implementation. A team approach with comprehensive and clear documentation ensures the survival of the therapeutic plan through all transitions of care.

NOTE *Rapid diagnostics using molecular platforms and disease markers like procalcitonin have shortened the time from days to hours for usable lab/microbiology data. However, it is helpful to know your local lab tools and institutional protocols for result turn around and result interpretation.*

MOMENT 4: Duration

“What duration of antibiotic therapy is needed for this patient’s diagnosis?”

Most common infections can be treated in 5 days or fewer. The total antibiotic duration count should include the first day appropriate empiric therapy was provided plus the days of targeted therapy. Minimizing excessive antibiotic exposure reduces the likelihood of drug side-effects, drug- drug interactions, antibiotic associated diarrhea including *C. difficile*, and resistance. Durations should be based on the current literature and initial clinical response.

ANTIBIOTIC RESISTANCE PEARLS

Regional resistance trends in the Pacific Northwest were utilized to drive agent selection for the UW TASP Antibiotic guide. Some customization of this guide may be warranted based upon your local antibiogram or drug formulary.

To learn more about regional antibiotic resistance, visit your state's Department of Health website for posted regional antibiograms or your local hospital antibiogram.

The following is a summary of observations for drugs and bugs that may help you in antibiotic selection:

GRAM-NEGATIVE BACTERIA AND ANTIMICROBIAL RESISTANCE:

Gram-negative bacteria like *E. coli*, *Klebsiella spp.*, *Enterobacter*, *Acinetobacter*, and *Pseudomonas* are becoming increasingly drug resistant. Some of these organisms are intrinsically resistant due to structure or the production of specific beta-lactamases. Over time, the repeated introduction of new genes on mobile plasmids is increasing the risk of resistance. This is especially concerning for empiric therapy for community-acquired infections since that therapy needs to cover essentially all probable bacterial pathogens. Although this is a very broad and complex topic, we are including a few examples below to help as you think through potential treatment options and/or interpret guidelines.

There has been a slow increase in resistance to the fluoroquinolone class of antimicrobials over the last 20 years. Fluoroquinolones may not be the best option as empiric treatment for upper tract UTIs or gastrointestinal infections. In Washington state surveillance data demonstrate about 15% fluoroquinolone resistance in *E. coli*, the most common community-acquired Gram-negative pathogen. Treatment guidelines discourage empiric use of TMP/ SMX for *E. coli* coverage when local susceptibility trends demonstrate resistance rates $\geq 20\%$, which is consistently observed in the Pacific NW. Similarly, ampicillin/sulbactam is no longer reliable for empiric coverage of *E. coli* due to rates of resistance commonly in the 30-40% range.

ESBL (extended spectrum beta-lactamase) Producers

Typical organisms: *E. coli*, *Klebsiella spp.*, *Proteus*

Incidence: Between 25-30% of *Enterobacteriales* (e.g. *E. coli*) in US hospitals according to CDC data published in 2023.

Resistance pattern: Can be susceptible to cephamycins (cefoxitin and cefotetan) and resistant to first and third generation cephalosporins

Recommended treatment: Although cephamycins show in-vitro susceptibility, they are **NOT** used for clinical ESBL infections. For serious infections due to ESBL-producing bacteria, carbapenems or non-beta lactam antibiotics demonstrating susceptibility (fluoroquinolones, trimethoprim-sulfamethoxazole) are the best option, even if the organism is susceptible to drugs like piperacillin-tazobactam or cefepime.

GRAM-POSITIVE BACTERIA AND ANTIMICROBIAL RESISTANCE:

Drug-resistance in Gram-positives has been prevalent since the 1990s, most commonly in *Staphylococcus aureus* and *Enterococcus faecium*.

Staphylococcus aureus

S.aureus is a highly virulent organism and can cause a variety of clinical syndromes from mild skin and soft tissue infections to life-threatening endovascular infections.

Methicillin-sensitive *Staphylococcus aureus* (MSSA)

Resistance pattern: *S. aureus* isolates sensitive to methicillin/oxacillin are also sensitive to naftillin, ampicillin-sulbactam, amoxicillin-clavulanate, cefazolin and cephalexin. Often remains highly sensitive to the tetracycline class and TMP-SMX.

Recommended treatment: Cefazolin and in some cases, naftillin, is appropriate first-line therapy for treatment of serious MSSA infections. Although ceftriaxone is active against MSSA, it should not be used first line as clinical failures have been reported in the literature. The preferred oral agents for MSSA infections are cephalexin (should be avoided in serious infections such as bacteraemia, endocarditis or osteomyelitis), dicloxacillin or TMP- SMX.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Resistance pattern: MRSA are resistant to essentially all beta-lactams, including cefazolin. Clindamycin is utilized in pediatric MRSA infection however susceptibility is variable and should be confirmed.

Recommended treatment: Vancomycin remains the drug of choice to treat hospitalized patients for MRSA infections; linezolid is also an option for patients who can tolerate oral administration. TMP-SMX and doxycycline are preferred for ambulatory patients. Daptomycin has reliable MRSA coverage and may be easier to dose compared to vancomycin. It is associated with greater expense and should not be used in pulmonary infection given its inactivation by pulmonary surfactant. Note that

NOTE

- *Ceftaroline, a 5th generation cephalosporin with anti-MRSA activity, may be warranted in patients with persistent bacteremia, often in combination with daptomycin. Cases with persistent bacteremia may benefit from expert ID consultation.*
- *Staphylococcus lugdenensis is a coagulase-negative staphylococcus but has more invasive potential. It can cause infections similar to S.aureus, and it should not be treated as a contaminant until proven otherwise in clinical specimens*

Rifampin should not be used as monotherapy for *S.aureus* due to rapid development of resistance and subsequent clinical failure.

Streptococci

Among *Streptococcus pneumoniae* in the United States, there are high rates of resistance to macrolides and TMP-SMX. As a result, azithromycin and TMP-SMX are not recommended for empiric treatment options where coverage for *S. pneumoniae* is critical, such as most pediatric upper respiratory infections.

Groups A, B, C and G Streptococci are universally susceptible to penicillin and cefazolin; therefore, local testing and reporting is not necessary.

Streptococcus pyogenes (Group A strep) and *S. agalactiae* (Group B strep) may exhibit clindamycin resistance in up to >20% of cases, and up to 50% in certain areas. Confirm clindamycin susceptibility in serious streptococcal infections prior to use.

Enterococcus

Enterococci are generally low virulence organisms that grow well in bacterial cultures and are often over-treated with antibiotics. Urinary tract infections due to enterococci are often catheter or instrumentation-associated; bacteremia from a urinary source occurs infrequently. *Enterococcus* is a component of mixed flora in intra-abdominal and pelvic cultures and therapy specifically directed against this pathogen may not be warranted. Non-antimicrobial treatments for enterococcal infections include catheter removal, percutaneous or surgical drainage, I&D and debridement.

Enterococcus faecalis

Resistance pattern: remain highly sensitive to ampicillin, nitrofurantoin, and vancomycin. Piperacillin and amoxicillin activity can be extrapolated from ampicillin susceptibility. Note that trimethoprim-sulfamethoxazole (TMP-SMX) has unreliable activity against enterococci and is not tested due to the inherent ability of the organisms to take up exogenous folate.

Recommended treatment: cephalosporins and nafcillin **cannot** be used to treat enterococcal infections due to intrinsic resistance. Ampicillin alone is reasonable treatment for most *E. faecalis* infections. Endocarditis merits combination therapy.

Enterococcus faecium

Resistance pattern: high-level beta-lactam resistance is common.

Intrinsic resistance to cephalosporins and most carbapenems.

These

organisms are often resistant to vancomycin as well, otherwise known as vancomycin-resistant enterococci (VRE).

Recommended treatment: Linezolid or daptomycin should be reserved for complicated VRE infections with or without bacteremia. Higher doses of daptomycin (10-12mg/kg) are recommended when used for severe enterococcal infections. VRE cystitis has been successfully treated with amoxicillin, despite documented lab resistance, because of high concentrations drug achieved in the bladder.

NOTE

- *Daptomycin should not be used to treat pneumonias due to drug degradation in the presence of surfactant. Linezolid has been associated with very rare but serious serotonergic reactions especially in combination with other agents (e.g. SSRIs, methadone). Patients should be educated of signs and symptoms and instructed to contact a clinical provider immediately should they occur.*

IS IT REALLY A PENICILLIN ALLERGY?

An accurate medication allergy history is the responsibility of every health care provider. It is imperative that antibiotic allergies be clarified, captured and, when appropriate, corrected in the electronic medical record. Here we will focus on Type I allergic reaction, which is an immunoglobulin E-mediated adverse reaction that would be expected to be reproducible upon re-challenge. A credible antibiotic allergy history includes two elements:

1. A specific recollection of the drug taken, the time elapsed between drug administration and drug reaction, and a specific description of symptoms that occurred during the drug reaction, AND
2. The symptoms during drug reaction being consistent with a serious hypersensitivity reaction. The more specific the symptoms of a drug reaction resemble an anaphylactic reaction, the more concerning and “credible” the history.

FACTS ABOUT PENICILLIN ALLERGY (TYPE 1, IMMUNOGLOBULIN E (IgE)-MEDIATED)

1. Approximately 10% of all U.S. patients report having an allergic reaction to a penicillin class antibiotic in their past.
2. However, many patients who report penicillin allergies do not have true IgE-mediated reactions. When evaluated, fewer than 1% of the population are truly allergic to penicillins.
3. Approximately 80% of patients with IgE-mediated penicillin allergy lose their sensitivity after 10 years.
4. Broad-spectrum antibiotics are often used as an alternative to penicillins. The use of broad-spectrum antibiotics in patients labeled “penicillin-allergic” is associated with adverse drug effects, sub-optimal antibiotic therapy, higher healthcare costs, and an increased risk for antibiotic resistance. Patients with a reported penicillin allergy had a 50% increased risk of developing a surgical site infection, attributable to the receipt of second-line perioperative antibiotics.
5. Correctly identifying those who are not truly penicillin allergic can decrease unnecessary and inappropriate use of antimicrobials.
6. Updated national expert Allergy guidelines state that cephalosporins with dissimilar side chains can be safely given to patients with a penicillin allergy (even if there is a history of anaphylaxis).

TAKING A HISTORY

Before prescribing, administering, or considering broad-spectrum antibiotics to a patient thought to be penicillin-allergic, evaluate the patient for true penicillin allergy (Ig-E mediated) by conducting a history.

Questions to ask to understand a patient's penicillin allergy:

- What medication were you taking when the reaction occurred?
- What kind of reaction occurred and how soon after taking the medication did the reaction occur?
- How long ago did the reaction occur?
- How was the reaction managed?
- What was the outcome?
- Have you ever received amoxicillin, ampicillin or penicillin since having the allergy?

Characteristics of an Immediate, IgE-mediated (Type 1) reaction:

Reactions that generally occur within 1 hour, but in some cases ≤6 hours after drug exposure. Phenotypically, these reactions may present with:

- Hives: Multiple pink/red raised areas of skin that are intensely itchy
- Angioedema: Localized edema without hives affecting the abdomen, face, extremities, genitalia, oropharynx, or larynx
- Bronchospasm: Wheezing and shortness of breath

Anaphylaxis is an acute, life-threatening, systemic IgE mediated reaction that occurs minutes and within 6 hours of exposure. Though several diagnostic criteria exist, anaphylaxis is likely if two or more of the following suddenly occur after exposure to likely allergen:

- 1) Skin or mucosal symptoms: generalized hives, itch-flush, swollen lips-tongue-uvula
- 2) Respiratory symptoms: shortness of breath, wheezing, cough, stridor, hypoxemia
- 3) Reduced blood pressure or symptoms of end-organ dysfunction: collapse, incontinence
- 4) Severe Gastrointestinal symptoms: crampy abdominal pain, vomiting

The PENFAST score is a clinical decision-making tool designed to determine risk of reaction to penicillin antibiotics. The PENFAST score has a high negative predictive value (NPV) that can help identify patients with low-risk penicillin allergy who do not require skin testing prior to oral penicillin challenge.

