Additional References		
Intraperitoneal antimicrobial dosing	7/2023	--
Augmentin concentrations and dosing	9/2022	--
Duplicate Anaerobic Policy	9/2022	--
Lock Therapy – Patient Care Policy 2058	7/2024	--
Beta-lactam allergy delabeling guideline	1/2024	--
Penicillin Skin Testing Policy – Patient Care Policy 5006	8/2024	--
Pediatric bone marrow transplant guidelines: CMV Adenovirus EBV/BK/RSV Infection prophylaxis	--	--
Treatment Guideline References		

Restricted Antimicrobials Pharmacotherapy approved: 6/21/2024

Prescriber must contact a member of the Antimicrobial Management Team (AMT) directly via Perfect Serve between 7 am and 10 pm for adult sites and 7 am and 10 pm for APH/NICU daily for approval of restricted indications (see below for list). Pharmacy may not obtain approval on behalf of the prescriber. A discussion between the prescriber and AMT about the appropriateness of the restricted medication is expected to occur to obtain approval. If an ID provider is recommending the restricted medication, the ID provider must directly communicate approval to the pharmacy or prescribe the restricted antimicrobial.

- **ORMC/UFHCC, SSH, WPH, DPH, HCH, HWH, SOLK**: Antimicrobial Management Team (AMT) via PerfectServe
- **APH and NICU**: APH/NICU Antimicrobial Management Team (AMT) via PerfectServe

AMT Members - list of designated pharmacists at each site who are authorized to approve restricted antimicrobials. Infectious disease physicians are allowed to prescribe restricted antimicrobials outside of the pre-approved indications.

All non-formulary antimicrobials require AMT approval

Fluoroquinolones	
	Approved Indications (do not require AMT approval)
Ciprofloxacin	• Cystic Fibrosis Flares/Exacerbations • Gram negative bacteremia, known ciprofloxacin susceptible (PO therapy only) • Gram negative osteoarticular infections, known ciprofloxacin susceptible (PO therapy only) • *Pseudomonas* spp. pneumonia, known ciprofloxacin susceptible (PO therapy only) • Mycobacterial infections, combination therapy • Prophylaxis for meningococcal exposures • Prostatitis/Epididymal Orchitis • Spontaneous bacterial peritonitis (SBP) prophylaxis (oral only) • Shigella/Salmonella/Cholera infections **Additional indication for APH/NICU Only**: Treatment of UTI caused by *Pseudomonas* spp., known ciprofloxacin susceptible (PO therapy only)
Levofloxacin	**Adult sites**: • Prophylaxis of bacterial infections in patients with hematological malignancies or bone marrow transplant (BMT) patients who have an expected period of severe neutropenia > 7 days • Community acquired pneumonia in patients with severe penicillin AND cephalosporin allergies • Treatment of mycobacterial infections (continuation of home regimen) **APH:** • Prophylaxis of bacterial infections in patients with high-risk leukemias, allogenic BMT patients with GVHD, patients with HLH, and patients with bone marrow failure syndromes who have an expected period of severe neutropenia > 7 days (See full Guideline for comprehensive list of indications) • Sinus and pulmonary infections as oral stepdown therapy in patients with severe penicillin AND cephalosporin allergies

Carbapenems	
	Approved Indications (do not require AMT approval)
Ertapenem	• Infection due to ESBL-producing organism other than cystitis • Treatment of *Enterobacter* spp. or *Klebsiella aerogenes* infection other than cystitis • Continuation of home regimen/OPAT (Outpatient parenteral antimicrobial therapy)
Imipenem-cilastatin	None – all indications require AMT approval
Meropenem	**Adult sites:** • Empiric use for an ICU or BMT patient, 72 hours only (includes N2E and N8W at ORMC) • One time dose to ER at ORMC/DPH/SSH/HCH/HWH **APH:** • Empiric use for a BMT patient, 48 hours only • Orders between 7AM and 7PM: Approved x 1 dose pending ID consultation/approval for all indications. • Orders after 7PM: Approved x 2 doses pending ID consultation/approval for all indications.

Beta-lactam/Beta-lactamase Inhibitors	
	Approved Indications (do not require AMT approval)
Ceftazidime-avibactam	None – all indications require AMT approval
Ceftolozane-tazobactam	None – all indications require AMT approval
Meropenem-vaborbactam	None – all indications require AMT approval

Gram-positive Agents	
	Approved Indications (do not require AMT approval)
Ceftaroline	• None – all indications require AMT approval
Dalbavancin	• **See Restricted Antimicrobials Appendix I for Dalbavancin Use Criteria** • Ordered by ED physician AND patient is expected to be discharged in <24 hours • **No overnight release for unapproved indications – prescribers must use alternative therapy 2201 to 659.**
Daptomycin	• VRE bacteremia or other VRE infections and intolerant to linezolid • MRSA/MRSE with vancomycin contraindication (allergy, nephrotoxicity, h/o failure) • Gram-positive osteoarticular infections within 1 day of planned discharge (x48 hours only)
Linezolid	• Proven/suspected VRE • MRSA/MRSE with vancomycin contraindication (allergy, nephrotoxicity, h/o failure) • Proven/suspected severe MRSA pneumonia
Vancomycin (IV)	**APH and NICU ONLY** • Empiric use x 48 hours • Orders extended past initial 48-hour period that don't meet approved indications below require ID/AMT approval; approved x 2 doses pending ID/AMT approval between hours of 7PM and 7AM • Proven MRSA or coagulase negative Staphylococcal infections • Infections due to beta-lactam resistant, vancomycin susceptible Gram- positive organisms • Ampicillin resistant *Enterococcus* spp. infections • Treatment of infections caused by Gram-positive organisms in patients who have a severe type-1 allergic reaction to beta-lactam antibiotics • Proven beta-lactam resistant Streptococcal infections • Prophylaxis in cardiac patients for open chest > 48 hours, until chest closure

Other Antibiotics	
	Approved Indications (do not require AMT approval)
Aztreonam	None – all indications require AMT approval
Cefiderocol	None – all indications require AMT approval
Eravacycline	None – all indications require AMT approval
Fidaxomicin	• Ordered by GI physician • Confirmed recurrent *Clostridioides difficile* infection (CDI). Recurrent CDI is defined as: Reappearance of signs and symptoms of CDI AND a positive *C. difficile* screen within 8 weeks of a prior CDI episode for which signs and symptoms had resolved.
Polymyxin B IV	None – all indications require AMT approval
Colistin IV	• **Adult sites:** None. All indications require AMT/ID approval. • **APH:** Cystic fibrosis exacerbation. All other indications require AMT approval
Ribavirin	• Ordered by BMT service

Antifungals	
	Approved Indications (do not require AMT approval)
Amphotericin B IV	**Adult sites**: Ordered by BMT service. All other non-ID providers require AMT approval. **APH**: • Ordered by BMT service • Empiric use of the deoxycholate formulation ordered in the NICU x 48 hours • Empiric use of the deoxycholate formulation ordered at APH/NICU for Amoeba encephalitis x 48 hours
Flucytosine	Suspected or confirmed cryptococcal meningitis
Isavuconazole	Continuation of home regimen or ordered by BMT service.
Posaconazole	Tablets: Continuation of home regimen or ordered by hematology/oncology or BMT provider IV: None – all indications require AMT approval
Voriconazole	Continuation of home regimen or ordered by hematology/oncology or BMT provider

Antivirals	
	Approved Indications (do not require AMT approval)
Cidofovir	• Intralesional therapy performed by an EENT physician • Intravesicular administration ordered by BMT service
Ganciclovir	Ordered by BMT service. All other non-ID providers require AMT approval.
Letermovir	Ordered by BMT service. All other non-ID providers require AMT approval.
Paxlovid (Nirmatrelvir/ Ritonavir)	**Available at ORMC, APH, and WPH only:** All adults and pediatric patients aged > 12 years and at least 40 kg with mild/moderate COVID-19 (signs/symptoms of respiratory infection but maintaining oxygen saturation > 94% on room air) and with risk factors to for progression to severe disease
Peramivir	ICU patient with documented influenza and unable to take oral alternatives (1 dose only)
Remdesivir	**Adult Sites:** • Hospitalized for COVID-19, not requiring oxygen, unable to receive Paxlovid, and high risk for progression to severe disease – **Limited to 3-day duration** • Hospitalized for COVID-19 and requiring oxygen supplementation to maintain oxygen saturation > 94%, but who are not yet requiring high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), noninvasive positive-pressure ventilation (NPPV), or invasive mechanical ventilation – **Limited to 5-day duration** **APH/NICU:** No pre-approved indications.
Valganciclovir	**Adult Sites Only – Valganciclovir not restricted at APH/NICU** • Continuation of home regimen • Ordered by BMT service All other indications require AMT approval

Antiparasitics	
Pyrimethamine	**No pre-approved indications.** **All indications must be approved by AMT for all NEW orders (unless patient has own home supply – pharmacist to verify home supply before verifying order). At ORMC, AMT approval must be obtained by an ID Pharmacist (Monday-Friday 7 am to 5 pm). Providers must use an alternative until approval (see below).** **For all orders**, providers must use an alternative agent until pyrimethamine is available. Recommended alternative is sulfamethoxazole-trimethoprim 10 mg/kg/day (based on trimethoprim component) in two divided doses. Patients with renal insufficiency may require dose adjustment. For patients with sulfa allergies, discuss alternatives with ID/ AMT service.
Artesunate	**No pre-approved indications, all indications must be approved by ID/AMT** Supply for initial dose stocked at ORMC; see procurement process for details

Non-Antimicrobials Restricted to Infectious Diseases When Used for COVID-19 Treatment	
	Approved Indications (do not require AMT approval)
Baricitinib (NF)	Requires Infectious Diseases prescriber approval (or AMT approval at HCH only)
Tocilizumab	**Adult Sites:** Ordered by CCM (or other specialty when covering and acting on behalf of CCM) for non-pregnant patients with confirmed COVID-19 hospitalized within previous 3 days ***and*** admitted to the ICU within previous 24 hours requiring heated/humidified high flow nasal canula > 40% FiO_2/30 L/min, non-invasive ventilation (CPAP, BiPAP, NPPV), or invasive mechanical ventilation. See the Orlando Health Treatment Guidance for Inpatients with COVID-19 Pneumonia for additional considerations in who to avoid use in. All other use for COVID-19 treatment requires ID approval. **APH/NICU:** Requires Infectious Diseases prescriber approval *In situations of medication shortage identified by the Drug Shortages Management Team, preference will be given to oncological indications consistent with the process outlined in Patient Care Policy 5142 Medication Shortages and Backorders*

Restricted Antimicrobials Appendix I: Dalbavancin Use Criteria

Dalbavancin use in outpatient areas (including Emergency Department and Infusion Center) do not require ID/AMT approval.

All inpatient use (including observation patients) requires AMT approval. No overnight release (2200-0659) will be permitted - refer to the Management of Skin and Soft Tissue Infections in Adults guidelines for alternative treatment options during these times. Orders placed during these hours will be held until AMT is available again at 0700.

Use should be limited to the following:

- Acute bacterial skin and skin structure infections highly suspected or known to be caused by Gram-positive bacteria **PLUS** unable to take oral antibiotics* **PLUS** does not meet any exclusion criteria below
- Exclusion criteria:
    - Reason to admit the patient outside of needing intravenous antibiotics
      Known hypersensitivity to vancomycin, televancin, oritavancin, or dalbavancin
    - Clinical suspicion of severe sepsis or septic shock
    - Fournier's gangrene
    - Necrotizing fasciitis
    - Involvement of the eye, face, genitals
      Treatment for diabetic foot infections
      Suspicion of Gram-negative organisms
      Immunosuppressed or on active chemotherapy

Financial Considerations

- Average Wholesale Pricing (AWP)^: $5,861 per 1500mg course
- **Emergency Department and Infusion Center patients:**
    - Uninsured patients with financial hardship may be eligible for assistance
    - From Abbvie: https://www.abbvie.com/patients/patient-assistance/program-qualification/dalvance- program-selection.html#myabbvie
    - Product replacement may also be available with the above program

Follow-up

Patients should be instructed to follow-up with their primary care provider or return to the ED if infection does not improve or worsens within 48 hours of dalbavancin therapy

Approved by AUSS and Pharmacotherapy: 7/2021

APH & ED Antimicrobial Susceptibility Report January 2024 to December 2024

Microbiology Laboratory Number: 321-841-5226

	No. Tested	Ampicillin$	Clindamycin$$	Daptomycin$$$	Doxycycline$$$	Linezolid$$$	Nitrofurantoin$ urine only	Nafcillin$$$	Trimeth/Sulfa$$$	Vancomycin$
MIC breakpoint, mcg/mL		≤8[e]	≤0.5	≤1[bc]/≤4[e]	≤4	≤4[bc]/≤2[e]	≤32	≤2[b]/≤0.5[c]	≤2/38	≤4[ce]/≤2[b]
All *Staphylococcus aureus*[a]	245	-	81	100	99	100	99[g]	68[d]	88	100
MRSA (31%)	77	-	84	100	98	100	100[g]	0	80	100
MSSA (69%)	169	-	79	100	99	100	99[g]	100[d]	91	100
Staphylococcus epidermidis^	27	-	69	100	92	100	100	59	81	100
Enterococcus faecalis[a]	54	100	-	100	36	100	100	-	-	100

	No. Tested	Ceftriaxone$	Clindamycin$$	Linezolid$$$	Levofloxacin$	Penicillin$$$	Tetracycline$$$	Trimeth/Sulfa$$$	Vancomycin$
MIC breakpoint, mcg/mL		≤1/≤0.5[h]	≤ 0.25	≤2	≤1	≤2/≤0.06[h]	≤2	≤0.5/9.5	≤1
Streptococcus pneumoniae[i]	44	95/77	84	100	100	92/60	87[f]	77	100

Values reflect hospital acquisition cost to treat a 70 kg patient per day (IV formulation if available): $ = 0-14, $$= 15-24, $$$=25-49, $$$$=50-99 $$$$$=100-200, $$$$$$= >300

[a] **MRSA rate = 31%; VRE rate = 0%**

[b] Breakpoints for *Staphylococcus aureus.*

[c] Breakpoints for *Staphylococcus epidermidis*.

[d] *Staphylococcus aureus* susceptibility to nafcillin predicts susceptibility to cefazolin.

[e] Breakpoints for *Enterococcus spp*. For daptomycin, an MIC of 4 mcg/mL is considered susceptible if using high dose therapy.

[f] Organisms susceptible to tetracycline can be considered susceptible to doxycycline and minocycline.

[g] Presence of *Staphylococcus aureus* in the urine should always prompt consideration of possible *S. aureus* bacteremia and/or renal abscess.

[h] *Streptococcus pneumoniae* susceptibility breakpoints differ for CSF isolates/meningitis: 0.5 mcg/mL for ceftriaxone and 0.06 mcg/mL for penicillin.

[i] The percent susceptibility was calculated using ~2 years of data (January 2023-December 2024).

^ Susceptibility data from fewer than 30 isolates may carry less statistical significance.

APH & ED Antimicrobial Susceptibility Report January 2024 to December 2024

Microbiology Laboratory Number: 321-841-5226

	No. Tested	Amikacin[$]	Ampicillin[$]	Ampicillin/ Sulbactam[$]	Aztreonam[$$$$$]	Cefazolin[$] urine only	Cefepime[$]	Ceftriaxone[$]	Ciprofloxacin[$]	Ertapenem[$$$$]	Gentamicin[$]	Meropenem[$]	Nitrofurantoin[$] urine only	Piperacillin/ Tazobactam[$]	Trimeth/Sulfa[$$$]	Tobramycin[$]
MIC breakpoint, mcg/mL		≤ 4[a]/ ≤16[g]	≤8	≤8	≤4	≤16[b]	≤8	≤1[a]	≤0.25[a]/ ≤ 0.5[e]	≤0.5	≤2	≤1[a]/ ≤2[e]	≤32	≤16[f]	≤2/38	≤2[a]/ ≤1[e]
Enterobacter cloacae[^]	25	96	-	-	64	-	92	-[*]	96	95	100	100	36	64	84	100
Escherichia coli[cd]	377	99	43	55	95	93	99	92	79	100	87	99	97	88	63	86
E. coli – non-ESBL[cd]	352	99	46	56	99	98	100	99	84	100	88	100	97	95	65	88
Klebsiella pneumoniae[cd]	66	100	-	71	81	76	95	83	84	100	90	100	2	95	90	87
Pseudomonas aeruginosa	108	100[g]	-	-	-[h]	-	96	-	94	-	-	94	-	89	-	78
Serratia marcescens	31	87	-	-	93	-	100	83	90	100	87	100	-	100	96	70
Proteus mirabilis	37	97	76	81	97	89	100	94	100	100	94	100	-	100	84	91

Values reflect hospital acquisition cost to treat a 70 kg patient per day (IV formulation if available): $ = 0-14, $$= 15-24, $$$=25-49, $$$$=50-99 $$$$$=100-200, $$$$$$= >300

[a] Breakpoints for Enterobacterales (*Enterobacter* spp., *E. coli*, *Klebsiella* spp., etc.)

[b] Urinary breakpoint for Enterobacterales; only includes urinary isolates

[c] **ESBL rate: *E. coli* = 5.9%, *K. pneumoniae* = 16.7%**

[d] **CRE rate: *E. Coli* = 0.2%, *K. Penumoniae* = 0%**

[e] Breakpoint for *Pseudomonas aeruginosa*

[f] The CLSI MIC susceptibility breakpoint for piperacillin/tazobactam to Enterobacterales is 8 mcg/mL. An MIC breakpoint of 16 mcg/mL is used here which is susceptible-dose-dependent based on a dosage of 100 mg/kg of piperacillin (max 4000 mg) administered every 8 hours as a 4-hour infusion.

[g] Urinary breakpoint for *P. aeruginosa*, only includes urinary isolates

[h] Susceptibility not reported due to < 50% of isolates tested

^ Susceptibility data from fewer than 30 isolates may carry less statistical significance.

[*] Clinical failures during therapy have been reported due to hyperproduction of AmpC beta-lactamases. Avoid treatment with ceftriaxone against Enterobacter *cloacae* and *Klebsiella aerogenes* (formerly *Enterobacter aerogenes*).

Stenotrophomonas maltophilia[^] (16 isolates): 81% susceptible to minocycline, 93% susceptible to trimeth/sulfa

Salmonella enterica spp^ (18 isolates; 2 years of data): 100% susceptible to ampicillin; 100% susceptible to ampicillin/sulbactam, ceftriaxone, and trimeth/sulfa)

NICU Antimicrobial Susceptibility Report January 2023 to December 2024

Microbiology Laboratory Number 321-841-5226

	No. Tested	Ampicillin[$]	Clindamycin[$$]	Daptomycin[$$$]	Linezolid[$$$]	Nafcillin[$$$]	Trimethoprim/ Sulfamethoxazole [$$$]	Vancomycin[$]
MIC breakpoint, mcg/mL		≤8[e]	≤0.5	≤1[bc]/≤4[e]	≤4[bc]/≤2[e]	≤2[b]/≤0.5[c]	≤2/38	≤4[ce]/≤2[b]
All *Staphylococcus aureus*[a]	111	-	70	100	100	68[d]	95	100
MRSA (37%)	38	-	76	100	100	0	81	100
MSSA (63%)	76	-	65	100	100	100[d]	100	100
Staphylococcus epidermidis	87	-	21	100	100	16	62	100
Enterococcus faecalis^	26	100	-	100	100	-	-	100

Values reflect hospital acquisition cost to treat a 70 kg patient per day (IV formulation if available): $ = 0-14, $$= 15-24, $$$=25-49, $$$$=50-99 $$$$$=100-200, $$$$$$= >300

[a] The NICU **MRSA rate is 36.5% and the VRE rate is 0%**.

[b] Breakpoints for *Staphylococcus aureus.*

[c] Breakpoints for *Staphylococcus epidermidis*.

[d] *Staphylococcus aureus* susceptibility to nafcillin predicts susceptibility to cefazolin.

[e] Breakpoints for *Enterococcus spp*. For daptomycin, an MIC of 4 mcg/mL is considered susceptible if using high dose therapy.

^ Susceptibility data from fewer than 30 isolates may carry less statistical significance.

NICU Antimicrobial Susceptibility Report January 2023 to December 2024

Microbiology Laboratory Number 321-841-5226

	No. Tested	Amikacin[$]	Ampicillin[$]	Ampicillin/ Sulbactam[$]	Cefazolin[$] urine only	Cefepime[$]	Ceftriaxone[$]	Ciprofloxacin[$]	Gentamicin[$]	Meropenem[$]	Piperacillin/ Tazobactam[$]	Trimethoprim/ Sulfamethoxazole [$$$]	Tobramycin[$]
MIC breakpoint, mcg/mL		≤ 4[a]/ ≤16[g]	≤8	≤8	≤16[b]	≤8	≤1[a]	≤0.25[a]/ ≤ 0.5[e]	≤2	≤1[a]/ ≤2[e]	≤16[f]	≤2/38	≤2[a]/ ≤ 1[e]
Enterobacter cloacae	34	100	-	-	-	100	-[*]	100	100	100	76	97	100
Escherichia coli[cd]	58	87	22	39	86	100	91	70	86	100	98	44	86
Klebsiella pneumoniae[cd]	55	96	-	74	86	96	87	89	93	98	97	84	91
Klebsiella oxytoca	21	100	-	76	95	100	95	100	100	100	-	100	100
Pseudomonas aeruginosa	48	100[g]	-	-	-	100	-	97	-	94	79	-	81
Serratia marcescens	38	97	-	-	-	100	97	100	97	97	100^	100	76

Values reflect hospital acquisition cost to treat a 70 kg patient per day (IV formulation if available): $ = 0-14, $$= 15-24, $$$=25-49, $$$$=50-99 $$$$$=100-200, $$$$$$= >300

[a] Breakpoints for Enterobacterales (*Enterobacter* spp., *E. coli*, *Klebsiella* spp., etc.).

[b] Urinary breakpoint for Enterobacterales; for other sites of infection, a breakpoint of ≤ 2 mcg/mL should be used for interpretation.

[c] **ESBL rate: *E. coli* = 10.3%, *K. pneumoniae* = 12.2%**.

[d] **CRE rate: *K pneumoniae* = 0.02%**

[e] Breakpoint for *Pseudomonas aeruginosa.*

[f] The CLSI MIC susceptibility breakpoint for piperacillin/tazobactam to Enterobacterales is 8 mcg/mL. An MIC breakpoint of 16 mcg/mL is used here which is susceptible-dose-dependent.

[g] Urinary breakpoint for *P. aeruginosa*.

^ Susceptibility data from fewer than 30 isolates may carry less statistical significance.

[*] Clinical failures during therapy have been reported due to hyperproduction of AmpC beta-lactamases. Avoid treatment with ceftriaxone against *Enterobacter cloacae* and *Klebsiella aerogenes* (formerly *Enterobacter aerogenes*).

Stenotrophomonas maltophilia^ (12 isolates): 100% susceptible to minocycline, 100% susceptible to trimeth/sulfa)

APH Pediatric Skin and Soft-Tissue Infection Empiric Antibiotic Therapy Guideline

Excluded patients: immunocompromised (examples: malignancy on chemotherapy, neutropenia, severe immunodeficiency disorder), neonates (< 30 days and premature < 41 weeks CGA), hospital acquired, surgical site infections, device associated infections, pressure ulcers

Table of contents:

Impetigo & Bullous Impetigo

Most common organism	*Staphylococcus aureus, Streptococcus pyogenes*
Impetigo	Mupirocin topically to affected areas three times daily
Bullous impetigo	Mupirocin topically to affected areas three times daily Extensive lesions add PO therapy: Cephalexin 25 mg/kg/dose (max 500 mg) every 8 hours
For MRSA risk factors*, ADD the following if need for PO therapy	PO: SMX/TMP† 4 mg/kg/dose TMP (max 160 mg TMP) every 12 hours (preferred) OR doxycycline^ 2 mg/kg/dose (max 100 mg) every 12 hours
Duration of therapy	5-7 days

Cellulitis, non-purulent

Most common organism	*Streptococcus pyogenes*
First line PO therapy	Cephalexin 25 mg/kg/dose (max 500 mg) every 8 hours Note: if documented GAS by culture, use amoxicillin 25 mg/kg/dose (max 500 mg) every 12 hours
First line IV therapy	Cefazolin 25 mg/kg/dose (max 2g) every 8 hours Note: if documented GAS by culture, use ampicillin 50 mg/kg/dose (max 2000 mg) every 6 hours
Second line therapy Indications: failed outpatient first-line therapy, MRSA risk factors* Note: recommend ID consult if no improvement within 48 hours	PO: SMX/TMP† 4 mg/kg/dose TMP (max 160 mg TMP) every 12 hours OR doxycycline^ 2 mg/kg/dose (max 100 mg) every 12 hours IV: Vancomycin, pharmacy to dose
Toxic appearing or failure of therapy after 48 hours	Vancomycin, pharmacy to dose
Duration of therapy	5-7 days

Cellulitis, purulent or skin abscess (suspected or definite)

Most common organism	*Staphylococcus aureus*
If lesion ≤ 5 cm, adequate I&D, no significant associated cellulitis, AND low risk (≥ 1 year, no fever, well-appearing, adequate I&D, no significant comorbidities, adequate follow-up)	No antibiotics
First line therapy	PO: SMX/TMP† 4 mg/kg/dose TMP (max 160 mg TMP) every 12 hours OR doxycycline^ 2 mg/kg/dose (max 100 mg) every 12 hours IV: Vancomycin, pharmacy to dose
Second line therapy Indications: failed first line therapy	Linezolid 10 mg/kg/dose (max 600 mg); Q8H for patients < 12 years old, Q12H for patients ≥ 12 years

Toxic appearing or failure of therapy after 48 hours	Vancomycin, pharmacy to dose
Duration of therapy	7 days if adequate I&D, 10-14 days may be required without adequate I&D Tailor antibiotics based on culture results if appropriate

Staphylococcal scalded skin syndrome (SSSS)

Most common organisms	*Staphylococcus aureus*
First line IV therapy	Nafcillin 50 mg/kg/dose (max 2 g) every 6 hours + Clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours OR Cefazolin 50 mg/kg/dose (max 2 g) every 8 hours + Clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours
PO stepdown therapy	Clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours Note: if documented MSSA by culture, use cephalexin 25 mg/kg/dose (max 500 mg) every 8 hours
Duration of therapy	10-14 days

Note: Clindamycin should be changed to linezolid for patients with a history of or currently documented clindamycin resistant *Staphylococcus aureus*

Preseptal or periorbital cellulitis secondary to sinusitis

Most common organisms	*Streptococcus spp.*, oral anaerobes, *H. influenzae, Moraxella catarrhalis*
First line PO therapy	Amoxicillin/clavulanate 30 mg/kg/dose (amoxicillin component, max 875 mg) every 8 hours
First line IV therapy	Ampicillin/sulbactam 75 mg/kg/dose (ampicillin component, max 2 g) every 6 hours
Second line therapy Indications: type-1 penicillin allergy, failed outpatient first line therapy	Ceftriaxone 50 mg/kg/dose (max 2g) every 24 hours + clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours
Toxic appearing or failure of therapy after 48 hours	Ceftriaxone 50 mg/kg/dose (max 2g) every 24 hours + metronidazole 10 mg/kg/dose (max 500 mg) every 8 hours + vancomycin, pharmacy to dose & consult ID
Duration of therapy	10 days

Preseptal or periorbital cellulitis secondary to transdermal inoculation[$]

Most common organisms	*Staphylococcus spp.* MRSA/MSSA nares culture recommended (aerobic culture, source nares, comment to lab – looking for presence of/susceptibilities for MRSA or MSSA)
First line PO therapy	Cephalexin 25 mg/kg/dose (max 500 mg) every 8 hours
First line IV therapy	Cefazolin 25 mg/kg/dose (max 2g) every 8 hours OR nafcillin 50 mg/kg/dose (max 2 g) every 6 hours
Second line therapy Indications: failed first line therapy, MRSA isolated on nares culture	PO: SMX/TMP[†] 4 mg/kg/dose TMP (max 160 mg TMP) every 12 hours OR doxycycline[^] 2 mg/kg/dose (max 100 mg) every 12 hours IV: Vancomycin, pharmacy to dose
Toxic appearing or failure of therapy after 48 hours	Vancomycin, pharmacy to dose
Duration of therapy	10 days

[$]Trauma, bug bite, laceration, etc.

