ORLANDO HEALTH®

Pediatric Infectious Diseases Treatment Guideline

Antimicrobial Utilization and Stewardship Subcommittee

Table of Contents

Miscellaneous	Approval Date	Page Number
Management of Febrile Infants ≤ 60 Days Old Clinical Pathway	1/2024	97
Surgical Site Infection Prophylaxis Guide	7/2025	102
Duplicate Anaerobic Policy	9/2022	--
Beta-lactam Allergy Delabeling Guideline	1/2024	--
Penicillin Skin Testing Policy—Patient Care Policy 5006	8/2024	--

Treatment Guideline References

APH & ED Antimicrobial Susceptibility Report
January 2025 to December 2025

Microbiology Laboratory Number: 321-841-5226

	No. Tested	Ampicillin[$]	Clindamycin[$$]	Daptomycin[$$$]	Doxycycline[$]	Linezolid[$$$]	Nitrofurantoin[$] urine only	Nafcillin[$$$]	Trim/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]	267	-	77	100	99	100	100[g]	69[d]	85	100
MRSA (31%)	84	-	78	100	98	100	100[g]	-	70	100
MSSA (69%)	183	-	77	100	100	100	100[g]	100[d]	92	100
Staphylococcus epidermidis	30	-	56	100	93	100	100	43	66	100
Enterococcus faecalis[a]	57	100	-	98	25	98	98	-	-	100

	No. Tested	Ceftriaxone[$]	Clindamycin[$$]	Linezolid[$$$]	Levofloxacin[$]	Penicillin[$$$]	Tetracycline[$$$]	Trim/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]	40	98/83	85	100	97	98/60	90	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 2024-December 2025).

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

APH & ED Antimicrobial Susceptibility Report
January 2025 to December 2025

Microbiology Laboratory Number: 321-841-5226

	No. Tested	Amikacin[$]	Ampicillin[$]	Ampicillin/ Sulbactam[$]	Aztreonam[$$$$$]	Cefazolin[$] urine only	Cefepime[$]	Ceftriaxone[$]	Ciprofloxacin[$]	Ertapenem[$$$$]	Gentamicin[$]	Meropenem[$]	Minocycline[$$$$$]	Levofloxacin [$$$$]	Nitrofurantoin[$] urine only	Piperacillin/ Tazobactam[$]	Trim/Sulfa[$$$]	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]	≤1	≤2	≤32	≤16[f]	≤2/ 38	≤2[a]/ ≤1[e]
Enterobacter cloacae	31	100	-	-	90	-	100	-*	80	96	90	100	-	-	50	-*	68	87
Escherichia coli[cd]	402	97	43	57	94	89	99	91	80	100	84	100	-	-	97	96	65	84
Non-ESBL *E. coli*[cd]	365	99	47	60	99	96	100	99	85	100	87	100	-	-	97	96	67	88
ESBL *E. coli*[cd]	38	76	-	-	-	-	-	-	28	100	58	100	-	-	100	-	47	53
Klebsiella oxytoca^	25	96	-	68	92	92	100	88	92	100	88	100	-	-	100	100	92	88
Klebsiella pneumoniae[cd]	57	100	-	77	86	81	100	88	81	100	91	100	-	-	20	94	72	90
Non-ESBL *K. pneumoniae*[cd]	49	100	-	83	98	88	100	100	100	100	98	100	-	-	27	98	78	96
Proteus mirabilis	45	96	64	93	98	94	100	100	96	100	93	100	-	-	-	100	89	96
Pseudomonas aeruginosa	119	100[g]	-	-	-[h]	-	92	-	93	-	-	88	-	-	-	90	-	79
Salmonella enterica^	20	-	100	100	100	-	100	100	100	-	-	-	-	-	-	-	100	-
Serratia marcescens	35	100	-	-	89	-	100	83	80	100	89	100	-	-	-	94	97	79
Stenotrophomonas maltophilia^[i]	18	-	-	-	-	-	-	-	-	-	-	-	78	83	-	-	89	-

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* = 9.5%, *K. pneumoniae* = 14 %**

[d] **CRE rate: *E. coli* = 0%, *K. pneumoniae* = 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

[i] The percent susceptibility was calculated using ~2 years of data (January 2024-December 2025).

^ 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 or piperacillin/tazobactam against Enterobacter *cloacae* and *Klebsiella aerogenes* (formerly *Enterobacter aerogenes*).

Pediatric Antimicrobial Dosing Recommendations

Dosing card only to be used for pediatric patients corrected to > 44 weeks gestation and > 30 days old (unless otherwise noted)
For patients ≥ 40 kg, refer to the Orlando Health Adult Antimicrobial Dosing Guideline (unless otherwise noted)
*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	**< 40 kg:** 20 mg/kg/dose Q6H **≥ 40 kg:** - HSV treatment: 400 mg q8h - HSV prophylaxis 400 mg q12h - VZV treatment: 800 mg 5 times daily	**25-50**: usual dose **10-24**: usual dose Q8H **< 10**: usual dose Q12H Space to Q24H in patients undergoing HSV prophylaxis **HD**: 5 mg/kg/dose Q12H (max: 200 mg/dose) - Space to Q24H in patients undergoing VZV treatment (max 800 mg/day) **PD**: 20 mg/kg/dose Q24H **CRRT**: usual dose	Give after HD on HD days **Max single dose:** 800 mg **Max daily dose:** 3200 mg
Amikacin IV	15-30 mg/kg/dose Q24H Pharmacy consult	**Renal dose adjustments to be guided by Aminoglycoside CTMP**	**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 **Max daily dose:** 1.5mg/kg/day
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 **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	**Max single dose:** 3000 mg **Max daily dose:** 12000 mg
Ampicillin/ sulbactam IV (dosing based on ampicillin component)	Dosing based on indications match ampicillin as above **Carbapenem resistant *Acinetobacter baumannii* 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 carbapenem resistant *Acinetobacter baumannii* 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	Give after HD on HD days **Max single dose:** 2000 mg **Max daily dose:** 8000 mg
Cefazolin IV	25-50 mg/kg/dose Q8H	**30-49**: 25 mg/kg/dose Q12H **10-29**: 25 mg/kg/dose Q24H **< 10**: 25 mg/kg/dose Q48H **HD**: 50 mg/kg after dialysis (maximum 2000 mg) **PD**: 25-30 mg/kg/dose Q24H (maximum 1000 mg/dose) **CRRT**: 25 mg/kg/dose Q8H (maximum 2000mg/dose)	Give after HD on HD days **Max single dose:** 2000 mg, 1000 mg for cystitis, 3000 mg for surgical prophylaxis in patients $\geq$ 120 kg **Max daily dose:** 12000 mg
Cefepime IV/IM	**Severe sepsis/shock, CF patients, Confirmed or recent (≤1 year) *P. aeruginosa* infection, Febrile neutropenia (24–48 h pending cultures), SDD isolates:** 50 mg/kg/dose Q8H **Other:** 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) **PD**: 50 mg/kg/dose Q48H (Q24H may be considered for septic shock) (maximum 1000 mg/dose) **CRRT**: 50 mg/kg/dose Q8H (maximum 2000mg/dose)	IV doses for Severe sepsis/shock, CF patients, Confirmed or recent (≤1 year) *P. aeruginosa* infection, Febrile neutropenia (24–48 h pending cultures), or SDD isolates should be administered as a 3-hour infusion Give after HD on HD days **Max single dose:** 2000 mg, 1000 mg for CrCl < 10 **Max daily dose:** 6000 mg
Cefiderocol* IV	**All doses infused over 3 hours (consider a 1-hour infusion for patients < 3 months)** **Infants:**	**30-59**: 75% of usual dose administered Q8H; maximum 1500 mg/dose **15-29**: 50% of usual dose administered Q8H; maximum 1000 mg/dose **< 15**: 33% of usual dose administered Q8H; maximum 750 mg/dose	**Max single dose:** 2000 mg **Max daily dose:** 8000 mg

	< 2 months and < 32 weeks gestational age at birth: 30 mg/kg/dose Q8H < 2 months and ≥ 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 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	**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 ▪ 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	**Skin and Soft Tissue Infections:** **< 2 months:** 6 mg/kg/dose Q8H **≥ 2 months - < 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)	**< 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**: No data **CRRT**: 33% dose reduction at usual interval **≥ 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**: No data **CRRT**: 33% dose reduction at usual interval **≥ 2 years and ≤ 33 kg**: **30-≤50**: 8 - 10 mg/kg/dose Q8H (maximum 300mg/dose) **15-29**: 6 - 8 mg/kg/dose Q8H (maximum 200mg/dose) **< 15**: 5 mg/kg/dose Q8H **HD**: 5 mg/kg/dose Q8H **PD**: No data **CRRT**: 33% dose reduction at usual interval **≥ 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**: No data **CRRT**: 33% dose reduction at usual interval	**Max single dose:** 600 mg **Max daily dose:** 1800 mg
	Bacteremia and Osteoarticular Infections: **< 2 months:** 6 mg/kg/dose Q8H **≥ 2 months – 6 months: 10 mg/kg q8h** **> 6 months: 15 mg/kg q8h (max 600 mg/dose)**		
Ceftazidime IV/IM	50 mg/kg/dose Q8H Higher doses (Up to 100 mg/kg/dose Q8H) may be warranted in severe pseudomonal infections	**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:** 30mg/kg/dose Q8H **≥ 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) **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	Give after HD on HD days **Max single dose:** 2000 mg **Max daily dose:** 6000 mg
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, 1000 mg for cystitis **Max daily dose:** 2000mg or 4000 mg (CNS infections)
Cephalexin PO	25 mg/kg/dose Q6-8H	***Dose adjustment recommendations based on Q6H dose for patients with eGFR > 50** **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 <30: usual dose Q24H **HD**: 5 mg/kg/dose three times weekly after dialysis **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	**< 50 mL/min:** use not recommended in patients < 18 years; consider extrapolating from below as appropriate Max dose in renal dose adjustment is dependent on indication for treatment. **30-49**: 10 mg/kg/dose Q8H; (max 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	Give after HD on HD days **Max single dose**: 1000 mg (2000 mg for severe infections) **Max daily dose:** 6000 mg