Link to calculator: https://qxmd.com/calculate/calculator_752/pen-fast-penicillin-allergy-risk-tool

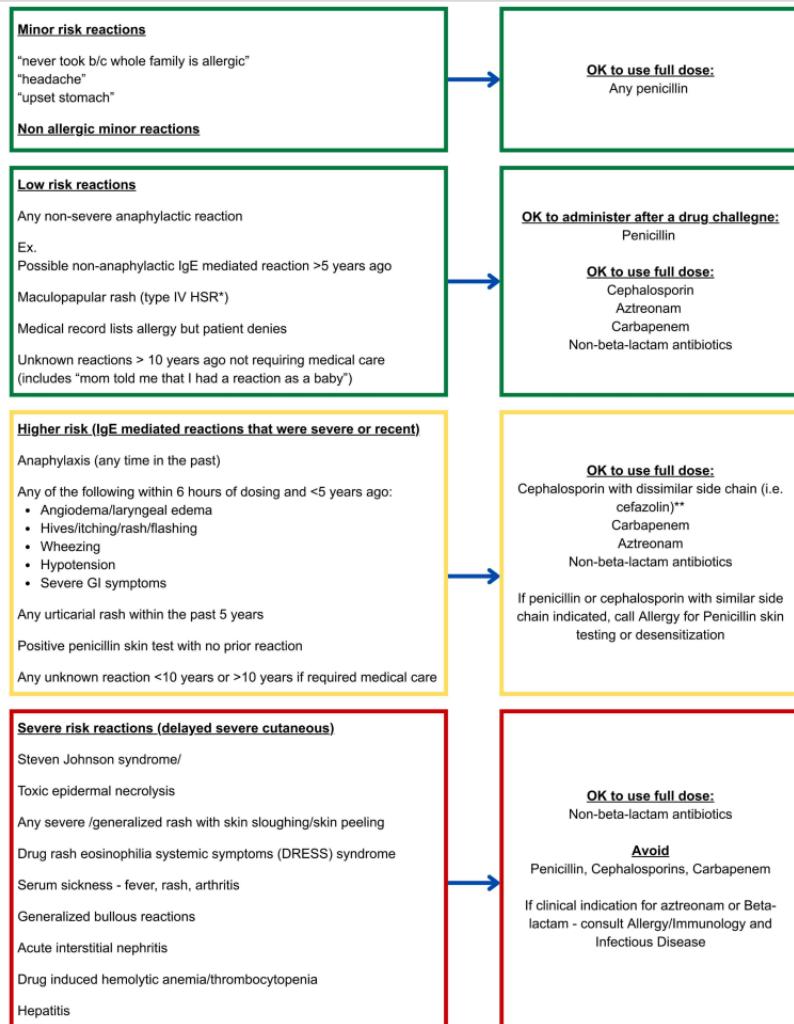
Characteristics of a Delayed, T Cell-mediated reaction:

Reactions that generally evolve over days to weeks following exposure to the drug. These reactions may present as:

- Benign exanthems: morbilliform drug eruption
- Drug reaction with eosinophilia and systematic symptoms (DRESS)
- Stevens-Johnson Syndrome (SJS)
- Toxic epidermal necrolysis (TEN)

Guidance on the evaluation and management of delayed hypersensitivity reactions will not be discussed in this review. Consult Allergy/Immunology and Infectious Disease if a delayed cutaneous reaction is suspected.

If Patient Has a Reported Penicillin Allergy Follow This:



*HSR: Hypersensitivity reaction. **See below for inpatient test dose procedure. For outpatient test dose and skin testing, refer to allergy clinic. Cefazolin in Penicillin allergy - see reference 13 and 14. ** See beta lactam cross-reactivity table

BETA-LACTAM CROSS REACTIVITY

Cross-reactivity refers to drugs with similar chemical structures that can cause similar allergic reactions. Penicillin and cephalosporins share common structures and cross-reactivity is largely based on the agent's R1 side chains. Structurally similar and/or identical R1 side chains between various beta-lactams puts patients at risk for cross-reactivity. Beta-lactams with dissimilar R1 side chains are at a low risk for cross-reactivity. Figure 2 describes the risk of cross-reactivity between R-side chains of beta-lactam antibiotics.

NOTE *Patients with more severe delayed hypersensitivity reactions — SJS, TEN, serum sickness, acute interstitial nephritis, hemolytic anemia, and DRESS—should not use the offending drug in the future.*

How to safely give beta-lactams in patients with penicillin allergies

Cephalosporins

Soon after the introduction of cephalosporins, anaphylaxis was reported in patients with prior reactions to penicillin. In the 1970s, a number of reviews examined the rate of allergic reactions to cephalosporins in penicillin allergic patients. One study found that 4.5% of about 16,000 patients exposed to penicillin had an allergy history; of the patients with allergy histories, 8% had a reaction to a cephalosporin. The 8% figure, rounded to 10%, has often been cited as the “rate” of cross-reactivity. However, more recent observations discredit the magnitude of this figure.

If a patient reports an allergy to penicillin, and a cephalosporin is ordered, the following recommendations can be made:

1. For a patient with a non-anaphylactic penicillin reaction (such as non-severe type IV reaction like maculopapular rash anytime in the past, non-anaphylactic IgE mediated reactions like isolated hives or swelling not affecting the airway >5 years ago, itching with no rash) cephalosporins can be given safely. This is especially true for a history of skin eruptions that do not involve itching or edematous wheals .
2. For patients with a history of a severe IgE-mediated penicillin reaction, the risk of a repeat reaction to an agent with a similar side chain is about 0.4%. The risk is nearly zero with agents with dissimilar side chains, therefore **most** cephalosporins can be given normally. If a cephalosporin with a structurally similar side chain is desired in a patient with a severe IgE-mediated penicillin allergy, penicillin skin testing, if available, should be utilized to guide further treatment.

NOTE *The cephalosporins that share the same side chain with ampicillin or amoxicillin include cefaclor, cefadroxil, and cephalexin. Therefore, these agents should not be given to patients with a history of anaphylaxis to ampicillin, amoxicillin or penicillin.*

NOTE Cefotaxime, cefpodoxime, ceftriaxone and cefepime share the same side chains and have the potential for cross-reactivity amongst the third and fourth generation cephalosporins also due to side chain cross-reactivity, but do not have cross-reactivity with penicillin or amoxicillin.

NOTE Cefazolin has a unique side chain and does not cross-react with penicillins.

3. For patients with a history of severe delayed hypersensitivity reactions (SJS, TEN, DRESS, hemolytic anemia, serum sickness), avoidance of all beta-lactam agents is recommended. Skin testing and drug challenges are also not appropriate in this setting.

Piperacillin-tazobactam

Some patients can be specifically allergic to piperacillin-tazobactam but tolerate other penicillins. Since this requires additional testing, the conservative approach remains to avoid other penicillin antibiotics such as ampicillin, amoxicillin, cefadroxil, cephalexin, cefaclor, or cefprozil. See Figure 2.

Carbapenems

The risk of cross-reactivity between penicillin and any carbapenem is low. A recent systematic review including 1127 penicillin-allergic patients demonstrated a 0.87% risk of cross-reactivity. Patients with a penicillin or cephalosporin allergy (excluding those with a severe delayed cutaneous or organ-involved reaction) can safely receive any carbapenem without prior testing.

Aztreonam

Aztreonam is a monobactam with no risk of cross-reactivity for IgE mediated hypersensitivity reactions between penicillins or cephalosporins, except for ceftazidime (due to the shared R1 side chain). Patients with a penicillin or cephalosporin allergy, except for ceftazidime, can safely receive aztreonam without prior testing.

NOTE Aztreonam does not have activity against aerobic and anaerobic gram-positive bacteria.

ANTIMICROBIAL DENSENSITIZATION AND DRUG CHALLENGE

Guidance on induction of tolerance (ie desensitization) and drug challenges (ie test doses) are not discussed in this review. Please refer to Drug Allergy Update 2022.

Figure 2: Beta-lactam R1 Side Chain Cross-reactivity Matrix

		β-Lactam Side Chain Cross Reactivity Chart																																					
		PEN			1st GEN		2nd GEN			3rd GEN			4th		5th		None	CARB	M																				
		Amoxicillin	Ampicillin	Nafcilin/Oxacillin	Penicillin G/V	Piperacillin	Pivmecilinam	Cefadroxil	Cefazolin*	Cephalexin	Cefaclor	Cefotetan	Cefoxitin	Cefprozil	Cefuroxime	Cefdinir	Cefixime	Cefotaxime	Ceftriazone	Cefepime	Ceftriaxone	Cefuroxime	Ceftriaxone	Cefuroxime	Cefdinir	Cefixime	Cefotaxime	Ceftriazone	Cefotiprole	Cefiderocol	Ertapenem	Imipenem	Meropenem	Aztreonam					
PEN	Amoxicillin	X	X	X	X	X	X			X	X			X																									
	Ampicillin	X		X	X	X	X			X	X			X																									
	Nafcilin/Oxacillin	X	X		X	X	X																																
	Penicillin G/V	X	X	X	X	X	X			X	X	X			X																								
	Piperacillin	X	X	X	X	X	X			X	X	X			X																								
1st GEN	Pivmecilinam																																						
	Cefadroxil	X	X	X	X	X	X																															X	
	Cefazolin*																																					X	
	Cephalexin	X	X	X	X	X	X																														X		
	Cefaclor	X	X	X	X	X	X																														X		
2nd GEN	Cefotetan																																					X	
	Cefoxitin																																					X	
	Cefprozil	X	X	X	X	X	X																														X		
	Cefuroxime																																					X	
	Cefdinir																																					X	
3rd GEN	Cefixime																																					X	
	Cefotaxime																																					X	
	Cefpodoxime																																					X	
	Ceftazidime																																					X	
	Ceftriaxone																																					X	
4th GEN	Cefepime																																					X	
	Ceftaroline																																					ND	
	Ceftolozane																																					X	
	Ceftobiprole		X	X	X	X	X																																
	Cefiderocol																																					X	
CARB	Ertapenem																																					X	
	Imipenem																																					X	
	Meropenem																																					X	
MONO	Aztreonam																																						

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x = identical or similar R1 or R2 side chains (at risk for cross reactivity)

blank = not cross reactive

ND = No data to support or deny cross reactivity

*cefazolin has unique side chains that do not cross react any beta-lactams (EXCEPT FOR CEFTOBIPROLE)

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Resources for additional information:

Penicillin Allergy Delabeling - Washington State Department of Health: <https://doh.wa.gov/public-health-provider-resources/healthcare-professions-and-facilities/healthcare-associated-infections/antimicrobial-resistance-and-antimicrobial-stewardship/antibiotic-stewardship/penicillin-allergy-delabeling>

ORGAN SYSTEM:	SYNDROME:
Upper Respiratory	Acute Otitis Media in Pediatrics

SYMPTOMS AND/OR RISK FACTORS

Differential Diagnosis Details / non-AOM Conditions

- Middle ear effusion without inflammation suggests Otitis Media with Effusion (OME), a collection of non-infected fluid in the middle ear that may be due to viral URI, allergies, irritant exposure, eustachian tube dysfunction, or resolving AOM.
- Pain with mild traction to outer ear and normal appearing ear drum may indicate otitis externa. Inflammation of ear canal may be present but does not warrant systemic antibiotics.

AOM

- New onset otorrhea (not due to acute otitis externa)
- Mild bulging tympanic membrane and recent (less than 48 hours) onset of ear pain
- Moderate to severe bulging tympanic membrane
- Intense erythema of the tympanic membrane with presence of middle ear effusion
- Non-severe AOM is defined as mild otalgia for < 48 hours and temperature < 39°C (102°F)
- Severe AOM is defined as toxic-appearing child, moderate or severe otalgia, otalgia for > 48 hours, or temperature > 39°C (102°F) in past 48 hours
- Recurrent AOM (> 2 episodes in 6 months or > 3 episodes in 1 year) in children is an indication for referral for tympanostomy tube placement.

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

- High-dose amoxicillin is recommended for pediatric otitis media because >10% *Strep pneumoniae* surveillance isolates are intermediate in Washington.
- Culture of ear fluid is not typically indicated.

RECOMMENDED TREATMENT AND DURATION

The following cases should always be treated with antibiotics:

- AOM with otorrhea
- Severe AOM (unilateral or bilateral)
- Bilateral non-severe AOM without otorrhea in children 6-23 months
- Any AOM in infants < 6 months (infants < 2 months may require additional infectious work up)

FIRST LINE:

Amoxicillin (high-dose) 45 mg/kg PO BID (max 2000mg per dose)

NOTE: For children with AOM and concurrent purulent conjunctivitis, use of amoxicillin in prior month, or history of recurrent treatment failures on amoxicillin, prescribe amoxicillin-clavulanate or a 2nd or 3rd generation cephalosporin.