Orbital cellulitis

Most common organisms	*Streptococcus spp., S. aureus,* oral anaerobes*, H. influenzae, Moraxella catarrhalis*
First line PO therapy	Amoxicillin/clavulanate 30 mg/kg/dose (amoxicillin component, max 875 mg) every 8 hours

APH Pediatric Skin and Soft-Tissue Infection Empiric Antibiotic Therapy Guideline

First line IV therapy	Ampicillin/sulbactam 75 mg/kg/dose (ampicillin component, max 2 g) every 6 hours
Second line therapy Indications: type-1 penicillin allergy, failed outpatient first line therapy, MRSA risk factors*	Ceftriaxone 50 mg/kg/dose (max 2g) every 24 hours + clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours
Toxic appearing or failure of therapy after 48 hours	Ceftriaxone 50 mg/kg/dose (max 2g) every 24 hours + metronidazole 10 mg/kg/dose (max 500 mg) every 8 hours + vancomycin, pharmacy to dose & consult ID
Duration of therapy	10-14 days after surgical drainage Longer therapy up to 28 days may be warranted for undrained collections or bony involvement (ID consult recommended)

Neck infections

Most common organisms	*Streptococcus pyogenes, Staphylococcus spp.,* anaerobes
First line PO therapy	Amoxicillin/clavulanate 30 mg/kg/dose (amoxicillin component, max 875 mg) every 8 hours
First line IV therapy	Ampicillin/sulbactam 75 mg/kg/dose (ampicillin component, max 2 g) every 6 hours
Second line therapy Indications: type-1 penicillin allergy, failed outpatient first line therapy, MRSA risk factors*	PO: Cefdinir 7 mg/kg/dose (max 300 mg) every 12 hours PLUS metronidazole 10 mg/kg/dose (max 500 mg) every 8 hours IV: Ceftriaxone 50 mg/kg/dose (max 2000 mg) every 24 hours plus metronidazole 10 mg/kg/dose (max 500 mg) every 8 hours If MRSA risk factors: add vancomycin, pharmacy to dose PO MRSA coverage only recommended for step down therapy if isolated on culture
Toxic appearing or failure of therapy after 48 hours	Add vancomycin, pharmacy to dose
Duration of therapy	10-14 days after appropriate source control if needed (I&D) Tailor therapy based on culture results as appropriate

Dental abscess

Most common organisms	*Streptococcus spp.*, oral anaerobes
First line PO therapy	Amoxicillin/clavulanate 15 mg/kg/dose (amoxicillin component, max 875 mg) every 8 hours For non-severe infection, consider amoxicillin/clavulanate 15 mg/kg/dose (amoxicillin component, max 875 mg) every 12 hours
First line IV therapy	Ampicillin/sulbactam 50 mg/kg/dose (ampicillin component, max 2 g) every 6 hours
Second line therapy Indications: type-1 penicillin allergy, failed outpatient first line therapy	Clindamycin (IV or PO) 13 mg/kg/dose (max 600 mg) every 8 hours
Duration of therapy	7 days after surgical drainage

Animal bites (dog and cat)

Most common organisms	*Pasturella spp., S. aureus, Streptococcus spp.*, anaerobes
First line PO therapy	Amoxicillin/clavulanate 15 mg/kg/dose (amoxicillin component, max 875 mg) every 8 hours For non-severe infection, consider amoxicillin/clavulanate 15 mg/kg/dose (amoxicillin component, max 875 mg) every 12 hours
First line IV therapy	Ampicillin/sulbactam 50 mg/kg/dose (ampicillin component, max 2 g) every 6 hours

APH Pediatric Skin and Soft-Tissue Infection Empiric Antibiotic Therapy Guideline

Second line therapy Indications: type-1 penicillin allergy, failed outpatient first line therapy, MRSA risk factors*	PO: Clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours + SMX/TMP† 4 mg/kg/dose TMP (max 160 mg TMP) every 12 hours IV: Ceftriaxone 50 mg/kg/dose (max 2g) every 24 hours + clindamycin 13 mg/kg/dose (max 600 mg) every 8 hours
Duration of therapy	Prophylaxis 3-5 days; Treatment of infection 10-14 days
Other	Assess need for tetanus and/or rabies prophylaxis

Necrotizing fasciitis

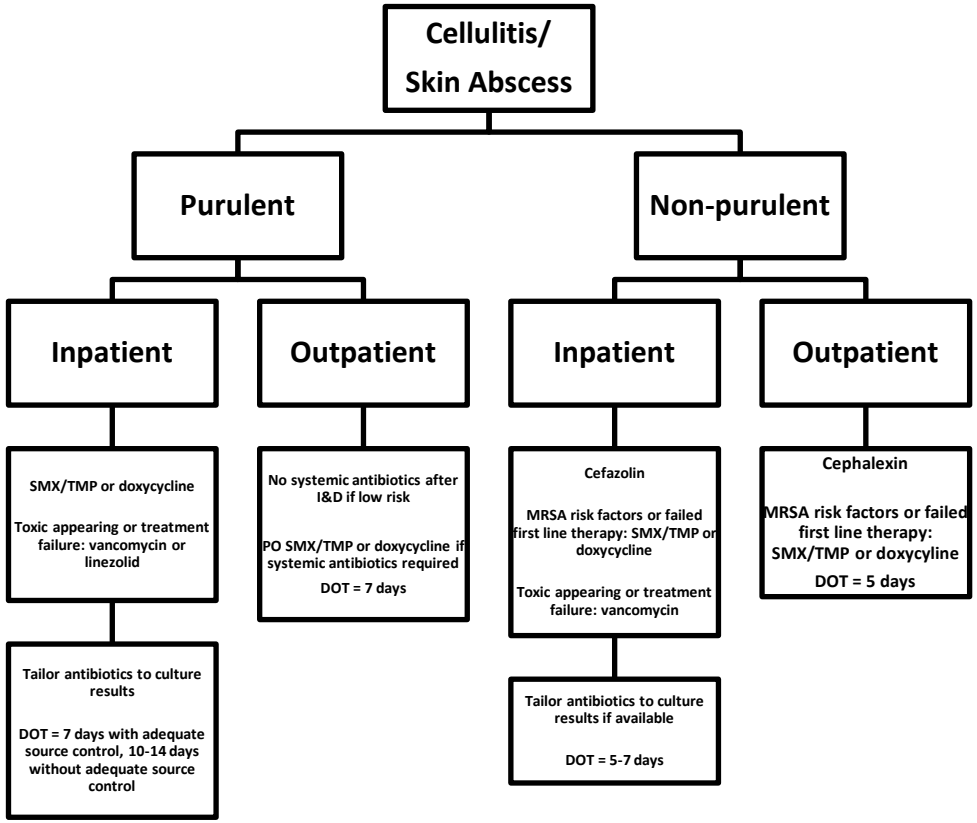
Most common organisms	*Streptococcus pyogenes*, polymicrobial including anaerobes
First line IV therapy	Emergent surgery Suspected or known GAS: IV penicillin 100,000 units/kg/dose (max 4 million units) every 6 hours + IV clindamycin 13 mg/kg/dose (max 900 mg) every 8 hours Unknown cause: Piperacillin/tazobactam 100 mg/kg/dose (piperacillin component, max 3g) every 8 hours, doses infused over 4 hours + clindamycin 13 mg/kg/dose (max 900 mg) every 8 hours + vancomycin, pharmacy to dose ID consult highly recommended including for decisions on second line therapies, role of IVIG, and determining duration of therapy

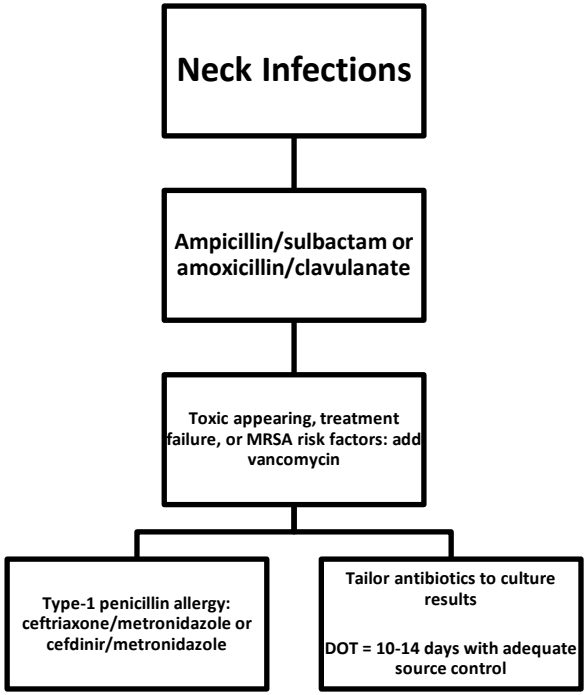
Definitions and Antibiogram

- All dosing assumes normal renal function, contact pharmacist for renal dose adjustments
- GAS = Group A Streptococcus (*Streptococcus pyogenes*); MRSA = Methicillin resistant *Staphylococcus aureus*
- ***MRSA risk factors**: known MRSA nasal colonization, recent prolonged hospitalization, history of recurrent skin infections, penetrating trauma, evidence of MRSA infection elsewhere, injection drug use, sepsis
- ^Doxycycline can safely be used for short durations (≤ 21 days) regardless of patient age
- †Sulfamethoxazole/trimethoprim (Bactrim)
- Type-1 penicillin allergy: anaphylaxis, shortness of breath, hives, swelling
- Failure of first line therapy: minimal improvement or worsening after 48-72 hours of therapy
- All GAS universally susceptible to penicillin; resistance to clindamycin has been reported as high as 10%

When to consider an ID consult: rapidly progressing disease, ill-appearing, sepsis, suspected or confirmed necrotizing fasciitis, fresh or salt water contact associated SSTI, concern for deep extremity infection (septic arthritis, osteomyelitis)
When to consider a general surgery consult: perianal abscess, perineal abscess, breast abscess, pilonidal cyst, suspected or confirmed necrotizing fasciitis, large or complex skin abscess
When to consider an ENT consult: neck abscess
When to consider an orthopedics consult: deep extremity infection (septic arthritis, osteomyelitis)

APH Pediatric Skin and Soft-Tissue Infection Empiric Antibiotic Therapy Guideline





Low risk: lesion ≤ 5 cm, adequate I&D, no significant associated cellulitis, ≥ 1 year old, no fever, well-appearing, no significant comorbidities, adequate follow-up

*__MRSA risk factors__: known MRSA nasal colonization, recent prolonged hospitalization, history of recurrent skin infections, penetrating trauma, evidence of MRSA infection elsewhere, injection drug use, sepsis

Arnold Palmer Hospital for Children: Management of Acute Hematogenous Osteomyelitis (AHO) & Septic Arthritis

1. Definitions:

Acute osteomyelitis: bone infection within 4 weeks from onset of clinical manifestations in a previously uninfected bone

Chronic osteomyelitis: protracted, often indolent disease process, lasting at least 6 weeks; presence of a sequestrum and/or relapse of infection in the same site (bone) weeks to years after apparently successful treatment of the initial infection in that site may be present

Sequestrum: piece of devitalized bone that has been separated from its surrounding bone during the process of necrosis

Complicated osteomyelitis: infection of the bone with ≥ 2 more bones involved, ≥ 2 surgeries required for source control, additional soft tissue sites of infection beyond the bone, lack of clinical response > 5 days such as resolution of fever and marked improvement in clinical signs, ≥ 72 hours prolonged bacteremia, venous thrombosis, endocarditis, or pathologic fracture

Septic arthritis: bacterial infection in the joint (synovial) fluid and joint tissues

Hemodynamic instability: hypotension, tachypnea, tachycardia, mental status changes, or organ dysfunction

Allergy: type 1 hypersensitivity reaction; involves immunoglobulin E (IgE) mediated release of antibodies (anaphylaxis, shortness of breath, hives, swelling)

Subperiosteal abscess: complication of osteomyelitis involving purulent material that ruptures through the thin cortex into the subperiosteal space

2. Inclusions/Exclusions

- Inclusion
  - Hospitalized
  - 1 month – 18 years old
  - Diagnosis of acute hematogenous osteomyelitis or septic arthritis
- Exclusion
  - Diagnosis of chronic osteomyelitis
  - Presence of orthopedic device or prosthesis
  - Infections from penetrating trauma
  - Immunocompromised
  - Sickle cell disease
  - Postoperative infection
  - Osteomyelitis associated with chronic pressure ulcers
  - Osteomyelitis associated with diabetic foot ulcers

3. Initial Evaluation

- Initial Laboratory Studies:
    - Blood culture
    - Complete blood count (CBC) with differential
    - Complete metabolic panel (CMP)
    - C-reactive protein (CRP)
    - Erythrocyte sedimentation rate (ESR)
    - Consider *Neisseria gonorrhea* screening for sexually active teenagers with new onset musculoskeletal infection

- Surgical specimens/culture recommendations
    - Aspirates and/or biopsy specimens of bone and/or associated purulent fluid collections for aerobic culture and Gram stain
    - *Kingella kingae* PCR test for all patients 18 months to < 5 years old (send synovial fluid in sterile cup)

- Initial Imaging Studies:
    - Plain radiography
        - Not sensitive for diagnosis of acute osteomyelitis, however, can rule out other diagnosis such as fracture or malignancy
    - Magnetic resonance imaging (MRI) with and without contrast
        - Modality of choice to establish the diagnosis of osteomyelitis or to delineate the location and extent of bone involvement
        - Preferred for all ill appearing patients

4. Initial Treatment

- Other than small bones of hands or feet, all patients should be treated with intravenous antibiotics initially
- If feasible, obtain proper tissue samples and cultures prior to starting antibiotics, unless hemodynamically unstable
- For empiric therapy, start intravenous antibiotic treatment and assess clinical response (Table 1 or Table 2)
- If blood or tissue culture positive, narrow therapy to cover organism (Table 3)
- For patients with a beta-lactam allergy, place a “Pharmacy general consult” for a beta-lactam allergy interview

MSSA = methicillin susceptible *Staphylococcus aureus*
MRSA = methicillin resistant *Staphylococcus aureus*
GAS = *Streptococcus pyogenes*

Management Algorithm

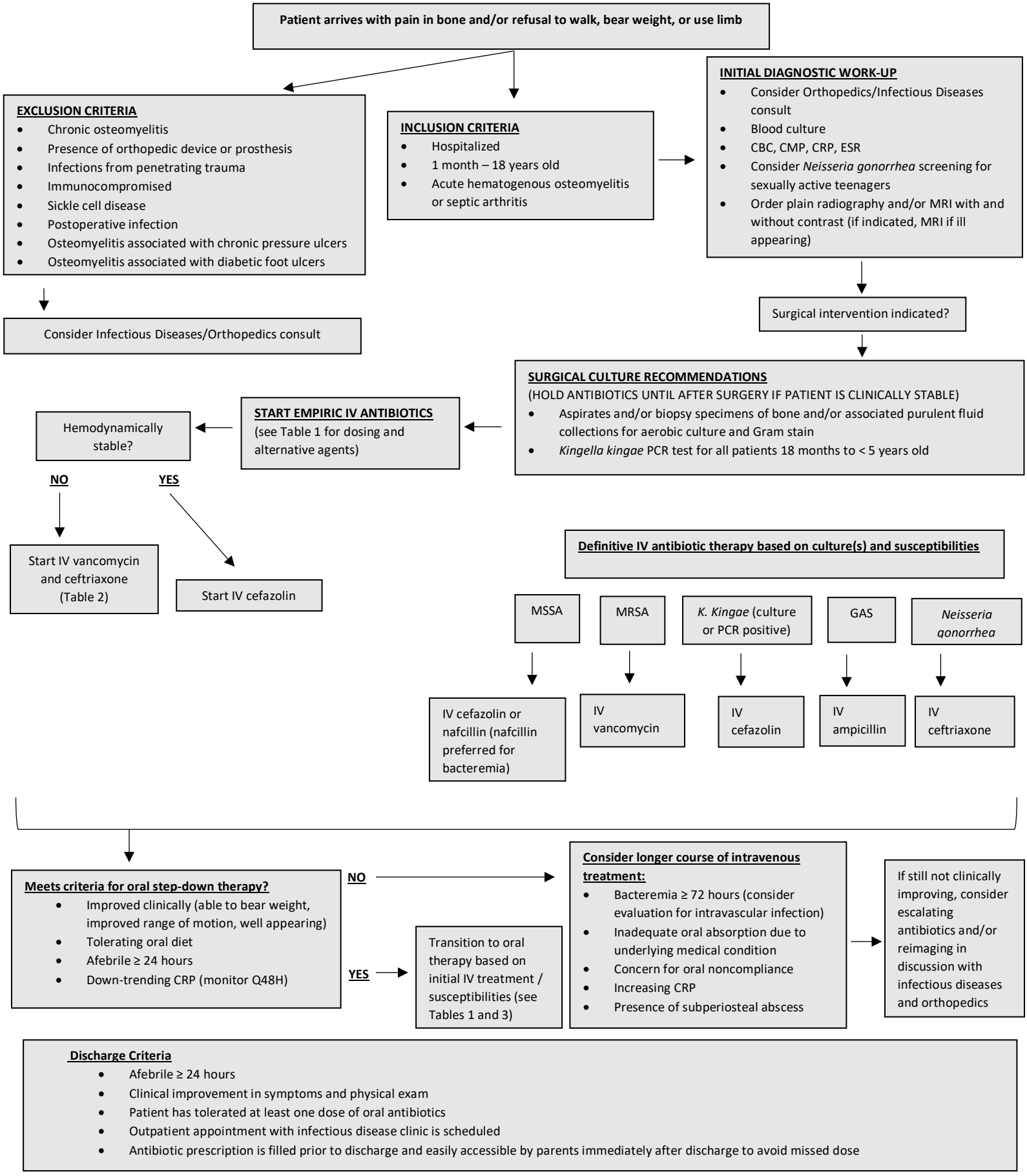


Table 1: Empiric or Culture Negative Antibiotic Therapy Recommendations		
	Intravenous Treatment	**Oral Step-Down Therapy (Culture Negative and Clinically Improving on Empiric Therapy)**
Hemodynamically stable patients **30 days - 4 years old** **Most common pathogens:** *S. aureus* *S. pyogenes* *K. kingae*	**First line:** Cefazolin 50 mg/kg/dose Q8H (max 2000 mg/dose) OR Ampicillin/sulbactam 50 mg/kg/dose Q6H (max 2000 mg ampicillin/dose) **Alternative treatment (allergy):** Levofloxacin (max 750 mg/dose) < 5 y/o: 10 mg/kg/dose Q12H ≥ 5 y/o: 10 mg/kg/dose Q24H	**First line:** Amoxicillin/clavulanate 30 mg/kg/dose Q8H (max 875 mg amoxicillin/dose) **Alternative treatment (allergy):** Levofloxacin (max 750 mg/dose) < 5 y/o: 10 mg/kg/dose Q12H ≥ 5 y/o: 10 mg/kg/dose Q24H Other options as appropriate based on culture and susceptibilities
Hemodynamically stable patients **5 – 18 years old** **Most common pathogens:** *S. aureus* *S. pyogenes*	**First line:** Cefazolin 50 mg/kg/dose Q8H (max 2000 mg/dose) **Alternative treatment (allergy):** Vancomycin 15 mg/kg/dose (max 2000 mg/dose) 30 days – 11 years: Q6H 12 – 18 years: Q8H	**First line:** Cephalexin 25 mg/kg/dose Q6H (max 1000 mg/dose) **Alternative treatment (allergy):** Linezolid* < 12 y/o: 10 mg/kg/dose Q8H ≥ 12 y/o: 10 mg/kg/dose Q12H (max 600 mg/dose) OR Amoxicillin/clavulanate 30 mg/kg/dose Q8H (max 875 mg amoxicillin/dose) Other options as appropriate based on culture and susceptibilities

Table 2: Other Patient Populations	
Hemodynamic instability (ICU)	Vancomycin 15 mg/kg/dose (max 2000 mg/dose) 30 days – 11 years: Q6H 12 – 18 years: Q8H AND Ceftriaxone 75 mg/kg/dose Q24H (max 2000 mg/dose)
Sexually active teenagers who test positive for: *Neisseria gonorrhea*	Ceftriaxone 75 mg/kg/dose Q24H (max 2000 mg/dose)

Table 3: Definitive Antibiotic Therapy Recommendations		
Pathogen	**Intravenous Treatment**	**Oral Step-Down Therapy**
Methicillin-susceptible *Staphylococcus aureus*	**First line:** Cefazolin 50 mg/kg/dose Q8H (max 2000 mg/dose) **Alternative treatment (allergy):** Nafcillin 200 mg/kg/day divided Q4-6H (max 3000 mg/dose, 12000 mg/day)	**First line:** Cephalexin 25 mg/kg/dose Q6H (max 1000 mg/dose) **Alternative treatment (allergy):** Dicloxacillin 100 mg/kg/day divided Q6H (max 500 mg/dose)
Methicillin-resistant *Staphylococcus aureus*	**First line:** Vancomycin 15 mg/kg/dose (max 2000 mg/dose) 30 days – 11 years: Q6H 12 – 18 years: Q8H	**First line:** Clindamycin 13 mg/kg/dose Q8H (max 600 mg/dose) – if documented susceptibility **Alternative treatment (allergy or clindamycin resistance)** Linezolid* < 12 y/o: 10 mg/kg/dose Q8H ≥ 12 y/o: 10 mg/kg/dose Q12H (max 600 mg/dose) OR Doxycycline: 2.2 mg/kg/dose Q12H (max 100 mg/dose) OR Sulfamethoxazole/trimethoprim 20 mg/kg/day of trimethoprim Q6-12H (max 320 mg trimethoprim/dose)
Kingella kingae **(culture or PCR positive)**	**First line:** Cefazolin 50 mg/kg/dose Q8H (max 2000 mg/dose) **Alternative treatment (allergy):** Ceftriaxone 75 mg/kg/dose Q24H (max 2000 mg/dose) OR Levofloxacin (max 750 mg/dose) < 5 y/o: 10 mg/kg/dose Q12H ≥ 5 y/o: 10 mg/kg/dose Q24H	**First line:** Amoxicillin/clavulanate 30 mg/kg/dose Q8H (max 875 mg amoxicillin/dose) **Alternative treatment (allergy):** Levofloxacin (max 750 mg/dose) < 5 y/o: 10 mg/kg/dose Q12H ≥ 5 y/o: 10 mg/kg/dose Q24H
Streptococcus pyogenes	**First line:** Ampicillin 50 mg/kg/dose Q6H (max 2,000 mg/dose) **Alternative treatment (allergy):** Cefazolin 50 mg/kg/dose Q8H (max 2000 mg/dose)	**First line:** Amoxicillin 30 mg/kg/dose Q8H (max 1000 mg/dose) **Alternative treatment (allergy):** Cephalexin 25 mg/kg/dose Q6H (max 1000 mg/dose)

* For children receiving linezolid for more than 2 weeks, recommend weekly screening for thrombocytopenia and neutropenia
All dosing assumes normal renal function, contact pharmacist for renal dose adjustment

5. Rationale for Empiric Antibiotic Recommendations

- Based on local data, methicillin susceptible *Staphylococcus aureus* (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA) are the most likely organisms recovered from blood or tissue cultures in musculoskeletal infections at Arnold Palmer Hospital for Children, with MSSA isolated in > 70% of culture positive patients. This justifies the use of cefazolin as first line intravenous treatment for most clinically stable patients.
- Empiric antibiotic regimens for patients < 5 years old should include coverage for *K. kingae*.

6. Transition to Oral Therapy

- For most patients, continue intravenous antibiotic therapy for ≤ 72 hours
- Treat intravenously until:
    - Improved clinically (able to bear weight, improved range of motion, well appearing)
    - Tolerating oral diet
    - Afebrile ≥ 24 hours
    - Down-trending CRP (repeat every 48 hours)

- Consider longer course of intravenous treatment if:
    - Bacteremia ≥ 72 hours (consider evaluation for intravascular infection)
    - Inadequate oral absorption
    - Concern for oral noncompliance
    - Increasing CRP
    - Prescence of subperiosteal abscess

7. Discharge Criteria

- Afebrile ≥ 24 hours
- Clinical improvement in symptoms and physical exam
- Patient has tolerated at least one dose of oral antibiotics
- Outpatient appointment with infectious disease clinic is scheduled
- Antibiotic prescription is filled prior to discharge and easily accessible by parents immediately after discharge to avoid missed dose

8. Total Duration of Therapy:

- Follow outpatient for clinical improvement, antibiotic tolerance/compliance, and normalization of inflammatory markers such as CRP and ESR
- Septic arthritis: total duration of 2 weeks for most patients
- Acute hematogenous osteomyelitis: total duration of 3-4 weeks for most patients
- Consider ≥ 3 weeks for MRSA, poor/slow response (limited clinical improvement after 2 – 5 days of IV antibiotics), complicated osteomyelitis, or septic arthritis

Arnold Palmer Hospital Diagnostic & Treatment Algorithm for *Clostridioides difficile* Infection (CDI) in Children

CDI Risk Factors:

- Previous history of CDI or recent exposure to person with known CDI
- Recent antibiotic exposure and/or hospitalization
- Complex chronic conditions (malignancy, solid organ transplant, inflammatory bowel disease, etc.)
- Acid suppressing medications (H2RAs >> PPIs)
- Presence of G or J tube

Who to test:

- Patients ≥ 2 years old
- Unexplained and new-onset ***≥3 unformed stools*** in 24 hours

*Decision to test in patients < 2 years old should be made on a case-by-case basis in consultation with Infectious Diseases[1]
*Do not perform repeat testing (within 7 days) during the same episode of diarrhea
*Do not test asymptomatic patients

Clinical suspicion of CDI?[2]

Discontinue systemic antimicrobials if possible[3]
Discontinue all bowel regimens[8]
Discontinue use of antimotility agents[4]

Yes →

Send *C. difficile* Screen x 1

*Note: lab will not test formed stool without approval from ID

(+) Screen, (+) Diarrhea

Initial episode

Non-severe: No manifestations of severe disease

Severe: WBC ≥ 15,000 cells/mL; serum creatinine level > 1.5 mg/dL (or > 50% from baseline), little/no urine output, clinical signs of dehydration

Fulminant: Hypotension or shock, ileus, megacolon

Note: for ileus or toxic megacolon, consult ID, GI and surgery

Yes →

Non-severe (immunocompetent):
Metronidazole 10 mg/kg/dose PO/NG q8h (max: 500 mg q8h) *OR* vancomycin 10 mg/kg/dose PO/NG q6h (max: 125 mg q6h)
Non –severe (immunocompromised):
Vancomycin (see above dose)
Severe[5]: Vancomycin 10 mg/kg/dose PO or PR q6h (max: 500 mg q6h)
Fulminant[5]: Vancomycin 10 mg/kg/dose PO and/or PR q6h (max: 500 mg q6h) ± metronidazole 10 mg/kg/dose IV q8h (max: 500 mg q8h)

No ↓

First recurrence
****ID consult****

Yes →

Vancomycin 10 mg/kg/dose q6h PO/NG (max: 125 mg q6h)
*Avoid metronidazole for recurrent CDI[6]
*For severe or fulminant follow above[5]

No ↓

Second or subsequent recurrence
****ID consult****

Yes →

Vancomycin taper, fecal transplant, fidaxomicin, etc.[10]

(+) Screen, (-) Diarrhea

Rule out excess opioid use

Ileus or toxic megacolon suspected?

Yes → Consult ID, GI, and surgery

No → Patient is an asymptomatic carrier, CDI treatment is **not** warranted[7]

(-) Screen, (+) Diarrhea

CDI highly unlikely

Consider alternative causes of diarrhea[8]

Continued clinical suspicion/diarrhea →

Repeat screen within 7 days of initial negative test is ***NOT*** recommended[9]

Response Assessment

- Diarrhea should improve within 4-6 days of treatment
- Criteria:
  - Number of diarrhea episodes
  - Stool consistency
  - Severity of abdominal pain/cramping
  - Fever and WBC trend
- Repeat screen is **not** recommended to assess response or colonization[7]
- Continue to re-evaluate need for systemic antimicrobials

Responding →

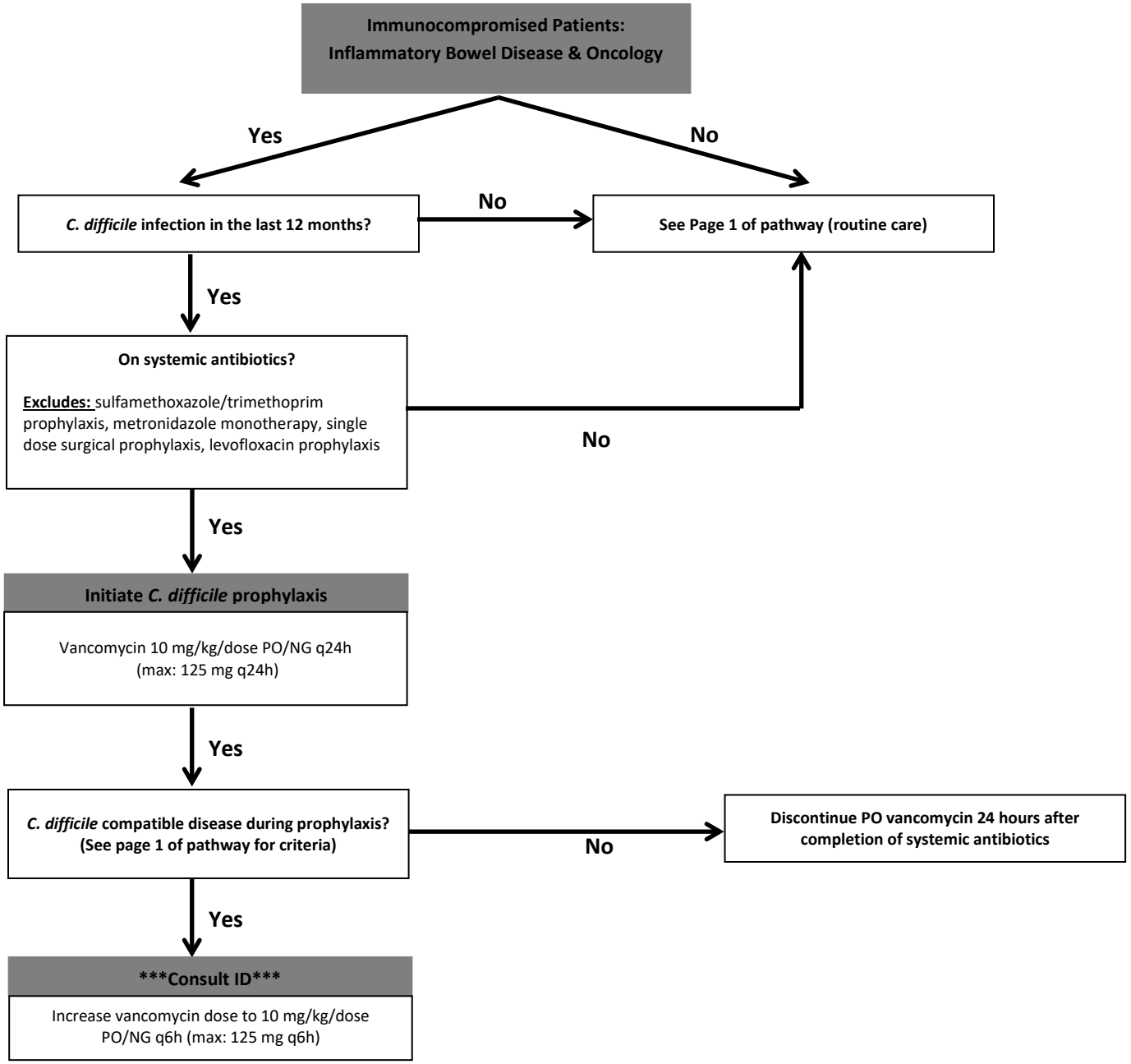
- ***Treat x 10 days***[11]
- Recommendations for secondary prophylaxis[12]

Not responding after 4-6 days of therapy →

- **ID and/or GI consult**
- If on metronidazole, escalate to vancomycin 10 mg/kg/dose PO q6h (max: 125 mg/dose)
- If on PO vancomycin, consider[5]:
  - Increasing vancomycin dose to 10 mg/kg/dose q6h (max: 500 mg/dose) or adding vancomycin enema (500 mg/100mL in NS) if GI motility or ileus is a concern
  - Adding IV metronidazole 10 mg/kg/dose q8h (max: 500 mg per dose)
  - Switching to PO fidaxomicin 16 mg/kg/dose q12h (max: 200 mg per dose)

1. Testing is not to be routinely recommended in neonates or infants ≤ 12 months of age with diarrhea due to a high prevalence of asymptomatic carriage of toxigenic *C. difficile* in this population. In children between 1-2 years of age testing may be completed if other infectious or noninfectious causes of diarrhea have been excluded.
2. Initiate contact precautions and use soap and water to wash hands when leaving the patient's room until CDI ruled out. Antibacterial foam is ineffective against *C. difficile* spores.
3. Systemic antimicrobials kill off natural gut flora allowing *C. difficile* to proliferate, decreasing cure rates and increasing chance of recurrence. With non-CDI antimicrobials, whenever possible ***discontinue*** antimicrobial therapy. If unable to stop antimicrobials, then narrow therapy and use as short a duration as possible.
4. Do not use anti-motility agents (loperamide, bulking agents, bowel regiments, etc.) in known/suspected CDI. They delay toxin excretion, causing complications including toxic megacolon.
5. Severe/Fulminant disease (**Consider ID consult**)
    a. High dose (10 mg/kg/dose; max 500 mg/dose) PO/NG vancomycin is recommended, as oral vancomycin is the preferred agent for fulminant CDI (intravenous vancomycin cannot be used for CDI as it does not achieve therapeutic concentrations in the colon).
    b. IV metronidazole and per rectum (PR) vancomycin are recommended as adjunct therapy in fulminant CDI since ability of oral agents to reach the colon may be compromised. PR vancomycin should be utilized in the setting of ileus. As patients improve and bowel function normalizes, these agents may be discontinued with PO vancomycin continuing to complete therapy.
    c. Dosing for per rectum vancomycin (500 mg/100mL in NS): 50 mL per dose for ages 1-3 years, 75 mL per dose (4-9 years), and 100 mL per dose (≥ 10 years). PR vancomycin is dosed Q6h.
    d. PO metronidazole adds no benefit to PO vancomycin therapy and these agents should not be used in combination for the treatment of CDI.
    e. If a patient is NPO (no matter the severity of CDI) IV metronidazole should be initiated. As soon as PO therapy can be given, the treatment algorithm should be followed.
6. Prolonged metronidazole use can cause irreversible peripheral neuropathy. Metronidazole is not preferred for recurrent *C. difficile* infections due to the increased risk of irreversible side effects with cumulative exposure.
7. Patients who have a positive *C. difficile* screen should remain in contact isolation for their entire hospitalization, and hand washing with soap and water should occur when leaving the room. Patients should not be re-tested for *C. diff* in the hopes of removing them from isolation, whether they are asymptomatic carriers or patients with resolved symptoms after treatment (> 50% of patients may remain *C. difficile* positive for up to 4 weeks after successful treatment).
8. Consider alternative causes of diarrhea: stop all bowel regimens, consider non-infectious causes, consider bacterial and parasitic causes if patient had diarrhea within 72 hours of admission , consider antibiotic related diarrhea, consider tube feeds, consider colonoscopy
9. If patient remains symptomatic and there is continued strong clinical suspicion of CDI, a second screening test may be ordered; however, a positive screen within 7 days of an initial negative test is highly unlikely
10. Consult ID. Options for second or subsequent recurrence:
    a. Vancomycin in a tapered and pulsed regimen
        i. 10 mg/kg/dose (max dose: 125 mg) PO every 6 hours x 10 – 14 days, then
        ii. 10 mg/kg/dose (max dose: 125 mg) PO every 12 hours x 7 days, then
        iii. 10 mg/kg/dose (max dose: 125 mg) PO once daily x 7 days, then
        iv. 10 mg/kg/dose (max dose: 125 mg) PO 2-3 times weekly x 2-8 weeks
    b. Fecal microbiota transplantation (See policy on SWIFT for more details)
    c. Fidaxomicin 16 mg/kg/dose twice daily (max: 200 mg per dose) for 10 days
    d. IVIG (see Orlando Health IVIG Guideline on SWIFT)
11. Treatment duration
    a. Immunocompetent patients receiving systemic antibiotics:
        i. Complete 10-day course of treatment and then consider decreasing vancomycin dose to 10 mg/kg/dose (max: 125 mg/kg/dose) PO/NG BID for duration of systemic antibiotics
    b. Immunocompromised patients (inflammatory bowel disease (IBD) or oncology): If patient continues to be neutropenic or continues on systemic antibiotics following completion of 10 days of PO vancomycin therapy, decrease dose to 10 mg/kg/dose (max: 125 mg/dose) PO/NG once daily and continue until 24 hours after discontinuation of systemic antibiotics
12. Secondary prevention of CDI
    a. Probiotics – lack of consistent evidence for use as prevention in CDI
        i. Do ***not*** recommend in patients with central venous line or immunocompromised patients
    b. Bezlotoxumab – human monoclonal antibody against *C. difficile* toxin B
        i. 10 mg/kg IV over 60 minutes x 1
        ii. Used as adjunctive therapy (in conjunction with antimicrobials)
        iii. *Outpatient use only;* ID consult preferred
    c. Secondary prophylaxis (refer to Appendix A. Recurrent *C. difficile* Infections in Immunocompromised Patients Pathway for more detailed recommendations for subsequent admissions and chemotherapy cycles)
        i. Recommended in IBD and oncology patients with a history of *C. difficile* in the last 12 months. Not routinely recommended in immunocompetent patients.