		CRRT: 10 mg/kg/dose Q8H (max 500-1000 mg/dose)	
Ciprofloxacin* IV	10 mg/kg/dose Q8-12H	**30-49**: usual dose **10-29**: 10 mg/kg/dose Q18H **< 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 Q18H **< 10**: 10-15 mg/kg/dose Q24H **HD**: 10 mg/kg/dose Q24H **PD**: 10 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:** 10-12 mg/kg/dose Q24H **≥ 12 years:** 8-10 mg/kg/dose Q24H	**< 2 months:** **30-49**: usual dose **15-29**: usual dose Q24H **< 15**: 4 mg/kg Q48H **HD**: usual dose Q48H **PD**: usual dose Q48H **CRRT**: usual dose Q48H **2 months to 6 years:** **30-49:** usual dose **15-29:** usual dose Q48H **< 15:** 8 mg/kg Q48H **HD**: usual dose Q48H **PD**: usual dose Q48H **CRRT:** usual dose Q48H **7-11 years:** **30-49:** usual dose **15-29:** usual dose Q48H **< 15:** 6-8 mg/kg Q48H **HD**: usual dose Q48H **PD**: usual dose Q48H **CRRT:** usual dose Q48H **≥ 12 years:** **30-49:** usual dose **15-29:** usual dose Q48H **< 15:** 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
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:** 7.5 mg/kg Q12H **HD:** 7.5 mg/kg Q12H **PD:** 7.5 mg/kg Q12H **CRRT:** usual dose **≥ 13 years**: **30-49**: usual dose **<30**: 500 mg/dose Q24H **HD**: 500 mg/dose Q24H, supplemental dose of 150mg following HD if	Give after HD on HD days **Max single dose:** 500 mg if < 13 years, 1000 mg if ≥ 13 years **Max daily dose:** 1000 mg

		ertapenem daily dose given within 6 hours prior to HD **PD**: 500 mg/dose Q24H **CRRT**: usual dose	
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:** **< 50**: Usual dose q48h (dose reduce to 50% q24h if loading dose give) **HD**: usual dose after each HD session **PD**: 50% of usual dose q24h **CRRT**: usual dose **Other:** **< 50:** Usual dose q48h **HD**: usual dose after each HD session **PD**: 50% of usual dose Q24H **CRRT**: usual dose	Give after HD on HD days **Max dose:** 800 mg (may consider up to 1600 mg)
Flucytosine PO	25 mg/kg/dose Q6H	**30-50**: 25-37.5 mg/kg/dose Q8H **10-29**: 25-37.5 mg/kg/dose Q12H **< 10**: 25-37.5 mg/kg/dose Q24H **HD**: 25-37.5 mg/kg/dose Q24H **PD**: no data	Give after HD on HD days See ANTIFUNGAL GUIDELINE for therapeutic drug monitoring recommendations
Gentamicin IV/IM	7-8 mg/kg/dose Q24H Pharmacy consult	**Renal dose adjustments to be guided by Aminoglycoside CTMP**	**Dosing weight**: if total body weight ≥ 120% of ideal body weight, use obese (adjusted) dosing weight
Isavuconazole* IV/PO (dosing based on isavuconazonium sulfate - total drug) ^Start all maintenance doses 12-24H after the last loading dose	**IV:** **< 3 years:** Loading dose: 15 mg/kg/dose Q8H x 6 doses Maintenance dose: 15 mg/kg/dose Q24H^ **≥ 3 years and < 18 years:** Loading dose: 10 mg/kg/dose Q8H x 6 doses Maintenance dose: 10 mg/kg/dose Q24H^ **≥ 18 years:** Loading dose: 372 mg Q8H x 6 doses Maintenance dose: 372 mg Q24H^ **PO:** **≥ 6 years and < 18 years:** 16 to < 18 kg: 149 mg Q8H x 6 doses followed by 149 mg Q24H^ 18 to < 25 kg: 223.5 mg Q8H x 6 doses followed by 223.5 mg Q24H^ 25 to < 32 kg: 298 mg Q8H x 6 doses followed by 298 mg Q24H^ ≥ 32 kg: 372 mg Q8H x 6 doses followed by 372 mg Q24H^ **≥ 18 years:** 372 mg Q8H x 6 doses followed by 372 mg Q24H^	**None**	Capsules may be opened and mixed with an acidic beverage or soft food; contents may also be mixed with water, saline, or tube feeds for enteral feeding tube administration The IV formulation may be administered PO (within 1 hour of reconstitution) **Max single dose:** 372-744 mg **Max daily dose:** 372-1116 mg Maximum doses may be exceeded based on therapeutic drug monitoring See ANTIFUNGAL GUIDELINE for therapeutic drug monitoring recommendations
Itraconazole PO	**Prophylaxis:** 5 mg/kg/dose Q24H **Treatment (most indications):** 2-5 mg/kg/dose Q12H	**None**	Formulations are not interchangeable. Capsules should be administered immediately after a full meal, ideally high fat, with an acidic

	<u>Cryptococcal meningitis or histoplasmosis</u>: 2.5-5 mg/kg/dose Q8H x 3 days, followed by 2-5 mg/kg/dose Q12H		beverage. The oral solution should be administered on an empty stomach. **Max single dose:** 200 mg Maximum doses may be exceeded based on therapeutic drug monitoring See ANTIFUNGAL GUIDELINE for therapeutic drug monitoring recommendations
Levofloxacin* IV/PO	**< 5 years:** 10 mg/kg/dose Q12H **<u>≥</u> 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**: 10mg/kg Q24H **<u>≥</u> 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	**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 **<u>≥</u> 12 years:** 600 mg/dose Q12H	**None** **Therapeutic drug monitoring suggested; adverse effects more common in patient with impaired renal function**	Give after HD on HD days **Max single dose:** 600 mg **Max daily dose:** 1800 mg
Meropenem* IV	**CNS infections, cystic fibrosis:** 40 mg/kg/dose Q8H **Other:** 20 mg/kg/dose Q8H	**CNS infections, cystic fibrosis:** **26-49**: 40 mg/kg/dose Q12H **10-25**: 20 mg/kg/dose Q12H **< 10**: 20 mg/kg/dose Q24H **HD**: 25 mg/kg/dose Q24H **PD**: 20 mg/kg/dose Q24H **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**: 250 mg/kg/dose Q24H, max 2000mg/dose **PD**: 10 mg/kg/dose Q24H, max 1000mg/dose **CRRT**: 20 mg/kg/dose Q8H	Doses for cystic fibrosis should be administered as a 3-hour infusion Give after HD on HD days **Max single dose:** 2000 mg, - 1000 mg for CrCl ≤25 for CNS infections/cystic fibrosis - 500 mg for CrCl ≤25 for other infections **Max daily dose:** 6000 mg for CNS infections/cystic fibrosis, 3000 mg for other infections
Meropenem-vaborbactam (Dosed based on meropenem component)	**<u>≤</u> 3 months of age:** 20 mg/kg Q8H **> 3 months of age:** 40 mg/kg Q8H	**30 -50:** 50% of usual dose Q8H **15-29:** 50% of usual dose Q12H **< 15:** 25% of usual dose Q12H **HD:** 25% of usual dose Q12H **PD:** 25% of usual dose Q12H **CRRT:** 50% of usual dose Q12H	Give at least one dose after HD on HD days **Max single dose:** 2000 mg of meropenem
Metronidazole IV/PO	10 mg/kg/dose Q8H (10 mg/kg/dose Q12H associated with same clinical efficacy) Alternatively, total daily dose may be divided Q6H	**None**	Evaluate need for further 50% dose reduction if severe hepatic dysfunction present Administer after HD on HD days **Max single dose:** 500 mg (or 1500 mg if giving IV once daily) **Max daily dose:** 1500 mg

	When given IV, the total daily dose may be given Q24H (30 mg/kg/dose Q24H)		
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 **Max single dose:** 2000 mg **Max daily dose:** 12000 mg for CNS/endocarditis/invasive infections
Oseltamivir	**Treatment:** **< 9 months of age:** 3 mg/kg/dose twice daily **≥ 9 months of age:** 3.5 mg/kg/dose twice daily	**≥ 60**: usual dose **30-59:** 50% dose adjustment administered twice daily **10-29:** 50% dose adjustment administered once daily **< 10:** 50% dose adjustment administered every other day	**Max single dose:** 75 mg **Max daily dose:** 150 mg
Penicillin G (Parenteral/ Aqueous) IV/IM	**Caution: doses in units/kg/DAY** **CNS infections:** 300,000 - 400,000 units/kg/**DAY** Q4-6H **Other:** 100,000 -300,000 units/kg/**DAY** Q4-6H	**≥ 50:** usual dose **30-49**: 75% of usual daily dose divided q4-6h **10-29**: 50% of usual daily dose divided Q4-6H **< 10:** 25% of usual daily dose divided Q4-6H **HD**: 150,000 - 200,000 units/kg/**DAY** Q4-6H **PD**: 25% of usual daily dose divided Q4-6H **CRRT:** 75% of total daily dose divided Q4-6H	**Max single dose:** 4 million units (MU), 3 MU for CrCl 10-50, 2 MU for CrCl < 10 **Max 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)	**Cystic fibrosis:** 100 mg/kg/dose Q6H **Other:** 100 mg/kg/dose Q8H	**Cystic fibrosis:** **≥ 40:** usual dose **20 to < 40:** 70 mg/kg/dose Q6H **< 20:** 70 mg/kg/dose Q8H **HD:** 75 mg/kg/dose Q8H **PD:** 75 mg/kg/dose Q8H **CRRT:** usual dose **Other:** **≥40:** usual dose **20 to <40:** 70mg/kg/dose Q8H **<20:** 70mg/kg/dose Q12H **HD**: 75 mg/kg/dose Q12H **PD**: 75 mg/kg/dose Q12H **CRRT:** usual dose	Give after HD on HD days **Max single dose:** 4000 mg for cystic fibrosis, 3000 mg for all other infections **Max daily dose:** 16000 mg
Posaconazole* IV/PO (PO dosing for delayed-release suspension/tablets only)	**IV:** **≥ 2 years to < 18 years:** 6 mg/kg/dose Q12H x 2 doses followed by 6 mg/kg/dose Q24H **≥ 18 years:** 300 mg Q12H x 2 doses followed by 300 mg Q24H	**None**	DR tablets may be crushed; DR tablets and suspension may be given via tube Note: IV posaconazole is non-formulary **Max single dose:** 300-400 mg **Max daily dose:** 800 mg