SECOND LINE:

Amoxicillin-clavulanate (ES 600mg/42.9mg) 45mg/kg PO BID (max 2000mg/dose)

Penicillin Allergy (including anaphylaxis): Cefdinir 7mg/kg BID (max 600mg/day); Cefpodoxime 5mg/kg PO BID (max 200mg/dose); Cefuroxime (Infants > 2 months) 15mg/kg PO BID (max 500mg/dose); Ceftriaxone 50mg/kg IM/IV daily (max 2gm/dose)

NOTE: For children experiencing treatment failure (48-72 hours after initial antibiotic) alternatives include amoxicillin-clavulanate or ceftriaxone or clindamycin 10mg/kg PO TID (max 450mg/dose) or clindamycin PLUS 2nd or 3rd generation cephalosporin.

DURATION:

- 1-3 days if treating with ceftriaxone IM/IV daily
- 5 days for non-severe AOM and age 2-5 years
- 7 days for non-severe AOM and > 6 years
- 10 days for severe AOM or age < 2 years

Consider watchful waiting without antibiotic therapy:

- For children > 23 months with either bilateral non-severe AOM without otorrhea or unilateral non-severe AOM without otorrhea.
- For children 6-23 months with unilateral non-severe AOM without otorrhea.

Continued



NOTE When watchful waiting is used, ensure follow-up and begin antibiotic therapy if patient is worsening or not improving within 48-72 hours

SYMPTOMATIC TREATMENT for all patients:

- Extra rest, warm drinks, oral hydration
- Analgesics/antipyretics, as needed
 - Acetaminophen 15mg/kg PO q4-6hr PRN pain or fever, not to exceed 75mg/kg in 24 hours (max 4000 mg in 24 hours)
 - Ibuprofen 10mg/kg PO q4-6hr PRN pain or fever, not to exceed 40mg/kg in 24 hours (max 400mg/dose; 2400mg/day)
- Avoid cigarette smoke; offer smoking cessation resources to family members, if indicated

CONSIDERATIONS

- Ensure vaccinations are up to date.
- Amoxicillin, amoxicillin/clavulanate, cefdinir, and cefpodoxime are available as oral suspensions
- Cefdinir, cefuroxime, cefpodoxime, and ceftriaxone are highly unlikely to be associated with cross-reactivity with penicillin allergy due to their distinct chemical structures.
- Consider ENT referral if no sign of improvement after 48-72 hours **WITH** failure of alternative agent.
- It is reasonable to treat AOM in adults with the same approach as pediatrics using adult dosing strategies for outlined regimens.

Best practices for communicating with patients

- Identify and validate patient and parent concerns.
- Provide clear recommendations including specific symptom treatment and contingency plan for if symptoms worsen.
- Confirm agreement and answer questions.
- Provide education about antibiotic use and associated risks, including bacterial resistance, and *C. difficile*.

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ORGAN SYSTEM:	SYNDROME:
Upper Respiratory	Sinusitis in Pediatrics and Adults

SYMPTOMS AND/OR RISK FACTORS

Cardinal Criteria for Acute Bacterial Sinusitis

Must have purulent nasal discharge

PLUS

Nasal obstruction AND/OR facial pain/pressure/fullness

AND

Persistent & not improving (>10 days) OR symptoms worsen within 10 days after initial improvement from a typical upper respiratory infection that lasted 5-6 days

NOTE *thick, colored, or purulent nasal secretions do NOT necessarily indicate bacterial infection*

Items to consider for Risk of Antibiotic Resistance:

- Prior Abx in past 30 days
- Age <2 or >65
- Comorbidities e.g. diabetes, chronic cardiac, renal, or hepatic disease
- Prior hospitalization in past 5 days
- Attend daycare
- Immunocompromised
- Moderate to severe or prolonged signs and symptoms
 - Failure of prior ABX treatment
- Frontal or sphenoidal sinusitis
- Smoker or smoking in the family

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

- > 95% of cases are of viral origin and do not warrant antibiotics.
- Approximately 1/4 of *H. influenza* isolates produce beta-lactamases and are resistant to amoxicillin.
- > 10% of *Strep pneumoniae* surveillance isolates are non-susceptible to standard dosing of amoxicillin warranting higher dose in select patients.
- Macrolides are NOT recommended for empiric therapy due to high rates of resistance among *S. pneumoniae*.
- Sulfamethoxazole/Trimethoprim is NOT recommended for empiric therapy due to high rates of resistance to *S. pneumoniae* and *H. influenzae*.

- Routine coverage for MRSA is NOT recommended for initial empiric therapy.

NOTE *Endoscopic-guided culture and/or empiric *Staphylococcus aureus* (trimethoprim-sulfamethoxazole or doxycycline) should be considered in patients who have had recent sinus surgery.*

RECOMMENDED TREATMENT AND DURATION

Watchful waiting:

- Acceptable to observe mild bacterial sinusitis for 7 additional days before prescribing antibiotic if follow up is assured and focus instead on symptomatic treatment.
- Consider delaying the initiation of antibiotics for any severity of symptoms.
- Initiate treatment if condition fails to improve by 3 days in children or 7 days in adults.
- Consider wait-and-see-prescription (WASP).

Exceptions to watchful waiting:

- Patients with Chronic Rhinosinusitis or recurrent Acute Rhinosinusitis in multiple chronic conditions such as: asthma, ciliary dyskinesia, cystic fibrosis, or immunocompromised state.
- Watchful waiting may not be reasonable for advanced age, impaired cardiopulmonary status or multiple co-morbidities and overall poor general health.

If cardinal criteria are met and at least 10 days of symptoms or double worsening occurs:

FIRST LINE ADULT:

Amoxicillin clavulanate 875mg/125mg PO BID x 5 days

SECOND LINE ADULT:

Penicillin allergy (including anaphylaxis): Cefpodoxime 200mg PO BID x 5 days

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Doxycycline 100mg PO BID; or Levofloxacin 500mg PO Q 24 Hours x 5 days

At Risk for Antibiotic resistance: Amoxicillin-clavulanate 2gm PO BID; if high-dose extended-release formulation not available: Amoxicillin-clavulanate 875mg/125mg PO BID plus Amoxicillin 1gm PO BID x 5 days; or Levofloxacin 500mg PO Q 24 Hours

UPDATE: *Fluoroquinolone FDA Safety Alert: Disabling & potentially permanent adverse effects outweigh benefit in sinusitis. Only use levofloxacin when no other alternatives exist.*

Continued >

FIRST LINE PEDIATRIC:

Amoxicillin (high-dose) 45 mg/kg PO BID (max 2000mg per dose) x 10 days

SECOND LINE PEDIATRIC:

Penicillin allergy (including anaphylaxis): Cefdinir 7mg/kg BID

(max 600mg/day) x 10 days

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies Levofloxacin [max dose of 500mg] 6 months to 5 years old: 8-10mg/kg PO BID x 10 days or 5 to 16 years of age: 8-10mg/kg PO Q 24 Hours x 10 days

At Risk for Antibiotic resistance: Amoxicillin-clavulanate (High dose-ES 600mg/42.5mg/5mL) 45mg/kg PO BID x 10 days or use second line options listed above.

NOTE *In children < 2 years with a penicillin allergy and more severe sinusitis, it may be prudent to use a combination of clindamycin 10mg/kg PO TID plus cefdinir 14 mg/kg/day x 10 days*

Symptomatic Relief/ Adjunctive Treatment:

- Intranasal saline irrigation is safe and effective for symptom relief & does not lead to resistance.
- Intranasal corticosteroids are recommended for patients with h/o allergic rhinitis at standard approved dosing strategies.
- Control pain/fever with ibuprofen or acetaminophen.
- Nasal decongestants like oxymetazoline 1-3 sprays each nostril daily for up to 5 days if used concomitantly with intranasal steroids are safe and effective in adults with sinusitis.

CONSIDERATIONS

Identify and validate patient's concerns and provide clear recommendations including specific symptom treatment and contingency plan for if symptoms worsen.

During follow-up, if patient worsens or lack of improvement at 7 days from presentation:

- Reassess and confirm diagnosis, exclude other causes, and detect complications
- If watch and wait management, initiate FIRST LINE treatment
- If FIRST LINE treatment already completed, consider treatment from "At risk for ABX resistance" above

During follow-up, if NO improvement after 2 courses of antibiotics or if concern for orbital/CNS complications of bacterial sinusitis, order contrast-enhanced CT scan (preferred) or MRI of the paranasal sinuses and refer to the appropriate specialist.

NOTE Chronic sinusitis is defined as symptoms lasting > 12 weeks

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ORGAN SYSTEM:	SYNDROME:
Upper Respiratory	Pharyngitis in Pediatrics & Adults

SYMPTOMS AND/OR RISK FACTORS

Symptoms

- Abrupt onset of sore throat
- Headache
- Myalgia
- Occasionally nausea/vomiting/abdominal pain followed by spontaneous resolution in 2-5 days

Physical Exam consistent with Bacterial Pharyngitis

- Patchy tonsillopharyngeal exudate
- Anterior cervical adenitis (tender nodes)
- Tonsillopharyngeal inflammation
- Fever >100.4 F
- Palatal Petechia
- Scarlatiniform rash
- Absence of cough

NOTE If severe signs/symptoms (drooling, dysphonia, “potato” voice, neck swelling) consider: epiglottitis, peritonsillar abscess, retropharyngeal abscess, submandibular space infections, or primary HIV. Obtain lateral neck x-ray, and consider transfer to the emergency department.

Viral Features

- Conjunctivitis
- Rhinorrhea
- Coryza
- Cough
- Oral ulcers
- Hoarseness (laryngitis)
- Viral exanthema
- Diarrhea
- Ear pain

NOTE > 95% of pharyngitis cases are of viral etiology and do not require antibiotics. Provide symptomatic relief.

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

Test:

- Testing for Group A Streptococcus (GAS) is NOT recommended for acute pharyngitis with clinical & epidemiologic features that strongly suggest a VIRAL etiology.
- Routine use of back up throat cultures for those with a negative RADT is NOT necessary for adults; there is a low incidence of GAS pharyngitis in adults & risk of subsequent acute rheumatic fever is exceptionally low.
- Rapid Diagnostic Test (RADT) Recommended for adults with two or more symptoms and for children with signs and symptoms of strep throat who do not have viral symptoms.
- Reflex/Back up throat culture for negative RADT is only indicated in children/adolescence (3-15 years), patients at high-risk for severe disease (eg. poorly controlled diabetes, immunocompromised, on chronic corticosteroids), or those in close contact with elderly, infants or immunocompromised individuals.

NOTE *It is NOT recommended to test for GAS under the age of 3 years.*

RECOMMENDED TREATMENT AND DURATION

NOTE *treat patients who are RADT or throat culture positive or those with known exposure 2 weeks prior to symptom onset.*

FIRST LINE PEDIATRIC:

- Pen VK 250mg PO BID - TID (>27kg 500mg BID - TID) x 10 days
- Amoxicillin 50mg/kg PO daily or divided in 2 doses (MAX 1gm/ day) x 10 days
- Penicillin G Benzathine (<27kg) single IM dose 600,000 units x 1 dose

UPDATE: *Drug shortages of IM Penicillin G Benzathine warrant oral treatment options as first line consideration.*

SECOND LINE PEDIATRIC:

- For patients with penicillin allergy (NOT including anaphylaxis): Cephalexin 20mg/kg PO BID (MAX 500mg/dose) x 10 days
- Anaphylaxis to penicillin or severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Azithromycin (2-15 years of age) 12mg/kg PO once, then 6mg/kg PO daily days 2-5 (MAX 500mg/ dose); Azithromycin 20mg/kg PO once daily (max 1000mg/ dose) x 3 days; or Clindamycin 7mg/kg PO TID (MAX 300mg/ dose) x 10 days

Continued



FIRST LINE ADULT:

- Pen VK 500mg PO BID-TID x 10 days
- Amoxicillin 500mg PO BID x 10 days
- Penicillin G Benzathine ($\geq 27\text{kg}$) 1.2 million units IM x 1 dose

SECOND LINE ADULT:

- For patients with penicillin allergy (NOT including anaphylaxis): Cephalexin 500mg PO BID x 10 days
- Anaphylaxis to penicillin or severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Azithromycin 500mg PO on day one, 250mg PO daily on days 2-5; Azithromycin 500mg PO daily x 3 days, or Clindamycin 300mg PO TID x 10 days

Symptomatic Relief for all Patients (viral or bacterial infections):

- Rest
- Adequate fluid intake
- Antipyretics (no ASA (i.e. aspirin) under age 2)
- Magic mouthwash
- > 6yrs of age: gargle with warm salt water
- > 3yrs of age: sucking on hard candy

NOTE *Medicated throat lozenges/sprays (not recommended in children/adolescents)*

CONSIDERATIONS

- Stay home for the first 24h after beginning treatment to reduce transmission.
- Treatment for non-symptomatic GAS carriers is NOT routinely recommended.
- Testing or empiric tx of asymptomatic household contacts is NOT routinely recommended.
- There is no evidence of benefit for glucocorticoids in children or adolescents. Short term dosing may be beneficial in adults.
- Treatment for Group C & G are the same recommendations.