Appendix A: Preventing Recurrent *C. difficile* Infections in Immunocompromised Patients – Pathway



Arnold Palmer Hospital for Children: Prevention and Management of Infection in Pediatric Oncology and Bone Marrow Transplant Patients

Definitions

A. Fever: core body temperature ≥ 38.3°C (101°F) once, or ≥ 38°C (100.4°F) for ≥ 1 hour or measured on two separate occasions over an hour apart
B. Neutropenia: Absolute Neutrophil Count (ANC) < 500/mm^3 or < 1000/mm^3 with a predicted decline to < 500/mm^3
C. Severe sepsis: presence of sepsis-induced organ dysfunction; hypotension not responsive to fluid resuscitation
D. Marrow recovery: ANC or APC > 200/mm^3 and rising
E. Antibiotic administration: Antibiotic therapy should be started ≤ 1 hour from first contact or documented fever and after blood cultures are drawn
F. Clinically unstable: hypotension, tachypnea, tachycardia, mental status changes, organ dysfunction, etc.
G. Type-1 IgE mediated allergy: hives, anaphylaxis, bronchospasm, edema
H. Autologous hematopoietic stem cell transplant (HSCT): the use of a patient's own hematopoietic cells to reconstitute the bone marrow
I. Allogeneic HSCT: the use of another person's hematopoietic cells to reconstitute the bone marrow
J. Engraftment: absolute neutrophil count (ANC) ≥ 500/uL for three consecutive days AND platelet count ≥ 20/uL at least 7 days after last platelet infusion

Levofloxacin Prophylaxis

A. Indications:
   1. The following patients when expected to have significant and prolonged neutropenia (> 7 days):
      a) AML
      b) Relapsed ALL
      c) Bone marrow failure syndromes or MDS on intense chemotherapy
         1. Bone marrow failure syndrome examples: Fanconi anemia, aplastic anemia, amegakaryocytic thrombocytopenia, diamond blackfan anemia, deficiency of ADA2, dyskeratosis congenita, MIRAGE syndrome, paroxysmal nocturnal hemoglobinuria, Pearson syndrome, Shwachman diamond syndrome, etc.
      d) Hemophagocytic lymphohistiocytosis (HLH)
      e) The following leukemias
         1. Down syndrome (pre-maintenance)
         2. High-risk B-cell ALL/LLy (induction and DI phases)
         3. T-cell ALL/LLy and PH+ ALL (pre-maintenance)
         4. Infant ALL (pre-maintenance)
      f) HSCT
         1. Allogeneic patients
         2. Patients with GVHD on high dose steroids (amoxicillin preferred), see HSCT infection prophylaxis guideline link below
   2. Initiate when ANC < 200 or on day 0 of HSCT
   3. Discontinue when ANC > 200 and rising OR if started on systemic antibiotics (other than PJP prophylaxis)
B. Levofloxacin dose:
   1. < 5 years old: 10 mg/kg/dose every 12 hours
   2. ≥ 5 years old: 10 mg/kg/dose every 24 hours
   3. Maximum total dose per day = 750 mg
C. Contraindications to levofloxacin prophylaxis:
   1. Allergy to fluoroquinolones

2. Chronic active arthritis
3. Known prolonged QTc (only check if anticipated to be on levofloxacin > 2 weeks)
4. Pregnant or breast feeding
5. While on systemic antibiotics (other than PJP prophylaxis)
6. History of an infection due to a levofloxacin resistant organism
7. Note: In patients with a contraindication to levofloxacin, cefpodoxime may be used as an alternative agent (dose: 5 mg/kg/dose every 12 hours, maximum total dose per day = 400 mg)

D. *C. difficile*: Patients with a history of *C. difficile* should not receive PO vancomycin prophylaxis while on levofloxacin

Fungal Prophylaxis

A. Indications
   a. Patients at high risk of invasive fungal disease expected to have significant and prolonged neutropenia (> 7 days), including:
      i. Relapsed ALL and autologous HSCT recipients: fluconazole
      ii. AML/MDS on intense chemotherapy: voriconazole
      iii. Allogenic HSCT recipients (pre-engraftment) or if receiving immunosuppression for acute or chronic GVHD (prednisone equivalent ≥ 1 mg/kg/day): voriconazole
   b. If the patient has contraindications (see section C below) to the recommended agent, micafungin should be used as an alternative
   c. Initiate when ANC < 200 or on day 0 of HSCT or at onset of GVHD
   d. Discontinue when ANC > 200 and rising for autologous patients OR until engraftment for allogenic patients OR until prednisone equivalent dose of ≤ 1 mg/kg/day for GVHD patients OR if started on systemic antifungal therapy for all patients

B. Dosing
   a. Fluconazole: 6 mg/kg/dose every 24 hours
      i. Maximum total dose per day = 400 mg
   b. Voriconazole:
      i. 2-12 years of age OR >12 to 14 years of age and < 50 kg:
         1. IV: 9 mg/kg/dose every 12 hours x 2 doses (day 1), followed by 8 mg/kg/dose every 12 hours
         2. PO: 9 mg/kg/dose every 12 hours
         3. Maximum 350 mg per dose
      ii. >12 years to 14 years of age and ≥ 50 kg OR ≥ 15 years of age:
         1. IV/PO: 4 mg/kg/dose every 12 hours
         2. Maximum 200 mg per dose
      iii. See therapeutic monitoring recommendations
   c. Micafungin:
      i. ≥ 4 months: 1 mg/kg/dose IV every 24 hours
      ii. < 4 months: 2 mg/kg/dose IV every 24 hours
      iii. Maximum total dose per day = 50 mg

C. Contraindications to fungal prophylaxis
   a. Voriconazole:
      i. Allergy to voriconazole
      ii. Known prolonged QTc (only check if anticipated to be on voriconazole > 2 weeks)
      iii. LFTs > 3x ULN or known liver failure
      iv. Co-administration with major CYP3A4 substrates (such as vinca alkaloids like vincristine)
   b. Fluconazole:
      i. Allergy to fluconazole
      ii. Known prolonged QTc (only check if anticipated to be on fluconazole > 2 weeks)
      iii. LFTs > 3x ULN or known liver failure
      iv. Co-administration with major CYP3A4 substrates
         1. Hold fluconazole 24 hours before initiation of vinca alkaloids (vincristine) and resume 24 hours after vinca alkaloid therapy completed
   c. Micafungin:
      i. Allergy to micafungin or an echinocandin

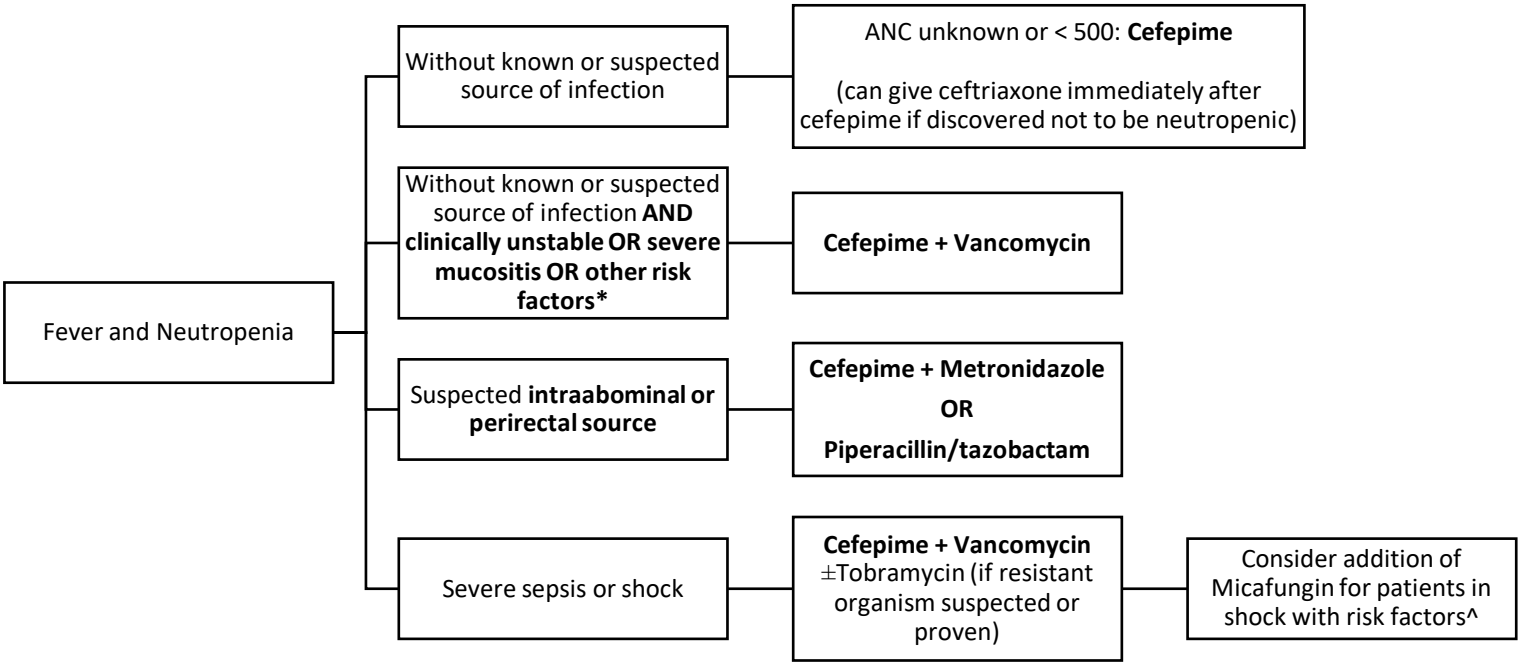
ii. LFTs > 5x ULN or known liver failure

Click HERE for expanded recommendations regarding infection prophylaxis in HSCT patients (including additional recommendations for PJP, HSV, VZV, CMV, and RSV)

Febrile Neutropenia Initial Workup

A. Blood cultures
   a. Draw 2 sets of aerobic blood cultures from each lumen of the central venous line (CVL) prior to antibiotic administration
   b. If no CVL, draw 2 peripheral cultures
   c. Draw blood cultures 5-15 minutes apart
B. Chest X-ray and respiratory PCR if respiratory signs/symptoms such as cough, shortness of breath, chest pain, crackles, etc.
C. Other imaging/workup as appropriate to assess for potential sources of infection based on patient presentation, such as a UA and urine culture if patient presents with symptoms of a urinary tract infection (dysuria, urinary frequency, urinary urgency, suprapubic pain)
D. Initial ID consult recommended for:
   a. History of vancomycin-resistant *Enterococcus* (VRE) or documented VRE infection, including empiric use of daptomycin or linezolid
   b. History of multi-drug-resistant organism (MDRO) or known infection due to MDRO, including empiric use of meropenem (consult mandatory for carbapenem resistant organisms)
   c. Empiric use of other restricted antimicrobial agents
   d. Bacteremia (consult mandatory for *Staphylococcus aureus* [MSSA or MRSA] or coagulase negative *Staphylococcus spp*. with 2 positive blood cultures)

Empiric Antimicrobial Therapy for Febrile Neutropenia



A. The addition of vancomycin is recommended for the following risk factors*:
   1. HSCT, AML, or relapsed ALL
   2. History of invasive MRSA or *Streptococcus viridans* infection
   3. Vascular line exit site infection or other skin/soft tissue infection suspected
   4. Recent high dose cytarabine ($\geq$ 1,000 mg/m^2/day)
   5. Positive blood cultures for Gram-positive bacteria (prior to identification and susceptibility)
B. The addition of empiric antifungal coverage with micafungin is recommended for patients in shock with the following risk factors^:

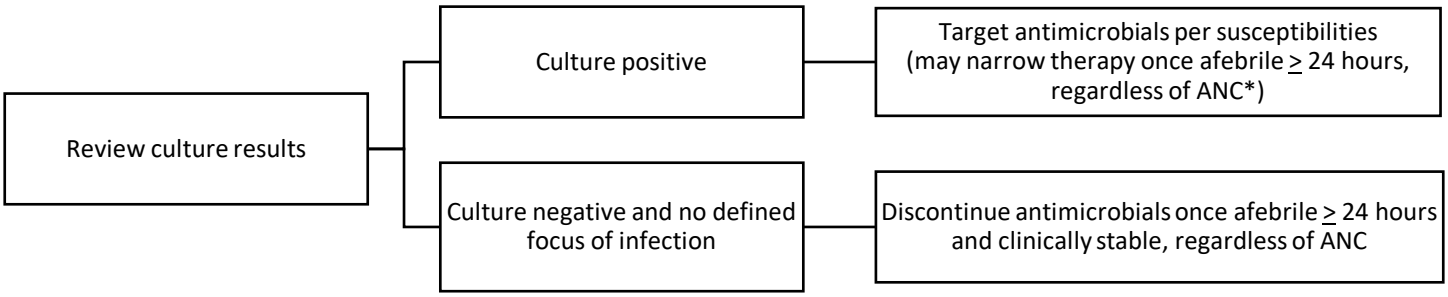
1. Exposure to broad-spectrum antibiotics for more than 7 days in last 2 weeks, recent major abdominal surgery, necrotizing pancreatitis, gastrointestinal perforation, steroid use in last 2 weeks including high doses (prednisone 2 mg/kg/day or a total dose of 20 mg/day or its equivalent) or prolonged durations (> 7 days), or in patients with AML,high-risk/relapsed ALL, or s/p HSCT

C. For patients with β-lactam allergies:
    1. For patients with <u>any</u> penicillin allergy or a non-type-1 allergy to a cephalosporin (such as rash): utilize a cefepime-based regimen
    2. For patients with a type-1 allergy to cephalosporins: replace cefepime with aztreonam and <u>add</u> vancomycin
D. For patients with a history of *C. difficile* in the last 12 months: initiate PO vancomycin prophylaxis (dose: 10 mg/kg every 24 hours, max 125 mg)

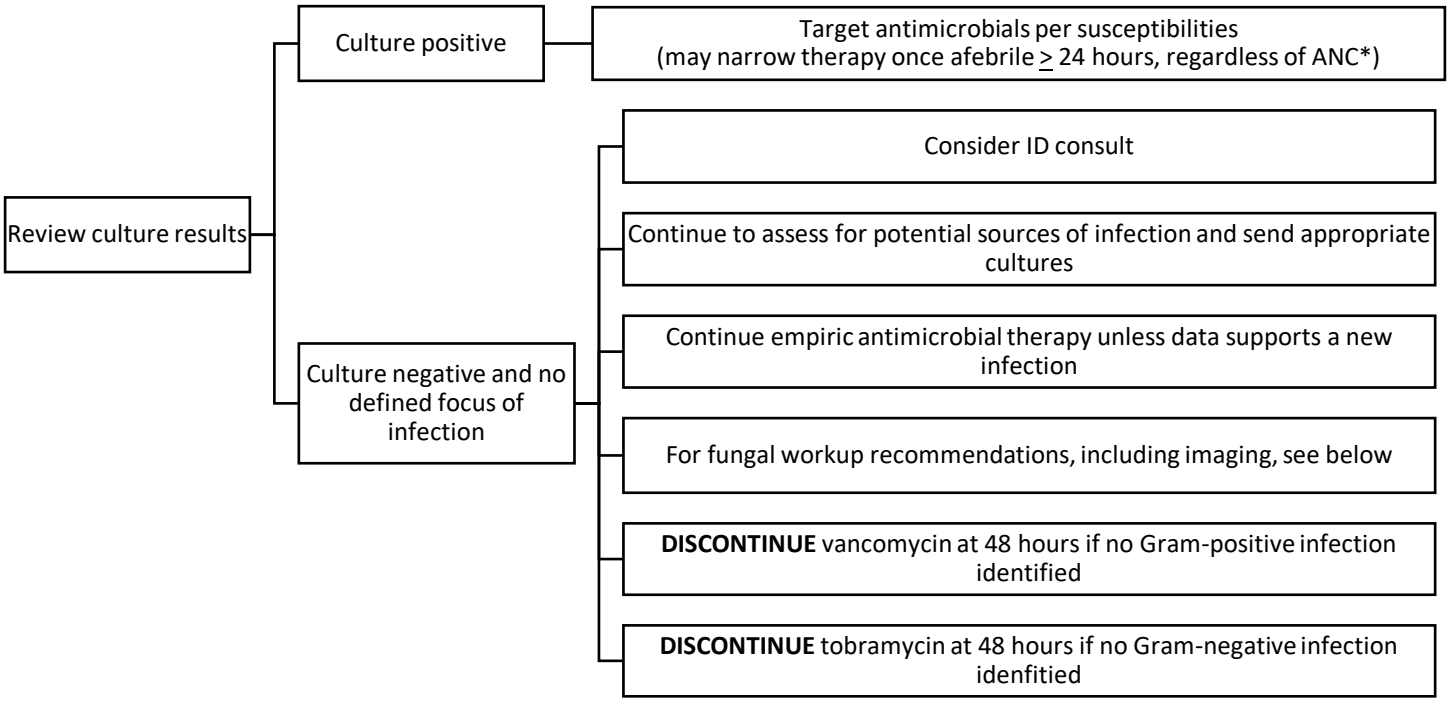
Reassessment of Antimicrobial Therapy for Febrile Neutropenia

A. All patients should be reassessed after 48 hours of antimicrobial therapy
B. ID consult recommended for persistent fever after 5 days or clinical instability after 48-72 hours despite appropriate empiric antimicrobials
C. Discontinuation of empiric antimicrobials
    a. Culture negative patients (without a defined focus of infection)
        i. Discontinuation of empiric antimicrobial therapy is recommended in clinically stable patients who have been afebrile <u>≥</u> 24 hours, regardless of ANC
        ii. Resume levofloxacin prophylaxis if applicable
    b. Culture positive patients and culture negative patients with a defined focus of infection
        i. Discontinuation of antimicrobial therapy is appropriate in clinically stable patients who are afebrile and have completed a full course of therapy for the defined infection
        ii. Resume levofloxacin prophylaxis if applicable
D. De-escalation of empiric antimicrobials
    a. Empiric antimicrobial therapy should be streamlined to the <u>most narrow</u> option for the identified organism in clinically stable patients who have been afebrile <u>≥</u> 24 hours, regardless of ANC
    b. ***Exception**: In patients with AML or relapsed ALL and s/p HSCT, wait until marrow recovery (ANC > 200 and rising) before streamlining therapy

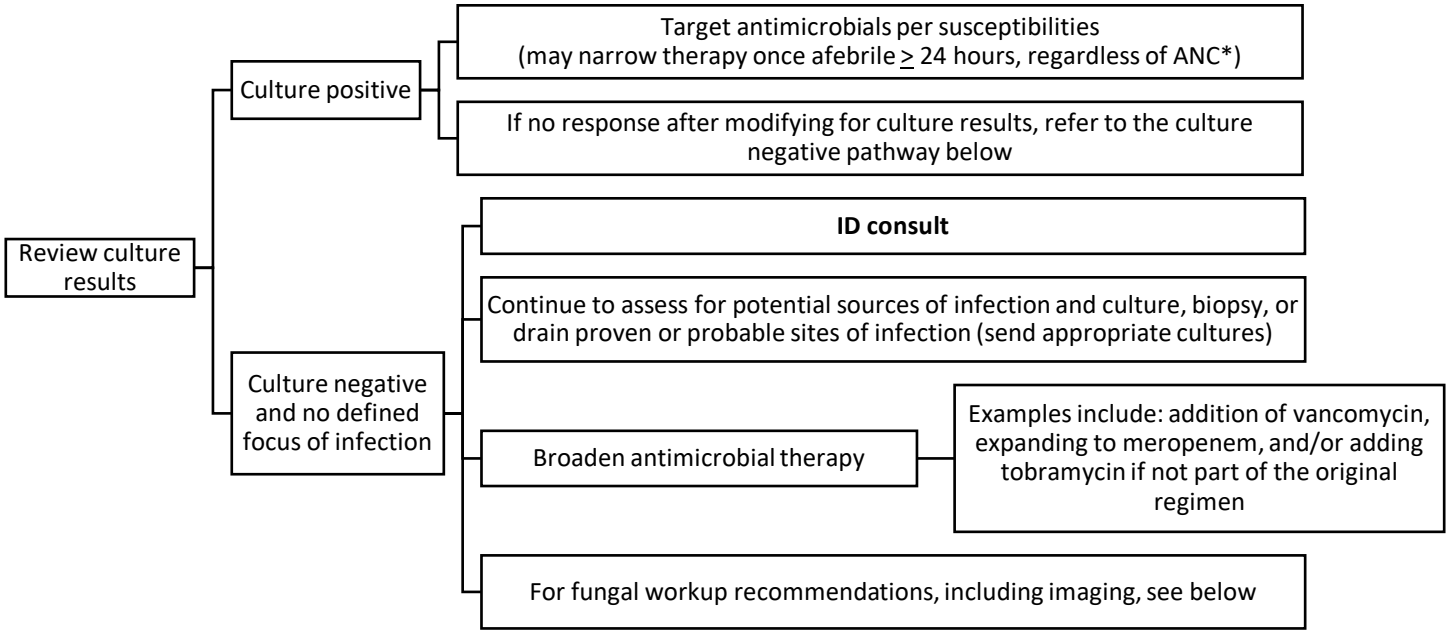
Clinical response – defervesced



Persistent fever – clinically stable



Persistent fever – clinically unstable



Febrile Neutropenia Fungal Workup

A. Initiate workup for invasive fungal infection in patients with fever **and** prolonged neutropenia ≥ **5 days** (persistent fever despite broad-spectrum antimicrobial therapy)
B. Initial workup:
    a. Consult ID
    b. Imaging:
        i. Abdominal ultrasound

1. Consider CT abdomen with contrast if significant GI signs/symptoms (see typhlitis section below)

ii. CT chest without contrast

iii. CT sinuses with and without contrast only if localized signs/symptoms

1. Sinus endoscopy evaluation is strongly recommended for HSCT patients
2. Purulent nasal discharge, nasal congestion/obstruction, facial congestion/fullness, facial pain/pressure, headache, ear pain/pressure

c. If above imaging is abnormal/suggestive of invasive fungal infection, send:

i. Serum fungal biomarkers

1. Aspergillus Antigen (Galactomannan)
2. Beta-D-Glucan (Fungitell): send only if high suspicion for PJP
    a. False positives are common and can be caused by the any of the following within a 3-4 day time period in relation to the lab draw: IVIG, albumin, hemodialysis, receipt of blood products (PRBCs, FFP), presence of bacteremia, use of certain types of surgical gauze, IV antimicrobial use (colistin, ertapenem, cefazolin, SMX/TMP, cefepime, ampicillin/sulbactam, piperacillin/tazobactam), Peg-asparaginase, presence of mucositis or other disruptions in GI integrity, enteral nutrition

ii. Pulmonology consult for BAL evaluation if CT chest suggestive of invasive fungal infection

iii. ENT consult if CT sinuses suggestive of invasive fungal infection

iv. Karius may be considered in patients unable to undergo lung biopsy or BAL – must have ID approval

C. Initiate empiric antifungal therapy – do not delay initiation while waiting for fungal workup results

a. First line: Micafungin

b. Second line: Liposomal Amphotericin B (may be preferred in patients previously on antifungal prophylaxis active against molds, such as voriconazole)

D. Discontinuation of empiric antifungal therapy in patients with negative fungal workup

a. Continue empiric antifungal therapy until afebrile ≥ 48 hours AND evidence of marrow recovery

b. In patients who remain persistently neutropenic, empiric therapy should be continued up to a maximum of 14 days

i. Transition to antifungal prophylaxis if appropriate

Footnote: Patients at high risk for invasive fungal infection include: AML, relapsed ALL, allogeneic HSCT, prolonged neutropenia (> 7 days), steroid use in last two weeks including high doses (prednisone 2 mg/kg/day or a total dose of 20 mg/day or its equivalent) or prolonged durations (> 7 days)

Neutropenic Enterocolitis (Typhlitis)

A. ID consult recommended

B. Initiate workup for typhlitis in patients with febrile neutropenia AND clinically significant diarrhea, bloody stool, emesis, abdominal pain, or abdominal distention not explained by other diagnoses

a. If diarrhea present:

i. *C. difficile* screen (if ≥ 2 years old and unexplained new-onset ≥ 3 loose/watery stools in last 24 hours)

ii. Enteric bacterial PCR

b. Aerobic and anaerobic blood cultures if not already sent

c. Abdominal CT with PO and IV contrast; abdominal ultrasound if unable to CT

C. Criteria for diagnosis

a. Fever and neutropenia

b. Bowel wall thickening seen on abdominal imaging

c. Other differential diagnoses excluded (*C. difficile*, GVHD, *Salmonella spp.* enteritis, etc.)

D. Initiate empiric antimicrobial therapy

a. First line: Cefepime + Metronidazole

b. Second line: Piperacillin/tazobactam

E. Duration of therapy:

a. 10-14 days or 7 days following marrow recovery, whichever is longer, AND until complete resolution of signs and symptoms

b. Longer durations may be necessary in patients with ongoing evidence of perforation or undrained abscess

Pediatric *Pneumocystis jirovecii* Pneumonia (PJP) Prophylaxis Guideline
(Non-Oncologic Conditions)

This guideline will provide standardized recommendations for PJP prophylaxis in patients receiving high-dose steroids and/or other combinations of immunosuppressive medications and is specific to conditions such as inflammatory bowel disease (IBD), rheumatologic disorders, non-malignant hematologic conditions, and other diseases requiring immunosuppressive therapy. This guideline does not provide PJP prophylaxis recommendations for patients with oncologic conditions on chemotherapy, patients on prophylaxis due to solid organ transplant (SOT), bone marrow transplant (BMT), CAR-T therapy, or patients with human immunodeficiency virus (HIV).

Indications for PJP prophylaxis:

1. Patients expected to be on high-dose corticosteroids (≥ 2 mg/kg/day prednisolone equivalent if < 7.5 kg or ≥ 15 mg/day of prednisolone equivalent) for more than 28 days
2. Patients expected to be on 3 or more immunosuppressive agents for > 28 days
3. Patients expected to be on combinations of 2 or more immunosuppressive therapies, *especially* if one if a calcineurin inhibitor (i.e. tacrolimus, cyclosporine) or includes high-dose corticosteroids for > 28 days
    - Examples of immunosuppressants include:
        - Anti-CD20 agents (i.e. rituximab)
        - Anti-TNFα agents (i.e. infliximab)
        - Calcineurin inhibitors (i.e. tacrolimus, cyclosporine)
        - Methotrexate
        - Thiopurines (i.e. azathioprine, 6-mercaptopurine)
        - Biologic agents (i.e. anakinra, risankizumab, adalimumab, etc.)

FIRST-LINE MEDICATION THERAPY (Prophylaxis)		
Drug	**Dose**	**Comments**

Trimethoprim-Sulfamethoxazole (TMP-SMX)	5 mg/kg/day (max 160 mg/dose) divided into 2 doses given on consecutive days (i.e. Saturday and Sunday)	• First-line therapy (patients > 1 month old)
		• IV formulation should only be used if there is a strict contraindication to oral therapy (i.e. critical illness preventing oral medication therapy) and should be avoided if possible
		• Incidence of myelosuppression is unclear as most studies included patients being treated with chemotherapy; may use with caution
		• G6PD deficiency is **not** a contraindication to receive TMP-SMX; risk of hemolytic anemia is minimal and is outweighed by the benefit of use
		• Requires renal dose adjustment
		• Available as tablets and oral solution
		  ○ Single strength tablets: 80 mg TMP-400 mg SMX
		  ○ Double strength tablets: 160 mg TMP-800 mg SMX
		  ○ Oral solution: 40 mg TMP-200 mg SMX per 5 mL

SECOND-LINE MEDICATION THERAPY (Prophylaxis)		
Pentamidine	4 mg/kg IV (max 300 mg) every 3 to 4 weeks	• Only IV pentamidine is available at APH (no inhaled)
Atovaquone	1 to 3 months: 30 mg/kg/day PO once daily 4 to 24 months: 45 mg/kg/day PO once daily > 24 months: 30 mg/kg/day PO once daily Max dose 1500 mg once daily	• Available as 750 mg/5 mL oral solution only • Taken with food to increase bioavailability • Use with cation in patients with severe hepatic impairment
Dapsone	2 mg/kg (max 100 mg) PO once daily OR 4 mg/kg (max 200 mg) every week	• Contraindicated in G6PD deficiency (high risk of hemolytic anemia) • Cross-reactivity in patients with sulfa allergy is possible and use not recommended; however, may use with caution only in patients with a remote history of a mild allergic reaction • Dapsone does not have a commercially available oral solution, but tablets may be crushed or a 2 mg/mL oral solution can be compounded ○ Tablets come as 25 mg or 100 mg formulations

Duration	
Non-malignant hematologic disorder	Up to 3 months after discontinuation of immunosuppression
High-dose corticosteroids	Until steroid dose is < 2 mg/kg/day (if < 7.5 kg) or < 15 mg/day
Other immunosuppressive conditions	After cessation of immunosuppression or upon maintenance on a single immunosuppressive agent • May consider extending prophylaxis with consideration to the half-life of the immunosuppressant (i.e. 3 half-lives or more) • For patients who had received rituximab in combination with other immunosuppressant(s), consider extending to 3 – 6 months after last rituximab dose

Arnold Palmer Hospital for Children: Management of Community Acquired Pneumonia (CAP)

Definitions

A. Community Acquired Pneumonia (CAP): infection of airways and lung (including a viral and bacterial etiology) acquired outside of the hospital
B. Complicated CAP: pneumonia with significant effusion (moderate to large), empyema, severe or impending respiratory failure, and/or signs/symptoms of sepsis or shock
C. Pleural Effusion: excess fluid in the pleural space
D. Parapneumonic Effusion: pleural fluid that results from pneumonia or lung abscess; evolves through three stages:
    a. Exudative: sterile, free-flowing fluid, 2-5 days after the onset of the effusion
    b. Fibro-purulent: deposition of fibrin over the visceral and parietal pleurae, fluid becomes loculated or septated 5-10 days after the onset of the effusion
    c. Organized: a thick and stiff pleural peel or rind develops and is attached to both visceral and parietal pleurae 10-14 days after the onset of the effusion
E. Empyema: accumulation of pus in pleural space
F. Bronchopleural Fistula: occurs when erosion in the airway or parenchyma communicates directly with the pleura such that air enters the pleural space
G. Necrotizing Pneumonia: occurs as a complication of both lobar and bronchopneumonia and is defined by a combination of parapneumonic effusion, loculation, and septation of the effusion and abscesses
H. Under-immunized: patient who has not received at least 2 Pneumococcal vaccinations
I. Un-immunized: patient who has not received any Pneumococcal vaccinations
J. Type-1, IgE mediated allergy: hives, bronchospasm, anaphylaxis, swelling

Inclusions/Exclusions

A. Inclusion:
    1. Hospitalized
    2. > 3 months of age with diagnosis of CAP
B. Exclusion:
    1. Cystic fibrosis
    2. Immunocompromised
    3. Ventilator associated pneumonia/tracheitis/other nosocomial infections
    4. Sickle cell disease
    5. Trauma
    6. Lung abscess, pneumatocele

Uncomplicated CAP

A. Clinical Management
    a. Initial Evaluation: Laboratory and Imaging
        i. CBC with differential
        ii. BMP
        iii. Procalcitonin
        iv. Microbiology
            1. Sputum gram stain and culture, if child is able to provide it
                a. A high quality sputum is usually defined by <10 squamous epithelial cells and > 25 WBCs per low power field
            2. See Appendix I: Rapid RSV/Flu versus Respiratory Viral Panel (PCR)

a. Consider full respiratory viral panel regardless of season for patients not responding to antibiotic treatment and for patients with clinical course/labs not consistent with bacterial pneumonia

v. CXR (PA, lateral) – determine presence of effusion

vi. Blood culture is not routinely recommended for patients with uncomplicated CAP

b. Treatment

i. Start empiric antibiotics therapy based on patient scenario below AFTER obtaining a procalcitonin

1. Tailor coverage based on identification/susceptibilities

ii. Empiric antibiotic choice:

Clinical Scenario	Antibiotic Therapy	Duration of Therapy
Mild/Moderate Pneumonia, Uncomplicated		
Fully Immunized	Ampicillin 50-75 mg/kg/dose Q6h, max dose 2000mg PO step down: Amoxicillin 30 mg/kg/dose Q8h, max dose 1000 mg	5 days
Under-immunized/ Un-immunized without: **Exposure to amoxicillin in last 30 days or recent failure of therapy**	**1st line**: Ampicillin 75 mg/kg/dose Q6h, max dose 3000 mg OR **2nd line**: Ampicillin/sulbactam 75 mg/kg/dose (ampicillin component) Q6h, max dose 2000 mg (ampicillin component) PO step down: **1st line**: Amoxicillin 30 mg/kg/dose Q8h, max dose 1000 mg **2nd line**: Augmentin ES 30 mg/kg/dose Q8h (amoxicillin component), max dose 1300 mg (amoxicillin component; max of 2000 mg/dose Q12h if using XR tablets) *For patients > 40 kg, use non-ES formulation	
Any patient, regardless of immunization status with: **Exposure to amoxicillin in last 30 days or recent failure of therapy**	**1st line**: Ampicillin/sulbactam 75 mg/kg/dose (ampicillin component) Q6h, max dose 2000 mg (ampicillin component) OR **2nd line**: Ceftriaxone 50 mg/kg/dose Q24h, max dose 2000 mg PO step down: **1st line**: Augmentin ES 30 mg/kg/dose (amoxicillin component) Q8h, max dose 1300 mg (amoxicillin component; max of 2000 mg/dose Q12h if using XR tablets) *For patients > 40 kg, use non-ES formulation **2nd line**: Levofloxacin < 5 yo 10 mg/kg/dose Q12h, ≥ 5 yo 10 mg/kg/dose Q24h, max dose 750 mg OR Linezolid	