	PO DR suspension: **≥ 2 years and at least 10 kg:** 10 to < 12 kg: 90 mg Q12H x 2 doses followed by 90 mg Q24H 12 to < 17 kg: 120 mg Q12H x 2 doses followed by 120 mg Q24H 17 to < 21 kg: 150 mg Q12H x 2 doses followed by 150 mg Q24H 21 to < 26 kg: 180 mg Q12H x 2 doses followed by 180 mg Q24H 26 to < 36 kg: 210 mg Q12H x 2 doses followed by 210 mg Q24H 36 to 40 kg: 240 mg Q12H x 2 doses followed by 240 mg Q24H > 40 kg: 300 mg Q12H x 2 doses followed by 300 mg Q24H **PO DR tablets:** 5-7 mg/kg/dose Q12H x 2 doses followed by 5-7 mg/kg/dose Q24H **OR** 15 to 22 kg: 100 mg Q12H x 2 doses followed by 100 mg Q24H > 22 to 40 kg: 200 mg Q12H x 2 doses followed by 200 mg Q24H > 40 kg: 300 mg Q12H x 2 doses followed by 300 mg Q24H		Maximum doses may be exceeded based on therapeutic drug monitoring See ANTIFUNGAL GUIDELINE for therapeutic drug monitoring recommendations
Tobramycin IV/IM	7-8 mg/kg/dose Q24H Pharmacy consult	**Renal dose adjustments to be guided by Aminoglycoside CTMP**	**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**: 3-5 mg/kg/dose Q24H (use Q12H if treating pneumocystic pneumonia) **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 **Max single dose:** 320 mg, 160 mg for CrCl < 50 **Max daily dose:** none
Vancomycin* IV	10-20 mg/kg/dose Q6-8H Pharmacy consult	**Renal dose adjustments to be guided by Vancomycin CTMP**	
Vancomycin PO	10 mg/kg/dose Q6H	**None**	**Max single dose:** 125 mg, 500 mg for severe/fulminant *C. difficile* **Max 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 (max 350mg/dose) **≥ 15 years OR ≥ 12 years and ≥ 50 kg:** Loading dose: 6 mg/kg/dose IV Q12H x 2 doses	**None**	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 Usual maximum doses may be exceeded based on therapeutic drug monitoring **See ANTIFUNGAL GUIDELINE for therapeutic drug monitoring recommendations**

	Maintenance dose: 4 mg/kg/dose IV Q12H PO Maintenance dose: 200mg Q12H		

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

Amoxicillin/Clavulanic acid Concentrations (PEDIATRIC)

- Dosing based on amoxicillin component and indication
- Incorrect amoxicillin:clavulanic acid (a.k.a clavulanate) ratio could result in subtherapeutic clavulanic acid concentrations or severe diarrhea
    - **Pharmacists must ensure the right product is dispensed based on the ordered dose**
- Required clavulanic acid dose:
    - Pediatric patients < 40 kg
        - 3.6 – 10 mg/kg/day clavulanate
    - For patients ≥ 40 kg, follow adult recommendations below
        - Minimum recommended clavulanic acid per dose = 125 mg
        - Maximum daily clavulanic acid per day = 375 mg

Table 1: All Available Amoxicillin/Clavulanic Acid Products Components

Strength	Amoxicillin	Clavulanic acid
Suspension (amoxicillin and clavulanic acid strength per 5mL)		
125 mg / 5mL*	125 mg	31.25mg
200 mg / 5mL*	200 mg	28.5mg
250 mg / 5mL	250 mg	62.5mg
400 mg / 5mL	400 mg	57.0 mg
600 mg / 5mL (ES)	600mg	42.9mg
Tablets		
250 mg*	250 mg	125 mg
500 mg	500 mg	125 mg
875 mg	875 mg	125 mg
200 mg chewable*	200 mg	28.5 mg
400mg chewable*	400 mg	57 mg
1000mg XR*	1000 mg	62.5 mg

*Products currently NOT on formulary

- Examples of wrong product being dispensed and leading to errors:
    - Two 250 mg tablets should **not** be interchanged for one 500 mg tablet → patient will receive double the amount of clavulanic acid
        - 2 x 250 mg tablets = 250mg clavulanic acid
        - 500 mg tablet = 125mg clavulanic acid
    - Same principle applies for the 500 mg tablets → should **not** be interchanged for the 1000 mg tablets
- Pediatric clinical pearls
    - 600 mg/5 mL (ES) formulation should be used if the following two criteria are met:
        - Patients weighs < 40 kg
        - Administering high dose, 80-100 mg amoxicillin/kg/day

Amoxicillin/Clavulanic acid Concentrations (PEDIATRIC)

Table 2: Augmentin Dosing Recommendations (Standard-Dose)

Disease state	Dose	Indication
Skin and Soft Tissue Infection (cellulitis, skin abscess, dog bite, dental infection)	**< 40 kg**: 45 mg/kg/day divided every 8-12 hours Suspension: Use 400 mg-57mg/5 mL formulation **≥ 40 kg and adults**: Tablets: 875 mg every 8-12 hours Suspension: Use 400 mg-57 mg/5 mL formulation875 mg every 8-12 hours	• Coverage of: o Group A *Streptococcus* (*Streptococcus pyogenes*) o MSSA o Various Gram-negatives and anaerobes
Intra-abdominal Infection		• Coverage of: o Gram-negatives o Anaerobes o *Enterococcus faecalis*
Urinary Tract Infection		• Coverage of: o Gram-negatives o *Enterococcus faecalis*

Table 3: Augmentin Dosing Recommendations (High-Dose)

Disease state	Dose	Indication
Otitis Media	**< 40 kg**: 90 mg amoxicillin/kg/day divided every 8-12 hours Suspension (ES-600): Use 600mg-42.9mg/5 mL formulation **≥ 40 kg and adults with BMI < 30**: Tablets: 875 mg every 8 hours Suspension: Use 400-57 mg/5 mL formulation: 875 mg every 8 hours **≥ 40 kg and adults with BMI ≥ 30**: Tablets: High Dose (XR tablets): 2 grams XR* twice daily (interchanged to amoxicillin/clavulanate plus amoxicillin) Suspension (ES-600): Use 600 mg/5 mL suspension: 2000 mg twice daily (16.7 mL twice daily)	• Coverage of: o β-lactamase positive *H. influenzae* o *M. catarrhalis* o *Streptococcus pneumoniae* • Areas with high endemic rates of penicillin-non-susceptible *S. pneumoniae* • Patients who are immunocompromised or if initial therapy fails • Recent β-lactam use in the past month
Rhinosinusitis		
Pneumonia, Preseptal, Periorbital, or Orbital Cellulitis, Neck infections		
Osteomyelitis		• Optimize bone penetration • Coverage of: o Group A *Streptococcus* (*Streptococcus pyogenes*) o MSSA o Salmonella o Kingella

*Must give 2 tablets of the 1000 mg/62.5 mg XR tablets; interchange to amoxicillin/clavulanate plus amoxicillin at OH (see table 5)

Amoxicillin/Clavulanic acid Concentrations (PEDIATRIC)

Table 4: Augmentin –Equivalent Liquid to Tablet Formulations

If changing from liquid to tablets, total dose of clavulanate must remain < 10 mg/kg/day

Amoxicillin/clavulanate Suspension	Amoxicillin/clavulanate Tablet	Ratio (Amoxicillin:Clavulanate)
250 mg/62.5 mg per 5 mL	500 mg/125 mg	4:1
400 mg/57 mg per 5 mL	875 mg/125 mg	7:1
600 mg/42.9 mg per 5mL	1000 mg/62.5 mg XR tablets*	14:1

*Must give 2 tablets/dose for sufficient clavulanate concentration; interchange to amoxicillin/clavulanate plus amoxicillin at OH (see table 5)

Table 5: XR Tablet Interchange at OH

Drug name	Interchange criteria: - Ordered concentration/formulation - Ordered dose	Interchange to:
Amoxicillin/clavulanate	Concentration: 1,000 mg-62.5 mg tablet, extended release (XR) Dose: 2000 mg/125 mg twice daily	Amoxicillin/clavulanate 500 mg/125 mg twice daily PLUS Amoxicillin 1500 mg twice daily (use 500 mg capsules) *Enter as a linked order

References:

1. Lexi comp Online® , Adult, Pediatric, and Neonatal Lexi-Drugs® , Hudson, Ohio: Lexi-Comp, Inc.; October 30, 2018
2. Augmentin ES 600® [package insert]. Dr. Reddy's Laboratories Inc., Briston, TN; 1984. Accessed June 30, 2017.
3. Augmentin® [package insert]. Dr. Reddy's Laboratories Inc., Bridgewater, NJ; 1984. Accessed June 30, 2017.