Best Practices for Communicating with Patients:

- Identify and validate patient's and parent's concerns.
- Provide clear recommendations including specific symptom treatment and contingency plan for if symptoms worsen.

- Confirm agreement and answer questions.
- Provide education about antibiotic use and associated risks, including bacterial resistance and *C. difficile*.

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ORGAN SYSTEM:	SYNDROME:
Lower Respiratory	Acute Uncomplicated Bronchitis in Adults

SYMPTOMS AND/OR RISK FACTORS

Presenting Symptoms:

- Cough > 5 days in a patient WITHOUT COPD
- Purulent sputum occurs in 50% of cases and does NOT necessarily indicate bacterial infection
- Low-grade fever is common early in illness (<100.5 F or <38C)
- Diffuse wheezes or rhonchi on exam, but NOT rales or signs of consolidation
- Mild dyspnea
 - Chest wall pain due to coughing

Comorbidities to consider:

- COPD or other chronic lung disease
- Asthma
- Elderly (> 75 years)
- Immunocompromised
- Heart failure
- Underlying bronchiectasis

Testing:

- Vital signs including SpO₂ on ambient air
- Obtain chest x-ray if: hemoptysis, ill-appearing, focal abnormality on auscultation, age >70, RR >24 bpm, temperature > 100.4F or >38C for longer than 4 days OR recurrent after having resolved for longer than 24 hours, HR > 100 bpm, resting O₂ sat < 90% cough not improving after > 6-8 weeks
- A low procalcitonin (if available) may help confirm decision to withhold antibiotics

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

Bronchitis is a self-limited inflammation of the bronchi due to respiratory infection by viruses (>90% of cases), including:

- Influenza A or B
- Parainfluenza

- Human metapneumovirus
- Rhinovirus
- RSV
- Pertussis
- Consider influenza PCR during flu season if high risk or <48 hours of symptoms
- Consider pertussis PCR if paroxysms, post-tussive emesis, inspiratory whoop or known exposure to pertussis case. Report suspect, probable or confirmed pertussis to local public health.
- Respiratory pathogen testing is discouraged in uncomplicated acute bronchitis in otherwise healthy, non-pregnant adults

NOTE *the most common causes of acute uncomplicated bronchitis DO NOT require antibiotics*

RECOMMENDED TREATMENT AND DURATION

NOTE *Antibiotic therapy may be indicated for bronchitis in patients with comorbidities such as immunosuppression, COPD/chronic bronchitis, cystic fibrosis, or other underlying lung disease other than asthma. Recommendations for these patients is beyond the scope of this guideline.*

Symptoms without comorbidities present < 14-21 days:

- Guaifenesin Q4H prn cough
- Dextromethorphan Q4H prn cough

NOTE *Narcotic medications should not be used for cough suppression in acute bronchitis.*

- Albuterol inhaler PRN difficulty breathing or wheezing present on exam in patients with asthma or underlying pulmonary disease

Symptoms and comorbidities present:

- Evaluate for pneumonia or COPD exacerbation or alternative causes
- If positive evaluation, treat accordingly
- If negative evaluation, follow guideline for symptoms without comorbidities above
- Adjunctive medications Ibuprofen 400mg PO Q6-8H prn pain or inflammation
- Naproxen 500mg PO Q12H prn pain or inflammation
- Acetaminophen 325mg-650mg PO Q6h prn pain

CONSIDERATIONS

- Expected duration of cough due to bronchitis is 2-3 weeks (average 18 days).
- Persistent cough, especially cough lasting > 6-8 weeks, may be a sign of another disease process ranging from minor to serious, such as post-nasal drip syndrome, medication use (e.g., lisinopril), irritant exposure, asthma, gastroesophageal reflux disease (GERD), smoking or second-hand smoke exposure, chronic bronchitis, bronchiectasis, tuberculosis, or malignancy.
- Antihistamines are NOT effective for bronchitis
- Provide patient education on rationale for NOT prescribing antibiotics, expected duration of symptoms, importance of smoking cessation and smoke-free environment, avoidance of irritants, adequate hydration, rest, humidified air, and to follow-up for worsening symptoms. Describe the diagnosis as “viral illness” or “chest cold”

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ORGAN SYSTEM:	SYNDROME:
Lower Respiratory	Pneumonia in Pediatrics

SYMPTOMS AND/OR RISK FACTORS

Initial Testing/Imaging

- Vital Signs: Temp, BP and Pulse Oximetry

NOTE Routine labs or chest x-ray are **not** indicated for children well enough to be managed as outpatient

- Labs:

- Blood work: CBC with differential, CRP, blood cultures if not fully immunized OR failure to improve after initiation of antibiotics
- Viral Testing: SARS-CoV-2 testing at all times and Influenza PCR during influenza season
- If atypical pathogen suspected: PCR Respiratory Panel if available
- Sputum gram stain and culture: if intubating, collect at time of initial ET tube placement; consider testing in older children who can produce sputum sample
- Urinary antigen detection testing is not recommended in children as false-positive tests are common.

- Imaging:

- AP and lateral chest x-ray if failure to improve on initial antibiotic therapy
- AP and lateral chest x-ray 4-6 weeks after diagnosis if recurrent pneumonia involving the same lobe

Criteria for Outpatient Management

- Mild CAP: no signs of respiratory distress and SpO₂ >=90% on room air
- Able to tolerate food and water
- No concerns for pathogen with increased virulence (ex. CA-MRSA)
- Family able to carefully observe child at home, comply with therapy plan, and attend follow up appointments

Inpatient Admission Criteria

PEDIATRIC FLOOR

- Respiratory distress (tachypnea, dyspnea, apnea, retractions, grunting, nasal flaring)
- SpO₂ <90% on room air
- Unable to tolerate PO
- Suspected or documented CAP caused by pathogen with increased virulence (ex. CA-MRSA)

- Concerns about observation at home, inability to comply with therapy, inability to be followed up

PICU

- Respiratory support: Intubated or requiring non-invasive positive pressure ventilation
- Concern for respiratory failure
- Concern for sepsis
- FiO_2 needs HFNC $>50\%$ to keep saturation $\geq 92\%$
- Altered mental status

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

- The most common suspected pathogens are viral. For bacterial pneumonia common pathogens include: *Streptococcus pneumoniae* and *Mycoplasma pneumoniae*.
- Atypical pneumonia is highly unlikely in children <5 years old. For children > 5 years of age, empirically add a macrolide if atypical pneumonia cannot be ruled out.
- For suspected viral pneumonia, the most common pathogens include: Respiratory syncytial virus (RSV), human rhinovirus, human metapneumovirus, and adenovirus

RECOMMENDED TREATMENT AND DURATION

UNCOMPLICATED PNEUMONIA

Previously healthy and fully immunized children:

Inpatient Treatment:

FIRST LINE:

Ampicillin 50mg/kg IV q6h (max 2000mg/dose)

SECOND LINE:

Ceftriaxone 100mg/kg IV once, then 50mg/kg IV q24h (max 2000mg/dose)
For patients with penicillin allergies (including anaphylaxis): Ceftriaxone is safe

Severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergy: Levofloxacin: 6 month-5 years old: 8-10mg/kg PO BID (max 375mg/dose) or ≥ 5 to 16 years of age: 8-10mg/ kg PO q24h (max 750 mg/dose)

Continued 

Outpatient Treatment:

FIRST LINE:

Amoxicillin 45mg/kg PO BID (max 2000mg/dose)

SECOND LINE:

For patients with penicillin allergy (including anaphylaxis): Cefuroxime or cefprozil in children > 6 months of age needing a liquid formulation

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies:
Levofloxacin

COMPLICATED PNEUMONIA

Not fully immunized with PCV13 & Hib or suspicion for *H. influenzae* or severe disease and/or complicated pneumonia:

Inpatient Treatment:

FIRST LINE:

Ceftriaxone 100mg/kg IV once, then 50mg/kg IV BID (max 2000mg/dose)

For patients with penicillin allergies (including anaphylaxis): Ceftriaxone is safe

SECOND LINE:

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Levofloxacin: 6 month-5 years old: 8-10mg/kg PO BID (max 375mg/dose) or \geq 5 to 16 years of age: 8-10mg/kg PO q24h (max 750 mg/dose)

For suspicion of Methicillin resistant *Staphylococcus aureus*:

- ADD: Clindamycin 13mg/kg PO TID (max 600mg/dose)
- For PICU or Severe Infection, ADD Vancomycin

Outpatient Treatment:

FIRST LINE:

Amoxicillin/clavulanate 45mg amoxicillin component/kg PO BID (max 2000mg/dose of amoxicillin component)

SECOND LINE:

Penicillin Allergy (including anaphylaxis): cefuroxime 15mg/kg PO BID (max 500mg/dose) or cefprozil 15mg/kg PO BID (max 500mg/dose) in children > 6 months of age needing a liquid formulation

Continued



RECOMMENDED TREATMENT AND DURATION *Continued*

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Levofloxacin.

For pneumonia in children > 5 years of age and atypical pneumonia cannot be ruled out:

FIRST LINE:

ADD azithromycin 10mg/kg IV/PO daily for 1-2 days then transition to oral step down if possible (max 500mg/dose).

A 3-day total azithromycin course is sufficient for atypical coverage.

SECOND LINE:

(For children > 7 years only) ADD Doxycycline 1-2 mg/kg PO BID (max dose 200mg/day) for 7-10 days.

DURATION:

- Uncomplicated pneumonia: 7-10 days. Although a 10-day duration is recommended in the most recent IDSA guidelines, shorter courses (3-5 days outpatient or 5-7 days inpatient) may be considered for mild disease in children aged ≥ 6 months.
- Complicated pneumonia: duration is dependent on clinical response, in general 2-4 week course.

CONSIDERATIONS

- Viral pneumonia is most common in children < 5 years of age. Antibiotics are not typically necessary. If influenza positive, treat with oseltamivir.
- Children should show clinical signs of improvement within 48- 72 hours allowing de-escalation of therapy based on available culture results and consideration of transition to oral step-down therapy.
- If no improvement or worsening, pursue further diagnostic work up as indicated. Consider broadening antibiotics and formal infectious disease consultation.

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ORGAN SYSTEM:	SYNDROME:
Lower Respiratory	Pneumonia in Adults

SYMPTOMS AND/OR RISK FACTORS

Symptoms: productive cough, chest pain, dyspnea, diminished breath sounds, crackles not cleared with coughing, abdominal pain, with or without fever.

Assess: Chest x-ray; pulse oximetry on room air

Determine if patient should be admitted using CURB-65 Scoring:

1 point each for the criteria below:

Manage inpatient for score ≥ 2 , Manage outpatient for score (0-1)

- Confusion
- Blood Urea nitrogen > 20 mg/dL
- Respiratory rate > 30 breaths/min
- Blood pressure SBP < 90 or DBP < 60 mmHg
- Age > 65 years

For patients already hospitalized with CAP use Severe CAP Scoring:

3 minor OR 1 major criteria: consider ICU level care.

Minor Criteria:

- Respiratory rate ≥ 30 breaths/min
- $\text{Pa}_{\text{O}_2}/\text{Fi}_{\text{O}_2} \leq 250$
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (BUN ≥ 20 mg/dl)
- WBC < 4000 cells/ μl (leukopenia due to infection alone, not chemotherapy induced)
- Platelet $< 100,000/\mu\text{l}$
- Temp $< 36^\circ\text{C}$
- Hypotension requiring aggressive fluid resuscitation

Major Criteria:

- Septic shock with need for vasopressors
- Respiratory failure requiring mechanical ventilation

UPDATE: *Healthcare associated pneumonia (HCAP) is no longer a designated category of pneumonia. This is because HCAP risk factors are poor at predicting prevalence of multidrug resistant organisms and lead to unnecessary use of broad-spectrum antibiotics without improved outcomes.*

Patients should be treated according to specific risk factors (detailed below) and their severity of illness.

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION FOR ALL PATIENTS

Routine Sputum and Blood cultures are NOT necessary for all non-severe cases of CAP.