	< 12 yo 10 mg/kg/dose Q8h, ≥ 12 yo 10 mg/kg/dose Q12h, max dose 600 mg	
Type 1 penicillin allergy	Ceftriaxone 50 mg/kg/dose Q24h, max dose 2000 mg PO step down: **1st line**: Cefpodoxime 5 mg/kg/dose Q12h, max dose 200 mg OR **2nd line**: *Preferred if Beta-lactam exposure in last 30 days or recent failure of therapy Levofloxacin < 5 yo 10 mg/kg/dose Q12h, ≥ 5 yo 10 mg/kg/dose Q24h, max dose 750 mg OR Linezolid < 12 yo 10 mg/kg/dose Q8h, ≥ 12 yo 10 mg/kg/dose Q12h, max dose 600 mg	
Atypical Pneumonia	Treatment of atypical pneumonia in the absence of severe respiratory compromise is generally not recommended due to the self-limiting nature of the illness; greatest benefit seen in school age children > 7 years old **1st line**: Azithromycin 10 mg/kg/dose Q24h, max dose 500 mg **2nd line**: Doxycycline (if ≥ 8 years old) 2 mg/kg/dose Q12h, max dose 100 mg OR Levofloxacin < 5 yo 10 mg/kg/dose Q12h, ≥ 5 yo 10 mg/kg/dose Q24h, max dose 750 mg Note: discontinuation recommended if respiratory PCR negative for atypical organisms	3 days – azithromycin 5 days – doxycycline or levofloxacin

Notes:
For type 1 cephalosporin allergy, consult with ID for antibiotic recommendations
Use of levofloxacin or linezolid requires ID/AMT approval

iii. Rationale for antibiotic recommendations
    1. For ampicillin as first line therapy regardless of immunization status in patients who have not failed previous therapy or had recent beta-lactam exposure
        a. The IDSA guidelines for management of CAP in infants and children recommend use of ampicillin as first line therapy for most hospitalized children in places where local rates of penicillin-resistant Pneumococcus (for invasive isolates) is low
            i. Based on our antibiogram, invasive isolates of Pneumococcus at APH are >90% susceptible to penicillin
            ii. Empiric therapy with ceftriaxone in children who are not fully immunized is only recommended when local susceptibilities for invasive Pneumococcal strains indicate high-levels of penicillin resistance, which ours do not
        b. Use of pneumococcal vaccines has decreased penicillin resistant strains of Pneumococcus
            i. Penicillin resistant Pneumococcal serotypes (14, 6B, 19F, 23F) are covered by the current PCV vaccines

ii. Currently circulating isolates are mostly susceptible to penicillin

c. Use of high dose ampicillin or amoxicillin allows us to overcome intermediate penicillin resistance for Pneumococcus
    i. Particularly, use of amoxicillin 90 mg/kg/d divided every 8 hours is appropriate to achieve lung exposure for Pneumococci MICs up to 2 mcg/mL and is predicted to achieve clinical and microbiological cure in 90% of pediatric patients treated
    ii. This likelihood decreases to 65% if the amoxicillin is given divided every 12 hours for high MIC isolates
d. No oral cephalosporin studied has activity against Pneumococcus in the lungs that equates to using high-dose amoxicillin

2. For ampicillin/sulbactam as first line therapy regardless of immunization status in patients who have failed previous therapy or have recent beta-lactam exposure
    a. While *Streptococcus pneumoniae* remains the number one cause of CAP in infants and children, *Haemophilus influenzae* and *Moraxella catarrhalis* are also known to be the next most common organisms causing disease
        i. Ampicillin coverage of these two organisms is usually not reliable due to their production of beta-lactamases
    b. Given that these are the two second most common organisms causing CAP in pediatric patients, adding a beta-lactamase inhibitor with ampicillin/sulbactam or amoxicillin/clavulanate provides adequate coverage for these organisms and ceftriaxone offers little benefit
    c. Benefit of ceftriaxone is really for penicillin resistant Pneumococcus, which is rare
    d. Hospitalized patients can be watched for clinical improvement on ampicillin/sulbactam therapy for 24-48 hours before deciding to escalate to ceftriaxone

c. Failure of Initial Therapy
    i. Patients should respond to initial therapy within 48-72 hours of starting antimicrobials
    ii. Consider trending procalcitonin (as shown in Appendix II) to determine if therapy should be escalated
    iii. ID consult should be considered for patients failing first line therapy above

Failure of First Line Inpatient Treatment Below	**Recommended Escalation**
Ampicillin; amoxicillin OR Ampicillin/sulbactam; amoxicillin/clavulanate	Ceftriaxone
Ceftriaxone	Vancomycin

Complicated CAP

A. Clinical Management
    a. Assess history for specific exposures
        i. TB risk assessment
        ii. Travel history: Middle East (MERS), Asia (SARS), others
    b. Assess severity
        i. Normal respiratory rates in children

Age	**Respiratory rate (breaths/min)**
Newborn ≤1 month	40-60
Infant (1-12 months)	30-53
Toddler (13 months – 3 years)	22-37
Preschool (4-6 years)	20-28
School Age (7-12 yeas)	18-26
Adolescent (13-19 years)	12-20

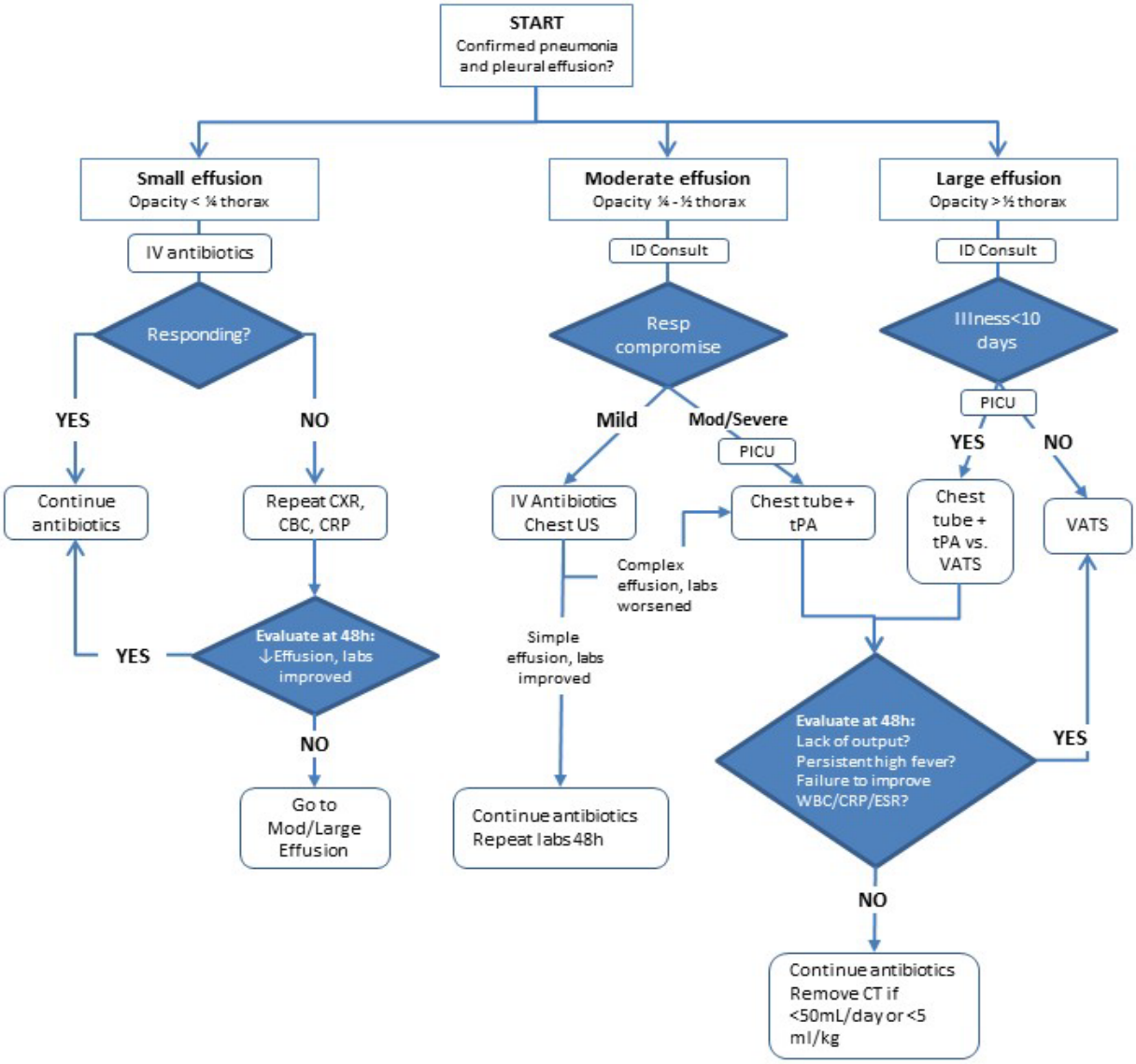
    c. Assess fluid status: patients have increased sensible losses
    d. Diet: NPO if pleural drainage anticipated; assess whether respiratory rate allows for oral intake
    e. Initial Evaluation: Laboratory and Imaging
        i. CBC with differential
        ii. BMP
        iii. Procalcitonin (also consider C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR])
        iv. Microbiology

1. Sputum gram stain and culture, if child is able to provide it
    a. A high quality sputum is usually defined by <10 squamous epithelial cells and > 25 WBCs per low power field
2. See Appendix I: Rapid RSV/Flu versus Respiratory Viral Panel (PCR)
    a. Consider full respiratory viral panel regardless of season for patients not responding to antibiotic treatment and for patients with clinical course/labs not consistent with bacterial pneumonia
3. Blood culture is recommended
4. Consider TST vs IGRA (Quantiferon)

v. CXR (PA, lateral) – determine presence of effusion
vi. ABG if significant compromise

f. Treatment
    i. Empyemas develop primarily because of delayed presentation by the patient with advanced pneumonia and progressive pleural infection, and from inappropriate clinical management. Early antibiotic treatment prevents progression of pneumonia and the development of a parapneumonic effusion. Appropriate early antibiotic treatment will prevent development of an uncomplicated PPE and progression to empyema. Manage according to algorithm below.
    ii. Start empiric antibiotics therapy based on patient scenario below AFTER obtaining a procalcitonin
        1. Tailor coverage based on identification/susceptibilities
    iii. If pleural drainage; send fluid for:
        1. Gram stain and culture
        2. Cell count, glucose, protein, LDH
        3. Consider sending:
            a. Rapid *S. pneumoniae* antigen test (Binax NOW)
            b. Broad range 16S rDNA PCR if negative Gram stain
    iv. Fibrinolytics
        1. < 1yr of age: 0.1-0.2 mg/kg tPA (alteplase)
        2. > 1yr of age: 4 mg tPA (alteplase)
        3. Instill via pigtail/chest tube, clamp for a dwell time of 1 hour, encourage mobilization/rotation of patient, then allow 8 hours of drainage with negative pressure suction at -10-20 cm H2O. Repeat daily x 3.
    v. VATS versus chest tube +/- fibrinolytics: RCTs demonstrate similar efficacy in terms of length of stay but favor chest tube with fibrinolytics in terms of cost versus VATS in terms of needing additional drainage procedures

vi. Management algorithm



Chest tube
8-36 Fr chest tube
8.3 Fr pigtail for neonates

Pleural fluid studies
- Cell count
- LDH
- Glucose
- Protein
- Gram stain, Culture
- *XX TBD by ID XXX*

tPA dosing
- 0.1-0.2 mg/kg up to 4mg in 40mL Saline x 1h-dwell q24h x 3. Rotate patient

J Pediatr Surg 2012;47:2101
Eur J Pediatr 2014;173:1339
Clin Infect Dis2007;45:1480

vii. Empiric antibiotic choice:

Clinical Scenario	Antibiotic Therapy	Duration of Therapy/Comments
Complicated Pneumonia (moderate to large effusion): ID consult		
Complicated Pneumonia, clinically stable	Ampicillin 75 mg/kg/dose Q6h, max dose 2000 mg OR Ampicillin/sulbactam 75 mg/kg/dose Q6h, max dose 2000 mg ampicillin Underimmunized, type 1 penicillin allergy, or exposure to amoxicillin in last 30 days/recent failure of therapy: Ceftriaxone 75-100 mg/kg/dose Q24h, max dose 2000 mg Staphylococcus pneumonia suspected: ADD Vancomycin (pharmacy consult) OR Clindamycin 10-13 mg/kg/dose Q8h, max dose 600 mg *Send MRSA/MSSA nasal PCR	7 days from chest tube placement/drainage of effusion or 7 days from resolution of fever Note: some complicated infections may require up to 4 weeks of treatment
Complicated Pneumonia, critically ill or necrotizing (ICU, intubated, sepsis)	Ceftriaxone 75-100 mg/kg/dose Q24h, max dose 2000 mg PLUS: Vancomycin (pharmacy consult) OR Clindamycin 10-13 mg/kg/dose Q8h, max dose 600 mg *Send MRSA/MSSA nasal PCR	
PO step down for complicated pneumonia (depending on initial IV therapy)	Amoxicillin 30 mg/kg/dose Q8h, max dose 1000 mg OR Augmentin ES 30 mg/kg/dose Q8h, max dose 1300 mg (amoxicillin component; max of 2000 mg/dose Q12h if using XR tablets) *For patients > 40 kg, use non-ES formulation OR Levofloxacin < 5 yo 10 mg/kg/dose Q12h, ≥ 5 yo 10 mg/kg/dose Q24h, max dose 750 mg OR Linezolid < 12 yo 10 mg/kg/dose Q8h, ≥ 12 yo 10 mg/kg/dose Q12h, max dose 600 mg	
Atypical Pneumonia	See above in uncomplicated CAP section	

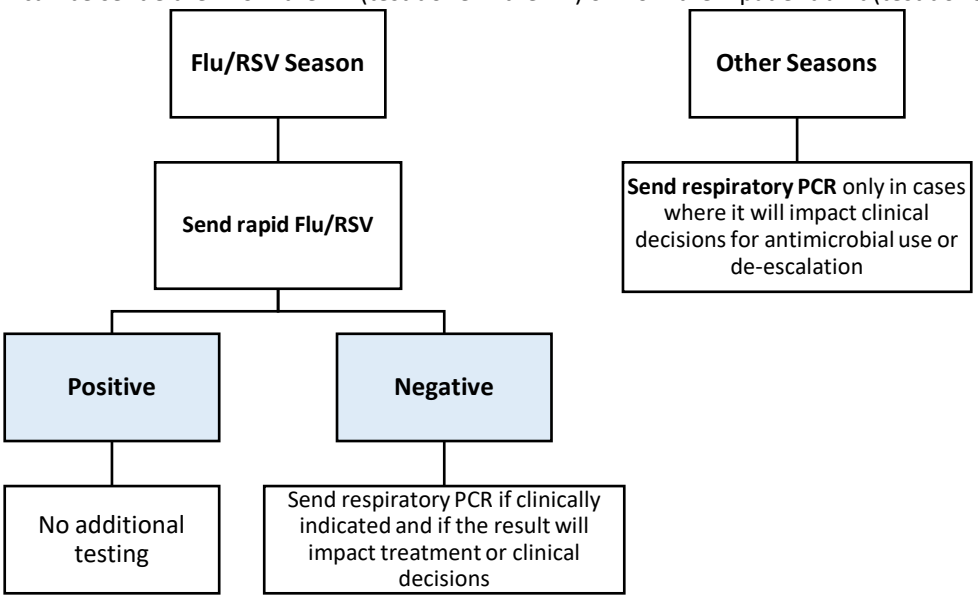
Notes:
For type 1 cephalosporin allergy, consult with ID for antibiotic recommendations
Use of levofloxacin or linezolid requires ID/AMT approval

Aspiration Pneumonia

A. Clinical Management
    a. Initial Evaluation:
        i. Empiric antibiotics are not indicated after an aspiration event or for aspiration pneumonitis
            1. Typically resolves withing 24-48 hours
        ii. For patients who develop a pneumonia after an aspiration event, coverage of anaerobes is not recommended unless lung abscess or empyema is present
        iii. Procalcitonin will be falsely elevated in these patients and use in decision making is not recommended
    b. Treatment
        i. Empiric antibiotic choice (dosing per uncomplicated CAP section above):
            1. IV: ampicillin/sulbactam or ceftriaxone
            2. PO: amoxicillin/clavulanate or cefpodoxime
            3. Tailor coverage based on identification/susceptibilities if cultures obtained
        ii. Duration: 5 days

Appendix I: Rapid RSV/Flu versus Respiratory Viral Panel (PCR)

A. Rapid Flu/RSV can be sent either from the ED (test done in the ED) or from the inpatient unit (test done in the lab)



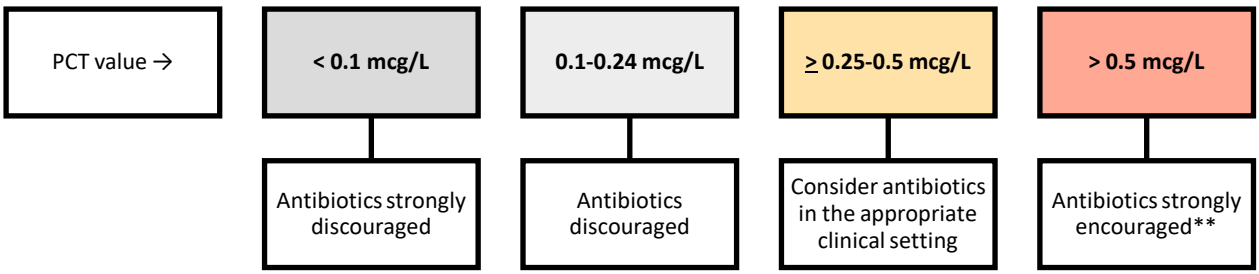
Appendix II: Procalcitonin

A. Procalcitonin (PCT) is a precursor of calcitonin, which under normal circumstances is produced by thyroid C-cells. Serum concentrations of PCT are usually < 0.05 ng/mL, but in the setting of bacterial infection, PCT is produced in large quantities by many body tissues. Presence of bacterial infection stimulates production of PCT in parenchymal tissues and then PCT is rapidly released into the bloodstream. Cytokines in the presence of viral infection actually inhibit PCT production. PCT peaks within 6-12 hours (versus a peak of 24-48 hours for CRP). The more severe the infection, the higher the PCT result. Higher serum PCT levels have also been correlated to increased risk of mortality.
B. Advantages of PCT over CRP:
    a. Specific for bacterial infection
    b. Rapid rise after the insult (peaks within 6-12 hours)
    c. Rapid decline with control of infection (half-life of 24 hours)
    d. Correlation with severity of illness and outcomes
    e. Lack of impact of other inflammatory states on production
C. Cautions:
    a. PCT should be used in clinical context of each patient scenario in combination with other pertinent clinical data
    b. PCT may not rise with localized infections (osteomyelitis, localized abscess, etc.)
    c. PCT may be elevated in newborns in the first 48-72 hours of life
    d. Renal dysfunction (particularly significant compromise, especially hemodialysis patients) will decrease PCT excretion and lead to falsely elevated levels

e. Surgical trauma, cardiopulmonary bypass, cardiac arrest, intracranial hemorrhage, and burns can all falsely elevate PCT
f. PCT may also be elevated after receipt of immunomodulatory agents, in patients with neuroendocrine tumors, and in patients with Kawasaki disease

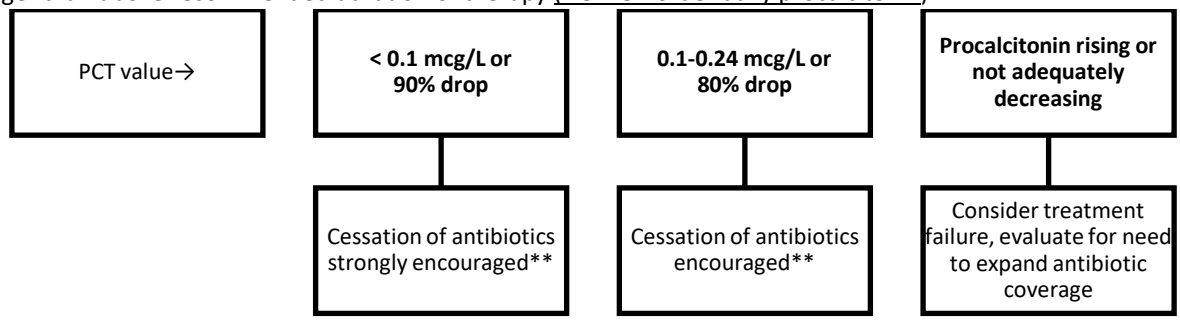
D. PCT results are run in the lab the same day, turnaround time ~30 mins from time it is put on the machine

E. **Initial procalcitonin value on admission:**



a. For PCT values < 0.24 mcg/L:
   i. Consider alternative diagnoses
   ii. Repeat PCT in 6-12 hours if antibiotics not started and no clinical improvement
b. For PCT values > 0.25 mcg/L:
   i. If antibiotics not started, repeat PCT in 6-12 hours if no clinical improvement

F. **Follow-up procalcitonin values while inpatient**, recommended after 48 hours of antibiotic therapy only if considering doing longer than above recommended duration of therapy (DO NOT order daily procalcitonin):



a. Procalcitonin should not be used as the sole factor for deciding to initiate antibiotics and should be interpreted in the context of the patient's clinical picture. Typical LRTI bacteria (i.e. *Streptococcus pneumoniae* or *Haemophilus influenzae*) tend to cause higher rises in PCT than atypical bacteria.
b. **Minimum recommended duration of therapy is 5 days

Arnold Palmer Hospital for Children – Management of Central Line Associated Infections

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Inclusion

- All patients at Arnold Palmer Hospital for Children with suspected or confirmed Central Vascular Catheter (CVC) Infection
    - Includes **all** inpatients and Emergency Department patients AND **all** outpatients in the Kid's Kidney Center and Hematology Oncology Outpatient Center

Exclusions

- Patients without a central catheter (see definition below)
- NICU patients

Definitions

Device Definitions

- Central vascular catheter (CVC): A catheter placed within a vein or artery whose distal end is intended to be located within a central vein or artery, usually the vena cava (inferior or superior).
    - This includes peripherally inserted central catheters (PICCs), tunneled and non-tunneled central venous catheters (such as hemodialysis catheters), central and pulmonary arterial catheters, and subcutaneous ports or reservoirs. See select specific definitions below.
    - Short-term central vascular catheter: Central catheter placed into a central vein or artery without tunneling or cuffs, including non-tunneled hemodialysis catheters. These are generally intended for short-term use (less than 30 days). These include catheters placed at the subclavian, internal jugular or femoral sites, as well as peripherally inserted central catheters (PICCs) intended for use < 30 days.
    - Long-term central catheter: Surgically implanted central catheter with a tunneled portion under the skin and a cuff just inside the exit site. These catheters are intended for use longer than 30 days.
    - Peripherally inserted central catheter (PICC): A short-term central vascular catheter inserted into a peripheral vein (usually basilic or cephalic), with distal tip ending in a central vein, usually the superior vena cava.
    - Hemodialysis catheter: A long-term central venous catheter, either non-tunneled or tunneled, temporary or permanent, which is used to dialyze the blood.
    - Port: Implantable subcutaneous port or reservoir with self-sealing septum tunneled beneath the skin and accessed by a needle through the skin. These are intended for long-term use and managed similarly to long-term catheters.

Infection Definitions

- Exit site infection: Infection, as indicated by exudate, erythema, induration and/or tenderness, at the catheter exit site, < 2cm from the exit line site
- Tunnel infection: Infection, as indicated by erythema, induration, and/or tenderness, >2cm proximal to the catheter exit site, or anywhere along the tract of the tunneled catheter.
- (Port) Pocket infection: Infection in the subcutaneous pocket of an implanted port site; usually associated with tenderness, erythema, and/or swelling over the pocket/port area.
- Complicated infection:
    - Clinical symptoms or bacteremia persist despite 72 hours of appropriate antimicrobial therapy
    - Persistence of sepsis or septic shock
    - Presence of endovascular hardware (e.g., mechanical valve, vascular graft, recent cardiovascular surgery with endocardial manipulation (within previous 14 days), presence of pacemaker with endocardial leads, or AICD)
    - Disseminated disease by septic seeding or suppurative complications (e.g. pulmonary abscesses, endocarditis, osteoarticular infection, or suppurative thrombophlebitis)
- Severe sepsis/septic shock:
    - Infection – proven or suspected infection caused by any pathogen OR clinical syndrome associated with a high probability of infection
    - SIRS – Systemic Inflammatory Response Syndrome to a variety of clinical insults which include temperature changes, heart rate changes, respiratory changes, and changes in white blood cells
    - Sepsis – life-threatening organ dysfunction caused by a dysregulated host response to infection
    - Severe Sepsis – 1) greater than or equal to 2 age-based systemic inflammatory response syndrome (SIRS) criteria, 2) confirmed or suspected invasive infection, and 3) cardiovascular dysfunction, acute respiratory distress syndrome (ARDS), or greater than or equal to 2 non-cardiovascular organ system dysfunctions
    - Septic Shock – severe infection leading to cardiovascular dysfunction (including hypotension, need for treatment with a vasoactive medication, or impaired perfusion)
- Central Vascular Catheter Infection: Primary bloodstream infection in a patient with a CVC, without another infectious source.

Diagnosis

- Blood cultures should be obtained prior to the initiation of antibiotics, unless the patient is unstable or critically ill
- Obtain two blood cultures prior to starting antibiotics
    - One peripheral (excluding oncology patients)
        - If patient/guardian refuses peripheral culture, obtain second central culture
    - One culture from central line (from each lumen, if applicable)
      Note: efforts should be made to collect same volume of blood for all cultures
    - Central line site culture if exit site infection is suspected
    - Do not culture catheter tips

Management

- Remove short-term catheters immediately
- Remove (or exchange if removal is not feasible) non-tunneled catheters immediately in patients with sepsis or septic shock
    - Tunneled catheters (port, Broviac, HD catheter, etc.) should be removed as soon as possible in hemodynamically unstable patients
- Review previous culture history in last 12 months as it may impact the empiric regimen suggested below
- Consult ID
- Start empiric antibiotic therapy (outlined below); antibiotics may be administered via the CVL while in place

- Note: the patient's clinical condition should always be considered regarding decisions for central vascular catheter management

Empiric Antimicrobial Therapy

Immunocompetent/Immunocompromised (Excluding Oncology Patients)

- Cefepime PLUS vancomycin
    - May consider ceftriaxone instead of cefepime if no history of *Enterobacter* spp., *Klebsiella aerogenes*, or *Pseudomonas spp.* in last 12 months

PLUS

- Hemodynamically unstable/toxic/clinical deterioration – add tobramycin

Immunocompromised Oncology Patients

- Cefepime

PLUS

- Hemodynamically unstable, acute myeloid leukemia (AML), or high-risk/relapsed acute lymphoblastic leukemia (ALL) – add vancomycin
- Toxic/clinical deterioration – add tobramycin
- Add antifungal coverage with micafungin for the following criteria:
    - Septic shock, exposure to broad-spectrum antibiotics > 7 days in the last 2 weeks, recent major abdominal surgery, necrotizing pancreatitis, gastrointestinal perforation, high-dose or prolonged (> 7 days) steroid use, AML or high-risk/relapsed ALL, or dialysis

Clinical status	Empiric Therapy	Sepsis	Severe sepsis
Immunocompetent/ Immunocompromised (Excluding Oncology Patients)	Vancomycin + Cefepime/Ceftriaxone	Vancomycin + Cefepime	Vancomycin + Cefepime + Tobramycin
Immunocompromised Oncology Patients	Cefepime	Vancomycin + Cefepime	Vancomycin + Cefepime + Tobramycin ± Micafungin

Negative culture management

Discontinue antibiotics if cultures are negative for 36 hours and patient's clinical course is reassuring

Positive culture initial management

1. Recommend Pediatric ID Consult
2. Evaluate for other sources of infection
    a. This may impact line removal decisions
3. Line removal
    a. Generally recommended for the following organisms:
        i. Methicillin-susceptible *Staphylococcus aureus* (MSSA)
        ii. Methicillin-resistant *Staphylococcus aureus* (MRSA)
        iii. Staphylococcus lugdunensis
        iv. Bacillus spp. (confirmed infection)

v. *Corynebacterium* spp.
vi. *Lactobacillus*
vii. Pseudomonas aeruginosa
viii. Multi-drug resistant Gram-negative bacteria
ix. Fungi (except in stable oncology patients)

b. Also recommended in the following situations
   i. Sepsis/septic shock
   ii. Failed line salvage
      1. Positive cultures for 72 hours despite appropriate antibiotic therapy

      OR

      2. Persistent fever, and hemodynamic changes despite 72 hours of appropriate antibiotic therapy
         a. Exception: oncology patients with a positive culture for *Streptococcus viridans* group (*S. mitis, S. sanguis, S. mutans*, and *S. anginosus* group)
   iii. Previous history of CVC infection in the last 12 months with the same organism from the same line
   iv. Exit site infection, tunneled infection, or pocket infection of the catheter site associated with the bacteremia
   v. Endovascular infection, including endocarditis
   vi. Suppurative thrombophlebitis
   vii. Presence of an intravascular prosthetic device

c. Other considerations for line removal
   i. Non-tunneled catheters: generally should be removed if possible for the majority of patients
   ii. Tunneled/long term catheters:
      1. Complicated infection as defined above: remove
      2. Uncomplicated infection:
         a. Line needed long term – line salvage unless above criteria are met; see criteria for failing line salvage and remove accordingly if necessary
         b. Line not needed for long term: remove
   iii. Polymicrobial line infections
      1. Line removal not always necessary (unless one of the organisms is noted above) but threshold for removal in these patients is low

4. Line salvage – lock therapy (see Appendix I)
   a. Preferred:
      i. Gram-positive organisms: vancomycin lock
      ii. Gram-negative organisms: gentamicin lock
      iii. Fungal organisms: amphotericin lock
   b. Ensure the organism is susceptible to the chosen lock therapy – for alternatives discuss with ID (examples: cefazolin, ceftazidime, ciprofloxacin)
   c. Lock each infected lumen. Lumen should not be used while the lock is in place.
   d. Lock therapy duration
      i. Dwell time: 4-24 hours depending on line access availability
         1. Minimum recommended dwell time = 4 hours
         2. May consider 72 hour dwells for dialysis patients on a three times weekly cadence
      ii. Total duration of lock therapy should match duration of antibiotic therapy
   e. For information on ethanol locks and sodium bicarbonate locks for prevention of central line infections, see Policy # 2058
5. The BIOFIRE Gram-positive and Gram-negative panels are run within approximately 2 hours of identification of a positive culture. **Results may influence empiric therapy choice.** Comments on the result will provide

information on drug of choice for the organism detected and will test for common resistance mechanisms that may necessitate expansion of therapy.

6. Repeat blood cultures every 24 hours until 48 hours of negative cultures have been documented
    a. For fungal line infections, it is recommended that 3 days of negative cultures be documented
7. Duration of therapy
    a. See specifics per organism below
    b. Day 1 of therapy starts on day of first documented negative blood culture without any positive blood cultures on the same day
    c. Duration of therapy may differ for complicated infections or exit site, tunnel, or pocket infections
    d. For patients with hemodialysis catheters, a 4-6 week course of antimicrobials is recommended if bacteremia or fungemia persists > 72 hours after catheter removal

Positive culture DEFINITIVE management by organism

Organism	**Drug of choice**	**Duration if catheter retained**	**Duration if catheter removed**
Coagulase negative *Staphylococcus*: Methicillin resistant Methicillin susceptible	 Vancomycin Nafcillin	10 days	Blood cultures positive < 72 hours: 5 days Blood cultures positive ≥ 72 hours: 7 days
***Staphylococcus aureus* and *Staphylococcus lugdunensis*:** Methicillin resistant Methicillin susceptible	 Vancomycin Nafcillin (preferred) Cefazolin appropriate for MSSA following clearance of blood cultures	Removal highly recommended 4-6 weeks	Uncomplicated: 14 days Hemodialysis: 21 days Complicated or immunocompromised: 4-6 weeks
***Enterococcus*:** *E. faecalis* *E. faecium*	 Ampicillin Daptomycin or linezolid Ampicillin only if susceptible	14 days	10 days
***Streptococcus* spp:** *S. pneumoniae* *S. pyogenes* (GAS) *S. anginosus*	Susceptibility dependent, usually ampicillin or ceftriaxone	10 days	10 days
Lactobacillus ***Bacillus* spp.**	Ampicillin Vancomycin	Removal highly recommended 10 days	7 days

Gram-negative bacilli (*E. coli, Klebsiella spp., Serratia, Acinetobacter, Enterobacter spp., Pseudomonas, Citrobacter spp., Proteus spp*., etc.)**:**	Susceptibility dependent, with the following considerations:	10 days if cultures positive < 72 hours and rapid defervescence If above criteria not met: 14 days	7 days if cultures negative within 72 hours after line removal and rapid defervescence If above criteria not met: 10 days In some cases, therapy may be extended up to 14 days
Enterobacter spp. and *Klebsiella aerogenes*	Cefepime preferred over narrower therapy even if ceftriaxone susceptible		
Acinetobacter spp.	Ampicillin/sulbactam is the drug of choice		
ESBL positive (ex: CTX-M)	Carbapenem is the drug of choice (meropenem or ertapenem, ertapenem preferred)		
Carbapenemase positive (ex: IMP, KPC, NDM, OXA, VIM)	Pseudomonas: ceftolozane/ tazobactam (Zerbaxa) Other Gram-negatives: ceftazidime/avibactam (Avycaz)		
Candida spp. Neutropenic or immunocompromised Other patients	Micafungin (Fluconazole appropriate following clearance of blood cultures/source control and documented susceptibility) Micafungin (Fluconazole appropriate empirically if not critically ill and if low risk for azole resistance [not on azole prophylaxis] or definitively following clearance of blood cultures/source control and documented susceptibility)	Removal recommended except in stable oncology patients 14 days	14 days

Criteria for PO antimicrobial therapy

- All patients must meet the following criteria:
  - Blood cultures negative > 48 hours for bacteria and > 5 days for Candida spp.
  - Sustained clinical improvement
  - Adequate PO absorption (i.e. intact bowel)
  - Immunocompetent
- Additional organism specific criteria:
  - *Candida spp.*:
    - PO treatment appropriate in above patients regardless of line removal
  - Bacterial organisms:
    - Line must be removed

Criteria for catheter replacement

- **Unless there is an urgent need for central vascular access, new CVC placement should be delayed until at least 5 days after the first negative blood culture** when treating a bloodstream infection, including CLABSI. This may be extended up to 7 days when the bloodstream infection is due to fungal organisms.
  - Insertion of a central vascular catheter in the presence of an active bloodstream infection may result in colonization and infection of the new catheter, resulting in relapse of bacteremia after treatment.
  - A recent small study showed that PICCs placed within two days of documented bacteremia had an increased risk of relapse of bacteremia (6.5%) when compared to PICCs place at least three days after documentation of negative blood culture (0.3%).[2]
  - In clinical scenarios where there is ongoing need for central vascular access, clinicians must weigh the risk/benefit of placing a new CVC in the setting of active bacteremia.
- **Considerations for midline catheter placement at the time of long-term catheter removal:**
  - In patients requiring removal of a long term central catheter (such as a Port or Broviac) and ongoing need for central access, the primary team can consider consulting vascular access to coordinate placement of a midline catheter at the time of long term catheter removal in the OR.
    - Examples may include patients requiring TPN, patients receiving medications that require central administration, or patients on multiple IV medications with compatibility issues.
  - Patients with fungemia are excluded from consideration for a midline catheter at the time of long-term catheter removal.
  - Discussion with ID is recommended, especially in patients who are requiring line removal due to hemodynamic instability in the setting of central venous catheter infection.