Prolonged Infusion of Beta-lactams In Pediatric Patients

Table of contents:

Definitions

Term	Definition
Intermittent infusion	Standard infusion times (usually 30 mins to 1 hour)
Extended infusion	Infusion over 3-4 hours
Continuous infusion (CI)	Total daily dose given over 24 hours
Prolonged infusion	Inclusive of both extended and continuous infusion strategies
Breakpoint	Concentration at which determination of susceptible or resistant is made
Minimum inhibitory concentration (MIC)	Lowest concentration of an antibiotic that prevents growth of an organism
Susceptible dose dependent (SDD)	Organism is susceptible to antibiotic at higher and/or more frequent doses or using regimens administered via extended or continuous infusion
Time over MIC ($fT_{>MIC}$)	Percentage of free drug over the MIC in a 24 hour time period
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)

Exclusion criteria for prolonged infusion

- Neonates (<28 days of life)
- NICU patients
- One-time doses (i.e. loading doses)
- Patients with compatibility or line access issues

Extended Infusion

Inclusion criteria

Table 2. Inclusion criteria for extended infusion

Antibiotic	Indication
Piperacillin/tazobactam	All indications
Meropenem	Cystic fibrosis patients
Cefepime	• Critically ill patients ○ Severe sepsis or septic shock • Cystic fibrosis patients • Empiric use for febrile neutropenia patients for initial 24-48 hours pending cultures • Confirmed *Pseudomonas aeruginosa* infections • Empiric use if history of *Pseudomonas aeruginosa* infection within the last year • Isolates with susceptibilities reported as SDD
Ampicillin/sulbactam	Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections

Administration times

Table 3. Extended infusion administration times

Antibiotic	Extended infusion administration time
Ampicillin/sulbactam	3 hours
Cefepime	3 hours
Meropenem	3 hours
Piperacillin/tazobactam	4 hours

- Initial loading doses should be given over 30 minutes.
- Time subsequent doses for 6 hours following initial dose for Q8H regimens and 4 hours following initial dose for Q6H regimens.
- Reload if >1 dosing interval is missed. If a patient is on a susceptible agent and narrowing to another agent, no re-load is necessary. For broadening when the initial agent was not susceptible, re-loading is required.

Refer to APH Systemic Antimicrobial Dosing reference for dosing.

Continuous Infusion

Inclusion criteria for continuous infusion

- Infectious diseases consult only

Table 4. Continuous infusion dosing

Antibiotic	Dose per 24H	Loading dose	Stability
Ampicillin	200 mg/kg	50 mg/kg	8 hours ***Doses should be given every 8 hours administered over 8 hours due to stability***
Cefazolin	150 mg/kg	50 mg/kg	24 hours
Cefepime	150 mg/kg	50 mg/kg	24 hours
Meropenem	120 mg/kg	20-40 mg/kg	8 hours ***Doses should be given every 8 hours administered over 8 hours due to stability***
Nafcillin	200 mg/kg	50 mg/kg	24 hours
Penicillin G (parenteral/ aqueous)	300,000-400,000 units/kg	75,000 units/kg	24 hours
Piperacillin/ tazobactam	300 mg/kg	100 mg/kg	24 hours

Table 5. Continuous infusion loading doses

Scenario	Loading Dose Recommendation
Initiating continuous infusion therapy with no therapeutic prior antibiotics	Give a loading dose
Narrowing to a susceptible agent *E.g. Switching from meropenem intermittent dosing to cefepime continuous infusion for a susceptible P. aeruginosa infection*	The patient is already receiving effective therapy. Additional loading is not required
Broadening after a non-susceptible agent *E.g. Switching from ceftriaxone intermittent dosing to cefepime continuous infusion for a P. aeruginosa infection*	Loading dose of new antimicrobial is recommended to ensure therapeutic drug levels quickly reach the target for effective treatment
Patients being transitioned from intermittent to continuous infusion of the same antimicrobial	Loading dose is recommended if the last intermittent dose was ≥3 hours prior

Compatibility Challenges:

Table 6. Compatibility of Common Intravenous Drugs

	Cefepime	Piperacillin/tazobactam	Meropenem
Epinephrine	C	C	C
Norepinephrine	ND	C	C
Dopamine	CD	C	C
Fentanyl	C	C	C
Midazolam	I	I	CD
Dexmedetomidine	C	C	C
Vancomycin	CD	CD	C
Tacrolimus	I	C	C
Morphine PCA	CD	C	C
Hydromorphone PCA	C	C	C
Naloxone	ND	C	C
TPN (without lipids)	C	C	ND
Intralipid	C	ND	C
SMOFlipid	ND	C	ND
D5W	C	C	C
NS	C	C	CD
½ NS	I	ND	I
LR	CD	C	CD

C: compatible, **I**: incompatible, **ND**: no data available- incompatible, **CD**: concentration dependent

Table 7. Common Scenarios

Scenario	Recommendation
Incompatible medications	For single IV lines: RN should stop continuous infusion, flush the line, administer the incompatible drug, flush the line again, and then restart the continuous infusion. The infusion rate of the continuous infusion will need to be adjusted on the pump to compensate for time the infusion was stopped (inpatient pharmacy may be called for assistance).
Concentration dependent incompatibility	Consult drug information resources or call inpatient pharmacy for assistance
Multiple lumen catheters	Medications can typically be administered through the other lumen at the same time the antibiotic is infusing through a different lumen
Managing interruptions	If > 3 hours interruption per day consider placing an additional line, changing to a multiple lumen line, or administering the drug by intermittent infusion
Excess volume at the end of infusion	Call inpatient pharmacy for assistance

Rationale for Prolonged Infusion

- Prolonging the infusion of beta-lactam antibiotics is an effective strategy to improve pharmacodynamic target attainment and help limit the development of antimicrobial resistance. Beta-lactams including penicillins, cephalosporins, and carbapenems exert time-dependent bactericidal activity, meaning their efficacy depends on maintaining drug concentrations above the minimum inhibitory concentration (MIC) for an adequate portion of the dosing interval. Traditional intermittent infusion regimens may fail to consistently achieve sufficient exposure, particularly when MIC values approach susceptibility breakpoints. Strategies such as prolonged infusion can help overcome elevated MICs and improve outcomes, especially in patient populations with altered pharmacokinetics. Literature for prolonged infusion of beta-lactams suggests it is associated with reduced mortality as well as shorter hospital and ICU stays. Additionally, this approach is considered both cost-effective and safer, as it minimizes peak-related toxicities like nephrotoxicity and neurotoxicity while maximizing the time the drug concentration remains above the MIC.

- Pharmacodynamics
    - For time dependent antibiotics including beta-lactams, their effectiveness depends on how long the free drug level stays above the MIC of the bacteria during a 24 hour period ($fT_{>MIC}$).

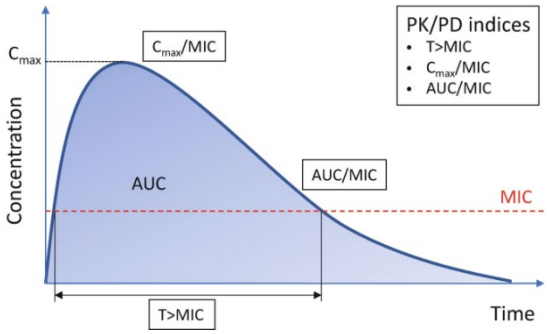


Figure 1.

Table 8. Goal target percentage of free drug over MIC to achieve bacterial killing

Infection type	Target
Mild/moderate infections (i.e., UTI, SSTI, intraabdominal infection with source control)	50-100% $fT_{>MIC}$
Severe infections (i.e., pneumonia, bacteremia, osteomyelitis, endocarditis, CNS infections)	100% $fT_{>4x\ MIC}$

Table 9. Populations that may benefit from prolonged infusion

Indication	Rationale for using prolonged infusion
Critically ill	• Reduction or augmentation of metabolism/clearance • Altered volume of distribution with fluid resuscitation and capillary leak • Changes in protein binding
Pseudomonas aeruginosa infections	• Cause of virulent infections often requiring higher targets of $fT_{>MIC}$ • Can be multi-drug resistant and require optimization of dosing to achieve target $fT_{>MIC}$
Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections	• Multi-drug resistant infection that requires optimization of dosing to achieve target $fT_{>MIC}$
Cystic fibrosis patients	• Frequent infections and multiple courses of antibiotics increase risk of infection with multi-drug resistant organisms, requiring optimization of dosing to achieve $fT_{>MIC}$ • Augmented renal clearance
Febrile neutropenia patients	• Risk of infection with multi-drug resistant organisms, requiring optimization of dosing to achieve $fT_{>MIC}$ • Absent neutrophil mediated bacterial killing
Organisms with susceptibilities reported as SDD	• Extending the infusion for these isolates achieves target $fT_{>MIC}$

- Continuous infusion
    - Continuous infusion beta-lactams have been shown to reduce 90-day mortality in critically ill adults with sepsis when compared to intermittent infusion. They have also been shown to better achieve target $fT_{>MIC}$ in critically ill pediatric patients when compared to intermittent infusion.
    - Advantages of continuous infusion over extended infusion
        - Optimal $fT_{>MIC}$
        - More convenient
        - Less interruptions

***Pseudomonas aeruginosa* MIC Distribution at APH for 2023-2026**

Studies have shown that intermittent dosing likely does not achieve adequate drug exposure for *Pseudomonas aeruginosa* at the breakpoint (MIC of 8 mcg/mL). When evaluating the APH MIC distributions for cefepime for *Pseudomonas aeruginosa*, it was found that nearly 10% of isolates fall at the breakpoint as shown in yellow below.