- If starting anti-MRSA or anti-pseudomonal treatment, collect a sputum sample.
- If starting anti-MRSA treatment, also collect a MRSA nares swab.
- Consider stopping anti-MRSA treatment if MRSA nares is negative for MRSA.

Obtain Chest x-ray

Send nasal swab for seasonal respiratory viruses if applicable

FOR PTs with SEVERE CAP (in addition to above):

Sputum and blood cultures should be sent severe CAP or ICU level patients or pts with sepsis

Optional:

- Urinary pneumococcal antigen and urinary legionella antigen. Suspected or confirmed Legionella may require longer macrolide therapy. Recognize that patients may have pneumococcal or legionella pneumonia with negative urinary antigens.
- Viral respiratory PCR and/or procalcitonin (PCT) if unclear diagnosis of pneumonia or acute exacerbation of COPD.

Most Common Etiologies:

Bacterial: *S. pneumoniae*, *H. influenza*, Mycoplasma, *Chlamydophila pneumoniae*

Respiratory viruses: Influenza A & B, adenovirus, respiratory syncytial virus, parainfluenza and SARS-COV2

Structural lung disease such as bronchiectasis or exacerbations of COPD with multiple courses of antibiotics and/or chronic steroid use may warrant coverage for *Pseudomonas aeruginosa*

RECOMMENDED TREATMENT AND DURATION

Community-acquired pneumonia (outpatient)

FIRST LINE

Patients with no co-morbidities:

FIRST CHOICE: Amoxicillin 1g PO TID

Continued 

OR

Doxycycline 100mg PO BID

Patients with comorbidities (chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; asplenia):

- Amoxicillin/Clavulanate 875/125mg BID PLUS Azithromycin
 - **Alternatives to Amoxicillin/Clavulanate: Cefuroxime 500mg PO BID or Cefpodoxime 200mg-400mg PO BID, or Cefdinir 300mg BID
 - Dose for Azithromycin is 500mg on day 1 then 250 mg daily x 4 days or Azithromycin 500mg q24h x 3 days
 - Doxycycline 100mg PO BID x 5 days is an alternative option to azithromycin
- OR Levofloxacin 750 mg PO Daily

DURATION: 5 days

NOTE Azithromycin is provided for atypical coverage and should not be relied upon as monotherapy for ambulatory or inpatient management of pneumonia due to increasing *Streptococcus pneumoniae* resistance.

Community-acquired pneumonia (inpatient)

FIRST LINE:

Ceftriaxone 1 to 2g IV daily PLUS Azithromycin 500mg PO/IV q24hr x 3 days unless confirmed Legionella pneumonia.

For patients with penicillin allergies (including anaphylaxis): Ceftriaxone is safe.

SECOND LINE:

Levofloxacin 750mg PO/IV q24hr

Indications for Broadening Antimicrobial Coverage:

- Add anti-MRSA and/or switch to anti-Pseudomonal coverage if prior culture history or if received IV antibiotics in preceding 90 days

NOTE Linezolid may be considered in place of vancomycin for anti-MRSA coverage. Alternative antibiotics with anti-pseudomonal coverage include ceftazidime, or piperacillin/tazobactam.

DURATION: Typically 3-5 days

Duration of therapy should be guided by measure of clinical stability.

A recent randomized controlled trial compared 3 vs 8 day antibiotic duration for patients hospitalized with CAP and found no difference in cure at 15 days. Three-day duration may be considered in patients with rapid clinical improvement.

Continued



RECOMMENDED TREATMENT AND DURATION *Continued*

Consider stopping antibiotics IF:

Afebrile x 48 hours

AND normalized vital signs or improved PCT:
(SBP \geq 90, HR $<$ 100, RR $<$ 24, arterial O₂ sat \geq 90%
on room air AND/OR PCT $<$ 0.25)

Hospital Associated Pneumonia (HAP) and Ventilator Associated Pneumonia (VAP)

- Defined as pneumonia occurring $>$ 48h after admission (HAP) or $>$ 48h after endotracheal intubation (VAP).
- Empiric coverage should include *P. aeruginosa* and MRSA and final treatment targeted to cultures and sensitivities. MRSA coverage is not necessary if MRSA is uncommon in the hospitalized patient population or there is recent documented absence of MRSA colonization of the nares or upper airway.
- Typical duration for HAP/VAP is 7 days

UPDATE: The 2019 CAP guidelines recommend against adding anaerobic coverage for aspiration pneumonia except in cases of suspected lung abscess or empyema

CONSIDERATIONS

Adjunct therapy

- Yeast and enterococcus in sputum, even in severe CAP, rarely represents true infection and does not warrant treatment.
- Corticosteroids can be considered for adults hospitalized with severe bacterial CAP. Stop once the patient improves or is discharged. Refer to CAPECOD trial for dosing.
- During flu season, send flu test and start empiric oseltamivir 75mg PO q12h.
- Higher doses (e.g. 150mg BID) offer no added benefit in critically ill or obese patients.
- Consider anti-MRSA coverage for post-influenza pneumonia in addition to coverage for *S. pneumoniae* and *H. influenzae*.

Transitions of care

- For inpatients, offer eligible vaccinations before discharge: pneumococcal conjugate vaccine, influenza, SARS-CoV-2, respiratory syncytial virus.
- Screen for and treat tobacco use, including cessation counseling and medications.

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ORGAN SYSTEM:	SYNDROME:
Intra-abdominal	Intra-abdominal Infections in Adults Inpatient

SYMPTOMS AND/OR RISK FACTORS

High Risk/Severe Criteria

- Albumin <2.5
- Age >70 years
- Immunocompromised state
- Severe sepsis/septic shock

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

Intra-abdominal infections are usually a polymicrobial process and may include the following pathogens:

- Enterobacteriales
- Enterococcus sp.
- Anaerobes (including Bacteroides sp.)

Anaerobes are less significant for biliary sources UNLESS bile duct to bowel anastomosis or fistula is present. Anaerobes are a special concern with liver abscesses due to the delivery of anaerobic bowel contents to the liver via the portal venous system.

Routine blood cultures are NOT recommended for community-acquired infections among immunocompetent patients without physiologic derangements. However, cultures SHOULD be obtained in patients with nosocomial infection or who require operation for prior treatment failure.

RECOMMENDED TREATMENT AND DURATION

EXTRA-BILIARY SOURCE:

appendicitis, diverticulitis, bowel perforation with peritonitis, hepatic abscess

Extra-biliary Source MILD-MODERATE Risk

FIRST LINE:

Ceftriaxone 2gm IV q24hr PLUS Metronidazole 500mg IV q8hr

For patients with penicillin allergies (including anaphylaxis): Ceftriaxone is safe

Continued 

SECOND LINE:

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Levofloxacin 750mg IV q24h PLUS Metronidazole 500mg IV q8hr

NOTE *Because many of the patients who are managed without a primary source control procedure may be treated in the outpatient setting, the oral regimens recommended can also be used as either primary therapy OR step-down therapy following initial intravenous antimicrobial therapy.*

Oral options: levofloxacin plus metronidazole, an oral cephalosporin with metronidazole; culture data may allow for the use of amoxicillin-clavulanate or moxifloxacin, but these agents should NOT be used empirically due to high rates of *B. fragilis* resistance.

Extra-biliary Source HIGH RISK/SEVERE

FIRST LINE:

Piperacillin-tazobactam 4.5gm IV q6hr (or extended infusion)

For patients with penicillin allergies (including anaphylaxis): Cefepime 2gm IV q8hr PLUS Metronidazole 500mg IV q8hr

SECOND LINE:

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Levofloxacin 750mg IV q24h PLUS Metronidazole 500mg IV q8hr

Consider the addition of Aztreonam 2gm IV q8hr

NOTE *IF previous colonization or concerns for highly resistant GNRs, may consider meropenem 1gm IV q8hr as a substitute for piperacillin-tazobactam or additional GNR coverage to levofloxacin. Or may use ertapenem IV q24 (if pseudomonas is not a concern)*

Duration of therapy

Without source control/surgery: 4 to 7 days total

With source control/surgery: 4 days post-operative therapy if adequate surgical source control

5 days for uncomplicated diverticulitis

If retained focus of infection, duration should be guided by clinical response (at least 7 to 14 days).

Continued 

BILIARY SOURCE: cholecystitis, cholangitis

Biliary source MILD-MODERATE Risk

FIRST LINE:

Ceftriaxone 2gm IV q24hr

For patients with penicillin allergies (including anaphylaxis): Ceftriaxone is safe

SECOND LINE:

For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies: Levofloxacin 750mg IV q24h

NOTE *Anaerobic therapy is NOT indicated unless a biliary-enteric anastomosis is present*

Biliary Source HIGH RISK/SEVERE

FIRST LINE:

Piperacillin-tazobactam 4.5gm IV q6hr (or extended infusion)

For patients with penicillin allergies (including anaphylaxis): Cefepime 2gm IV q8hr PLUS Metronidazole 500mg IV q8hr

SECOND LINE: For patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies:

Levofloxacin 750mg IV q24h

PLUS

Metronidazole 500mg IV q8hr

Consider the addition of Aztreonam 2gm IV q8hr

NOTE *IF previous colonization or concerns for highly resistant GNRs, consider meropenem 1gm IV q8hr as a substitute for piperacillin-tazobactam or additional GNR coverage to levofloxacin.*

Duration of therapy

Uncomplicated with operative or endoscopic management : \leq 24 hours

Uncomplicated, without operative or endoscopic management: 5 days

Complicated by inadequate source control: Duration should be determined on a case-by-case basis, depending on timing of source control and other clinical factors.

Continued 

NOTE In the event of uncomplicated IAIs, the infection involves a single organ and does not extend to the peritoneum. When the source of infection is treated effectively by surgical excision, post-operative antimicrobial therapy is not necessary, as demonstrated in managing uncomplicated acute appendicitis or cholecystitis.

CONSIDERATIONS

- Due to *E. coli* resistance >10%, empiric quinolone use alone is cautioned in high-risk/severe cases. Double coverage with the addition of aztreonam or an aminoglycoside should be considered in these high-risk/severe circumstances when using a quinolone as the backbone of therapy.
- Empiric ampicillin-sulbactam is NOT recommended for use because of high rates of resistance among community-acquired *E. coli* and *B. fragilis*.
- The IDSA definition of source control is a “single procedure or series of procedures that eliminate infectious foci, control factors that promote ongoing infection, and correct or control anastomotic derangements to restore normal physiologic function” Review of operative reports is often necessary to determine whether source control has been achieved.
- Empiric coverage of enterococcus or candida is NOT recommended for mild-moderate community-acquired intra-abdominal infections
- Empiric enterococcal treatment is recommended for healthcare associated infections with previous cephalosporin therapy, immunocompromised patients, and those with valvular heart disease or prosthetic intravascular materials.
- Bowel injuries from penetrating, blunt, or iatrogenic trauma repaired within 12hr of initial insult should be treated with antibiotics for < 24 hrs. Likewise, antibiotics should be used for < 24hrs when there is intraoperative contamination of the peritoneum by enteric contents.
- Use of ursodeoxycholic acid and/or antibiotics for the prevention of biliary stent occlusion or infection is NOT routinely recommended.
- Need for antibiotics in mild, outpatient diverticulitis disease remains controversial
- Aminoglycosides are NOT recommended for routine use in adults with community acquired intra-abdominal infection because of the availability of less toxic agents demonstrated to be at least equally effective. However, aminoglycosides may be necessary in high risk/severity patients in combination with a quinolone and metronidazole in patients with severe penicillin allergies with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergies.

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ORGAN SYSTEM:	
Urinary Tract	Appropriate Use of Urinalysis and Urine Culture

CLINICAL PEARLS

- Pyuria signifies inflammation in the GU tract and can be present in both asymptomatic bacteriuria and UTI.
- A urinalysis (UA) without pyuria (WBC) has a high **negative** predictive value for urinary tract infection (UTI). Therefore, if UTI is negative for pyuria, UTI is unlikely. Pyuria has a low positive predictive value for UTI, meaning it does not reliably discriminate between ASB and UTI.
- The diagnosis of UTI requires both compatible signs/symptoms and bacteriuria.
- Polymicrobial urine culture specimen without a predominant uropathogen is suggestive of a contaminated specimen; consider recollecting a new specimen if high clinical suspicion for UTI remains.