Appendix I: Antimicrobial lock therapy

Antimicrobial lock/concentration	Total volume per lumen
Vancomycin 5 mg/mL + heparin 100 units/mL	2 mL
Vancomycin 5 mg/mL + alteplase 0.5 mg/mL	2 mL
Gentamicin 2 mg/mL + heparin 100 units/mL	2 mL
Ciprofloxacin 0.2 mg/mL + heparin 5000 units/mL	2 mL
Ceftazidime 0.5 mg/mL + heparin 100 units/mL	2 mL
Cefazolin 5 mg/mL + heparin 2500 units/mL	2 mL
Ampicillin 10 mg/mL + heparin 5000 units/mL	2 mL
Amphotericin B liposomal 2 mg/mL	2 mL

Arnold Palmer Hospital Neonatal and Pediatric Meningitis Guideline

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INCLUSIONS

- All pediatric and neonatal patients at Arnold Palmer Hospital for Children and Winnie Palmer Hospital for Women and Babies (APH and NICU inpatients and APH Emergency Department patients) with suspected or confirmed meningitis
    - This includes patients with one or more of the following, all of whom should receive an LP to rule out meningitis:
        - Any neonate ≤ 28 days old presenting with fever
        - Infants 1-3 months of age triggered as high risk in the ED
        - Other infants and children with sepsis and signs concerning for CNS infection
        - Patients ≤ 6 weeks of age with bacteremia from any source
        - Infants < 3 months of age with Salmonella bacteremia

EXCLUSIONS

- Patients < 34 weeks gestation at birth admitted to the NICU
- Neurosurgical patients such as patients with neurologic hardware (i.e. ventricular shunt) or cochlear implant devices
- Patients with recent CNS surgery within the last 3 months
- Meningitis that resulted as an extension of other infected sites
- Patients with anatomic defects (i.e., dermal sinus, tract anomaly)
- Patients with penetrating head or spine trauma
- Patients with CSF otorrhea (including congenital defects, such as Mondini dysplasia) or CSF rhinorrhea/leak

DEFINITIONS

- CNS: central nervous system
- CSF: cerebrospinal fluid
- LP: lumbar puncture
- ICP: intracranial pressure
- Meningitis (bacterial, viral, aseptic):
    - Symptoms in infants: fever, hypothermia, bulging fontanel, lethargy, irritability, seizures, respiratory distress, poor feeding, vomiting
    - Symptoms in older children: fever, headache, photophobia, neck stiffness, nausea/vomiting, confusion/altered mental status, lethargy, irritability, neck/back pain, seizures, focal neurologic deficit
    - Positive Kernig or Brudzinski sign
    - Neonates and infants or children with neurodevelopmental disabilities may not present with usual signs or symptoms
- Traumatic LP
    - CSF containing at least 10 RBC per microliter
    - CSF WBC in setting of a traumatic LP does not have diagnostic utility
        - Correction (or ratios) for RBCs in CSF is discouraged due to lack of validating studies
- Pretreated meningitis
    - Signs/symptoms suggestive of meningitis but CSF culture negative on a non-traumatic LP AFTER administration of antibiotics (may occur as early as 15 minutes prior to LP for Meningococcal meningitis and 4 hours for Pneumococcal meningitis), regardless of molecular test result (e.g. PCR)
- CSF pleocystosis
    - Any elevation in WBC in the CSF
        - Neonates can normally have up to 6 WBCs/mm^3 and up to 5% neutrophils in the absence of meningitis

INITIAL MANAGEMENT/EMPICRIC THERAPY

- Initial laboratory evaluation:
  - Blood culture
  - CBC w/ differential
  - CRP, procalcitonin
  - CMP (preferred over BMP for viral meningitis or encephalitis to assess liver function)
  - Coagulation studies (PT, INR)
- CSF studies
  - LP with:
    - Cell count and differential
    - Protein
    - Glucose
    - Gram stain and culture
    - Meningitis/encephalitis PCR panel
      - The stand alone HSV CSF PCR is not recommended in addition to or in leu of this PCR
    - For CSF samples with inadequate volume for complete studies, the following should be prioritized in order of importance: PCR > Gram stain/culture > cell count/protein/glucose
      - Must contact the lab for the PCR to be run preferentially over the Gram stain/culture
  - The following patients may be at increased risk of complications from an LP, consider the risks/benefits:
    - Significant cardiopulmonary compromise
    - INR > 4, platelets < 50, active bleeding
    - Increased ICP
    - Papilledema
    - Skin infection over site for LP
    - Focal neurologic deficit
  - For guidance on CSF study interpretation, see **Appendix I**
- Start initial antibiotic therapy after LP as recommended below
  - If there is a contraindication or inability to perform an LP, antimicrobial therapy should not be delayed. At a minimum, obtain blood cultures before starting antimicrobials.
- Assess need for steroid initiation as recommended below
- Supportive care
  - Elevate head of bed
  - Treatment of hypoglycemia, acidosis, and coagulopathy if present
  - Treatment of seizures
  - Cardiopulmonary support
- Imaging
  - Recommended before LP for patients with:
    - Immunodeficiency
    - Papilledema
    - Focal neurologic deficit on exam
    - Dramatic changes in mental status or increased somnolence
  - CT without contrast

Initial Antimicrobial Therapy

- For patients with allergies to the preferred primary regimen, discuss with Infectious Diseases to ensure chosen alternative antimicrobial therapy has appropriate bactericidal activity and CNS penetration
- For dosing considerations, see **the APH Antimicrobial Dosing Card**

Age	Most Common Pathogens	First Line Empiric Therapy	Comments
≤ 28 days	• Group B *Streptococcus* (*Streptococcus agalactiae*, GBS) • Enteric Gram-negatives (*E. coli*) • *Listeria monocytogenes*	Ampicillin PLUS Gentamicin OR Ceftazidime Consider Ceftriaxone monotherapy for neonates ≥ 14 days with normal bilirubin Consider adding Acyclovir in neonates with: • Known HSV exposure • Hypothermia • Vesicular rash/mucus membrane ulcers • CSF pleocytosis • Seizures • Abnormal LFTs • Leukopenia and/or thrombocytopenia	Discontinue acyclovir if PCR negative for HSV If on gentamicin and any culture or PCR indicates Gram-negative organisms, switch to ceftazidime
> 28 days	• *Streptococcus pneumoniae* • *Neisseria meningitidis* • *Haemophilus influenzae* • GBS • Enteric Gram-negatives • *Listeria monocytogenes* (immunocompromised patients)	Ceftriaxone ADD Vancomycin if CSF abnormal ADD Ampicillin if patient is immunocompromised Consider adding Acyclovir in patients ≤ 6 weeks old with: • Known HSV exposure • Hypothermia • Vesicular rash/mucus membrane ulcers • CSF pleocytosis • Seizures • Abnormal LFTs • Leukopenia and/or thrombocytopenia	Discontinue acyclovir if PCR negative for HSV Discontinue ampicillin if PCR negative for *Listeria*

Steroid Considerations

- Consider steroids prior to LP in patients with risk factors for the organisms below:
  - Un-immunized
  - Sickle cell disease
  - Asplenia
- Patients with known *Haemophilus influenzae*
  - Gram stain = Gram-negative rods AND meningitis PCR panel positive for *H. influenzae*
  - Recommended to start before or at same time as first dose of antibiotics (no benefit if given more than one hour later)
- Patients with known *Streptococcus pneumoniae*
  - Gram stain = Gram-positive cocci in pairs and chains AND meningitis PCR panel positive for *S. pneumoniae*
  - Use in patients ≥ 18 years of age
    - No demonstrated benefit in pediatric patients, discuss with Infectious Diseases
      - If used, patient must be ≥ 6 weeks of age
- Dexamethasone
  - Dosing: 0.15 mg/kg per dose IV every 6 hours (max 10 mg/dose)
  - Duration: 2-4 days
    - A two-day course appears to be as effective as longer courses and is associated with a lower risk of toxicity

DEFINITIVE MANAGEMENT/DURATION OF THERAPY

Normal CSF Profile AND No Organism Identified

- For patients with normal CSF studies and negative blood and CSF cultures, discontinue empiric antimicrobial therapy if cultures remain negative at 48 hours

Neonatal Sepsis AND Inability to Obtain CSF

- For patients ≤ 6 weeks of age presenting for rule out sepsis OR with bacteremia and unable to obtain CSF studies, the decision to continue or discontinue empiric antimicrobial therapy should be individualized – consult Infectious Diseases

CSF Pleocytosis AND No Organism Identified

- For patients with abnormal CSF studies but negative blood and CSF cultures, the decision to continue or discontinue empiric antimicrobial therapy should be individualized – consult Infectious Diseases

Organism Identified

- Consult Infectious Diseases
- For patients with allergies to the preferred primary regimen below, discuss with Infectious Diseases to ensure chosen alternative antimicrobial therapy has appropriate bactericidal activity and CNS penetration
- For dosing considerations, see **the APH Antimicrobial Dosing Card**
- Repeat LP in the following circumstances:
    - All patients with poor clinical response at 36-48 hours despite appropriate antimicrobial therapy
    - Neonates with meningitis due to GBS, Gram-negatives, or *Listeria*, at 24-48 hours after starting appropriate antimicrobial therapy
    - All patients regardless of age with Gram-negative meningitis (except *Neisseria meningitidis* and *Haemophilus influenzae*), at 48-72 hours after starting appropriate antimicrobial therapy
    - All patients regardless of age with persistent or recurrent fever
    - All patients regardless of age with meningitis due to *Streptococcus pneumoniae* that is ceftriaxone intermediate or resistant OR who have received dexamethasone, at 48 hours after initial tap
    - All patients regardless of age with HSV meningitis, at 21 days of therapy
    - All patients regardless of age with Cryptococcal meningitis, at 14 days of therapy
- Imaging
    - Consider during treatment for the following:
        - Focal neurologic deficit
        - Persistent fever (otherwise unexplained)
        - Seizures
        - Persistently positive CSF cultures
        - All patients at 48-72 hours before anticipated end of therapy
    - MRI

Organism	**Preferred Regimen**	**Comments**
***E. coli* and other enteric Gram-negatives**	Neonates: Ceftazidime All other patients: Ceftriaxone *Consider ceftriaxone in neonates ≥ 14 days with normal bilirubin	Narrow to ampicillin if susceptible
Haemophilus influenzae	Ceftriaxone	Narrow to ampicillin if susceptible
Listeria monocytogenes	Ampicillin OR Penicillin PLUS Gentamicin	Continue gentamicin for ≥ 3 days and until patient clinically improves (usually 7-14 days)
Neisseria meningitidis	Ceftriaxone	Narrow to ampicillin if susceptible
Streptococcus agalactiae	Ampicillin OR Penicillin	

Streptococcus pneumoniae	Ceftriaxone PLUS Vancomycin	Penicillin susceptible (look for meningitis specific result as the MIC breakpoint is different): narrow to penicillin or ampicillin Penicillin intermediate or resistant/cephalosporin susceptible: discontinue vancomycin and continue ceftriaxone Penicillin and cephalosporin intermediate or resistant: continue ceftriaxone, continue vancomycin, ADD rifampin <u>if susceptible</u> AND one or more of the following is true: 1. If after 24-48 hours of vancomycin and ceftriaxone the clinical condition has worsened 2. The subsequent CSF culture indicates failure to eradicate or decrease substantially the number of organisms 3. The organism has a ceftriaxone MIC <u>≥</u> 4 mcg/mL
Cytomegalovirus (CMV)	Supportive care only	In certain patients with severe disease or immunocompromise, consider ganciclovir, decreasing immunosuppression, and CMV IgG
Enterovirus	Supportive care only *Discontinue antibiotics prior to rule out completion in all patients with CSF positive for Enterovirus by PCR if no other source of bacterial infection identified	In certain patients with severe disease or immunocompromise, consider IVIG and investigational antiviral therapy – must discuss with ID
Herpes simplex virus (HSV1/ HSV2)	Acyclovir	
Human herpes virus 6 (HHV-6)	Supportive care only	In certain patients with severe disease or significant immunocompromise, consider ganciclovir or foscarnet
Varicella-zoster virus (VZV)	Acyclovir	VariZIG or IVIG not recommended for established disease
Cryptococcus neoformans/gattii	Liposomal amphotericin B PLUS flucytosine	
Human parechovirus (HPeV)	Supportive care only	
Staphylococcus aureus	Vancomycin	MSSA: narrow to nafcillin MRSA: continue vancomycin
Salmonella spp.	Ceftriaxone	Narrow to ampicillin if susceptible

DURATION OF THERAPY

Organism	**Duration of Therapy**
GBS	14-21 days
Streptococcus pneumoniae	10-14 days
Haemophilus influenzae	7-10 days
Neisseria meningitidis	5-7 days
Listeria monocytogenes	21-28 days
Gram-negatives	21 days or 14 days from first sterile CSF culture, whichever is longer
Staphylococcus aureus (MRSA or MSSA)	14 days
Salmonella spp.	28 days
HSV	21 days minimum
Cryptococcus spp.	Induction therapy: 14 days minimum Consolidation therapy: 8 weeks minimum

<u>Note</u>: Duration of therapy may be extended for patients with meningitis and brain abscess. For organisms not included in above table, discuss with ID.

CHEMOPROPHYLAXIS OF CLOSE CONTACTS

- ***N. meningitidis***
  - Indicated in all household contacts (especially children < 2 years of age) of patients with meningococcal meningitis, regardless of their meningococcal vaccination status
  - Other high-risk groups that should receive prophylaxis:
    - Childcare or preschool contacts at any time during 7 days before onset of illness
    - Direct exposure to patient's secretions such as through kissing, sharing toothbrushes or sharing eating utensils, at any time during 7 days before onset of illness
    - Mouth-to-mouth resuscitation, unprotected contact during endotracheal intubation at any time 7 days before onset of illness or within 24 hours of initiation of effective antimicrobial therapy
    - Frequently slept in same dwelling as patient during 7 days before onset of illness
    - Passengers seated directly next to the index case during airline flights lasting more than 8 hours
  - Rifampin and ciprofloxacin are not recommended for pregnant women

Drug/Duration	Age Group	Dosing
Rifampin x 2 days (4 doses) PO	< 1 month	5 mg/kg/dose Q12H
	≥ 1 month	15-20 mg/kg/dose Q12H (max 600 mg/dose)
Ciprofloxacin x 1 dose PO	All ages	20 mg/kg (max 500 mg)
Ceftriaxone x 1 dose IM	< 15 years	125 mg
	≥ 15 years	250 mg
Azithromycin x 1 dose PO ***Not preferred**	All ages	10 mg/kg (max 500 mg)

- ***H. influenzae* type b (Hib)**
  - Indicated for certain close contacts of patients with Hib:
    - For all household contacts in the following circumstances:
      - Household with at least 1 contact younger than 4 years of age (other than the patient) who is un-immunized or incompletely immunized
      - Household with a child younger than 12 months who has not completed the primary Hib series
      - Household with a contact who is an immunocompromised child, regardless of that child's Hib immunization status or age
    - For preschool and childcare center contacts when 2 or more cases of Hib invasive disease have occurred within 60 days
    - For the patient him/herself, if younger than 2 years of age or a member of a household with a susceptible contact **AND** treated with a regimen other than ceftriaxone, chemoprophylaxis at the end of therapy is recommended
  - Drug/dosing/duration:
    - Rifampin x 4 days (4 doses) PO
    - Dose: 20 mg/kg/dose Q24H (max 600 mg/dose)
    - Prophylaxis is not recommended in pregnant women
  - Important definitions:
    - For Hib specifically, household contact is defined as: people residing with the patient or nonresidents who spent ≥ 4 hours with the patient for at least 5 of the 7 days preceding the day of hospital admission
    - Complete immunization is defined as having had at least 1 dose of conjugate vaccine at 15 months of age or older; 2 doses between 12 and 14 months of age; or the 2- or 3-dose primary series when younger than 12 months with a booster dose at 12 months of age or older

Appendix I:

CSF Interpretation, ≤ 60 days old

TABLE 2 CSF Values in Febrile Infants Without Evidence of UTI, IBI, HSV, Enterovirus, or Traumatic CSF

	Age, d	*n*	Mean	Median	Range
WBCs per mm^3	1–28	278	6.1	5.0	0–18
	29–60	318	3.1	3.0	0–8.5
Protein mg/dL	1–28	278	75.4	73.0	15.8–131.0
	29–60	318	58.9	54.0	5.5–105.5
Glucose	1–28	278	45.3	46.0	30.0–61.0
Glucose	29–60	318	48.0	48.0	20.6–65.5
RBCs per mm^3	1–28	278	95.5	5.5	0–236
RBCs per mm^3	29–60	318	75.5	2.0	0–64.5

Statistical outliers were removed. Other studies reveal slightly different ranges. Local laboratory tests may provide slightly different upper limits of normal. Adapted from Byington CL, Kendrick J, Sheng X. Normative cerebrospinal fluid profiles in febrile infants. *J Pediatr.* 2011;158(1):130–134.

CSF Interpretation, > 60 days old

CSF Finding	Leukocytes (mm^3)	Neutrophils	Protein (mg/dL)	Glucose (mg/dL)	Blood-to-glucose ratio
Viral	< 1000	20-40%	WNL or < 100	WNL	WNL
Bacterial	> 1000	> 85-90%	>100-150	< 40	< 0.4
Pretreated Bacterial	> 1000	> 80%	60 to > 100	< 40	< 0.4
Fungal	< 500	< 10-20%	> 100-200	< 40	< 0.4

WNL: within normal limits

Note: Neonates may have normal CSF studies in the setting of meningitis.

Arnold Palmer Hospital for Children: Management of Tracheitis and Ventilator Associated Pneumonia

1. Definitions

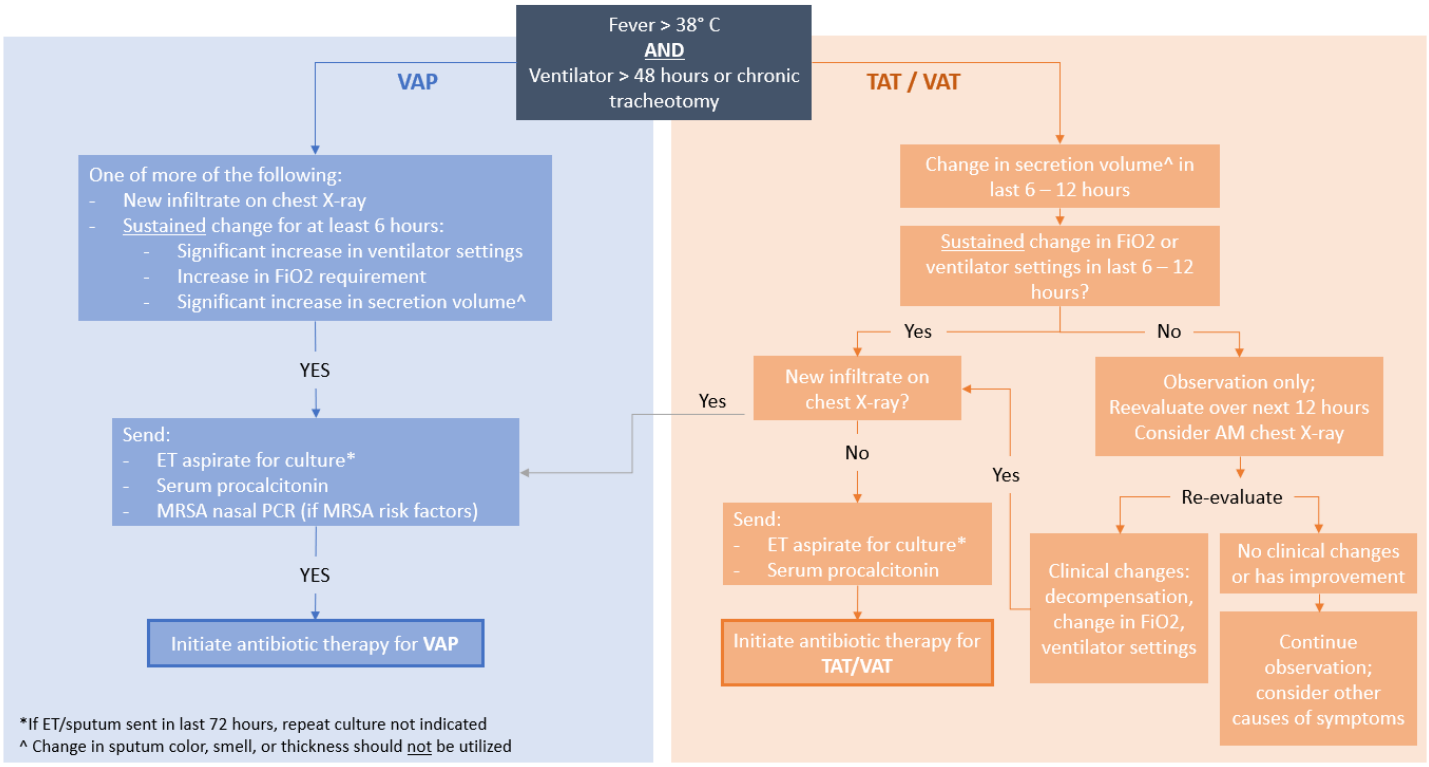
A. Tracheostomy or Ventilator Associated Tracheobronchitis/Tracheitis (TAT/VAT):
   a. Purulent tracheal secretions plus fever and change in respiratory requirements with no other known cause in the absence of new lung infiltrate on chest X-ray in a patient who has a chronic tracheostomy or who has been intubated > 48 hours

B. Ventilator Associated Pneumonia (VAP):
   a. New lung infiltrate on chest X-ray plus clinical evidence that the infiltrate is of an infectious process (new onset fever, purulent sputum, leukocytosis, elevated procalcitonin, change in respiratory requirements) in a patient who has been intubated for > 48 hours

C. Fever: temperature > 38°C

D. Change in secretion volume:
   a. Patient has an increased **quantity** of secretion production from baseline (changes in color or thickness of secretions are not relevant)

2. Diagnosis/Therapy Initiation Algorithm

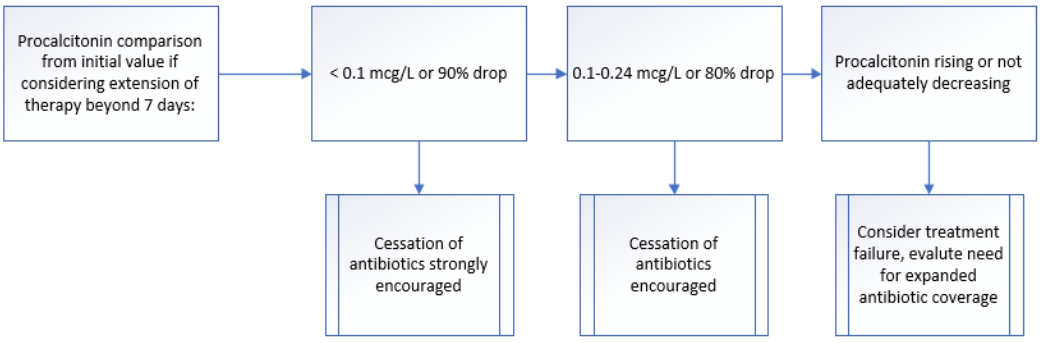


3. Empiric & Definitive Antibiotic Therapy

A. Use patient's previous culture data (in the last 6 months) to guide therapy for both TAT/VAT and VAP
B. TAT/VAT
    a. Cefepime
C. VAP
    a. Cefepime
    b. Add vancomycin for MRSA risk factors:
        i. Prior IV antibiotic use within last 90 days
        ii. History of invasive MRSA infection within last 12 months
        iii. Presence of invasive devices
        iv. History of recurrent skin infections or chronic wounds, etc.
D. Definitive Therapy
    a. Based on microbiological data (e.g. sputum culture and susceptibility)
    b. When changing from an empiric agent to a different definitive agent, the duration of the empiric agent should be included in the total duration of therapy (if empiric agent was active against the organism isolated)
    c. Step down to oral therapy (including via tube) is encouraged in clinically stable patients on other oral agents/receiving an oral diet
    d. For patients with no organism isolated, clinical judgement should be used to determine if empiric therapy should be continued or antibiotic therapy be stopped
E. Inhaled antibiotic therapy
    a. Not recommended in patients also on systemic antibiotic therapy
    b. Not enough evidence for recommendation of use as monotherapy

4. Antimicrobial Stewardship Tools

A. MRSA Nasal PCR
    a. MRSA nasal PCR will be sent on patients started on anti-MRSA antibiotic therapy for suspected VAP (i.e. vancomycin)
    b. Negative result indicates MRSA pneumonia is highly unlikely (negative predictive value > 95%)
        i. Anti-MRSA agents (vancomycin, clindamycin, etc.) are not warranted and can be avoided or discontinued (if already initiated)
    c. Positive results do NOT indicate need for anti-MRSA agents due to low positive predictive value
B. Procalcitonin
    a. Procalcitonin will be sent on all patients started on antibiotic therapy for suspected VAT/VAP
    b. Procalcitonin will be used to guide discontinuation of antibiotic therapy or escalation of therapy (if rising)



5. Duration of Antibiotic Therapy

A. TAT/VAT: 5 days
    a. Discontinue antibiotics sooner if patient is extubated (source control)
B. VAP: 7 days
    a. May require extension to 10-14 days for difficult to treat organisms such as *Staphylococcus aureus, Pseudomonas spp.* and *Acinetobacter spp.*
        i. Procalcitonin plus clinical criteria should guide discontinuation

Arnold Palmer Hospital for Children: Treatment of Pediatric Urinary Tract Infections (UTIs)

Table of contents:

Exclusion criteria: immunocompromised, renal abscess

A. **Indications for screening**:

Toilet trained AND without developmental delay or other reason for inability to express symptoms	**Non-toilet trained OR developmental delay or other reason for inability to express symptoms**
• Signs/symptoms (see below) referable to urinary tract or without explanation of another source • Fever in absence of another source of infection	• Signs (see below) without explanation of another source • Fever in absence of another source of infection

i. Toilet trained: daytime dryness without accidents
ii. Symptomology should be assessed in all patients with the ability to discuss; usually this occurs starting at age 3 (excluding patients with underlying developmental delay)
iii. **Signs/symptoms include**:
   a. Cystitis: urgency, dysuria, frequency
   b. Pyelonephritis: flank pain/CVA tenderness, vomiting
   c. Other signs/symptoms can include temperature instability (hyper/hypothermia; more common with pyelonephritis), diarrhea, abdominal pain, back pain, new bed-wetting, poor feeding, lethargy
   d. Foul smelling or cloudy urine without signs/symptoms referable to the urinary tract (if able to discuss) likely signify dehydration or asymptomatic bacteriuria (ASB; see below) – watchful waiting is recommended in these patients without any of the other signs/symptoms mentioned previously
   e. Note: Urinary catheters can cause micro-trauma resulting in some of the signs/symptoms above (such as dysuria, frequency, suprapubic pain/tenderness). In patients with urinary catheters in place or that have been placed or removed in the last 48 hours, consideration for screening of UTI should not be based on these signs/symptoms alone.