Table 10. *Pseudomonas aeruginosa* MIC Distribution at APH for 2023-2026

***Pseudomonas aeruginosa* isolates for cefepime, n = 354**		
% of isolates MIC <8 mcg/mL	**% of isolates MIC 8 mcg/mL**	**% of isolates MIC >8 mcg/mL**
85.6	9.8	4.5

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.

Arnold Palmer Hospital Neonatal and Pediatric Meningitis Guideline

Table of Contents

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 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

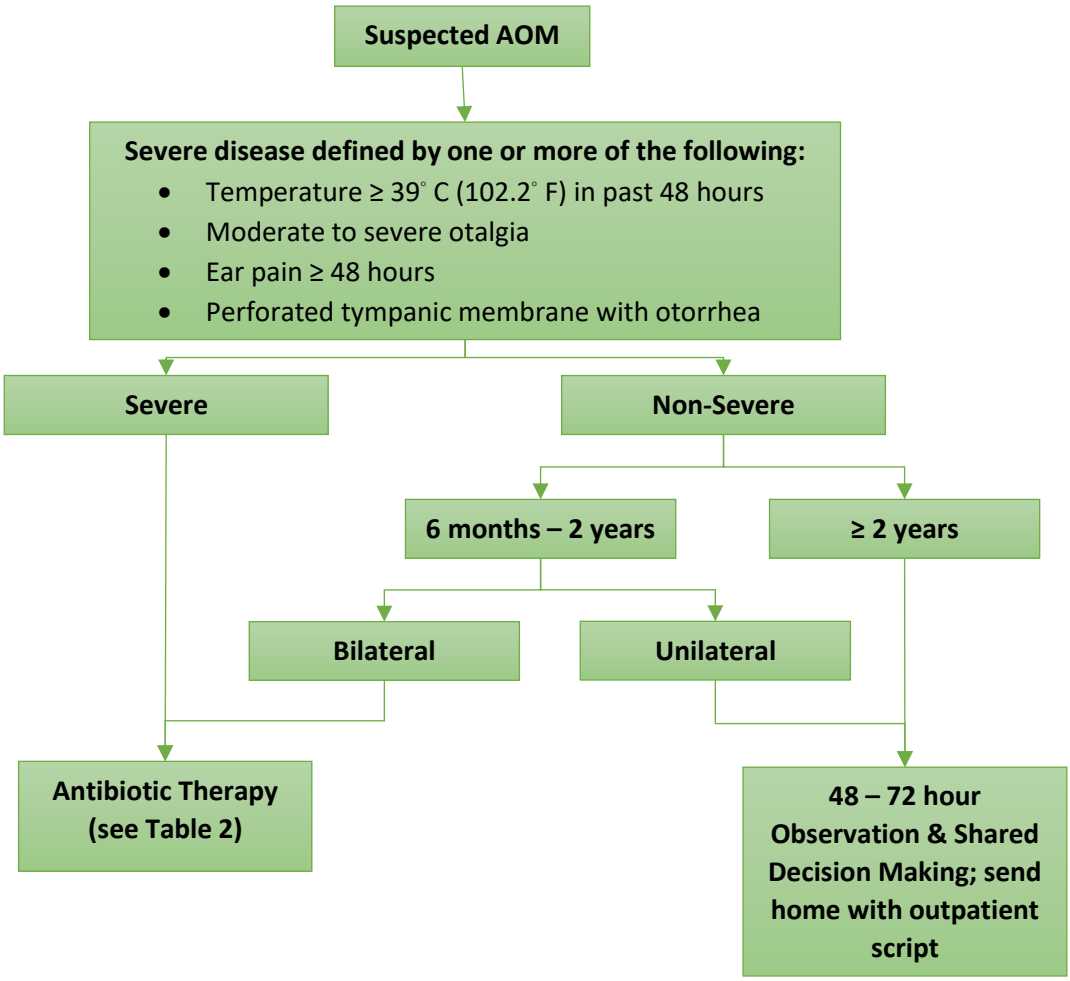
Metronidazole 10 mg/kg/dose q 8h (max 500 mg/dose)

PLUS

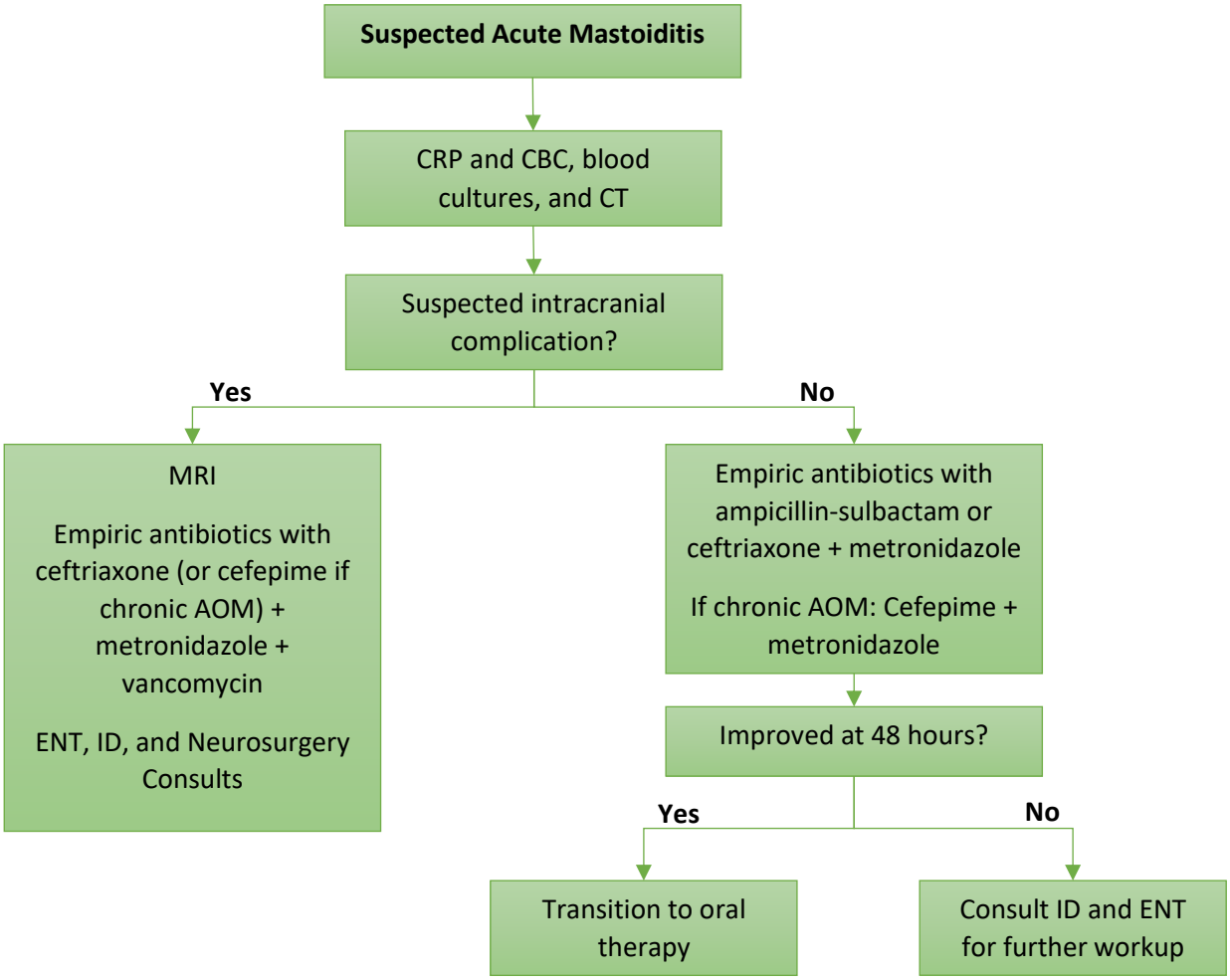
Vancomycin, pharmacy to dose

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 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