GENERAL GUIDELINES

- NOT a symptom of UTI: cloudy, high sediment, or malodorous urine
- NOT a symptom of UTI: altered mental status alone without urinary symptoms or sepsis
- UTI symptoms in patients with neurologic or spinal cord injury may be atypical
- CAUTION in catheterized patients: urinary symptoms may be due to catheter and colonization is common

DO order a urinalysis with reflex culture:	DO NOT order a urinalysis and culture:
<ul style="list-style-type: none"> • NEW signs or symptoms of UTI – e.g. burning, urgency or flank pain • Sepsis without known source • Screening for asymptomatic bacteriuria (pregnancy or prior urological surgery) <ul style="list-style-type: none"> ◦ For invasive urological procedures, screening is recommended only prior to procedures, screening is recommended only prior to procedures that cause mucosal injury (e.g. TURP, lithotripsy) 	<ul style="list-style-type: none"> • If the patient's only symptoms are delirium (AMS changes) or fall <u>without</u> localizing genitourinary symptoms or systemic signs of infection • If the patient has sediment in urine, foul-smelling urine, or "dirty" appearing urine <u>unless</u> there are other localizing symptoms • If the patient is undergoing a urologic procedure not involving mucosal injury (routine catheter change, diagnostic cystoscopy, removal or ureteral stents) • If the patient is undergoing <u>non-urologic</u> surgery (cardiac, ortho vascular) • If the patient has diabetes, cognitive impairment, resident in long-term care facility, or spinal cord injuries <u>without</u> other localizing symptoms

ORGAN SYSTEM:	SYNDROME:
Urinary Tract	Asymptomatic Bacteriuria (ASB)

SYMPTOMS AND/OR RISK FACTORS

ASB is the presence of one or more species of bacteria growing in the urine (with or without concurrent pyuria) in the absence of signs or symptoms of a UTI.

CULTURE & SUSCEPTIBILITY (C&S) INVESTIGATION

- Routine screening is NOT indicated in asymptomatic patients unless screening in pregnancy or prior to urologic procedure with compromise of the urothelial mucosa.
- **DO NOT screen for asymptomatic bacteriuria outside of pregnancy or upcoming urologic procedures.**
 - Bacteriuria identified on perioperative urine screening for non-urologic procedures (cardiac, ortho, vascular) is NOT an indication for antibiotics and does not decrease surgical site infections or prevent UTIs

RECOMMENDED TREATMENT AND DURATION

Pregnant women: (select one option)

- Nitrofurantoin 100mg PO q12h x 5d
contraindicated at > 38 weeks gestation or when the onset of labor is imminent.
- Cephalexin 500mg PO q6h x 5d

Patients undergoing urologic procedure with mucosal injury:

- Direct treatment based on pre-procedure screening C&S
- Treatment duration: 1 or 2 doses of an appropriate antibiotic given 30-60 minutes prior to the start of the procedure

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ORGAN SYSTEM:	SYNDROME:
Urinary Tract	Adult Lower Tract UTI (Cystitis)

SYMPTOMS AND/OR RISK FACTORS

Lower tract UTI: symptoms of dysuria, frequency, urgency, or suprapubic pain with no systemic or upper tract signs of infection in afebrile women or men. Patients with male anatomy should be evaluated for associated prostatitis, especially if there is a history of recurrent UTI with the same pathogen

CULTURE & SUSCEPTIBILITY (C&S) INVESTIGATION

- Agent selection should be guided by local susceptibilities (antibiogram) and patient-specific factors
- Consider deviation from the standard recommendations (or consult ID) if any of the following risk factors for multidrug resistant organisms are present:
 - Antibiotic exposure within 90 days
 - Presence of urinary invasive devices(s)
 - History of UTI with multi-drug resistant organism
- Interpretation of atypical urinary pathogens:
 - Yeast: Generally a non-pathogenic, colonizing organism, especially for patients with indwelling catheters. Rare cause of UTI and does not typically require treatment
 - Coagulase-negative *Staphylococcus*: Typically represents skin flora. Does not routinely cause UTI.
 - *Staphylococcus aureus*: Presence in the urine indicates bacteremia until proven otherwise. This organism typically seeds the urine via the bloodstream. Obtain blood cultures and assess patients for symptoms of bloodstream infection

RECOMMENDED TREATMENT AND DURATION

Outpatient treatment:

FIRST LINE:

Nitrofurantoin (monohydrate/macrocystals) 100 mg PO q12h x 5 days (avoid if CrCl<30 due to potential decreased urinary concentrations from impaired renal function)

TMP-SMX DS 1 tablet PO q12h x 3 days if E coli susceptibility is >80%

Continued



ALTERNATIVES:

- Cephalexin 500mg PO q12h or Cefadroxil 500mg PO q12h x 5 days
- Amoxicillin-clavulanate 875/125mg PO q12h x 5 days
 - Preferred for *Enterococcus faecalis*
- Ciprofloxacin 250mg PO q12h x 3 days

Inpatient treatment:

FIRST LINE:

- Nitrofurantoin (monohydrate/macrocystals) 100mg PO q12h x 5 days (avoid CrCl <30 due to potential for decreased urinary concentrations from impaired renal function)
- TMP/SMX 1 DS tablet PO q12h x 3 days

ALTERNATIVES (if unable to tolerate PO):

- Ceftriaxone 1g IV daily, transition to oral regimen when susceptibility returns

CONSIDERATIONS

- For ESBL (extended spectrum beta-lactamase) producing organisms, treat according to reported susceptibility with one of the following:
 - Nitrofurantoin (monohydrate/macrocystals) 100mg PO q12h x 5 days
 - TMP/SMX 1 DS tablet PO q12h x 3 days
 - Ciprofloxacin 250-750mg PO q12h x 3 days
 - Levofloxacin 750mg PO q24h x 3 days
 - Fosfomycin 3g PO x 1 dose (for *E.coli* only; susceptibility testing is recommended)
 - Gentamicin OR tobramycin 5 mg/kg/dose IV x once)
 - A single IV dose is generally effective for lower tract UTI with minimal toxicity (aminoglycoside-associated nephrotoxicity and ototoxicity are primarily duration-dependent). Thus, acute kidney injury in this setting is rare, even among patients with pre-existing renal impairment.
- Recurrent UTI
 - Empiric therapy for patients with recurrent UTIs should be based upon prior C&S results (<1 year)

- Chronic antibiotic prophylaxis/suppression for most patients with recurrent UTI is NOT typically recommended. Risk of resistance outweighs the slight reduction in infection rate.
- One randomized trial confirmed that pre-menopausal women with recurrent UTIs who drank more water (1.5L total fluid daily) had fewer UTIs.
- Other strategies to prevent UTIs, include topical vaginal estrogen in patients with low estrogen (e.g. post-menopause, estrogen-blocker therapy), cranberry products, or methenamine hippurate

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ORGAN SYSTEM:	SYNDROME:
Urinary Tract	Adult Upper Tract UTI (including Pyelonephritis)

SYMPTOMS AND/OR RISK FACTORS

Upper tract UTI: symptoms of UTI with 1 or more of the following that suggests extension beyond the bladder: fever, other signs or symptoms of systemic illness (chills, rigors, or hemodynamic instability), flank pain, costovertebral angle tenderness in women or men OR pelvic or perineal pain in men (which may suggest prostatitis).

- Consider deviation from the below recommendations (or consult ID) if any of the following risk factors for multidrug resistant organisms are present:
 - Antibiotic exposure within 90 days
 - Presence of urinary invasive device(s)
 - History of UTI with multi-drug resistant organism

CULTURE & SUSCEPTIBILITY (C&S) INVESTIGATION

- Agent selection should be guided by local susceptibilities (antibiogram) and patient-specific factors

RECOMMENDED TREATMENT AND DURATION

Outpatient/ED Management:

FIRST LINE:

- Ceftriaxone 1g IV/IM x once, followed by:
 - Ciprofloxacin 500mg PO q12h x 5-7 days
 - Levofloxacin 750mg PO q24h x 5-7 days
 - TMP/SMX 1DS tab PO q12h x 7 days
 - Beta-lactams (amoxicillin, amoxicillin-clavulanate, cefpodoxime, cefuroxime, cephalexin) x 7 days
- History of ESBL: ertapenem 1g IV q24h x once instead of ceftriaxone
For patients with penicillin allergies (including anaphylaxis): Ceftriaxone is safe

NOTE Above recommendations are for empiric antimicrobial therapy, tailor maintenance therapy to C&S report.

Inpatient:

- Ceftriaxone 1g IV q24h

Continued 

- For patients with a severe penicillin allergy (delayed, severe cutaneous reactions such as DRESS, SJS, TEN) or any cephalosporin allergy:
 - Ciprofloxacin 400mg IV q12h
 - Levofloxacin 750mg IV q24h
- History of ESBL: ertapenem 1g IV q24h
- When clinically stable, transition to PO antibiotic based on susceptibility:
 - Ciprofloxacin 500mg PO q12h
 - Levofloxacin 750mg PO q24h
 - TMP/SMX 1DS tab PO q12h
 - Beta-lactams (amoxicillin, amoxicillin-clavulanate, cefpodoxime, cefuroxime)
 - Use cefpodoxime with caution: this medication has a lower bioavailability than other beta lactams)
- Total duration = 7 days

CONSIDERATIONS

- Empiric therapy for patients with recurrent UTIs should be based upon prior C&S results (<1 year)
- Nitrofurantoin and Fosfomycin should be avoided if concern for kidney or prostate involvement due to poor tissue penetration.
- Among hospitalized patients with uncomplicated gram-negative bacteremia due to UTI who are hemodynamically stable and afebrile for at least 48 hours (and without ongoing focus of infection), we recommend a total duration of 7 days of antibiotic therapy (day 1 = first day of appropriate therapy). Transition from IV to PO agents is preferred.
- Persistent fever for 72 hours is within expected limits and does not warrant a change in therapy or imaging in the absence of hemodynamic instability. Consider imaging to evaluate for a perinephric abscess if there is persistent fever for >72 hours after the initiation of appropriate antibiotics.
- For ESBL (extended spectrum beta-lactamase) producing organisms, treat according to reported susceptibility with one of the following to complete a 7-day treatment course:
 - TMP/SMX 1 DS tablet PO q12h
 - Ciprofloxacin 750mg PO q12h
 - Levofloxacin 750mg PO q24h

- If resistant to all tested antibiotics or multiple allergies, consult Infectious Diseases for potential alternatives. ESBL pyelonephritis may require inpatient admission for IV carbapenem.

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ORGAN SYSTEM:	SYNDROME:
Urinary Tract	Catheter-Associated UTI (CAUTI)

SYMPTOMS AND/OR RISK FACTORS

CAUTI: presence of signs or symptoms consistent with UTI along with >105 colony-forming units of a bacteria species in patients with an indwelling urethral or suprapubic catheter or ongoing intermittent catheterization.

- Signs and symptoms in CAUTI: may include suprapubic tenderness, fever, rigors, flank pain, costovertebral angle tenderness, acute hematuria, and pelvic discomfort.
 - Patients with CAUTI may present with altered mental status, malaise, and lethargy. However, in hemodynamically stable patients without concurrent localizing UTI symptoms, we do not recommend screening, testing, or treating for CAUTI.
 - Patients may experience dysuria, urgency, frequency, or suprapubic pain following catheter removal. In the absence of other signs and symptoms (as above), watchful waiting (with good hydration) is recommended. If symptoms have not improved in 48 hours, perform follow-up UA with reflex culture to assess for infection.