B. **How to screen**:
i. Screening should occur prior to initiation of antibiotics if possible (antibiotics should not be delayed if there is an inability to obtain a urine sample)
ii. For uncircumcised males, ensure foreskin retraction
iii. For catheterized patients, remove the foley prior to collection when possible
   a. Do not collect sample directly from drainage container
iv. Cleaning prior to obtaining specimen
   a. Cleaning of the skin around the genital area is recommended, especially prior to obtaining a clean catch specimen (toilet trained patients only)
v. Clean catch versus catheterized specimen
   a. Clean catch should only be done in toilet trained patients (with help of the parent/guardian or nurse if applicable) and the sample should be obtained mid-stream
   b. Catheterized specimens (or a suprapubic aspiration) should be done in children who do not meet clean catch criteria

c. Urine samples obtained with cotton balls/gauze or via a bagged specimen should NOT be used for diagnosis

vi. Urinalysis (UA) interpretation

a. Urine culture to be sent if:
   1. Patient < 6 months of age, regardless of UA/urine dip results
   2. Urinalysis: pyuria, nitrites, or bacteriuria present
   3. Urine dip:
      a. LE positive and nitrite negative – send for microscopy and evaluate as above
      b. Nitrite positive

b. Note: A positive leukocyte esterase result is likely false if no WBCs are present – this should be considered when interpreting the UA

c. Do NOT obtain a repeat urinalysis in patients who clinically improve on appropriate antibiotic treatment

d. Presence of ≥ 10 per high-power field squamous epithelial cells on the UA is indicative of a contaminated specimen

vii. Urine culture interpretation

a. The following colony counts are considered a positive result based on type of specimen obtained BUT must be accompanied by positive signs/symptoms (if able to discuss) AND a positive urinalysis
   1. Suprapubic aspiration: > 1,000 CFU
   2. Catheterized: > 50,000 CFU
   3. Clean catch: > 100,000 CFU

b. Multiple pathogens and/or presence of yeast is usually more consistent with contamination
   1. A repeat specimen (prior to antimicrobials) is recommended if true clinical suspicion for UTI
   2. If there is presence of yeast and the patient has signs/symptoms consistent with a vulvovaginal yeast infection, single dose fluconazole should be considered (or up to three doses for severe or recurrent disease)
      a. Fluconazole 3 mg/kg (max 150 mg) x 1, or Q72H x 2-3 doses

c. Repeating urine cultures within 5-7 days of the initial culture is NOT recommended, including for test of cure, especially in children who are clinically improving

C. **Considerations for admission**

i. Inability to tolerate oral intake (including antibiotics)
ii. Toxic/ill appearing
iii. Severe dehydration
iv. Concerns related to follow-up

D. **Empiric/definitive therapy (antimicrobials and duration of treatment)**

i. Asymptomatic bacteriuria (ASB)

a. Definition: bacteria in the urine without signs/symptoms (as above) referable to urinary tract (if able to discuss)

b. In patients able to discuss symptomology, a positive UA and/or urine culture (regardless of colony count) is not indicative of UTI without signs/symptoms referable to the urinary tract

c. Antibiotics are **not** recommended
   1. Antibiotics do not improve clinical outcomes; rather, antibiotic use is associated with an increase in the risk of symptomatic UTI and development of antibiotic resistance
   2. ASB resolves spontaneously
   3. Exceptions include pregnant patients and patients undergoing endoscopic urologic procedures associated with mucosal bleeding

d. Note: All patients with chronic urinary catheters will eventually develop ASB. This is also common in patients with short term urinary catheters or who intermittently catheterize. Catheters should be removed as soon as possible to reduce the risk of catheter associated UTI (CAUTI).

ii. Considerations prior to making antibiotic choice
   a. Review history of previous microbiology for patients with history of a UTI in the previous 6 months
   b. If on UTI prophylaxis, hold this therapy and do not use the same antibiotic for empiric treatment
   c. Consider withholding antibiotics in patients who are afebrile and well-appearing if UA is mildly positive or equivocal (LE positive only, low WBC count) while awaiting culture results
      1. If history is consistent with UTI in this setting antibiotics should not be withheld (signs/symptoms referable to urinary tract as above)

iii. When to use intravenous (IV) versus oral (PO) therapy
   a. PO therapy is preferred and considered to be equally as effective as IV therapy
   b. IV should be used only in patients unable to tolerate PO

iv. Uncomplicated acute cystitis
   a. Definition: lower UTI (involving the bladder and urethra) resulting in dysuria, frequency, and/or urgency without fever, flank pain/CVA tenderness, or other signs/symptoms of pyelonephritis
   b. Antimicrobial choices:
      1. Fluoroquinolones (FQ) should be avoided in children unless resistance patters on susceptibility testing indicate that they are the only option for antibiotic therapy (example, Pseudomonas spp.)
         a. Note: inpatient FQ use requires AMT/ID approval
      2. Cefdinir should NOT be used due to poor urinary tract penetration
      3. Nitrofurantoin should be avoided in patients < 1 month of age due to risk of hemolytic anemia and sulfamethoxazole/trimethoprim (SMX/TMP) should be avoided in patients < 2 months of age due to risk of hyperbilirubinemia/kernicterus
         a. Use of these agents may be considered after discussion with infectious diseases if benefits outweigh risks
      4. Ceftriaxone can be safely used in children < 1 month of age (including those who have not corrected to full term) excluding the following:
         a. Patients with hyperbilirubinemia expected to received > 2 doses
         b. Patients who have received or will receive IV calcium-containing solutions within 48 hours
      5. Definitive therapy should be based on documented susceptibilities

Clinical Scenario	Antimicrobial	Dosing (patients > 1 month old with normal renal function; consult pharmacist for dosing adjustments)	Duration
Preferred empiric therapy	Cephalexin	25 mg/kg/dose (max 500 mg) Q8H	5 days
	Cefazolin	25 mg/kg/dose (max 2000 mg) Q8H	Transition to PO when possible, otherwise 3 days
Alternative empiric therapy	Nitrofurantoin	Macrodantin (capsules and suspension): 5-7 mg/kg/DAY (max 100 mg) Q6H Macrobid (capsules): 100 mg/dose Q12H (patients ≥ 40 kg only)	5 days
	Cefpodoxime	5 mg/kg/dose (max 100 mg) Q12H	5 days
	Ceftriaxone	50 mg/kg/dose (max 1000 mg) Q24H	Transition to PO when possible, otherwise 3 days
Preferred definitive therapy (once susceptibilities are known)	Amoxicillin	15 mg/kg/dose (max 500 mg) Q8H or 25 mg/kg/dose (max 875 mg) Q12H	5 days
	Amoxicillin/clavulanate (non-ES formulation)	25 mg/kg/dose (max 875 mg, amoxicillin component) Q12H	5 days
	Cephalexin	As above	5 days
	Cefpodoxime	As above	5 days
Alternative definitive therapy (once susceptibilities are known)	Nitrofurantoin	As above	5 days
	SMX/TMP	4 mg/kg/dose (max 160 mg, trimethoprim component) Q12H	3 days
	Gentamicin	5 mg/kg	Single dose
	Ciprofloxacin (PO only) – Pseudomonas and other organisms resistant to options above ONLY	15-20 mg/kg/dose (max 750 mg) Q12H	3 days
	Fosfomycin – patients ≥ 40 kg ONLY	3000 mg	Single dose

v. Complicated UTIs

a. Definition:
   1. Acute pyelonephritis: infection of the kidneys/ureters resulting in flank pain/CVA tenderness, fever, nausea/vomiting, as well as other symptoms described above
   2. Acute cystitis associated with: obstruction, reflux, azotemia, or in patients with certain underlying conditions (abnormalities of the urinary tract, neurogenic bladder, recent GU surgery in the last 3 months, etc.)
   3. CAUTI: UTI signs/symptoms in a patient with a catheter in place or who was catheterized in the previous 48 hours
   4. Patients < 2 months of age

b. Antimicrobial choices:
   1. Nitrofurantoin, fosfomycin and cefdinir are NOT recommended due to low blood and kidney concentrations
   2. Sulfamethoxazole/trimethoprim (SMX/TMP) should be avoided in patients < 2 months of age due to risk of hyperbilirubinemia/kernicterus
      a. Use may be considered after discussion with infectious diseases if benefits outweigh risks
   3. Ceftriaxone can be safely used in children < 1 month of age (including those who have not corrected to full term) excluding the following:
      a. Patients with hyperbilirubinemia expected to received > 2 doses

b. Patients who have received or will receive IV calcium-containing solutions within 48 hours

4. Definitive therapy should be based on documented susceptibilities

Clinical Scenario	Antimicrobial	Dosing (patients > 1 month old with normal renal function; consult pharmacist for dosing adjustments)	Duration
Preferred empiric therapy	Cephalexin (if able to take PO and discharging from ED)	25 mg/kg/dose (max 500-1000 mg) Q6H	7-14 days for all complicated UTIs, regardless of agent **7 days preferred for most patients** Extending therapy should be considered for: patients < 2 months of age and patients who take > 72 hours to clinically improve
	Cefazolin	25 mg/kg/dose (max 2000 mg) Q8H	
	Ceftriaxone	50 mg/kg/dose (max 2000 mg) Q24H	
Preferred empiric therapy if hemodynamic instability or history of *Pseudomonas spp*. in last 6 months	Cefepime	50 mg/kg/dose (max 2000 mg) Q8-12H	
Preferred empiric therapy if hemodynamic instability and history of ESBL organism in last 6 months	Ertapenem (or meropenem if < 3 months of age or also history of Pseudomonas in last 6 months)	< 13 years old: 15 mg/kg/dose (max 500 mg) Q12H ≥ 13 years old: 1000 mg/dose Q24H *For meropenem dosing, refer to APH Dosing Card	
Preferred definitive therapy (once susceptibilities are known)	Amoxicillin	20 mg/kg/dose (max 1000 mg) Q6-8H	
	Ampicillin	50 mg/kg/dose (max 2000 mg/dose) Q6H	
	Amoxicillin/clavulanate (non-ES formulation)	25 mg/kg/dose (max 875 mg, amoxicillin component) Q12H	
	Ampicillin/sulbactam	50 mg/kg/dose (max 2000 mg/dose, ampicillin component) Q6H	
	Cephalexin	As above	
	Cefazolin	As above	
	Cefpodoxime	5 mg/kg/dose (max 200 mg) Q12H	
	Ceftriaxone	As above	
Alternative definitive therapy (once susceptibilities are known)	Ertapenem (ESBL producing organisms only; meropenem if < 3 months of age)	As above	
	Gentamicin	5-7 mg/kg/dose Q24H	
	SMX/TMP	4 mg/kg/dose (max 160 mg, trimethoprim component) Q12H	
	Ciprofloxacin (PO only) – Pseudomonas and other organisms resistant to options above ONLY	15-20 mg/kg/dose (max 750 mg) Q12H	

E. **Considerations for discharge**

i. Overall clinical improvement

ii. Adequate PO intake, including tolerating PO antibiotics

iii. Appropriate follow-up

iv. Note: a specific amount if IV therapy is not recommended prior to discharge, even for younger patients, patients with complicated infections, or patients with bacteremia

F. **Additional management considerations**

i. Antibiotic prophylaxis
   a. Has not been shown to reduce risk of renal scarring but may decrease risk of UTI recurrence. This should be weighed with known increased risk of antimicrobial resistance.
   b. When used, antibiotic prophylaxis should be limited to patients with high risk of UTI recurrence and be used for the shortest appropriate period of time. Use in non-toilet trained patients should be re-evaluated once the patient is toilet trained.
   c. Should be considered in patients with proven bowel/bladder dysfunction or VUR especially patients <1 year of age
   d. Should involve consultation with Nephrology OR Urology and should NOT be prescribed without discussion with one of these services

ii. Renal ultrasound
   a. Should be obtained on all first time pyelonephritis or febrile UTI in patients < 2 years of age
   b. Does not have to be repeated for recurrent pyelonephritis unless there is a strong clinical suspicion for renal abscess, or a need to assess for scarring. Fever lasting longer than 72 hours should constitute a need for re-imaging to look for abscess or scarring.

iii. VCUG (voiding cystourethrography)
   a. Should be obtained based on the following:
      1. Any of the following on ultrasound: hydronephrosis, scarring, dilation of collecting system, or any other finding suggestive of high-grade vesicoureteral reflux (VUR) or obstructive uropathy
      2. Difficulty in urine flow during hospitalization
      3. Family history of VUR

iv. Infectious diseases consultation should be considered if:
   a. UTI associated with bacteremia
   b. Presence of renal abscess
   c. Resistant organisms, especially with limited oral treatment options (organisms with resistance to carbapenems required ID consult per hospital policy)
   d. Prolonged fever (expected for up to 7 days on appropriate antimicrobial therapy for patients with pyelonephritis)
   e. Pre-treated UTI (urine culture obtained after initiation of antibiotics) with negative urine culture, especially if not responsive to antimicrobial therapy

v. Nephrology/urology consultation:
   a. Nephrology consultation should be considered in a patient with recurrent pyelonephritis (>3 in 1 year)
   b. Urology consultation should be obtained in a patient with abnormal Ultrasound AND VCUG results concerning for high grade (grade III or greater) OR concern for urinary obstruction on VCUG
      1. Also for known history of urologic abnormalities or recent instrumentation
      2. Recurrent UTI evaluation (voiding dysfunction)

PEDIATRIC – BIOFIRE® Blood Culture Identification 2 Panel (BCID2) Empiric Therapy Guidance

Background

- The BIOFIRE® BCID2 panel tests for a list of 30 pathogens and 10 antibiotic resistance genes.
- The average sensitivity and specificity across all pathogens on the BCID2 panel is 99% and 99.8%, respectively; however, results should never supersede clinical judgement.
- Full antibiotic susceptibility results will still be performed by the microbiology lab and will appear 24-48 hours after the BCID2 results.
- Limitations of BIOFIRE® BCID2:
    - Reduced sensitivity in the setting of multiple organisms growing in the same specimen (i.e., polymicrobial infections).
    - A negative BIOFIRE® BCID2 result does NOT rule out a potential infection. If the culture is positive but no targets are detected, this means that the pathogen is likely not one of the 30 pathogens detected by BCID.

Table 1. List of Pathogens and Resistance Genes Detected

Gram-positive	Gram-negative	Yeast	Resistance Genes
Enterococcus faecalis *Enterococcus faecium* *Listeria monocytogenes* Staphylococcus genus *Staphylococcus aureus* *Staphylococcus epidermidis* *Staphylococcus lugdunensis* Streptococcus genus *Streptococcus agalactiae* *Streptococcus pneumoniae* *Streptococcus pyogenes*	*Acinetobacter baumannii* complex *Bacteroides fragilis* Enterobacterales Order *Enterobacter cloacae* complex *Escherichia coli* *Klebsiella aerogenes* *Klebsiella oxytoca* *Klebsiella pneumoniae* group *Proteus* spp. *Salmonella* spp. *Serratia marcescens* *Haemophilus influenzae* *Neisseria meningitidis* *Pseudomonas aeruginosa* *Stenotrophomonas maltophilia*	*Candida albicans* *Candida auris* *Candida glabrata* *Candida krusei* *Candida parapsilosis* *Candida tropicalis* *Cryptococcus neoformans/gattii*	Methicillin Resistance • mecA/C • mecA/C and MREJ Vancomycin Resistance • vanA/B ESBL • CTX-M Carbapenemases • IMP • KPC • OXA-48-like • NDM • VIM Colistin Resistance • mcr-1

Table 2: Gram-positive Blood Culture Empiric Therapy Guide: speciation and resistance genes detected

Gram Stain Result	BCID2 Group Target	BCID2 Organism Target	BCID2 Gene Target	1st line empiric therapy	2nd line empiric therapy	Comments
Gram-positive cocci in clusters **OR** Gram-positive cocci in pairs and chains	*Staphylococcus*	*Staphylococcus aureus*	No resistance marker	Nafcillin	Cefazolin	**ID consult required**
			mecA/C and MREJ	Vancomycin	Daptomycin	
		Staphylococcus epidermidis	No resistance marker	Nafcillin	Cefazolin	Often skin contaminant, treat if suspicion for infection; **ID Consult required for two positive blood cultures**
			mecA/C	Vancomycin	Daptomycin	
		Staphylococcus lugdunensis	No resistance marker	Nafcillin	Cefazolin	**ID consult required**
			mecA/C	Vancomycin	Daptomycin	
		none*	N/A	Vancomycin	Daptomycin	Often skin contaminant, treat if suspicion for infection; **ID Consult required for two positive blood cultures**
	Streptococcus	*Streptococcus agalactiae*	N/A	Penicillin G or ampicillin	Cefazolin	
		Streptococcus pneumoniae	N/A	Ceftriaxone	Vancomycin	If meningitis: ceftriaxone + vancomycin 2nd line: severe cephalosporin allergies only
		Streptococcus pyogenes	N/A	Penicillin G or ampicillin	Cefazolin	
		none±	N/A	Ceftriaxone	Vancomycin	*Streptococcus* spp. without BCID2 identification, see ±**footnote**
	none	*Enterococcus faecalis*	No resistance marker	Ampicillin	Vancomycin	
			vanA/B	Daptomycin	Linezolid	
		Enterococcus faecium	No resistance marker	Vancomycin	Daptomycin	
			vanA/B	Daptomycin	Linezolid	
	none	none∞	N/A	Vancomycin	Daptomycin	See ∞**footnote** for possible organisms
Gram-positive rods	none	*Listeria monocytogenes*	N/A	Ampicillin	Trimethoprim-sulfamethoxazole	If meningitis: add gentamicin 2nd line: severe penicillin allergies only
	none	none¥	N/A	Vancomycin	Daptomycin	See ¥**footnote** for possible organisms

***Other *Staphyloccocus* spp. detected:** *S. argenteus, S. auricularis, S. capitis, S. caprae, S. carnosus, S. cohnii, S. equorum, S. haemolyticus S. hominis, S. intermedius, S. lentus S. nepalensis, S. pasteuri, S. pettenkoferi, S. pseudointermedius, S. saprophyticus, S. schleiferi, S. schweitzeri, S. sciuri, S. simulans, S. warneri, S. xylosus*

±Other *Streptococcus* spp. detected: *S. anginosus, S. australis, S. bovis, S. canis, S. constellatus, S. cristatus, S. dysgalactiae, S. equi, S. equinis, S. gallolyticus, S. goronii, S. intermedius, S. pseudopneumoniae, S. salivarius, S. sanguinis, S. sobrinus, S. suis, S. vestibularis*

∞Examples of Gram-positive cocci NOT detected (not all inclusive): *Aerococcus* spp., *Enterococcus* spp. *(other than E. faecalis and E. faecium), Gemella* spp., *Lactococcus* spp., *Micrococcus* spp., *Peptostreptococcus* spp., *Rhodococcus* spp., *Rothia* spp.

¥Examples of Gram-positive rods NOT detected (not all inclusive): *Actinomyces* spp., *Arcanobacterium* spp., *Bacillus* spp., *Clostridium* spp., *Corynebacterium* spp., *Cutibacterium acnes, Granulicatella adiacens, Kocuria* spp., *Nocardia* spp., *Lactobacillus spp.* (if suspected, add ampicillin to above recommended agent)

Table 3: Gram-negative Blood Culture Empiric Therapy Guide: speciation and resistance genes detected

Gram Stain Result	BCID2 Group Target	BCID2 Organism Target	BCID2 Gene Target	Recommended Empiric Therapy	Comments
Gram - negative rod	none	*Acinetobacter baumannii* complex	No resistance marker	Ampicillin-sulbactam (high-dose)	
			KPC	Cefiderocol	**ID consult required**
			OXA		
			NDM/VIM/IMP		
	none	*Bacteroides fragilis*	N/A	Metronidazole	
	Enterobacterales	*Enterobacter cloacae* complex	No resistance marker	Cefepime	Avoid 3rd generation cephalosporins (e.g., ceftriaxone) as inducible resistance may lead to treatment failure
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	
			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		Escherichia coli	No resistance marker	Ceftriaxone	
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	
			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		Klebsiella aerogenes	No resistance marker	Cefepime	Avoid 3rd generation cephalosporins (e.g., ceftriaxone) as inducible resistance may lead to treatment failure
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	
			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		Klebsiella oxytoca	No resistance marker	Ceftriaxone	
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	
			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		Klebsiella pneumoniae	No resistance marker	Ceftriaxone	
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	

			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		Proteus spp.	No resistance marker	Ceftriaxone	
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	
			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		Salmonella spp.	N/A	Ampicillin or Ceftriaxone	
		Serratia marcescens	No resistance marker	Cefepime	
			CTX-M	Ertapenem < 3 months old or critically ill: meropenem	
			KPC	Ceftazidime-avibactam	**ID consult required**
			OXA	Ceftazidime-avibactam	
			NDM/VIM/IMP	Cefiderocol	
		none*	N/A	Cefepime	
	none	*Pseudomonas aeruginosa*	No resistance marker	Cefepime	
			KPC	Cefiderocol	**ID consult required**
			OXA		
			NDM/VIM/IMP		
	none	*Stenotrophomonas maltophilia*	N/A	Trimethoprim-sulfamethoxazole	
	none	none	N/A	Cefepime	See **∞footnote** for possible organisms
Gram-negative cocci	none	*Haemophilus influenzae*	N/A	Ceftriaxone	
	none	*Neisseria meningitidis*	N/A	Ceftriaxone	
	none	none	N/A	Ceftriaxone	See **¥footnote** for possible organisms

***Other Enterobacterales spp. detected:** *Cedeceae* spp., *Citrobacter* spp., *Cosenzaea* spp., *Erwinia* spp., *Hafnia* spp., *Kluyvera* spp., *Kosakonia* spp., *Leclercia* spp., *Lelliottia* spp., *Mixta* spp., *Morganella* spp., *Pantoea* spp., *Providencia* spp., *Pseudoescherchia* spp. *Rahnella* spp.* *Raoultella* spp., *Sodalis* spp., *Shigella* spp., *Tatumella* spp., *Trabulsiella* spp., *Yersinia* spp., *Yokanella* spp., and other *Enterobacter*, *Klebsiella*, and *Serratia* spp.

∞Examples of Gram-negative rods NOT detected (not all inclusive): *Achromobacter* spp., *Capnocytophaga* spp., *Fusobacterium* spp., other *Bacteroides* spp., *Burkholderia* spp., *Vibrio* spp., *Aeromonas* spp., *Campylobacter* spp.

¥Examples of Gram-negative cocci NOT detected (not all inclusive): *Pasteurella* spp., *Moraxella* spp., other *Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium* spp., *Eikenella* spp., *Kingella* spp., *Prevotella* spp.

Table 4: Yeast Blood Culture Empiric Therapy Guide

Gram Stain Result	BCID2 Organism Target	BCID2 Gene Target	Recommended Empiric Therapy	Comments
Yeast	*Candida albicans*	none	Micafungin NICU patients: Amphotericin deoxycholate	Fluconazole preferred in non-NICU patients if clinically stable
	Candida auris	none	Micafungin NICU patients: Amphotericin deoxycholate	
	Candida glabrata	none	Micafungin NICU patients: Amphotericin deoxycholate	
	Candida krusei	none	Micafungin NICU patients: Amphotericin deoxycholate	
	Candida parapsilosis	none	Micafungin NICU patients: Amphotericin deoxycholate	Fluconazole preferred in non-NICU patients if clinically stable
	Candida tropicalis	none	Micafungin NICU patients: Amphotericin deoxycholate	
	Cryptococcus (C. neoformans/C. gattii)	none	Liposomal Amphotericin B	ID consult recommended to determine need for flucytosine

Arnold Palmer Hospital for Children: Management of Acute Otitis Media and Mastoiditis

1. Definitions

A. Acute Mastoiditis: suppurative infection of mastoid air cells with symptoms of less than one month's duration
B. Acute Otitis Media (AOM): the rapid onset of signs and symptoms of inflammation in the middle ear
C. Chronic Otitis Media: purulent otorrhea associated with a chronic tympanic membrane (TM) perforation that persists for more than 6 weeks despite appropriate treatment for AOM
D. Complicated Mastoiditis: infection of mastoid air cells with epidural abscess, subperiosteal abscess, brain abscess, septic thrombus, or other intracranial or extracranial complication
E. Non-severe AOM: AOM with the presence of mild otalgia and a temperature below 39°C
F. Otitis externa: an infection of the external auditory canal
G. Otitis media with effusion (OME): inflammation of the middle ear with liquid collection, but signs and symptoms of acute infection are absent
H. Otorrhea: discharge from the ear, originating at 1 or more of the following sites; the external auditory canal, middle ear, mastoid, inner ear, or intracranial cavity
I. Recurrent AOM: 3 or more well-documented and separate AOM episodes in the preceding 6 months or 4 or more episodes in the preceding 12 months with at least 1 episode in the past 6 months
J. Severe AOM: AOM with the presence of moderate to severe otalgia, otalgia for ≥ 48 hours, otorrhea due to perforated tympanic membrane, or fever equal to or higher than 39°C in past 48 hours
K. Tympanometry: measuring acoustic immittance (transfer of acoustic energy) of the ear as a function of ear canal air pressure
L. Uncomplicated AOM: AOM without otorrhea

2. Inclusions/Exclusions

A. Inclusion: All patients at least 6 months of age with suspected or confirmed acute otitis media
B. Exclusion:
   a. Anatomic abnormalities, including:
      i. Cleft palate
      ii. Genetic conditions with craniofacial abnormalities (i.e. Down syndrome)
   b. Immunodeficiencies
   c. Cochlear implants
   d. OME without AOM

3. Uncomplicated Acute Otitis Media (AOM) Management

A. Microbiology
   a. Bacterial pathogens that most commonly trigger inflammatory changes of AOM include *Streptococcus pneumoniae, Haemophilus influenza,* and *Moraxella catarrhalis.*
   b. Viral infection is also frequently associated with AOM, and can include respiratory syncytial virus (RSV), influenza viruses, and human metapneumovirus.
B. Clinical Management
   a. Initial Evaluation
      i. AOM is diagnosed through a combination of otoscopic findings and patient signs and symptoms.
      ii. Otoscopic findings may include moderate to severe bulging tympanic membrane, erythema, decreased mobility of tympanic membrane, perforated tympanic membrane, and/or presence of middle ear effusion.
      iii. Poor or absent mobility of tympanic membrane and presence of fluid in the middle ear in absence of acute inflammation or bulging tympanic membranes favors diagnosis of OME and does **not** warrant antimicrobial treatment.

iv. Tympanocentesis is typically not necessary, but can be considered if child appears toxic, is immunocompromised, or has failed previous courses of antibiotic therapy.

b. Symptoms
   i. Acute (< 48 hours) onset of otalgia, new onset otorrhea not caused by otitis externa, nearing loss, fever
   ii. Pre-verbal children: tugging/rubbing/holding of the ear, excessive crying, changes in sleep or behavior pattern

C. Treatment
   a. Analgesics are recommended for symptoms of ear pain, fever, and irritability.
   b. Antimicrobial treatment:

Table 1: Recommendations for Initial Management for AOM

Age	Otorrhea With AOM [a]	Unilateral or Bilateral AOM [a] With Severe Symptoms [b]	Bilateral AOM [a] Without Otorrhea	Unilateral AOM [a] Without Otorrhea
6 months to 2 years	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy or additional observation [c]
≥ 2 years	Antibiotic therapy	Antibiotic therapy	Antibiotic therapy or additional observation [c]	Antibiotic therapy or additional observation [c]

[a] *Applies only to children with well-documented AOM with high certainty of diagnosis*

[b] *A toxic-appearing child, moderate to severe otalgia, persistent otalgia ≥ 48 h, temperature ≥ 39°C in the past 48 h, or if there is uncertain access to follow-up after the visit.*

[c] *This plan of initial management provides an opportunity for shared decision-making with the child's family for those categories appropriate for additional observation. If observation is offered, a mechanism must be in place to ensure follow-up and begin antibiotics if the child worsens or fails to improve within 48 to 72 h of AOM onset.*

Table 2: Initial Immediate or Delayed Antibiotic Treatment	
Recommended First-line Treatment	**Alternative Treatment (Type 1 Penicillin Allergy) [b] and no exposure to amoxicillin in past 30 days**
Amoxicillin (90 mg/kg/**day** in 2 divided doses; max single dose of 2 g or 4 g daily) **If received amoxicillin in previous 30 days or with otitis-conjunctivitis syndrome:** Amoxicillin-clavulanate (90 mg/kg/**day** of amoxicillin in two divided doses [oral suspension, ES, amoxicillin 600 mg and clavulanate 42.2 mg per 5 mL], max single dose of amoxicillin 2 g)	Ceftriaxone (50 mg/kg IM or IV for **1 dose,** max 1000 mg/**dose**)[c]
	Cefdinir (14 mg/kg/**day** in 1 or 2 doses, max 600 mg/**day**)
	Cefpodoxime^ (10 mg/kg/**day** in 2 divided doses, max 200 mg/**dose**)
Antibiotic Treatment After 48–72 h of Failure of Initial Antibiotic Treatment	
Recommended First-line Treatment	**Alternative Treatment**
If initial antibiotic was amoxicillin: Amoxicillin-clavulanate (90 mg/kg/**day** of amoxicillin in two divided doses [oral suspension, ES, amoxicillin 600 mg and clavulanate 42.2 mg per 5 mL], max single dose of amoxicillin 2g); consider first-line if received amoxicillin in previous 30 days or with otitis-conjunctivitis syndrome **If initial antibiotic was amoxicillin/clavulanate or Type 1 Penicillin Allergy:** Ceftriaxone (50 mg/kg/**dose** IM or IV daily for **3 doses**, max 1000 mg/**dose**) Alternatives: see levofloxacin, linezolid, and doxycycline options in next column	Levofloxacin: < 5 years old: 10 mg/kg/**dose** (max 750 mg/dose) PO q 12h ≥ 5 years old: 10 mg/kg/**dose** (max 750 mg/dose) PO q 24h Linezolid: < 12 years old: 10 mg/kg/**dose** (max 600 mg/dose) PO q 8h ≥ 12 years old: 10 mg/kg/**dose** (max 600 mg/dose) PO q 12h Doxycycline (may be used regardless of patient age): 2 mg/kg/**dose** (max 100 mg/dose) PO q 12h
	Tympanocentesis [a]
	Consult specialist [a]

[a] *Perform tympanocentesis/drainage if skilled in the procedure or seek a consultation from an otolaryngologist for tympanocentesis/drainage. If the tympanocentesis reveals multidrug-resistant bacteria, ID consult is recommended.*

[b] *Cefdinir, cefpodoxime, and ceftriaxone have no cross-reactivity with penicillin.*

[c] *Single dose ceftriaxone should NOT be used in patients with tympanic membranes that are heavily scarred, perforated, or obscured by purulent drainage*

^See rationale below for cefpodoxime crushing considerations

c. Rationale for antibiotic recommendations
    i. High-dose amoxicillin therapy (90 mg/kg/**day**) is recommended in all patients for empiric treatment of intermediate penicillin-resistant *S. pneumoniae.* Azithromycin is inferior to high-dose amoxicillin in this setting.
    ii. If the patient has been exposed to amoxicillin in the past 30 days or had failure of initial antibiotic treatment, coverage should be expanded to amoxicillin-clavulanate or ceftriaxone to include empiric treatment of beta-lactamase positive *H. influenzae* or *M. catarrhalis*.
    iii. In patients without exposure to amoxicillin in previous 30 days, a single dose of ceftriaxone is sufficient for treatment of AOM. For patients who have failed previous therapy, three doses of ceftriaxone are needed for treatment of presumed penicillin-resistant *S. pneumoniae*.
    iv. The recommended daily dose of clavulanate is 6.4 mg/kg/**day**, but doses between 3.4 – 10 mg/kg/day are also acceptable. Doses below this range may lead to antibiotic failure, and doses above this range may lead to excessive gastrointestinal side effects such as diarrhea, nausea, and vomiting.
    v. Despite low oral bioavailability (~20%), cefdinir achieves excellent concentrations in the middle ear.
    vi. Oral cephalosporins, including cefdinir and cefpodoxime should **not** be utilized after treatment failure with a previous antibiotic, as *S. pneumoniae* resistance to oral amoxicillin should be extrapolated to oral cephalosporins.
    vii. ^Cefpodoxime tablets may be crushed but may have a bitter taste. If insurance does not cover cefpodoxime oral suspension, consider prescribing tablets and advising patients to crush and take with a spoonful of food, such as applesauce.
d. Additional management considerations
    i. Immunization with PCV20 or PCV15 is recommended in all patients who meet age criteria, as defined by the CDC Vaccination Schedule.
    ii. Patients with recurrent AOM should be referred to ENT for possible surgical management.
    iii. Antibiotic prophylaxis is **not** recommended to reduce frequency of AOM in children with recurrent AOM.

D. Duration of Therapy
a. 10 days:
    i. All children < 2 years
    ii. Severe symptoms (otalgia for at least 48 hours, fever > 102.2°F, or otorrhea)
    iii. Tympanic membrane perforation
b. 5 days:
    i. Children ≥2 years with mild or moderate symptoms (otalgia < 48 hours or fever < 102.2°F)

E. Other Complications of Acute Otitis Media
a. Hearing Loss
    i. Persistent or fluctuating hearing loss occurs in the setting of middle ear fluid.
    ii. Despite treatment with antimicrobials, middle ear fluid with associated hearing loss may persist for weeks to months.
b. Perforated Tympanic Membrane
    i. Perforation allows drainage of middle ear fluid and relieves pressure.
    ii. The tympanic membrane usually heals on its own in a matter of hours to days.
    iii. Topical antibiotic ear drops may be considered in addition to systemic antibiotics (see recommended choices below).
    iv. Avoid topical analgesic agents (i.e. ear drops) in the setting of a perforated tympanic membrane.
    v. Pain in this setting is unlikely due to the relief of pressure; consider differential diagnosis of mastoiditis, or otitis externa (in which case a topical agent may be beneficial).
    vi. Advise against the use of topical home remedies in this setting.
    vii. If the perforation persists for three months or longer, patients should be referred to ENT for further management.
c. Acute Otitis Externa
    i. Inflammation of ear canal resulting in otalgia, itching, canal edema, canal erythema, and otorrhea
    ii. Commonly caused by swimming or minor trauma secondary to inappropriate cleaning
    iii. Microbiology: *P. aeruginosa* and *S. aureus* are most common pathogens
    iv. Topical antimicrobials (ear drops) are treatment of choice
        1. Tympanic membrane intact:
            a. Neomycin/polymyxin B/hydrocortisone

b. Hydrocortisone 2%/acetic acid 1%
c. Acetic acid 2%

2. Tympanic membrane not intact or unknown:
a. Ciprofloxacin 0.3%/dexamethasone 0.1%
b. Ofloxacin 0.3%

v. For patients on systemic antimicrobials, topical agents should be **continued**

d. Patients with AOM and tympanostomy tubes (AOMT)
i. Tympanostomy tubes may be utilized for recurrent AOM to decrease frequency of AOM episodes.
ii. For patients with acute otitis media/otorrhea in the setting of tympanostomy tubes, topical antibiotic monotherapy should be used for treatment.
iii. Recommended topical antibiotic therapy:
1. Ciprofloxacin 0.3%/dexamethasone 0.1%, 4 drops twice daily
2. Ofloxacin 0.3%, 5 drops once daily
3. Note: topical aminoglycoside agents should not be used due to risk of ototoxicity
iv. Duration of topical antibiotic therapy: 7 days
v. If otorrhea does not respond after 7 days of topical treatment, ENT consultation should be considered for culturing of the middle ear fluid and selection of a systemic antibiotic regimen.

e. Intracranial complications
i. Very rarely, untreated acute otitis media may lead to intracranial complications such as meningitis, brain abscess, epidural abscess, sinus or carotid artery thrombosis, or subdural empyema.

4. Mastoiditis Management

A. Microbiology
a. Bacterial species are similar to AOM and include *S. pneumoniae*, *S. pyogenes*, *H. influenzae*, and *Fusobacterium necrophorum*.
b. *S. aureus*, *P. aeruginosa* and anaerobes such as *Peptostreptococcus*, Gram-negative bacilli *(Prevotella, Porphyromonas,* and *Bacteroides*), and *Fusobacterium* should be considered for patients with a history of recurrent AOM, perforated tympanic membrane, or chronic symptoms of AOM.