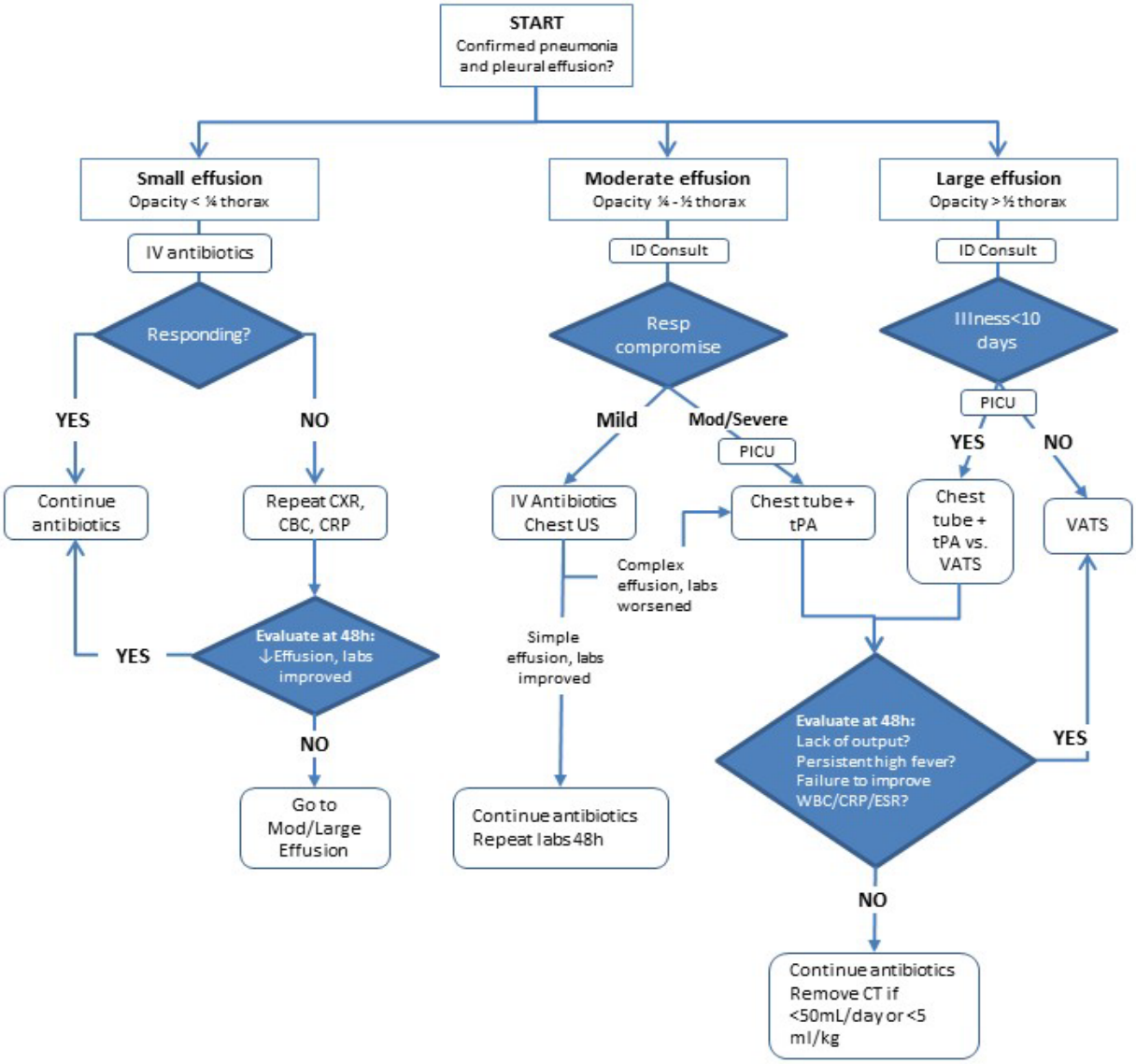
    c. Assess fluid status: patients have increased sensible losses
    d. Diet: NPO if pleural drainage anticipated; assess whether respiratory rate allows for oral intake
    e. Initial Evaluation: Laboratory and Imaging
        i. CBC with differential
        ii. BMP
        iii. Procalcitonin (also 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	

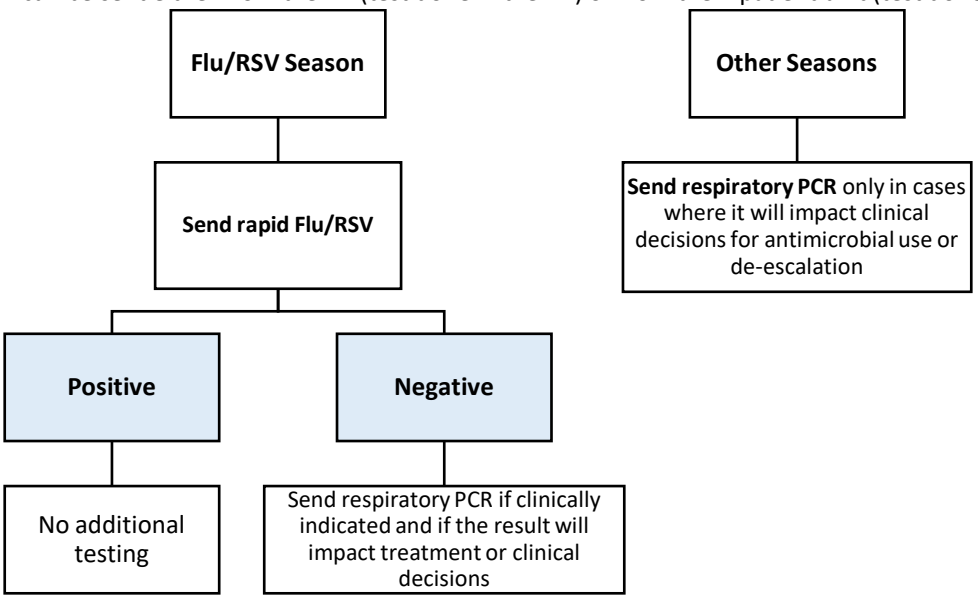
Notes:
For type 1 cephalosporin allergy, consult with ID for antibiotic recommendations
Use of levofloxacin or linezolid requires ID/AMT approval

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)



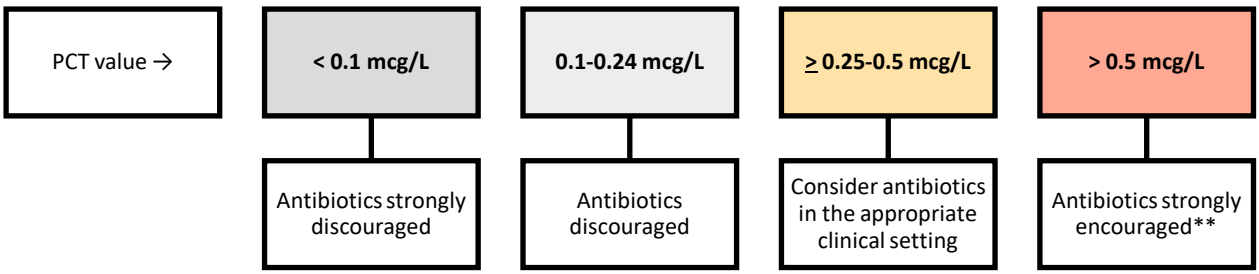
Appendix II: Procalcitonin

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

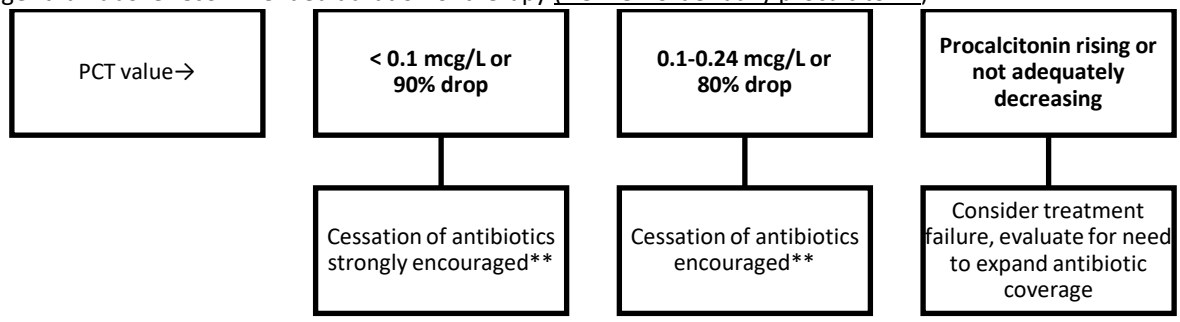
D. PCT results are run in the lab the same day, turnaround time ~30 mins from time it is put on the machine

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 Tracheitis and Ventilator Associated Pneumonia

1. Definitions

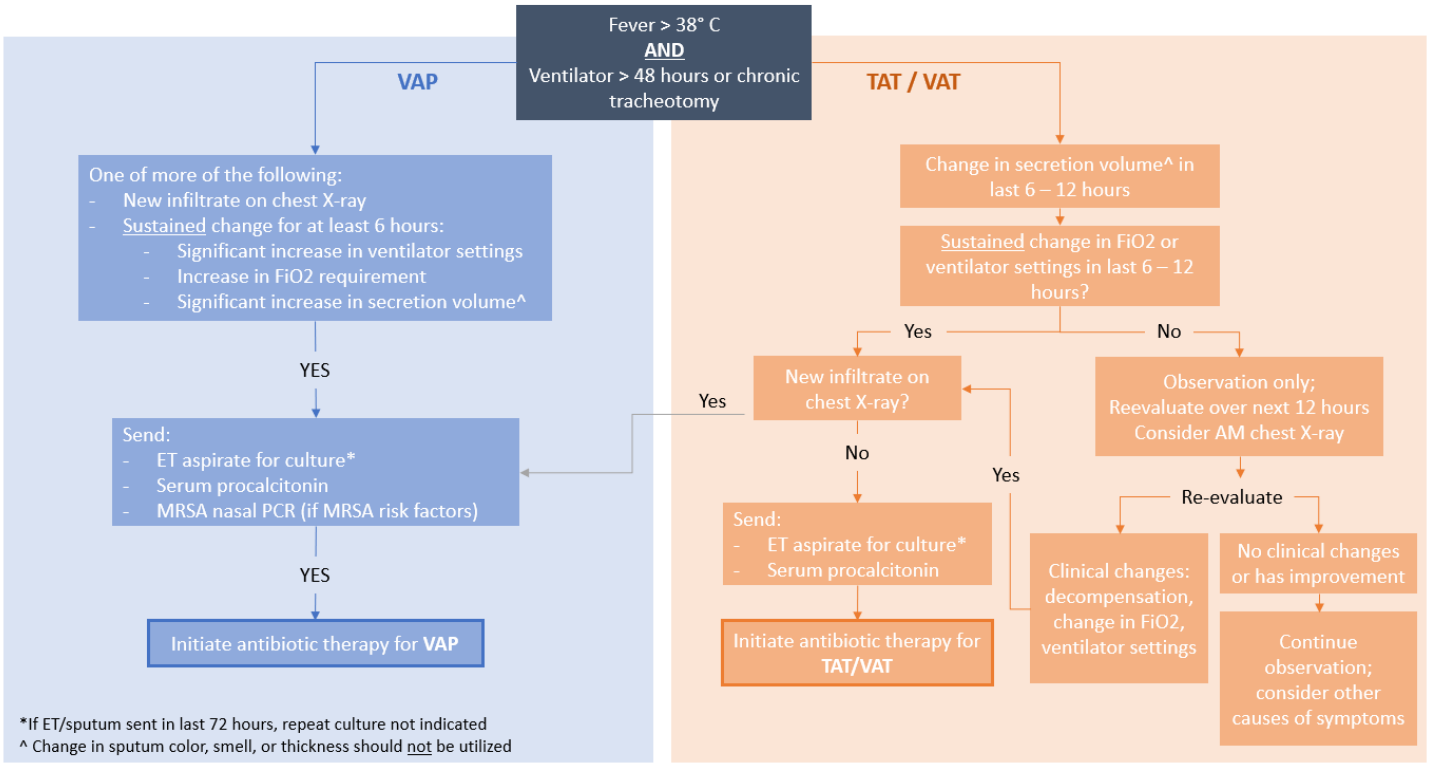
A. Tracheostomy or Ventilator Associated Tracheobronchitis/Tracheitis (TAT/VAT):
   a. Purulent tracheal secretions plus fever and change in respiratory requirements with no other known cause in the absence of new lung infiltrate on chest X-ray in a patient who has a chronic tracheostomy or who has been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