CULTURE & SUSCEPTIBILITY (C&S) INVESTIGATION

- Prevalence of bacteria in urine among individuals with a chronic catheter is 100%. Correlate treatment with the presence of symptoms.
- The presence or degree of pyuria alone is not diagnostic of CAUTI.
- Diagnosis of CAUTI:
 - Remove the catheter and obtain a clean-catch specimen
- Avoid sending urine cultures from old catheters: if urethral catheter has been in place for ≥ 5 days, remove or replace prior to culture (exclusions: difficult to place catheter, irrigation, end of life, recent urologic/gynecologic surgery or suprapubic catheters)

RECOMMENDED TREATMENT AND DURATION

Treatment:

- For antibiotic selection, please assess presenting signs/symptoms and refer to the above sections for upper and lower tract UTI

Continued 

Duration:

- Patients clinically improving:
 - 5-7 days of a fluoroquinolone
 - 7 days of a non-fluoroquinolone antibiotic
- Not clinically improving:
 - Assess for unresolved nidus of infection requiring source control
 - Reassess UTI diagnosis
 - Assess for drug-bug mismatch

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ORGAN SYSTEM:	SYNDROME:
Urinary Tract	Pediatric Urinary Tract Infection (Ages 2-24 months)

SYMPTOMS AND/OR RISK FACTORS

Definition of UTI (a combination of the following):

- Urinary tract symptoms
- Urinalysis with pyuria and/or bacteria
- At least 50,000 CFU/mL of a single uropathogen obtained from an appropriately collected specimen (catheterization or clean-catch; bagged specimens should be used)

*UTICalc tool to help with decision to test: <https://uticalc.pitt.edu/>

Risk Factors (in the absence of another source of infection):

- Girls: Temp \geq 39 C, fever \geq 2 days, age <12 months
- Boys: Temp \geq 39 C, fever \geq 2 days, age <6 months, uncircumcised

RECOMMENDED TREATMENT AND DURATION

Outpatient treatment:

FIRST LINE

- Cephalexin or TMP/SMX
 - Cephalexin dosing
 - 2 mo-14 years, <20 kg: 25 mg/kg q8h (max 500mg/dose for cystitis & max 1000mg/dose for febrile UTI/pyelonephritis)
 - 2mo-14 years, \geq 20 kg: 500mg q8h
 - TMP/SMX dosing: 4 mg/kg q12h of TMP component (max 160 mg TMP q12h)
 - Consider ceftriaxone IM if concern or PO tolerance
 - Follow up with primary care provider within 24 hours
 - Total duration:
 - Cystitis: 3 days
 - Febrile UTI: 7 days

NOTE Above recommendations are for empiric antimicrobial therapy, tailor maintenance therapy to C&S report.

Inpatient treatment:

- Cefazolin 150mg/kg/day IV divided 3 times daily (max 2000mg/dose), followed by transition to oral regimen when susceptibility returns

Continued 

- Total duration:
 - Cystitis: 3 days
 - Febrile UTI: 7 days

CONSIDERATIONS

- Renal/bladder ultrasound should be considered in the following scenarios:
 - Inpatient (to evaluate for abscess or obstruction), particularly in patients with:
 - Failure to response to antibiotics after 48 hours
 - Hemodynamic instability
 - Outpatient (to evaluate for structural abnormality if not previously performed), particularly in patients with:
 - Recurrent UTI
 - Non-*E. coli* UTI
 - Febrile UTI and children <24 months old

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ORGAN SYSTEM:	SYNDROME:
Skin and Soft Tissue	Uncomplicated Cellulitis in Adults

SYMPTOMS AND/OR RISK FACTORS

Complicating Risk Factors:

NOTE Guideline recommendations are for uncomplicated cellulitis in adults and excludes those with complicating risk factors; if complicating risk factors, treatment may vary and formal ID consultation should be considered.

Infected diabetic or vascular ulcer

- Critical illness
- Concern for necrotizing fasciitis
- Deep tissue infection
- Surgical site infection
- Human or animal bite
- Bacteremia
- Periorbital or orbital cellulitis
- Perineal/vulvar/perianal infection
- Water exposure wounds

FOR PATIENTS WITH SEPSIS – See Sepsis section

Diagnostic Studies:

- Do culture purulent drainage from abscess. Swabs from chronic wounds often represent colonization and are NOT recommended.
- Blood cultures are not routinely needed unless systemically ill or other immunosuppression
- The following are NOT routinely indicated for initial management of uncomplicated disease: ESR, CRP, Procalcitonin, blood cultures, plain films, CT or MRI

NOTE Necrotizing fasciitis is a clinical diagnosis. Surgical consultation should be obtained if there is any concern, regardless of imaging findings

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

- Non-purulent cellulitis is most commonly caused by beta- hemolytic streptococci
- Purulent cellulitis or cutaneous abscess is most commonly caused by *Staphylococcus aureus* and beta-hemolytic streptococci and warrants empiric coverage for MRSA, MSSA and group A Strep.

RECOMMENDED TREATMENT AND DURATION

IMPETIGO:

Topical treatment: soap, water, & mupirocin.
Avoid systemic antibiotics.

NON-PURULENT CELLULITIS:

FIRST LINE IV:

Cefazolin 2 gm IV q8hr

SECOND LINE IV:

Penicillin allergy (including anaphylaxis): cefazolin is safe

For patients with severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any severe cephalosporin allergy (anaphylaxis, delayed cutaneous reaction): Vancomycin IV

FIRST LINE ORAL:

Amoxicillin 500mg PO TID or Cephalexin 500mg PO QID or 1g BID

SECOND LINE ORAL:

Penicillin allergy (including anaphylaxis), severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any severe cephalosporin allergy: Clindamycin 300 PO TID or TMP/SMX DS 1 tab BID

In patients known to tolerate higher generation cephalosporins: other oral higher generation cephalosporins may be an option, discuss with your pharmacists. See beta-lactam cross reactivity chart.

PURULENT CELLULITIS OR CUTANEOUS ABSCESS:

FIRST LINE IV:

NOTE *I&D is PRIMARY TREATMENT*

Antibiotics may not be necessary for drained abscess without surrounding induration or erythema

Adjunctive antibiotics: Vancomycin IV

FIRST LINE ORAL:

NOTE *I&D is PRIMARY TREATMENT*

Antibiotics may not be necessary for drained abscess without surrounding induration or erythema

TMP/SMX DS 1 tab PO BID OR

Doxycycline 100mg PO BID +amoxicillin/cephalexin (see dosing above)

Duration of antibiotics: 5 days for uncomplicated cases including a well-drained abscess without surrounding cellulitis but may be extended for severe or poorly responsive disease

CONSIDERATIONS

Antibiotics with broad-spectrum gram-negative activity are NOT recommended except in necrotizing fasciitis.

Vancomycin serum concentration monitoring may not be needed for uncomplicated infections.

Treat tinea pedis if present.

Elevate affected area(s).

Consider MRSA decolonization with intranasal mupirocin and chlorhexidine rinses or bleach baths for patients with recurrent *S. aureus* infections.

Consider adding analgesia, such as ibuprofen or acetaminophen if no contraindications exist.

FAQ:

When is an antitoxin agent (i.e. clindamycin, linezolid) needed?

Antibiotics with antitoxin effects should be added when there is concern for a severe, toxin-mediated infection such as necrotizing fasciitis or toxic shock syndrome.

Does TMP/SMX treat Strep?

TMP/SMX was historically thought to be ineffective against streptococci due to flawed testing methodology which falsely indicated resistance. Modern susceptibility testing and clinical trials now support TMP/SMX monotherapy for many SSTIs, including those involving streptococci.

Should I use dual therapy for uncomplicated cellulitis?

Dual therapy is RARELY needed for uncomplicated cellulitis.

- For non-purulent cellulitis, early generation cephalosporins alone provide excellent coverage against streptococci.
- For purulent cellulitis/abscess, MONotherapy with agents such as TMP/SMX or vancomycin provide excellent coverage for both *Staph aureus* (including MRSA) and streptococci.
 - Switch to beta-lactam alone if MRSA is not found on culture/rapid test.
- Exception: for purulent cellulitis, doxycycline has variable activity against streptococci, so some clinicians add a beta-lactam (e.g., cephalexin) to ensure adequate coverage.

When should I include gram-negative coverage (e.g. ceftriaxone, pip/tazo)?

Gram-negative coverage is usually unnecessary unless there is direct anatomic communication between the GI or GU tract.

When should I add anaerobic coverage (e.g. metronidazole, amox/clav, pip/tazo)?

Anaerobic coverage is rarely needed in uncomplicated cellulitis and should only be considered in infections that involve the perineum or rectum, concern for necrotizing fasciitis, moderate/severe diabetic foot infections, or bite wounds.

How should I manage bilateral cellulitis?

Misdiagnosis of cellulitis is common. True bilateral cellulitis is RARE and should prompt consideration of alternative etiologies of lower extremity erythema. Clues for alternative diagnoses include bilateral involvement, lack of systemic signs of infection (leukocytosis, fever), chronic unchanging erythema and lack of improvement on standard antibiotics.

How should I manage a patient who has failed outpatient antibiotics?

- Reassess the diagnosis (cellulitis misdiagnosis is common).
- Extending erythema alone should not be considered treatment failure. Extension of erythema first 1-2 days of effective treatment is common; assess other parameters for improvement (fever, pain).
- Ensure the infected extremity is elevated (improves lymphatic drainage).
- Ensure the patient is taking and absorbing the oral antibiotics.
- If the above are met, consider escalating to IV or anti-MRSA agent if not initially given.

Is there a role for long-acting antibiotics (dalbavancin, oritavancin) in the treatment of cellulitis?

Dalbavancin and oritavancin are long-acting cousins to vancomycin with activity against *Staph aureus* (including MRSA) and streptococci, approved for the treatment of skin and soft tissue infections. Their use depends on insurance coverage and institutional access. They may be a useful option for patients with cellulitis who are poor candidates for oral therapy and wish to avoid hospital admission. Recommended dose:

- Dalbavancin 1500 mg IV x 1
- Oritavancin 1200 mg IV x 1

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ORGAN SYSTEM:	SYNDROME:
Skin and Soft Tissue	Adult Diabetic Foot Infection

SYMPTOMS AND/OR RISK FACTORS

Assessment

- Physical examination to assess for evidence of infection and depth
- Ankle brachial index (ABI) and/or transcutaneous oxygen tension measurement
- Plain film to assess for foreign bodies, deformity, boney destruction, soft tissue gas, and/or foreign bodies.

NOTE metal probe has a negative predictive value of 98% for osteomyelitis; plain film has a specificity 67%, sensitivity 60%

- When more specific imaging is needed to evaluate for either soft tissue abscess or osteomyelitis, an MRI is preferred

Osteomyelitis Evaluation:

- Consider osteomyelitis in any infected, deep, or large foot ulcer, particularly those that are chronic and over bony prominences
- Plain films along with the probe to bone test are reasonable first steps in evaluating for osteomyelitis
- Patients where the diagnosis remains unclear should undergo MRI
- Patients with findings suggestive of osteomyelitis should undergo debridement with bone culture before antibiotics are started if possible, assuming the patient is otherwise clinically stable
- Consult orthopedics or vascular surgery for potential surgical intervention if there is concern for osteomyelitis and/or arterial insufficiency
- If debridement is not an option, an IR guided bone biopsy should be obtained to determine the microbial etiology
- Consult an infectious diseases provider for evaluation and management of long-term antibiotics

Risk

- Infection related to ulceration to the bone, ulcers that have been present for longer than 30 days, recurrent trauma and peripheral arterial disease

Diagnostic Criteria

Obvious purulent drainage AND/OR 2 of the following: Erythema, Pain, Tenderness, Warmth, Induration

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

- Infected ulcers initially harbor staphylococci and streptococci.

- With increasing time, depth and size, wounds are colonized and/ or infected with multiple organisms, including gram negatives and anaerobes
- Do not culture a clinically uninfected lesion
- Consider obtaining ESR and CRP if concern for infection is unclear
- Do obtain an appropriate specimen for culture from INFECTED wounds and before antibiotics are started, if possible
- Cleanse and debride before collection of tissue
- Tissue collection using sterile scalpel or curettage or biopsy from the base
- Aspirate any purulent secretions using a sterile needle & syringe
- Do not routinely obtain a specimen by swabbing the wound or wound drainage

Clinical Manifestation of Infection	IWGDF grade	IDSA Infection Severity
No symptoms or signs of infection*	1	uninfected
Local infection* involving only skin and subcutaneous tissue. If erythema, must be >0.5 cm to ≤2 cm around the ulcer *Infection present as defined by 2 of the following: •Local swelling or induration •Erythema •Local tenderness or pain •Local warmth •Purulent discharge	2	mild
Local infection with erythema >2 cm or involving deeper than skin and subcutaneous tissues, and no systemic inflammatory response signs	3	moderate
Local infection with signs of SIRS, as manifested by fever, tachycardia, tachypnea, leukocytosis	4	severe

RECOMMENDED TREATMENT AND DURATION

MILD: Local infection with erythema <2cm.

FIRST LINE (Empiric)

Cephalexin 500mg PO QID OR Amoxicillin-clavulanate 875/125 mg PO BID

If MRSA concern add: Doxycycline 100 mg PO BID or TMP/SMX DS 1 tab PO BID

SECOND LINE (Empiric)

Penicillin allergy (including anaphylaxis), severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergy: Clindamycin 300 mg PO BID. Duration for mild infections of soft tissue only is 5-7 days.