B. Clinical Management
a. Initial Evaluation
i. Laboratory markers such as WBC, ESR, or CRP may be elevated but these are non-specific.
ii. Blood cultures
iii. CT with contrast
1. Indicated to rule out extracranial or intracranial complications.
2. Loss of definition of the bony septae that define the mastoid air cells is diagnostic of mastoiditis.
3. Absence of mastoid opacification excludes mastoiditis diagnosis. Mastoid air cell opacification alone in the absence of other radiographic abnormalities may be seen in AOM.
iv. MRI – if intracranial complication suspected
v. Consider ENT consult for aspiration/drainage of middle ear and possible surgical assessment.
1. If subperiosteal abscess or eroded outer cortex suspected on CT, consult ENT for possible mastoidectomy or myringotomy.
vi. ID Consult for antimicrobial management for all complicated mastoiditis patients or in acute mastoiditis patients if no improvement after 48 hours

C. Treatment
a. Empiric antimicrobial therapy (see table below) is indicated for all patients.
b. MRI and ENT consult for I&D, mastoidectomy, or myringotomy if no clinical improvement within 48 hours (continued fever, persistent erythema and swelling, new complications)
c. Proceed with pathogen-directed therapy if pathogen isolated on culture.
d. For mastoiditis without intracranial complications, if improved by 48 hours, switch to PO step down therapy

<table>
<tr><th colspan="2">Empiric Antimicrobial Therapy for Mastoiditis</th><th>Duration</th></tr>
<tr><td>Uncomplicated or complicated acute mastoiditis without intracranial features</td><td>1st Line:
Ampicillin-sulbactam 75 mg/kg/dose (ampicillin component) IV q 6h (max 2 g ampicillin per dose)

2nd Line (if penicillin allergy):
Ceftriaxone 75 mg/kg IV q 24h (max 2 g/dose)
PLUS
Metronidazole 10 mg/kg/dose IV q 8h (max 500 mg/dose)

If secondary to chronic AOM:
Cefepime 50 mg/kg/dose q 8h (max 2 g/dose)
PLUS
Metronidazole 10 mg/kg/dose IV q 8h (max 500 mg/dose)

PO Step Down:
1st Line:
Amoxicillin-clavulanate 90 mg/kg/day of amoxicillin in two divided doses (oral suspension, ES, amoxicillin 600 mg and clavulanate 42.9 mg per 5 mL, max single dose of amoxicillin 2g)

2nd Line (or preferred if secondary to chronic AOM):
Levofloxacin
< 5 y/o 10 mg/kg/dose Q12h, ≥ 5 y/o 10 mg/kg/dose Q24h, max single dose 750 mg</td><td>2 – 4 weeks depending on source control and severity:

Consider 2 weeks for acute uncomplicated mastoiditis, and 3-4 weeks for chronic or complicated mastoiditis

For culture positive patients, alternative antibiotic regimens may be considered; recommend discussion with Infectious Diseases</td></tr>
<tr><td>Intracranial complication (i.e. epidural or brain abscess)</td><td>Ceftriaxone 100 mg/kg/dose Q24H; for doses > 2g, split dose to 50 mg/kg/dose (max 2 g/dose) q 12h (max 4g/day)

PLUS

Metronidazole 10 mg/kg/dose q 8h (max 500 mg/dose)

PLUS

Vancomycin, pharmacy to dose

Neurosurgery and ID consult recommended</td><td rowspan="2">4 - 6 weeks

IV to PO and cessation of anaerobic coverage to be determined by Infectious Diseases</td></tr>
<tr><td>Intracranial complication (i.e. epidural or brain abscess), secondary to chronic otitis media</td><td>Cefepime 50 mg/kg/dose q 8h (max 2 g/dose) (cefepime preferred if secondary to chronic otitis media)

PLUS

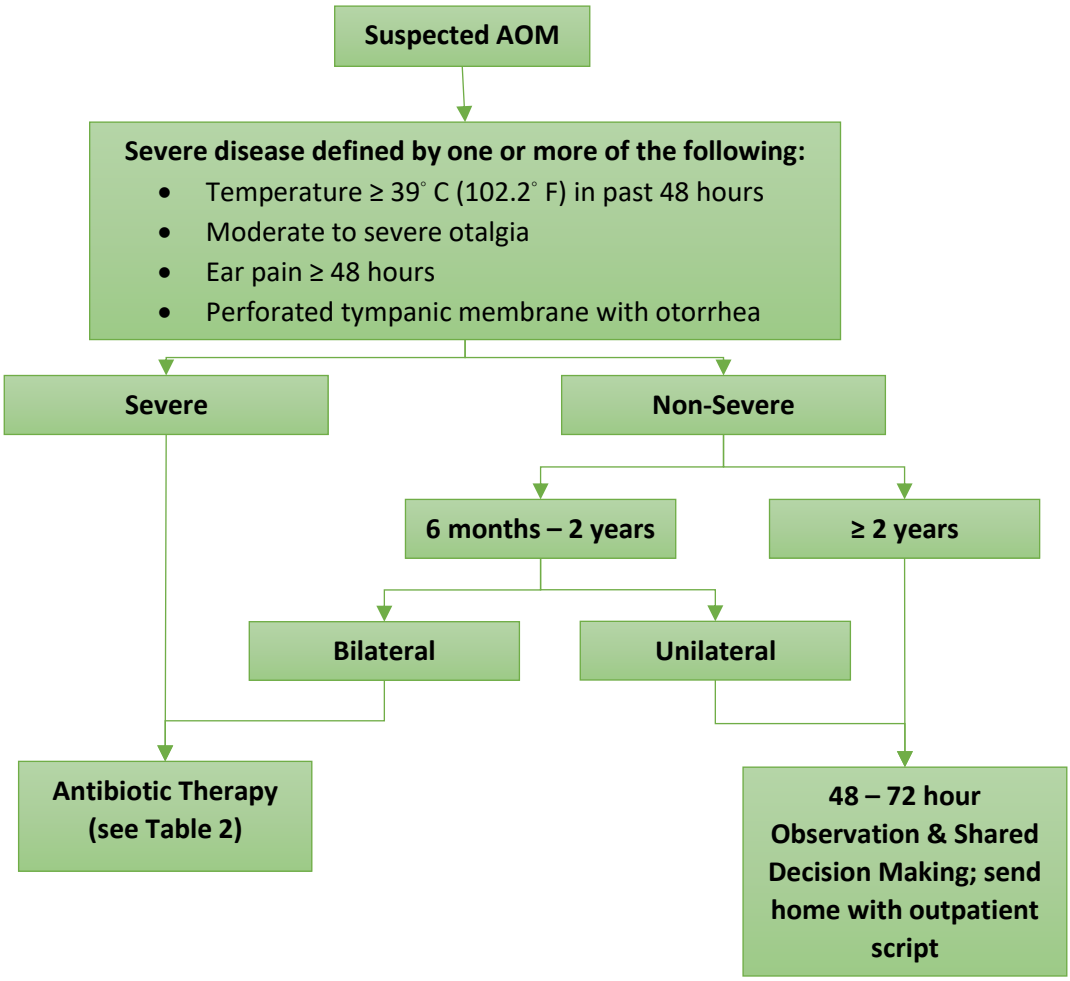
Metronidazole 10 mg/kg/dose q 8h (max 500 mg/dose)

PLUS

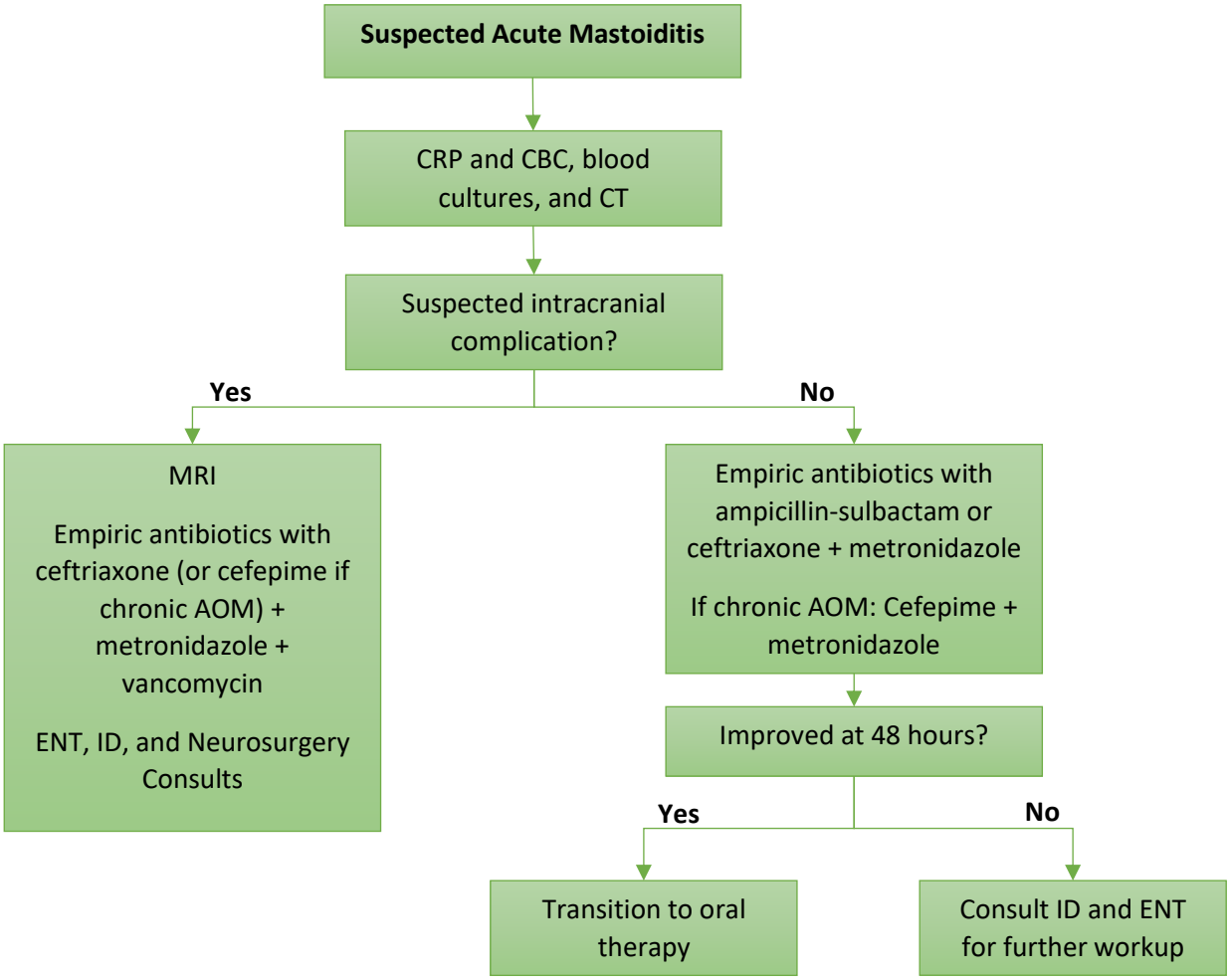
Vancomycin, pharmacy to dose

Neurosurgery and ID consult recommended</td></tr>
</table>

Algorithm for Management of Acute Otitis Media



Algorithm for Management of Acute Mastoiditis



Arnold Palmer Hospital for Children: Management of Febrile Infants ≤ 60 Days Old Clinical Pathway

1. Definitions
    a. Positive urinalysis
        i. Presence of any leukocyte esterase on dipstick
        ii. Pyuria (> 5- 10 WBC/mm^3), nitrites, or bacteriuria present
    b. Elevated inflammatory markers (IMs)
        i. Procalcitonin > 0.5 ng/mL
        ii. CRP > 2 mg/dL
        iii. ANC > 4000, > 5200 per mm3
    c. CSF Interpretation
        i. The CSF from a traumatic LP should be cultured and can be tested for HSV if indicated. In general, correction (or ratios) for red blood cells (RBCs) in CSF is discouraged because of lack of validating studies. It is reasonable to interpret CSF WBC counts at face value in CSF specimens with up to 10,000 RBCs per mm^3.

TABLE 2 CSF Values in Febrile Infants Without Evidence of UTI, IBI, HSV, Enterovirus, or Traumatic CSF

	Age, d	*n*	Mean	Median	Range
WBCs per mm^3	1–28	278	6.1	5.0	0–18
	29–60	318	3.1	3.0	0–8.5
Protein mg/dL	1–28	278	75.4	73.0	15.8–131.0
	29–60	318	58.9	54.0	5.5–105.5
Glucose	1–28	278	45.3	46.0	30.0–61.0
Glucose	29–60	318	48.0	48.0	20.6–65.5
RBCs per mm^3	1–28	278	95.5	5.5	0–236
RBCs per mm^3	29–60	318	75.5	2.0	0–64.5

Statistical outliers were removed. Other studies reveal slightly different ranges. Local laboratory tests may provide slightly different upper limits of normal. Adapted from Byington CL, Kendrick J, Sheng X. Normative cerebrospinal fluid profiles in febrile infants. *J Pediatr.* 2011;158(1):130–134.

    d. HSV risk factors
        i. Known HSV exposure
        ii. Maternal history of genital or mucocutaneous lesions
        iii. Maternal perinatal fevers (i.e. 48 hours prior to, or after, delivery)
        iv. Persistent hypothermia
        v. Mucus membrane ulcers
        vi. Skin vesicles
        vii. Seizure
        viii. Leukopenia and/or thrombocytopenia
        ix. Increased ALT or AST
        x. CSF pleocytosis in the absence of positive Gram stain results

2. Guideline Inclusion/Exclusion:

    a. Inclusion:
        i. Infants 0 – 60 days old
        ii. Documented rectal temperatures of ≥38.0^{o}C or ≥100.4^{o}F at home in the past 24 hours or determined in a clinical setting
        iii. Gestation between ≥ 37 and < 42 weeks
        iv. Patients presenting from home after discharge from a newborn nursery or born at home
    b. Exclusion:
        i. Focal bacterial infection (cellulitis, omphalitis, septic arthritis, osteomyelitis, etc.)
        ii. Clinical bronchiolitis
        iii. Documented or suspected immune compromise
        iv. Congenital/chromosomal abnormalities
        v. Requiring technology or therapeutic intervention to sustain life
        vi. Immunizations within the last 48 hours

Age 0 – 21 Day Old Algorithm
Age 22 – 28 Day Old Algorithm
Age 29 – 60 Day Old Algorithm

Age 0 – 21 Days Old:

Evaluation:

- Complete blood count with differential
- Complete metabolic panel
- Blood culture
- Lumbar puncture (LP)[o]
  - Culture
  - Cell counts
  - Glucose
  - Protein
  - Meningitis/encephalitis panel PCR
- Procalcitonin, C-reactive protein
- Catheterized urinalysis and urine culture
- Respiratory viral panel (if infectious respiratory symptoms present)
- If HSV suspected based on risk factors (as listed above), HSV PCR testing should include:
  - Blood
  - Skin lesions (if present)
  - Conjunctival/oropharyngeal/periumbilical/perirectal swab
- Stool PCR (if diarrhea present)

Empiric Antimicrobial Therapy (Use Newborn Antibacterial Rule Out Sepsis Order Set):

1 – 7 Days

- Ampicillin* 100 mg/kg IV every 8 hours x36 hours AND
- Gentamicin** 5 mg/kg IV x1 dose
  - Consider repeat dose of gentamicin 5 mg/kg IV x1 in 36 hours if positive urinalysis pending culture result or continued antibiotics clinically indicated
- If HSV suspected based on risk factors (as listed above)
  - Acyclovir 20 mg/kg IV every 8 hours

8 – 13 Days

- Ampicillin* 75 mg/kg IV every 6 hours x36 hours AND
- Gentamicin** 5 mg/kg IV x1 dose
  - Consider repeat dose of gentamicin 5 mg/kg IV x1 in 36 hours if positive urinalysis pending culture result or continued antibiotics otherwise clinically indicated
- If HSV suspected based on risk factors (as listed above)
  - Acyclovir 20 mg/kg IV every 8 hours

14 – 21 Days

- Ceftriaxone[¥] 50 mg/kg IV x1
  - If therapy continued, ceftriaxone 50 mg/kg IV every 12 hours (continued concern for meningitis) or ceftriaxone 50 mg/kg IV every 24 hours (if meningitis ruled out)
- If HSV suspected based on risk factors (as listed above)
  - Acyclovir 20 mg/kg IV every 8 hours

*May reduce dose to ampicillin 50 mg/kg IV every 8 hours in all neonatal patients with negative meningitis/encephalitis PCR and normal CSF
**Change gentamicin to ceftazidime 50 mg/kg every 8 hours if suspected/confirmed meningitis or Gram-negative bacteremia identified
[¥]Avoid ceftriaxone in neonatal patients receiving concomitant intravenous calcium (i.e. TPN)

Infection identified? **YES** → Treat as indicated and off pathway. Consider Infectious Diseases consult if there is confirmed meningitis, bacteremia, or UTI with Multi-Drug Resistant (MDR) organism (see UTI guideline if indicated)

If enterovirus detected in the CSF, DISCONTINUE antibiotics unless concern for concomitant bacterial infection due to abnormal inflammatory markers or abnormal urinalysis

- Although infants whose CSF is positive for enterovirus may be observed without antimicrobial agents, they should remain in a hospital setting for a minimum of 24 hours because of the small risk of progression to enteroviral sepsis

NO ↓

Is the patient improving? **NO** → Further evaluation and treatment required per primary team, consider Infectious Diseases consult

YES ↓

Discharge criteria:

- Infant is stable, well appearing and tolerating feeds
- Blood, urine, CSF results negative after 24-36 hours
  - Consider antibiotic discontinuation at 24 if cultures remain negative with negative urinalysis and patient shows clinical improvement
- No new symptoms of concern
- No persistent fever
- HSV studies negative if obtained
  - Discontinue acyclovir if HSV testing results as negative unless continued clinical concern for HSV (ID consult recommended if clinical concern for HSV despite negative testing, i.e. vesicles)
- Family understands discharge instructions and infant needs
- Follow-up provider identified, discharge plan and close follow-up arranged

Age 22 – 28 Days Old:

Evaluation:

- Complete blood count with differential
- Complete metabolic panel
- Blood culture
- Consider LP if elevated inflammatory marker(s), abnormal urinalysis, or if persistent fever[o]
  - Culture
  - Cell counts
  - Glucose
  - Protein
  - Meningitis/encephalitis panel PCR
- Procalcitonin, C-reactive protein
- Catheterized urinalysis and urine culture
- Respiratory viral panel (if infectious respiratory symptoms present)
- If HSV suspected based on risk factors (as listed above), HSV PCR testing should include:
  - Blood
  - Skin lesions (if present)
  - Conjunctival/oropharyngeal/periumbilical/perirectal swab
- Stool PCR (if diarrhea present)

Empiric Antimicrobial Therapy (Use Newborn Antibacterial Rule Out Sepsis Order Set):

22 – 28 Days

- Ceftriaxone[¥] 50 mg/kg IV x1
  - If therapy continued, ceftriaxone 50 mg/kg IV every 12 hours (continued concern for meningitis) or ceftriaxone 50 mg/kg IV every 24 hours (if meningitis ruled out)
- If HSV suspected based on risk factors (as listed above)
  - Acyclovir 20 mg/kg IV every 8 hours

[¥]Avoid ceftriaxone in neonatal patients receiving concomitant intravenous calcium (i.e. TPN)

Infection identified? **YES** → Treat as indicated and off pathway. Consider Infectious Diseases consult if there is confirmed meningitis, bacteremia, or UTI with Multi-Drug Resistant (MDR) organism (see UTI guideline if indicated)

If enterovirus detected in the CSF, DISCONTINUE antibiotics unless concern for concomitant bacterial infection due to abnormal inflammatory markers or abnormal urinalysis

- Although infants whose CSF is positive for enterovirus may be observed without antimicrobial agents, they should remain in a hospital setting for a minimum of 24 h because of the small risk of progression to enteroviral sepsis

NO ↓

Is the patient improving? **NO** → Further evaluation and treatment required per primary team, consider Infectious Diseases consult

YES ↓

Discharge criteria:

- Infant is stable, well appearing and tolerating feeds
- Blood, urine, CSF results negative after 24-36 hours
  - Consider antibiotic discontinuation at 24 if cultures remain negative with negative urinalysis and patient shows clinical improvement
- No new symptoms of concern
- No persistent fever
- HSV studies negative if obtained
  - Discontinue acyclovir if HSV testing results as negative unless continued clinical concern for HSV (ID consult recommended if clinical concern for HSV despite negative testing i.e. vesicles)
- Family understands discharge instructions and infant needs
- Follow-up provider identified, discharge plan and close follow-up arranged

Infant may be managed at home if parent and clinician agree that the following are present: reliable phone and transportation, parent willingness to observe and communicate changes in condition, and agreement to the infant being reevaluated in 24 hours

Age 29 – 60 Days Old:

Evaluation:

- Complete blood count with differential
- Complete metabolic panel
- Blood culture
- Consider LP if elevated inflammatory markers, abnormal urinalysis, or if persistent fever[o]
  - Culture
  - Cell counts
  - Glucose
  - Protein
  - Meningitis/encephalitis panel PCR
- Procalcitonin, C-reactive protein
- Catheterized urinalysis and urine culture
- Respiratory viral panel (if infectious respiratory symptoms present)
- If HSV suspected based on risk factors (as listed above), HSV PCR testing should include:
  - Blood
  - Skin lesions (if present)
  - Conjunctival/oropharyngeal/periumbilical/perirectal swab
- Stool PCR (if diarrhea present)

Empiric Antimicrobial Therapy (Use Newborn Antibacterial Rule Out Sepsis Order Set):

29 - 60 Days

- Clinicians need not use antimicrobial therapy while awaiting bacterial culture results if all of the following are met:
  - CSF analysis (if CSF obtained) is normal or enterovirus-positive
  - Urinalysis is negative
  - No IM obtained is abnormal
- If antimicrobial therapy indicated for patients 29 – 60 days:
  - Ceftriaxone[¥] 50 mg/kg IV x1
    - If therapy continued, ceftriaxone 50 mg/kg IV every 12 hours (continued concern for meningitis) or ceftriaxone 50 mg/kg IV every 24 hours (if meningitis ruled out)
- If HSV suspected based on risk factors (as listed above)
  - Acyclovir 20 mg/kg IV every 8 hours

Infection identified? **YES** → Treat as indicated and off pathway. Consider Infectious Diseases consult if there is confirmed meningitis, bacteremia, or UTI with Multi-Drug Resistant (MDR) organism (see UTI guideline if indicated)

If enterovirus detected in the CSF, DISCONTINUE antibiotics unless concern for concomitant bacterial infection due to abnormal inflammatory markers or abnormal urinalysis

- Although infants whose CSF is positive for enterovirus may be observed without antimicrobial agents, they should remain in a hospital setting for a minimum of 24 h because of the small risk of progression to enteroviral sepsis

NO → Is the patient improving?

NO → Further evaluation and treatment required per primary team, consider Infectious Diseases consult

YES

Discharge criteria:

- Infant is stable, well appearing and tolerating feeds
- Blood, urine, CSF results negative after 24-36 hours
  - Consider antibiotic discontinuation at 24 hours if cultures remain negative with negative urinalysis and patient shows clinical improvement
- No new symptoms of concern
- No persistent fever
- HSV studies negative if obtained
  - Discontinue acyclovir if HSV testing results as negative unless continued clinical concern for HSV (ID consult recommended if clinical concern for HSV despite negative testing i.e. vesicles)
- Family understands discharge instructions and infant needs
- Follow-up provider identified, discharge plan and close follow-up arranged

- Infant may be managed at home if parent and clinician agree that the following are present:
  - Reliable phone and transportation, parent willingness to observe and communicate changes in condition, and agreement to the infant being reevaluated in 24 hours
- Most 29- to 60-day-old infants with negative IM and urinalysis results may be observed at home; hospital observation is an option for infants when there are barriers to follow-up

Rationale for antibiotic recommendations:

1. For ceftriaxone as first line empiric therapy for patients ≥ 14 days old
    a. Use of ceftriaxone over aminoglycosides or ceftazidime preserves pseudomonal coverage and may decrease the risk for resistant infections
    b. The risk of kernicterus in neonatal patients receiving ceftriaxone due to the displacement of bilirubin is only theoretical and has not been seen in clinical practice
        i. Important to weight risks/benefits in patients with known hyperbilirubinemia and trend appropriately, as patients presenting with infection may have an elevated total bilirubin that is a normal part of the disease process
    c. Although cephalosporins do not provide adequate coverage for *Listeria monocytogenes*, improvements in food safety may have resulted in a decrease in the incidence of disease caused by *Listeria monocytogenes*
        i. More than 70% of infections caused by *Listeria monocytogenes* occur in first 7 days of life

2. For discontinuation of antimicrobial therapy after patient tests positive for enteroviral meningitis (even if this occurs prior to 24-36 hour antibiotic rule out)
    a. Patients with a positive enterovirus PCR result are at a very low risk of bacterial meningitis and might be safely treated as outpatients, assuming they appear to be well and are followed up adequately
    b. In multivariate analysis, having a positive cerebrospinal fluid enterovirus polymerase chain reaction result was associated with a 1.54-day decrease in the length of stay and a 33.7% shorter duration of antibiotic use

Pediatric Antimicrobial Dosing Recommendations

Dosing card only to be used for APH patients > 30 days old (NICU excluded)
For patients ≥ 40 kg, refer to the Orlando Health Adult Antimicrobial Dosing Guideline
*Restricted antimicrobial
¥For weight-based dosing, use total body weight unless otherwise noted in the comments
Note: Dosing recommendations for certain antimicrobials may be higher than recommended below and/or require continuous/extended infusions for patients with cystic fibrosis, resistant isolates, or augmented renal clearance

Antimicrobial	Usual Dose¥	Renal Dose Adjustment (CrCl in mL/min, unless otherwise noted)	Comments
Acyclovir IV	**< 3 months:** 20 mg/kg/dose Q8H **3 months to < 12 yo:** 5-15 mg/kg/dose Q8H **≥ 12 yo:** 5-10 mg/kg/dose Q8H	**25-50**: usual dose Q12H **10-24**: usual dose Q24H **< 10**: 50% of usual dose Q24H **HD**: 5 mg/kg/dose Q24H **PD**: 5 mg/kg/dose Q24H **CRRT**: 10 mg/kg/dose Q12H	Give after HD on HD days Dosing weight: patients < 1 year use total body weight; patients ≥ 1 year, if total body weight ≥ 120% of ideal body weight, use ideal body weight PHARMACY TDR Lower end of suggested dosing range recommended for non-CNS infections (esp. stomatitis/mucocutaneous infections); higher end of suggested dosing range recommended for more invasive infections
Acyclovir PO	20 mg/kg/dose Q6H	**25-50**: usual dose **10-24**: usual dose Q8H **< 10**: 10 mg/kg/dose Q12H **HD**: 10 mg/kg/dose x 1 followed by 5 mg/kg/dose Q12H plus 10 mg/kg/dose x 1 after each HD session **PD**: 20 mg/kg/dose Q24H **CRRT**: usual dose	**Max single dose:** 800 mg **Max daily dose:** 3200 mg
Amikacin IV	15-30 mg/kg/dose Q24H Pharmacy consult		**Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight
Amoxicillin or amoxicillin/clavulanate (dosing based on amoxicillin component) PO †If using amoxicillin/clavulanate, use ES formulation (or XR tablets – non formulary) as appropriate based on dose: DOSING GUIDANCE	**Pneumonia, bone/joint infections†:** 30 mg/kg/dose Q8H **AOM, sinusitis:** 45 mg/kg/dose Q12H **UTI, SSTI, other:** 22.5 mg/kg/dose Q12H or 15 mg/kg/dose Q8H	**Pneumonia, bone/joint infections, AOM, sinusitis†:** **30-49**: usual dose **10-29**: 20 mg/kg/dose Q12H **< 10**: 20 mg/kg/dose Q24H **HD**: 20 mg/kg/dose Q24H **PD**: 20 mg/kg/dose Q24H **CRRT**: usual dose **UTI, SSTI, other:** **30-49**: usual dose **10-29**: 10 mg/kg/dose Q12H **< 10**: 10 mg/kg/dose Q24H **HD**: 10 mg/kg/dose Q24H **PD**: 10 mg/kg/dose Q24H **CRRT**: usual dose	Give after HD on HD days **Max single dose:** 1300 mg – Q8H, 2000 mg – Q12H, 500 mg for CrCl < 30 **Max daily dose:** 4000 mg
Amphotericin deoxycholate (conventional)* IV	0.5-1 mg/kg/dose Q24H	**None**	Preferred formulation for neonates or urinary source of infection
Amphotericin B liposomal* IV	**Empiric:** 3 mg/kg/dose Q24H **Confirmed invasive fungal infection:** 5 mg/kg/dose Q24H	**None**	
Ampicillin IV/IM	**CNS infections, complicated pneumonia:** 75 mg/kg/dose Q6H **Other:** 50 mg/kg/dose Q6H	**CNS infections, complicated pneumonia:** **30-49**: usual dose **10-29**: 75 mg/kg/dose Q8H **< 10**: 75 mg/kg/dose Q12H **HD**: 75 mg/kg/dose Q12H	**Max single dose:** 3000 mg **Max daily dose:** 12000 mg

		PD: 75 mg/kg/dose Q12H **CRRT**: usual dose **Other:** **30-49**: usual dose **10-29**: 50 mg/kg/dose Q8H **< 10**: 50 mg/kg/dose Q12H **HD**: 50 mg/kg/dose Q12H **PD**: 50 mg/kg/dose Q12H **CRRT**: usual dose	
Ampicillin/ sulbactam IV (dosing based on ampicillin component)	Dosing based on indications match ampicillin as above ***Acinetobacter spp.* infections:** 100-150 mg/kg/dose (50-75 mg/kg/dose of sulbactam) Q8H; maximum 3000 mg of sulbactam/dose; extended infusion over 3 hours preferred	**30-49**: usual dose **15-29**: usual dose Q12H **5-14**: usual dose Q24H **HD**: usual dose Q24H **PD**: usual dose Q24H **CRRT**: usual dose Q8-12H	Give after HD on HD days **Max single dose:** 2000 mg **Max daily dose:** 8000 mg Note: dosing for *Acinetobacter spp.* infections will exceed typical maximum ampicillin dosing
Azithromycin IV/PO	5-10 mg/kg/dose Q24H Note: higher dosing may be needed for certain indications	**None**	**Max single dose:** 500 mg **Max daily dose:** 500 mg
Aztreonam* IV/IM	40 mg/kg/dose Q8H	**30-49**: usual dose **10-29**: 20 mg/kg/dose Q8H **< 10**: 10 mg/kg/dose Q12H **HD**: 10 mg/kg/dose Q12H **PD**: 10 mg/kg/dose Q12H **CRRT**: usual dose	**Max single dose:** 2000 mg, 1000 mg for CrCl < 50 **Max daily dose:** 8000 mg
Cefazolin IV	25-50 mg/kg/dose Q8H	**30-49**: 25 mg/kg/dose Q8H **10-29**: 25 mg/kg/dose Q12H **< 10**: 25 mg/kg/dose Q24H **HD**: 25 mg/kg/dose Q24H (maximum 1000 mg) or 50 mg/kg/dose three times weekly (maximum 2000 mg) **PD**: 25 mg/kg/dose Q24H (maximum 1000 mg) **CRRT**: 25 mg/kg/dose Q8H	Give after HD on HD days **Max single dose:** 2000 mg (3000 mg for surgical prophylaxis in patients $\geq$ 120 kg) **Max daily dose:** 8000 mg
Cefepime IV/IM	50 mg/kg/dose Q8-12H	**30-60**: 50 mg/kg/dose Q12-24H **10-29**: 50 mg/kg/dose Q24H **< 10**: 25-50 mg/kg/dose Q24H **HD**: 50 mg/kg/dose x 1 followed by 25 mg/kg/dose Q24H (maximum 1000 mg) or 50 mg/kg/dose three times weekly (maximum 2000 mg) **PD**: 50 mg/kg/dose Q24H (maximum 1000 mg) **CRRT**: 50 mg/kg/dose Q8-12H	Give after HD on HD days **Max single dose:** 2000 mg, 1000 mg for CrCl < 10 **Max daily dose:** 8000 mg
Cefiderocol* IV	**All doses infused over 3 hours (consider a 1-hour infusion for patients < 3 months)** **Infants:** < 2 months and < 32 weeks gestational age at birth: 30 mg/kg/dose Q8H < 2 months and $\geq$ 32 weeks gestational age at birth: 40 mg/kg/dose Q8H 2 to < 3 months and < 32 weeks gestational age at birth: 40 mg/kg/dose Q8H	**Infants**: adjust for renal dysfunction, extrapolating from below as appropriate **30-59**: 45 mg/kg/dose Q8H; maximum 1500 mg/dose **10-29**: 30 mg/kg/dose Q8H; maximum 1000 mg/dose **< 10**: 30 mg/kg/dose Q8H; maximum 1000 mg/dose **HD**: 22.5 mg/kg/dose Q12H; maximum 750 mg/dose **PD**: use not recommended **CRRT**: clearance is dependent on effluent flow rate; consider drug levels	**Max single dose:** 2000 mg **Max daily dose:** 8000 mg