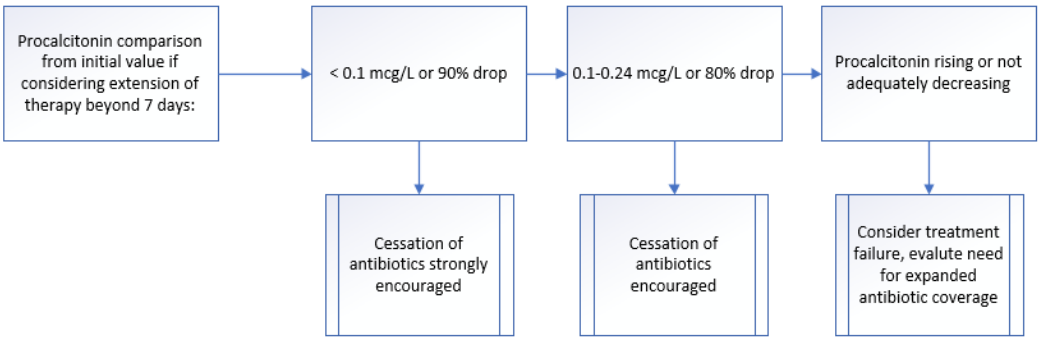


3. Empiric & Definitive Antibiotic Therapy

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 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 →

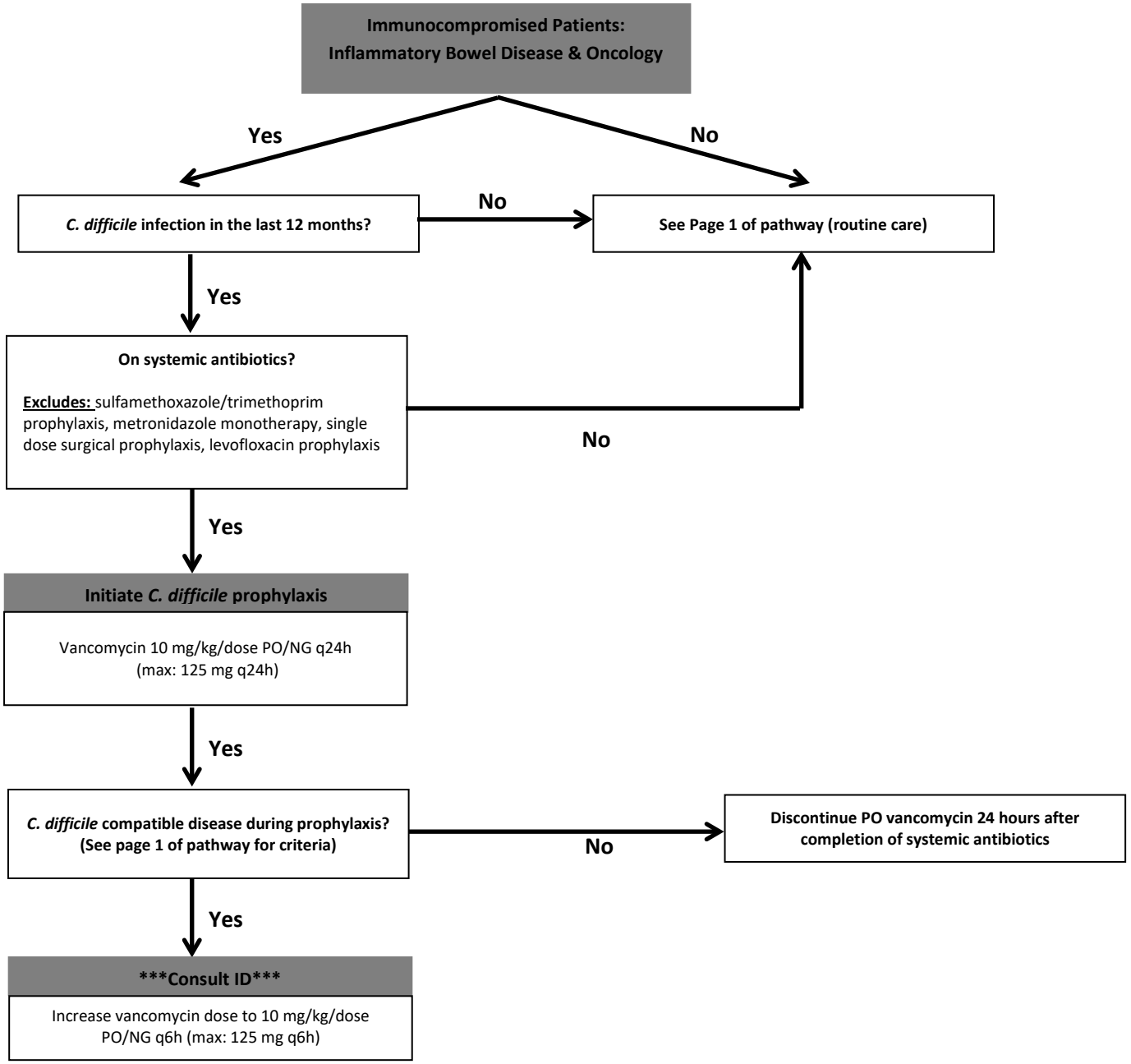
- ***Treat x 10 days***[11]
- Recommendations for secondary prophylaxis[12]

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: Treatment of Pediatric Urinary Tract Infections (UTIs)

Table of contents:

Exclusion criteria: immunocompromised, renal abscess, clinically unstable (septic shock)

Considerations for Admission/ Discharge

Admission	Discharge
Inability to tolerate oral intake (including antibiotics) Toxic/ill appearing Severe dehydration Concerns related to follow-up	Overall clinical improvement Adequate PO intake, including tolerating PO antibiotics Appropriate follow-up • 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

Signs/symptoms of UTI

- 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)

Cystitis	Pyelonephritis	Other signs/symptoms
Urgency Dysuria Frequency	Flank pain/ CVA tenderness Vomiting **Fever** *Fever may persist for several days despite an appropriate antibiotic regimen	Hyper/ hypothermia Diarrhea Abdominal pain Back pain New bed-wetting Poor feeding Lethargy

  - **Foul smelling or cloudy urine without signs/symptoms referring 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

  - **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.

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 above) referable to urinary tract or without explanation of another source • Fever in absence of another source of infection	• Signs (see above) without explanation of another source • Fever in absence of another source of infection

*Toilet trained: daytime dryness without accidents

How to screen

- 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)
- For uncircumcised males, ensure foreskin retraction
- For catheterized patients, remove the foley prior to collection when possible
    - Do not collect sample directly from drainage container
- Cleaning prior to obtaining specimen
    - Cleaning of the skin around the genital area is recommended, especially prior to obtaining a clean catch specimen (toilet trained patients only)

Clean Catch	Catheterized Specimen (or Suprapubic Aspiration)	Urine samples obtained with cotton balls/gauze or via a bagged specimen
Only performed in toilet trained patients (with help of the parent/guardian or nurse if applicable) and the sample should be obtained mid-stream	Only performed in children who do not meet clean catch criteria	Should NOT be used for diagnosis

Urinalysis (UA) and Urine Culture Indications

UA with Culture if Indicated	UA + Urine culture
Standard for all cases	Patient < 6 months of age Indicated for suspected structural abnormalities

Urinalysis (UA) interpretation

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

UA Results	Interpretation/ Recommendation
Patient < 6 months of age, regardless of UA/urine dip results	Possible UTI, send urine culture
Urinalysis: pyuria, nitrites, or bacteriuria present	Possible UTI, send urine culture
Urine dip: ▪ LE positive and nitrite negative – send for microscopy and evaluate as above ▪ Nitrite positive	Possible UTI, send urine culture
Positive leukocyte esterase result	Likely false if no WBCs are present – this should be considered when interpreting the UA
> 10 per high-power field squamous epithelial cells	Contaminated specimen