Continued >

MODERATE: Local infection with or involvement of deeper structures (abscess, osteomyelitis, septic arthritis) or more extensive erythema (>2 cm spread or associated lymphangitis) without systemic signs of inflammation

NOTE *May use oral or parenteral agents depending on care location and severity of infection. Treat for pathogens as above plus aerobic gram-negatives. Consider addition of MRSA active agent if history of MRSA infection/colonization.*

Oral Options:

FIRST LINE

Amoxicillin-clavulanate 875/125 mg PO BID

If MRSA concern add: Doxycycline 100 mg PO BID or TMP/SMX DS 1 tab PO BID

SECOND LINE

Penicillin allergy (including anaphylaxis) or severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS): Levofloxacin 750 mg PO daily PLUS Doxycycline 100 mg PO BID

IV Options:

FIRST LINE

Ceftriaxone 2 gm IV daily PLUS Metronidazole 500 mg IV/PO q8h OR Ampicillin/sulbactam 3 gm IV q6h OR

Ertapenem 1 gm IV daily

If MRSA concern add: Vancomycin 15 mg/kg IV Q12h

SECOND LINE

Penicillin allergy (including anaphylaxis): ceftriaxone and ertapenem are safe

Severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergy: Levofloxacin 750 mg IV daily PLUS Clindamycin 900 mg IV q8h

Moderate soft tissue only infections may require 1-2 weeks.

SEVERE: As above with systemic signs of infection (fever, tachycardia, leukocytosis, hypotension, sepsis syndrome, necrotizing infection, etc.) Generally, life- or limb-threatening.

NOTE *Increased frequency of polymicrobial infection. Treat gram-positive cocci including MRSA, aerobic gram-negative rods, and anaerobes. Do not*

Continued



RECOMMENDED TREATMENT AND DURATION *Continued*

include *Pseudomonas* coverage unless risk factors (water exposure, previous isolation of *Pseudomonas*). Consult a surgery team in all severe infections.

FIRST LINE

Vancomycin 15 mg/kg IV q12h PLUS Ceftriaxone 2 gm IV daily PLUS Metronidazole 500mg IV q8h (PREFERRED) OR

Vancomycin 15 mg/kg IV q12h PLUS Ertapenem 1 gm daily OR

Vancomycin 15 mg/kg IV q12h PLUS Piperacillin/tazobactam 4.5 gm IV q8h (or Extended Infusion)

NOTE If water exposure: Treat for *Pseudomonas* replacing ceftriaxone with cefepime 2gm IV q8hr until cultures return.

SECOND LINE

Penicillin allergy (including anaphylaxis): ceftriaxone, cefepime and ertapenem are safe

Severe penicillin allergy with delayed severe cutaneous reactions (DRESS, SJS) or any cephalosporin allergy: Vancomycin 15 mg/kg IV q12h PLUS Aztreonam 2g IV q8h PLUS Metronidazole 500mg IV q8h

Severe soft tissue infections with initial improvement on IV antibiotics can be switched early to highly bioavailable oral agents (FQ, TMP/SMX, linezolid, metronidazole, etc.) for a combined treatment duration of 2-4 weeks.

Antibiotics can be stopped 2-5 days post resection for bone or joint involvement if complete resection of infected tissue is confirmed post amputation.

If residual soft tissue infection exists after complete bone resection IV and oral antibiotics combined typically lasts 1-3 weeks. If residual infected bone an additional 1-3 weeks is recommended. Recommend infectious diseases consult for management of residual bone infection.

Extended durations are likely if no surgery or residual dead bone exists.

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ORGAN SYSTEM:	SYNDROME:
Skin and Soft Tissue	Uncomplicated Cellulitis in Pediatrics

SYMPTOMS AND/OR RISK FACTORS

NOTE Guideline recommendations are for uncomplicated cellulitis in children > 44 weeks and excludes those with complicating risk factors; if complicating risk factors, treatment may vary and formal specialty consultation may be warranted.

Guideline exclusion criteria:

- Hospital-acquired, surgical site & device-associated infections
- Presumed necrotizing fasciitis
- Orbital/periocular cellulitis
- Immunodeficiency
- Pressure ulcers
- Solitary dental abscess

Risk factors for MRSA:

- History of MRSA in the patient
- History of MRSA in the family
- Recurrent boils, pustules, “spider bites”, that required antibiotics, in patient or family

Specialty Consultation Considerations:

- Orthopedics if deep extremity infection (e.g., tenosynovitis, septic arthritis, osteomyelitis) · Deep puncture wound of hand/ fingers/feet
- General surgery if peri-anal abscess (within 1cm of anal verge) · Breast abscess · Perineal abscess · Pilonidal cyst · Large or complex abscess
- ENT if neck abscess
- Dental if facial cellulitis of dental origin

Low Risk Criteria:

Simple abscess · Adequate I&D · Age \geq 1 year · No fever · Well- appearing · No significant comorbidities · Follow up assured

Inpatient Admit Criteria (any one of the following):

Systemic illness, not tolerating PO, treatment failure on > 48 hrs of appropriate antibiotics, rapidly progressive lesion, pain control/wound care needed, inadequate follow-up, all < 2 months of age; consider if < 6 months

Diagnostic Studies:

- The following are NOT routinely indicated for initial management of uncomplicated disease: ESR, CRP, Procalcitonin, blood cultures, wound swab/ superficial cultures, fungal or AFB cultures, plain films, CT or MRI
- Perform bedside ultrasound unless clearly fluctuant or draining

- If fluctuant or abscess > 1cm on ultrasound, provide sedation/ pain control, I&D and wound culture of purulent drainage
- Obtain a CBC, CRP, and blood cultures in children with signs of systemic toxicity, including ill-appearance, rapidly spreading lesions, persistent fevers, and age < 1 year
- Plain film only if concern for foreign body or necrotizing fasciitis

CULTURE AND SUSCEPTIBILITY (C&S) INVESTIGATION

- Non-purulent cellulitis is most commonly attributed to beta- hemolytic streptococci
- Purulent cellulitis or cutaneous abscess is most commonly attributed to beta-hemolytic Streptococci and/or *Staphylococcus aureus* and warrants empiric coverage for MRSA.
- Recurrent MRSA infections need not be cultured at every presentation.
- Gram-negative or anaerobic coverage is usually unnecessary for purulent or non-purulent uncomplicated cellulitis.

RECOMMENDED TREATMENT AND DURATION

Non-purulent cellulitis:

INPATIENT

FIRST LINE INPATIENT

Cefazolin 50 mg/kg IV per day q8hr

SECOND LINE INPATIENT (β -Lactam Allergy)

If local *S. aureus* and GAS clindamycin susceptibility $\geq 85\%$, clindamycin 25-40 mg/kg per day q6-8hr or Vancomycin if systemic toxicity

OUTPATIENT

FIRST LINE OUTPATIENT OR ORAL STEP-DOWN

Cephalexin 25-50 mg/kg per day divided TID or QID

SECOND LINE OUTPATIENT (β -Lactam Allergy)

If local *S. aureus* and GAS clindamycin susceptibility $\geq 85\%$, clindamycin 25-30 mg/kg per day TID

Purulent cellulitis or cutaneous abscess:

INPATIENT

FIRST LINE INPATIENT

Clindamycin 10 mg/kg/dose IV q6-8hr (max does range 600- 900mg/dose IV)

SECOND LINE INPATIENT

Vancomycin 15mg/kg/dose IV q6-8hr (initial max 1gm/dose) if systemically ill, failed outpatient clindamycin, or abscess in an area difficult to drain completely

Continued >

OUTPATIENT

NOTE No systemic antibiotics are needed if adequate I&D and low risk

FIRST LINE OUTPATIENT or oral step-down

Clindamycin 10 mg/kg /dose PO TID (max single dose range 450-600mg/dose)

SECOND LINE OUTPATIENT

TMP/SMX 4-6 mg/kg/dose trimethoprim PO BID (max 160mg TMP/dose) or doxycycline if > 8 years 2mg/kg/dose PO BID (max 100mg/dose)

Duration of antibiotics for uncomplicated cellulitis in children is usually 7-10 days. May consider shorter durations (5-7 days) for non-severe infections with quick response to therapy or extended to 14 days for severe disease.

CONSIDERATIONS

- Antibiotics with broad-spectrum gram-negative activity are NOT recommended except necrotizing fasciitis, and in most cases should be avoided.
- Tailor antibiotics if culture results are available; utilize suggested empiric oral options when culture negative or not available.
- May consider oral de-escalation options if clinically improving in 2-3 days.
- If no improvement on adequate antibiotics after 48 hours or significant or rapid progression (ie. more than just 1-2 cm beyond margins) at any time, image (U/S preferred) to rule out abscess formation and consider modification to antibiotic therapy.

NOTE *The development of a new abscess within an area of previous infection while on antibiotics does not in and of itself constitute treatment failure. Likewise, it is not uncommon for erythema to spread after initiation of antibiotics due to release of toxin from killed organisms. Reasonable discharge criteria include: Lesion(s) show signs of improvement, tolerating PO, pain controlled, afebrile > 24 hours, F/U assured within 48 hours*

- Discuss with ID with there has been fresh or saltwater contact
- If worried about palatability or concerns about administration exist, a single oral antibiotic dose may be given prior to discharge.

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ORGAN SYSTEM:	SYNDROME:
Miscellaneous	Simplified Approach to Antibiotic Selection in Adults with sepsis-related organ dysfunction

ANTIMICROBIAL STEWARDSHIP KEY POINTS

1. Patients presenting with severe sepsis/septic shock are often infected with the same common bacteria that cause less severe presentations.
2. The key decision is whether to use an antibiotic (or antibiotic combination) that is based on a specific sepsis syndrome (pneumonia, UTI, etc.) or to treat sepsis as an undifferentiated disease state.
3. The most likely pathogens should be covered with the most effective and potent antibiotics. For example, *S. pneumoniae* is killed very effectively with ceftriaxone so should be included when an infection due to that pathogen is likely.
4. The risk for specific organisms or for drug-resistant infections can be determined by reviewing available data (e.g., an antibiogram), focusing on the presenting syndrome, and recent healthcare and antibiotic exposures.
5. Obtain cultures, especially blood cultures, as early as possible and preferably before administering antimicrobials. If there are barriers to getting cultures, antimicrobial administration should not be delayed.
6. Although supporting evidence is not as strong, other interventions for sepsis, including checking a lactate level (and repeating if elevated) and volume resuscitation, are important considerations. Sepsis presentations can mimic or overlap with other possible diagnoses, for example drug overdose or trauma, so the threshold for empiric treatment and sepsis-oriented diagnostics should be low until the patient's status is clearer.

SYMPTOMS AND/OR RISK FACTORS

How much room do you have to be wrong? Is the patient in acute care or critical care? Does the patient have evidence of end organ dysfunction? The more serious the patient's condition, the more delay to treatment matters.

What is the most likely source of infection, and which pathogens are the most common culprits for these infections?

Is the patient at risk for an infection with MRSA based upon prior infections or surveillance cultures?

Should anaerobes be covered based upon extra-biliary colonic source or necrotizing or cavitary pneumonia?

Is the patient at risk for pseudomonas or another MDRO (prior *P. aeruginosa* or MDR infections)

RECOMMENDED TREATMENT AND DURATION

Rapid initiation of broad-spectrum antibiotics is warranted for severe sepsis and/or shock.

FIRST LINE ADULT, UNKNOWN SOURCE

COMMUNITY ACQUIRED

Ceftriaxone 2g IV daily

Patient-specific risk factors: Consider the following for empiric coverage if the patient has risk factors

IF risk for Pseudomonas (e.g. hospital acquired)

Cefepime 2g q8hr OR Piperacillin/Tazobactam 4.5g q 6-8 hr

IF risk for ESBL (e.g. history of ESBL isolation)

Meropenem 1g q8hr OR Imipenem-Cilastatin 500mg IV q 6hr

IF risk for MRSA (e.g. hospital-acquired, prior positive MRSA cultures)

ADD Vancomycin IV X 1 (2g if $> 70\text{kg}$, 1.5g if $< 70\text{kg}$), then 15mg/kg IV q12hrs

IF risk for anaerobes (e.g. intra-abdominal source)

ADD Metronidazole 500mg IV q8hr if using cefepime or ceftriaxone

SECOND LINE ADULT (Penicillin Allergy)

Penicillin allergy (including anaphylaxis)	Ceftriaxone 2g IV daily OR Cefepime 2g IV q8hr OR Meropenem 1 g IV q8hr
Severe cutaneous adverse reaction (DRESS, SJS) OR Cephalosporin allergy	Aztreonam 2g IV q6hr PLUS Vancomycin IV x1 2g if $\geq 70\text{ kg}$, 1.5g if $< 70\text{ kg}$

NOTES