	2 to < 3 months and ≥ 32 weeks gestational age at birth: 60 mg/kg/dose Q8H **Pediatrics:** ≥ 3 months: 60 mg/kg/dose Q8H; maximum 2000 mg per dose	▪ Effluent flow rate < 2 L/hour (20-25 mL/kg/hour): 60 mg/kg/dose Q12H; maximum 2000 mg/dose ▪ Effluent flow rate ≥ 2 L/hour (20-25 mL/kg/hour): 60 mg/kg/dose Q8H; maximum 2000 mg/dose	
Ceftaroline* IV	**< 2 months:** 6 mg/kg/dose Q8H **≥ 2 months and < 2 years:** 8 mg/kg/dose Q8H **≥ 2 years and ≤ 33 kg:** 12 mg/kg/dose Q8H **≥ 2 years and > 33 kg:** 400 mg/dose Q8H or 600 mg/dose Q12H (600 mg/dose Q12H preferred for adolescents; 600 mg/dose Q8H may be considered for severe infections)	**< 2 months**: **30-59**: 4 mg/kg/dose Q8H **15-29**: 3.5 mg/kg/dose Q8H **< 15**: 2.5 mg/kg/dose Q8H **HD**: 2.5 mg/kg/dose Q8H **PD**: 2.5 mg/kg/dose Q8H **CRRT**: 4 mg/kg/dose Q8H **≥ 2 months and < 2 years**: **30-59**: 5 mg/kg/dose Q8H **15-29**: 4 mg/kg/dose Q8H **< 15**: 3 mg/kg/dose Q8H **HD**: 3 mg/kg/dose Q8H **PD**: 3 mg/kg/dose Q8H **CRRT**: 5 mg/kg/dose Q8H **≥ 2 years and ≤ 33 kg**: **30-59**: 8 mg/kg/dose Q8H **15-29**: 6 mg/kg/dose Q8H **< 15**: 5 mg/kg/dose Q8H **HD**: 5 mg/kg/dose Q8H **PD**: 5 mg/kg/dose Q8H **CRRT**: 8 mg/kg/dose Q8H **≥ 2 years and > 33 kg**: **30-49**: 400 mg/dose Q12H (Q8H for severe infection) **15-29**: 300 mg/dose Q12H (Q8H for severe infection) **< 15**: 200 mg/dose Q12H (Q8H for severe infection) **HD**: 200 mg/dose Q12H (Q8H for severe infection) **PD**: 200 mg/dose Q12H (Q8H for severe infection) **CRRT**: 8 mg/kg/dose Q8H	**Max single dose:** 600 mg **Max daily dose:** 1800 mg
Ceftazidime IV/IM	50 mg/kg/dose Q8H	**30-49**: 50 mg/kg/dose Q12H **10-29**: 50 mg/kg/dose Q24H **< 10**: 50 mg/kg/dose Q48H **HD**: 50 mg/kg/dose Q48H **PD**: 50 mg/kg/dose Q48H **CRRT**: 50 mg/kg/dose Q12H	Give after HD on HD days **Max single dose:** 2000 mg, 1000 mg for CrCl < 10 **Max daily dose:** 6000 mg
Ceftazidime/ avibactam* IV (dosing based on ceftazidime component)	**≥ 3 months to < 6 months:** 40 mg/kg/dose Q8H **≥ 6 months:** 50 mg/kg/dose Q8H	**< 50 mL/min:** use not recommended in patients < 2 years; consider extrapolating from below as appropriate **31-50**: 25 mg/kg/dose Q8H; maximum 1000 mg/dose **16-30**: 19 mg/kg/dose Q12H; maximum 750 mg/dose **6-15:** 19 mg/kg/dose Q24H; maximum 750 mg/dose **< 5**: 19 mg/kg/dose Q48H; maximum 750 mg/dose **HD**: 19 mg/kg/dose Q24H; maximum 750 mg/dose	Give after HD on HD days **Max single dose:** 2000 mg **Max daily dose:** 6000 mg

		PD: 19 mg/kg/dose Q24H; maximum 750 mg/dose **CRRT**: clearance is dependent on effluent flow rate; consider drug levels ▪ Effluent flow rate ≥ 2 L/hour (20-25 mL/kg/hour): 25 mg/kg/dose Q8H; maximum 1000 mg/dose	
Ceftriaxone IV/IM	**CNS infections:** 100 mg/kg/dose Q24H; divide Q12H for doses > 2000 mg **Other:** 50-75 mg/kg/dose Q24H	**None**	**Max single dose:** 2000 mg **Max daily dose:** 4000 mg
Cephalexin PO	25 mg/kg/dose Q6-8H	**30-49**: 10-20 mg/kg/dose Q8H **10-29**: 10-20 mg/kg/dose Q12H **< 10**: 10-20 mg/kg/dose Q24H **HD**: 10-20 mg/kg/dose Q24H **PD**: 10-20 mg/kg/dose Q24H **CRRT**: 10-20 mg/kg/dose Q8H	Capsules may be opened Give after HD on HD days **Max single dose:** 1000 mg, 500 mg for CrCl < 50 **Max daily dose:** 4000 mg
Cefpodoxime PO	5 mg/kg/dose Q12H	**30-49**: usual dose **10-29**: 5 mg/kg/dose Q24H **< 10**: 5 mg/kg/dose Q24H **HD**: 5 mg/kg/dose Q24H **PD**: 5 mg/kg/dose Q24H **CRRT**: usual dose	Give after HD on HD days **Max single dose**: 200 mg (400 mg for severe infections) **Max daily dose:** 800 mg
Ceftolozane/ tazobactam* IV (dosing based on ceftolozane component)	20 mg/kg/dose Q8H	**30-49**: 10 mg/kg/dose Q8H; maximum 500-1000 mg/dose **15-29**: 5 mg/kg/dose Q8H; max 250-500 mg/dose **< 15**: use not recommended **HD**: 10-15 mg/kg/dose x 1 (max 500-1500 mg/dose x 1) followed by 2-3 mg/kg/dose Q8H (max 100-300 mg/dose) **PD**: use not recommended **CRRT**: 10 mg/kg/dose Q8H (max 500-1000 mg/dose)	**Max single dose**: 1000 mg (2000 mg for severe infections) **Max daily dose:** 6000 mg
Ciprofloxacin* IV	10 mg/kg/dose Q8-12H	**30-49**: 10 mg/kg/dose Q12H **10-29**: 10 mg/kg/dose Q24H **< 10**: 10 mg/kg/dose Q24H **HD**: 10 mg/kg/dose Q24H **PD**: 10 mg/kg/dose Q24H **CRRT**: 10 mg/kg/dose Q12H	Give after HD on HD days **Max single dose:** 400 mg **Max daily dose:** 1200 mg
Ciprofloxacin* PO	10-20 mg/kg/dose Q12H	**30-49**: usual dose **10-29**: 10-15 mg/kg/dose Q24H **< 10**: 10-15 mg/kg/dose Q24H **HD**: 10-15 mg/kg/dose Q24H **PD**: 10-15 mg/kg/dose Q24H **CRRT**: usual dose	Do not administer liquid formulation via tube Give after HD on HD days **Max single dose:** 750 mg, 500 mg for CrCl < 50 **Max daily dose:** 1500 mg
Clindamycin IV/PO	7-13 mg/kg/dose Q8H Alternatively, total daily dose may be divided Q6H	**None**	Capsules may be opened **Max single dose:** 900 mg **Max daily dose:** 3600 mg
Daptomycin* IV	**< 2 months:** 6 mg/kg/dose Q12H **2 months to 6 years:** 12 mg/kg/dose Q24H **7-11 years:**	**30-49**: usual dose **10-29**: usual dose Q48H **< 10**: usual dose Q48H **HD**: usual dose Q48H **PD**: usual dose Q48H **CRRT**: usual dose Q48H	Give after HD on HD days **Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight

	10-12 mg/kg/dose Q24H **≥ 12 years:** 8-10 mg/kg/dose Q24H		
Doxycycline IV/PO	2.2 mg/kg/dose Q12H	**None**	**Max single dose:** 100 mg **Max daily dose:** 200 mg
Ertapenem* IV/IM	**3 months to < 13 years:** 15 mg/kg/dose Q12H **≥ 13 years:** 1000 mg/dose Q24H	**< 13 years**: **< 30:** no data, consider 50% dose reduction **≥ 13 years**: **30-49**: usual dose **10-29**: 500 mg/dose Q24H **< 10**: 500 mg/dose Q24H **HD**: 500 mg/dose Q24H **PD**: 500 mg/dose Q24H **CRRT**: usual dose	Give after HD on HD days **Max single dose:** 500 mg if < 13 years, 1000 mg if ≥ 13 years **Max daily dose:** 1000 mg
Fluconazole IV/PO	**Invasive infection:** 6-12 mg/kg/dose Q24H Consider 12-25 mg/kg x 1 loading dose **Other:** 3-6 mg/kg/dose Q24H	**Invasive infection:** **30-49**: usual dose **10-29**: 3-6 mg/kg/dose Q24H **< 10**: 3-6 mg/kg/dose Q48H **HD**: 3-6 mg/kg/dose Q48H **PD**: 3-6 mg/kg/dose Q48H **CRRT**: usual dose **Other:** **30-49**: usual dose **10-29**: 1.5-3 mg/kg/dose Q24H **< 10**: 1.5-3 mg/kg/dose Q48H **HD**: 1.5-3 mg/kg/dose Q48H **PD**: 1.5-3 mg/kg/dose Q48H **CRRT**: usual dose	Give after HD on HD days **Max dose:** 800 mg (may consider up to 1600 mg)
Gentamicin IV/IM	7-8 mg/kg/dose Q24H Pharmacy consult		**Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight
Levofloxacin* IV/PO	**< 5 years:** 10 mg/kg/dose Q12H **≥ 5 years:** 10 mg/kg/dose Q24H	**< 5 years:** **30-49**: usual dose **10-29**: 10 mg/kg/dose Q24H **< 10**: 10 mg/kg/dose Q48H **HD**: 10 mg/kg/dose Q48H **PD**: 10 mg/kg/dose Q48H **CRRT**: usual dose **≥ 5 years:** **30-49**: usual dose **10-29**: 5 mg/kg/dose Q24H **< 10**: 5 mg/kg/dose Q48H **HD**: 5 mg/kg/dose Q48H **PD**: 5 mg/kg/dose Q48H **CRRT**: usual dose	Give after HD on HD days **Max single dose:** 750 mg, 250-500 mg for CrCl < 30 **Max daily dose:** 750 mg
Linezolid* IV/PO	**< 12 years:** 10 mg/kg/dose Q8H **≥ 12 years:** 600 mg/dose Q12H	**None** **Therapeutic drug monitoring suggested; adverse effects more common in patient with impaired renal function**	**Max single dose:** 600 mg **Max daily dose:** 1800 mg
Meropenem* IV	**CNS infections:** 40 mg/kg/dose Q8H **Other:** 20 mg/kg/dose Q8H	**CNS infections:** **26-49**: 40 mg/kg/dose Q12H **10-25**: 20 mg/kg/dose Q12H **< 10**: 20 mg/kg/dose Q24H **HD**: 20 mg/kg/dose Q24H **PD**: 20 mg/kg/dose Q24H	Give after HD on HD days **Max single dose:** 2000 mg, 1000 mg for CrCl < 30 for CNS infections; 1000 mg, 500 mg for CrCl < 30 for other infections

		CRRT: 40 mg/kg/dose Q8H **Other:** **26-49**: 20 mg/kg/dose Q12H **10-25**: 10 mg/kg/dose Q12H **< 10**: 10 mg/kg/dose Q24H **HD**: 10 mg/kg/dose Q24H **PD**: 10 mg/kg/dose Q24H **CRRT**: 20 mg/kg/dose Q8H	**Max daily dose:** 6000 mg for CNS infections, 3000 mg for other infections
Metronidazole IV/PO	10 mg/kg/dose Q8H Alternatively, total daily dose may be divided Q6H When given IV, the total daily dose may be given Q24H (30 mg/kg/dose Q24H)	**30-49**: usual dose **10-29**: usual dose **< 10:** 5 mg/kg/dose Q8H **HD**: 5 mg/kg/dose Q8H **PD**: 5 mg/kg/dose Q8H **CRRT:** usual dose	Evaluate need for further 50% dose reduction if severe hepatic dysfunction present **Max single dose:** 500 mg (or 1500 mg if giving IV once daily) **Max daily dose:** 1500 mg
Micafungin IV	4-10 mg/kg/dose Q24H	**None**	**Max single dose:** 150 mg **Max daily dose:** 150 mg
Nafcillin IV/IM	**CNS infections, endocarditis, other invasive infections:** 50 mg/kg/dose Q6H **Other:** 37.5-50 mg/kg/dose Q6H	**None**	Evaluate need for dose adjustment if both renal and hepatic dysfunction present **Maximum single dose:** 3000 mg for CNS/endocarditis/invasive infections, 2000 mg for other infections **Maximum daily dose:** 12000 mg for CNS/endocarditis/invasive infections, 8000 mg for other infections
Penicillin G (Parenteral/ Aqueous) IV/IM	**Caution: doses in units/kg/DAY** **CNS infections:** 300-400,000 units/kg/**DAY** Q4-6H **Other:** 200-300,000 units/kg/**DAY** Q4-6H	**CNS infections:** **30-49**: usual dose **10-29**: 225-300,000 units/kg/**DAY** Q4-6H **< 10:** 150-200,000 units/kg/**DAY** Q4-6H **HD**: 150-200,000 units/kg/**DAY** Q4-6H **PD**: 150-200,000 units/kg/**DAY** Q4-6H **CRRT:** usual dose **Other:** **30-49**: usual dose **10-29**: 150-225,000 units/kg/**DAY** Q4-6H **< 10:** 100-150,000 units/kg/**DAY** Q4-6H **HD**: 100-150,000 units/kg/**DAY** Q4-6H **PD**: 100-150,000 units/kg/**DAY** Q4-6H **CRRT:** usual dose	**Maximum single dose:** 4 million units (MU), 3 MU for CrCl 10-50, 2 MU for CrCl < 10 **Maximum daily dose:** 24 MU
Penicillin G Benzathine IM	***Streptococcus,* group A:** ≤ 27 kg: IM: 600,000 units x 1 > 27 kg: IM: 1,200,000 units x 1 **Syphilis:** 50,000 units/kg/dose (maximum 2.4 MU/dose) x 1 or weekly	**None**	For IM administration only; do NOT give IV, intra-arterially or SUBQ
Piperacillin/ tazobactam IV (4 hour infusion; dosing based on piperacillin component)	100 mg/kg/dose Q8H	**30-49**: 75 mg/kg/dose Q8H **10-29**: 75 mg/kg/dose Q12H **< 10:** 75 mg/kg/dose Q12H **HD**: 75 mg/kg/dose Q12H **PD**: 75 mg/kg/dose Q12H **CRRT:** 75 mg/kg/dose Q8H	**Maximum single dose:** 3000 mg **Maximum daily dose:** 16000 mg
Tobramycin IV/IM	7-8 mg/kg/dose Q24H Pharmacy consult		**Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight

Trimethoprim/ sulfamethoxazole IV/PO (dosing based on trimethoprim component) ≥ 1 months only	**Caution: doses in mg/kg/DAY** 10-20 mg/kg/**DAY** Q6-12H	**30-49**: usual dose **15-29**: 5-10 mg/kg/**DAY** Q6-12H **< 15:** 2.5-5 mg/kg/**DAY** Q12H **HD**: 2.5-5 mg/kg/dose Q24H **PD**: 2.5-5 mg/kg/**DAY** Q12H **CRRT:** usual dose	Give after HD on HD days **Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight **Maximum single dose:** 320 mg, 160 mg for CrCl < 50 **Maximum daily dose:** none
Vancomycin* IV	10-20 mg/kg/dose Q6-8H Pharmacy consult		
Vancomycin PO	10 mg/kg/dose Q6H	**None**	**Maximum single dose:** 125 mg, 500 mg for severe/fulminant *C. difficile* **Maximum daily dose:** 2000 mg
Voriconazole* IV/PO	**< 12 years OR 12-14 years and < 50 kg:** Loading dose: 9 mg/kg/dose IV/PO Q12H x 2 doses Maintenance dose IV: 8 mg/kg/dose Q12H Maintenance dose PO: 9 mg/kg/dose Q12H **≥ 15 years OR ≥ 12 years and ≥ 50 kg:** Loading dose: 6 mg/kg/dose IV/PO Q12H x 2 doses Maintenance dose: 4 mg/kg/dose IV/PO Q12H	**None** PO preferred for CrCl < 50	Evaluate need for dose adjustment if cirrhosis is present **Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight **VORICONAZOLE DOSING AND MONITORING GUIDELINE**

Intraventricular Antimicrobial Dosing Recommendations

General Notes

- The intraventricular (IVT) route of administration is indicated in certain central nervous system infections when sufficient cerebrospinal fluid (CSF) concentrations cannot be obtained with intravenous antimicrobial dosing.
- The intrathecal and intraventricular routes of administration are NOT the same.

Administration Considerations

- IVT administration requires the placement of ventriculostomy (EVD or shunt) or a reservoir for instillation (e.g., Ommaya or Rickham).
- The estimated CSF volume in an adults is ~150mL total volume, ~25mL within the ventricular system. The estimated CSF volume in infants is ~ 50 mL, requiring a reduction in antimicrobial doses (by ~50-50%)
- Administration of antimicrobials is to be performed by a neurosurgeon or neurosurgery extender.
- Dose adjustments may be needed based on increased or decreased CSF output through the ventriculostomy.
- EVDs should be clamped for 15-60 minutes after administration to allow for the antimicrobial to distribute through the CSF.
- **NOTE:** Questions regarding antimicrobial administration should be directed to the attending neurosurgeon.

Suggested Duration: Continue for 3-4 days after negative CSF cultures.

Intraventricular Dosing

Drug	Dose Range and Frequency[a] (Starting Dose)	Diluent and Concentration[b]	Monitoring Parameters[c,d]
Amikacin	5-50 mg daily (30 mg)	• Preservative-free NS • 10 mg/mL	• Obtain CSF trough every 2-3 days • Goal CSF trough: 2-10 mcg/ml
Colistin *(in mg CBA)*	1-4 mg CBA daily (1 mg)	• Preservative-free NS 1 mg CBA/mL	None
Daptomycin	2-10 mg Q48-72H (5 mg Q48H)	• Preservative-free NS • 2.5 mg/mL	None
Gentamicin (preservative free)	1-2 mg daily (1 mg)	• Preservative-free NS • 5 mg/mL	• Obtain CSF levels every 2-3 days • Goal CSF trough: 2-10 mcg/mL
Polymyxin B	2 mg daily (2 mg)	• Preservative-free NS • 2.5 mg/mL	None
Tobramycin (preservative free)	5-20 mg daily (5 mg)	• Preservative-free NS • 5 mg/mL	• Obtain CSF levels every 2-3 days • Goal CSF trough: 2-10 mcg/ml
Vancomycin	5-20 mg daily (5mg)	• Preservative-free NS • 5 mg/mL	• Obtain CSF levels every 2-3 days • Goal CSF trough: 10-20 mcg/ml
Amphotericin B Deoxycholate	0.1 mg daily – increase Q24H to 0.5 mg daily (max 1 mg daily)	• Preservative-free D5W • 0.1 mg/mL • 0.25 mg/mL[e]	None
Amphotericin B LIPOSOMAL	1 mg daily (Clamp EVD 4H)	• Preservative-free D5W • 1 mg/3 mL	None

[a]Optimal dose and duration of vancomycin and the aminoglycosides are not well established. Clearance of antibiotics from CSF is variable and depends upon several factors: CSF production rate, anatomy of the ventricular system and communication between ventricles, presence of hydrocephalus and need for CSF drainage, CSF drainage volume, and the type of device present (i.e. reservoir vs. EVD). In general, higher initial doses are recommended in patients with high EVD output (>200mL / day).

[b]Neurosurgeon should specify the volume (preferred 2-3 ml of preservative free solution; max 4mL/dose).

[c]Successful treatment has been associated with CSF trough concentrations of 10-20 x MIC of the organism

[d]All antimicrobial levels from the CSF must be sent to an outside laboratory with an approximate turn-around time of 2-3 days. CSF concentration varies largely upon whether patients has an EVD, shunt, or reservoir.

[e]Use 0.25 mg/mL for doses ≥ 0.5 mg

Orlando Health Pediatric/Neonatal Peri-operative Antibiotic Prophylaxis Guideline

	Cefazolin	Clindamycin	Ampicillin/ Sulbactam	Gentamicin	Metronidazole	Vancomycin
Initial Dose Pediatric	30 mg/kg[3]	10 mg/kg	50 mg/kg	2.5 mg/kg[1]	10 mg/kg[2]	15 mg/kg
Initial Dose Neonatal	25-30 mg/kg	7.5 mg/kg	50 mg/kg	2 mg/kg	Pre-op: <1.2 kg: 7.5 mg/kg; ≥1.2 kg: 15 mg/kg Post-op: 7.5 mg/kg	10 mg/kg
Max Dose	<120kg: 2000 mg >120kg: 3000 mg	900 mg	3000 mg amp	N/A	500 mg	2000 mg
Administration	3-5 min IV Push	30 min infusion	30 min infusion	30 min infusion	10 min infusion	60 min/gram infusion
When to start infusion BEFORE incision	Within 60 minutes	Within 60 minutes	Within 60 minutes	Within 60 minutes	Within 60 minutes	Within 60-120 minutes
Minimum % of dose that should be administered prior to incision	100	100	100	100	100	50
Re-dosing if Surgical Delay > 60 minutes						
Repeat pre-op dose?	Yes, repeat	Yes, repeat	Yes, repeat	Do NOT re-dose	Yes, repeat	Yes, repeat for delay ≥ 8 hours. For a delay < 8 hours, give 5 mg/kg.
Re-dosing Interval During Surgeries > 2 hours						
CrCl > 50 mL/min	Q4H	Q6H	Q2H	Q8H	Do NOT re-dose	Do NOT re-dose
For patients with impaired renal function, the re-dosing interval is left to the discretion of the physician. Extending (e.g. doubling) the re-dosing interval is an option in patients with a CrCl between 30-50 mL/min. In patients with CrCL <30 mL/min, re-dosing is likely not needed for most surgeries. Clindamycin and metronidazole should not have the re-dosing interval adjusted for renal dysfunction as they are not cleared renally.						
Special Situations						
Estimated Blood Loss exceeds 20 mL/kg	Re-administration of prophylactic antibiotic is recommended for each > 20mL/kg of blood loss or hemodilution.					
Patients already receiving scheduled antibiotics	Scheduled antibiotics should not be held to be given at surgery and are NOT sufficient as prophylaxis unless given within 60 minutes of incision. The recommended prophylactic antibiotic(s) should be given as outlined above even in patients receiving scheduled antibiotics.					
Postoperative Duration						
Clean: NONE	**Clean-contaminated: 24 hours**	**Contaminated: 24 hours** **Note: extend for Grade III open fractures or ruptured viscous in intra-abdominal surgery**				

[1]Grade III open fracture prophylaxis is 7 mg/kg

[2]Consider metronidazole 30 mg/kg x 1 pre-op for appendicitis (post op dosing Q24H if being continued, infuse over 30 minutes)

[3]For cardiac bypass: 50 mg/kg bolus, followed by 10 mg/kg/hour (max 500 mg/hr) for the duration of bypass/skin closure

Recommended Regimens Are Preferred over Alternative Antibiotic Regimens Whenever Possible

- Recommended regimens typically have more data to support efficacy or have been associated with less toxicities.
- Cefazolin is the primary agent used for most surgical procedures and does not cross react with any other β-lactam agent. Use of the recommended regimen is strongly suggested unless the patient has a documented severe allergy to cefazolin. For patients with a documented severe penicillin allergy, use of the alternative regimen is recommended for procedures where ampicillin/sulbactam is listed as the recommended regimen.
- Severe allergy (IgE mediated) is defined as anaphylaxis, bronchospasm, or swelling (does not include unknown reactions). Patients with severe allergies to the recommended regimen should be verified for accuracy prior to antibiotic selection/use of an alternative regimen.
- **Add** pre-op vancomycin to the recommended regimen below for the following procedures in patients that screen positive for MRSA: orthopedic and neurosurgical procedures with hardware implantation, spinal procedures, hernia repairs, and cardiac/other thoracic procedures

Surgery Type	Recommended Regimen	Alternative
Cardiothoracic	Cefazolin	Vancomycin **OR** Clindamycin
Gastrointestinal		
Gastroduodenal (high-risk only), small bowel procedures (non-perforated), G-tube with or without Nissen (including revision or conversion)	Cefazolin **OR** Cefazolin/Metronidazole (if obstructed small bowel)	Vancomycin **OR** Clindamycin **with** Gentamicin
Biliary tract including cholecystectomy, exploration of common bile duct, etc. (open procedures or high-risk laprascopic procedures only)	Cefazolin	Vancomycin **OR** Clindamycin **with** Gentamicin
Hernia repairs	Cefazolin	Vancomycin **OR** Clindamycin
Colorectal	Cefazolin/Metronidazole	Clindamycin **plus** Gentamicin
Appendectomy (non-perforated)	Cefazolin/Metronidazole	Clindamycin **plus** Gentamicin
Any perforated bowel or abscess	Ceftriaxone **plus** Metronidazole *Ceftazidime instead of ceftriaxone for neonates	Piperacillin/tazobactam **OR** Cefepime plus Metronidazole
Head and Neck		
Dental, Oral, Respiratory Tract, or Esophageal	Cefazolin/Metronidazole **OR** Ampicillin/sulbactam	Clindamycin
Clean-contaminated or hardware placement (ENT)	Cefazolin **OR** Ampicillin/sulbactam	Clindamycin **WITH OR WITHOUT** Gentamicin
Neurosurgery	Cefazolin	Vancomycin
Orthopedic		
Hip/Knee Arthroplasty/ implantation of internal fixation devices/spinal procedures	Cefazolin	Clindamycin **OR** Vancomycin
Grade I and II open bone fracture prophylaxis	Cefazolin	Clindamycin **OR** Vancomycin
Grade III open bone fracture prophylaxis	Cefazolin **WITH OR WITHOUT** Gentamicin **OR** Ceftriaxone (monotherapy)	Clindamycin **WITH OR WITHOUT** Gentamicin
Thoracic	Cefazolin **OR** Ampicillin/Sulbactam	Clindamycin **OR** Vancomycin
Urologic		
High Risk Only (lower tract instrumentation with risk factors for infection) *Urine culture prior to surgery recommended to select effective pre-operative antibiotic	Cefazolin **OR** Gentamicin (if cefazolin resistant and gentamicin susceptible or susceptibility unknown)	Gentamicin *For other alternatives (such as if organism resistant to cefazolin and gentamicin), discussion with ID provider or pharmacist is recommended prior to surgery
Prosthetic material insertion, removal, revision	Cefazolin **plus** Gentamicin **OR** Ampicillin/sulbactam	Vancomycin **plus** Gentamicin
Removal epididymis or epididymis lesion	Cefazolin	Vancomycin
Involvment of bowel (clean-contaminated)	Cefazolin/Metronidazole	Gentamicin **plus** Metronidazole
Vascular Procedures	Cefazolin	Clindamycin **OR** Vancomycin
Plastic Surgery	Cefazolin **OR** Ampicillin/sulbactam	Clindamycin **OR** Vancomycin

Pediatric Antimicrobial Duration of Therapy for Common Infections – Expected Practice

I. PURPOSE:

This guideline details evidence-based recommendations regarding the duration of treatment of various types of pediatric infections, focusing on infections not otherwise covered in the Orlando Health Pediatric Infectious Diseases Treatment Guidelines. References are listed next to each recommendation for further guidance. The intent of this guideline is to provide general guidance regarding the expected practice for treatment length. This guideline may not be applicable to every patient and should be used to assist the prescriber in determining the most appropriate length of therapy.

II. DEPARTMENT GUIDELINE

Type of Infection	USUAL MAXIMUM Recommended Duration	REFERENCE
Central Nervous System		
Ventriculitis/Shunt Infection (Coagulase-negative *staphylococcus* or *Propionibacterium acnes*)	10 days Significant CSF WBC count, decreased CSF glucose, or clinical symptoms: 10-14 days *These recommendations apply for patients with shunt removal and source control. Complicated infections may require a longer duration of therapy.	Tunkel AR, et al. Clin Infect Dis. 2017; 64(6):34-65. PMID: 28203777
Ventriculitis/Shunt Infection (*Staphylococcus aureus* or Gram-negative bacilli)	14 days Gram-negative bacilli may be treated up to 21 days *These recommendations apply for patients with shunt removal and source control. Complicated infections may require a longer duration of therapy.	Tunkel AR, et al. Clin Infect Dis. 2017; 64(6):34-65. PMID: 28203777
Pulmonary		
Pertussis	5 days Alternatives to azithromycin may require a longer duration	Bradley JS, et a. Nelson's Pediatric Antimicrobial Therapy. 2018.
Cardiovascular		
Endocarditis	4 weeks for the following organisms: • Native valve Streptococci • Native or prosthetic valve *Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* spp. (HACEK) 4-6 weeks for the following organisms: • Native valve MSSA • Native or prosthetic valve *Enterococcus* • Native valve culture-negative endocarditis 6 weeks for the following organisms: • Prosthetic valve Streptococci • Native valve MRSA • Native or prosthetic valve *Enterococcus* treated with vancomycin • Prosthetic valve culture-negative endocarditis	Baltimore RS. Circulation. 2015; 132(15):1487-1515. PMID: 26373317 Baddour LM. Circulation. 2015; 132(15):1435-1486. PMID: 26373316

	AT LEAST 6 weeks for the following organisms: • Prosthetic valve Staphylococci • Enteric Gram-negative endocarditis	
Oropharyngeal		
Sinusitis	7 days *Patients without improvement or with complicated sinusitis may require a longer duration of therapy	Falagas ME, et al. Br J Clin Pharmacol. 2009; 67(2):161-171. PMID: 19154447 Wald ER, et al. Pediatrics. 2013; 132(1):262-280. PMID: 23796742
Epiglottitis	7 days	Bradley JS, et a. Nelson's Pediatric Antimicrobial Therapy. 2018.
Group A Streptococcal Pharyngitis (GAS)	10 days	Shulman ST, et al. Clin Infect Dis. 2012; 55(10):86-102. PMID: 22965026 Bradley JS, et al. Nelson's Pediatric Antimicrobial Therapy. 2018.
Non-Catheter Related Bloodstream Infection		
Bacteremia; *Staphylococcus aureus*	14 days following first negative blood culture	Bamberger DM, et al. Am Fam Physician. 2005; 72(12):2474-2481. PMID: 16370403 Bradley JS, et al. Nelson's Pediatric Antimicrobial Therapy. 2018.
Occult bacteremia; Coagulase-negative *staphylococcus*	5 days *If a source of infection is identified, duration of therapy should match the source	Kimberlin DW, et al. Red Book. 2018.
Occult bacteremia; *Streptococcus agalactiae* (GBS)	10 days *If a source of infection is identified, duration of therapy should match the source	Simonsen KA, et al. Clin Microbiol Rev. 2014; 27(1):21-47. PMID: 24396135 Kimberlin DW, et al. Red Book. 2018.
Occult bacteremia; *Streptococcus pneumoniae*	7-10 days *If a source of infection is identified, duration of therapy should match the source	Bachur R, Harper MB. Pediatrics. 2000;105(3 Pt 1):502-509. doi:10.1542/peds.105.3.502 PMID: 10699100 Boulos JM et al. Open Forum Infect Dis. 2021;8(Suppl 1):S205. doi:10.1093/ofid/ofab466.397 PMCID: 8645043
Bacteremia; *Enterococcus*	Duration of therapy should match the source of infection	Kimberlin DW, et al. Red Book. 2018.
Bacteremia; Gram-negative bacilli	Duration of therapy should match the source of infection	Yahav D, et al. Clin Infect Dis. 2018. doi: 10.1093/cid/ciy1054. [Epub ahead of print]. PMID: 30535100
Candidemia	14 days following first negative blood culture	Kimberlin DW, et al. Red Book. 2018.
Bone and Joint Infections		
Prosthetic Joint Infections	4-6 weeks followed by suppressive therapy if hardware retained	Osmon DR. Clin Infect Dis. 2013; 56(1):1-25. PMID: 23223583

Gastrointestinal		
Intra-abdominal infection	4-7 days with source control	Solomkin JS, et al. Clin Infect Dis. 2010; 50(2):133-164. PMID: 20034345
Appendicitis (non-perforated)	No antibiotics needed	Poon SHT, et al. World J Emerg Surg. 2017; 12:46. PMID: 29075315
Appendicitis (perforated)	3-7 days with source control	Van Rossem CC, et al. Br J Surg. 2014; 101(6):715-719. PMID: 24668341 Desai AA, et al. J Pediatr Surg. 2015; 50(6):912-914. PMID: 25812441 Fraser JD, et al. J Pediatr Surg. 2010; 45(6):1198-1202. PMID: 20620320
Salmonella gastroenteritis	Asymptomatic infection or uncomplicated gastroenteritis: antimicrobial therapy not indicated unless the patient is at increased risk of invasive disease (infants younger than 3 months, people with chronic gastrointestinal tract disease, malignant neoplasm, hemoglobinopathies, HIV infection, or other immunosuppressive illnesses or therapies) -Gastroenteritis: 5 days -Bacteremia: 7-10 days	Shane AL, et al. Clin Infect Dis. 2017;65(12):45-80. PMID: 29053792 Kimberlin DW, et al. Red Book. 2018.
Peritoneal dialysis associated infections	2 weeks: • Fungal peritonitis • Culture negative peritonitis • *E. coli* and *Klebsiella spp*. peritonitis susceptible to third-generation cephalosporins • Coagulase-negative *Staphylococcus spp*. peritonitis • *Streptococcus spp*. peritonitis 2-3 weeks: • *Enterobacter spp., Citrobacter spp., Serratia spp., and Proteus spp*. peritonitis • *Acinetobacter spp*. peritonitis • *Enterococcus spp*. peritonitis 3 weeks: • *E. coli* and *Klebsiella spp*. peritonitis resistant to third-generation cephalosporins • *Pseudomonas spp*. peritonitis • *Stenotrophomonas maltophilia* peritonitis • *Staphylococcus aureus* (MRSA and MSSA) peritonitis	Warady BA, et al. Peritoneal Dialysis International. 2012;32:S32-86. PMID: 22851742

	2-4 weeks: • Peritoneal dialysis catheter tunnel infections	
Genitourinary		
Epididymitis	10 days	Bradley JS, et al. Nelson's Pediatric Antimicrobial Therapy. 2018.

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Febrile infants ≤ 60 days old clinical pathway

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