Urine culture interpretation

Urine Culture Results	Interpretation/ Recommendation
Clean catch (voided), indwelling catheter (Foley), or Suprapubic catheter with 1-2 unique pathogens: ≤24 months: ≥50,000 CFU/mL >2 years: ≥100,000 CFU/mL **+** Positive signs/symptoms (if able to discuss) **+** Positive urinalysis	Positive results based on type of specimen obtained *Must have all 3 (signs/ symptoms, urinalysis, and adequate culture growth)
Multiple pathogens ± presence of yeast	More consistent with contamination • A repeat specimen (prior to antimicrobials) is recommended if true clinical suspicion for UTI
Presence of yeast + signs/symptoms consistent with a vulvovaginal yeast infection	Single dose fluconazole should be considered (or up to three doses for severe or recurrent disease)
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	

Common Bacteria

Common UTI Pathogens	Common Urogenital flora/ Contaminants
• *E. coli* • *K. pneumoniae* • *Proteus spp.* • *S. saprophyticus*	• *Lactobacillus* • *Corynebacterium* • Coagulase-negative *Staphylococci* • *Aerococcus*

Types of UTIs

Definitions of UTIs	
Asymptomatic bacteriuria (ASB)	Bacteria in the urine without signs/symptoms (as above) referable to urinary tract (if able to discuss)
Uncomplicated acute cystitis	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
Complicated UTIs	
Acute pyelonephritis	Infection of the kidneys/ureters resulting in flank pain/CVA tenderness, fever, nausea/vomiting, as well as other symptoms described above
CAUTI	UTI signs/symptoms in a patient with a catheter in place or who was catheterized in the previous 48 hours
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.)	

Empiric/definitive therapy (antimicrobials and duration of treatment)

- Considerations prior to making antibiotic choice
  - Review history of previous microbiology for patients with history of a UTI in the previous 6 months
  - If on UTI prophylaxis, hold this therapy and do not use the same antibiotic for empiric treatment
  - 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
    - If history is consistent with UTI in this setting antibiotics should not be withheld (signs/symptoms referable to urinary tract as above)
- When to use intravenous (IV) versus oral (PO) therapy
  - PO therapy is preferred and considered to be equally as effective as IV therapy
  - IV should be used only in patients unable to tolerate PO

Antibiotic Selection Considerations

Antibiotic	Pearl
Fluoroquinolones *(e.g. ciprofloxacin, levofloxacin)*	Avoid in children unless resistance patterns on susceptibility testing indicate that they are the only option for antibiotic therapy (e.g. treatment for *P. aeurginosa*) • Note: refer to the Restricted Antimicrobials List to determine pre-approved indications
Cefdinir	Do not use due to poor urinary tract penetration Not recommended for complicated UTI due to low blood and kidney concentrations
Nitrofurantoin	Avoid in patients < 1 month of age due to risk of hemolytic anemia Not recommended for complicated UTI due to low blood and kidney concentrations
Fosfomycin	Not recommended for complicated UTI due to low blood and kidney concentrations
Sulfamethoxazole/trimethoprim (SMX/TMP)	Avoid in patients < 2 months of age due to risk of hyperbilirubinemia/kernicterus • Use may be considered after discussion with infectious diseases if benefits outweigh risks
Ceftriaxone	Can be safely used in children < 1 month of age (including those who have not corrected to full term) excluding the following: • Patients with hyperbilirubinemia expected to received > 2 doses • Patients who have received or will receive IV calcium-containing solutions within 48 hours

Asymptomatic bacteriuria (ASB)

- 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
- 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).

Asymptomatic Bacteriuria (ASB) Treatment Recommendations

• Antibiotics are **not** recommended
  ○ 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
  ○ ASB resolves spontaneously
  ○ Exceptions include pregnant patients and patients undergoing endoscopic urologic procedures associated with mucosal bleeding

Uncomplicated Acute Cystitis

- Definitive therapy should be based on documented susceptibilities
- See the Antibiotic Selection Considerations section for restrictions and precautions

Uncomplicated Acute Cystitis Treatment Recommendations			
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~~ 1000 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	25 mg/kg/dose (max 500 mg) Q8H	5 days
	Cefpodoxime	5 mg/kg/dose (max 100 mg) Q12H	5 days
Alternative definitive therapy (once susceptibilities are known)	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
	SMX/TMP	4 mg/kg/dose (max 160 mg, trimethoprim component) Q12H	3 days
	Gentamicin	5 mg/kg	Single dose
	Ciprofloxacin (PO only) ***if 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*** ***MUST obtain susceptibility testing***	3000 mg	Single dose

Complicated UTIs

- Definitive therapy should be based on documented susceptibilities
- See the Antibiotic Selection Considerations section for restrictions and precautions

Complicated UTI Treatment Recommendations			
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)	100 mg/kg/day divided Q6-8H (max 1000 mg per dose)	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	
Alternative empiric therapy	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) Q8H ***administered over 3 hours***	
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	25 mg/kg/dose (max 500-1000 mg) Q6H	
	Cefazolin	25 mg/kg/dose (max 2000 mg) Q8H	
	Cefpodoxime	5 mg/kg/dose (max 200 mg) Q12H	
	Ceftriaxone	50 mg/kg/dose (max 2000 mg) Q24H	
Alternative definitive therapy (once susceptibilities are known)	Ertapenem (ESBL producing organisms only; meropenem if < 3 months of age)	< 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	
	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	

IV to Enteral Inferred Susceptibility

IV Antibiotic	Enteral Antibiotic
Ampicillin	Amoxicillin (cannot infer susceptibility to cephalosporins)
Ampicillin/ sulbactam	Amoxicillin/clavulanate
Cefazolin (MIC <16 for *Enterobacter spp.*)	Cephalexin, cefuroxime, cefpodoxime
Ceftazidime/ Ceftriaxone	N/A (cannot infer susceptibility to 3rd generation oral cephalosporins)
Ciprofloxacin	Ciprofloxacin
Trimethoprim/sulfamethoxazole	Trimethoprim/sulfamethoxazole

Additional management considerations

Antibiotic prophylaxis	• 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. • 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. • Should be considered in patients with proven bowel/bladder dysfunction or VUR especially patients <1 year of age • Should involve consultation with Nephrology OR Urology and should NOT be prescribed without discussion with one of these services
Renal ultrasound	• Should be obtained on all first time pyelonephritis or febrile UTI in patients < 2 years of age • 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

VCUG (voiding cystourethrography)	• Should be obtained based on the following:
	  ○ 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
	  ○ Difficulty in urine flow during hospitalization
	  ○ Family history of VUR

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

Nephrology/urology consultation	• Nephrology consultation should be considered in a patient with recurrent pyelonephritis (>3 in 1 year)
	• 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
	  ○ Also for known history of urologic abnormalities or recent instrumentation
	  ○ Recurrent UTI evaluation (voiding dysfunction)

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

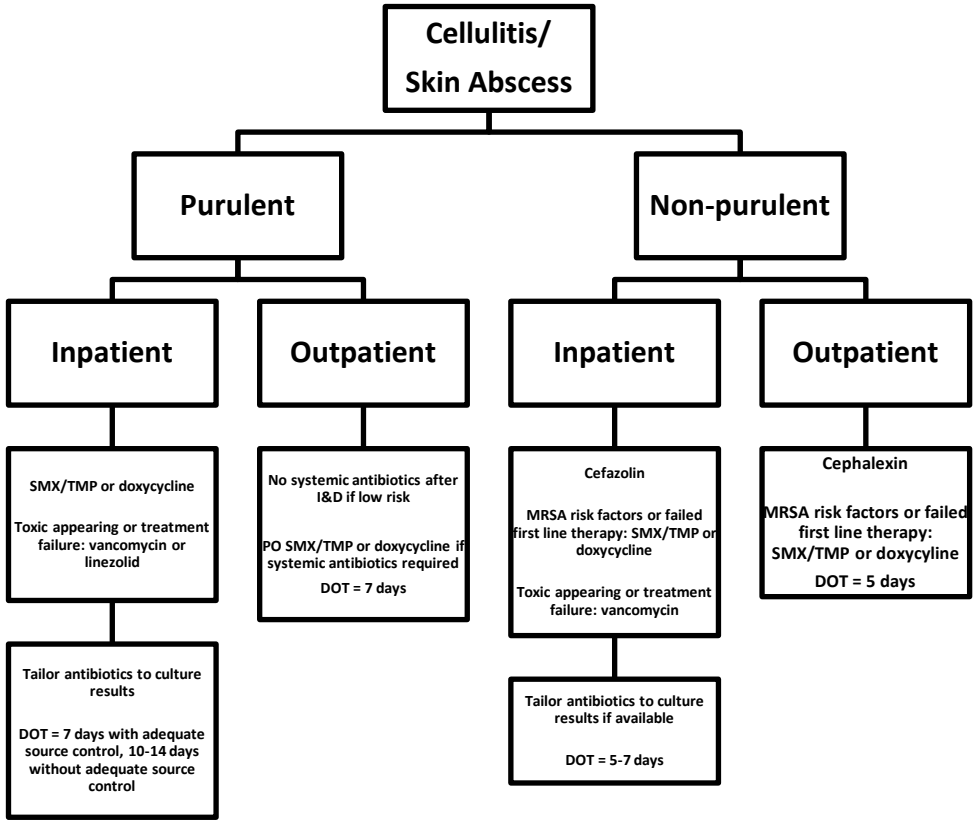
Most common organisms	*Streptococcus pyogenes*, polymicrobial including anaerobes
First line IV therapy	Emergent surgery Suspected or known GAS: IV penicillin 100,000 units/kg/dose (max 4 million units) every 6 hours + IV clindamycin 13 mg/kg/dose (max 900 mg) every 8 hours Unknown cause: Piperacillin/tazobactam 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

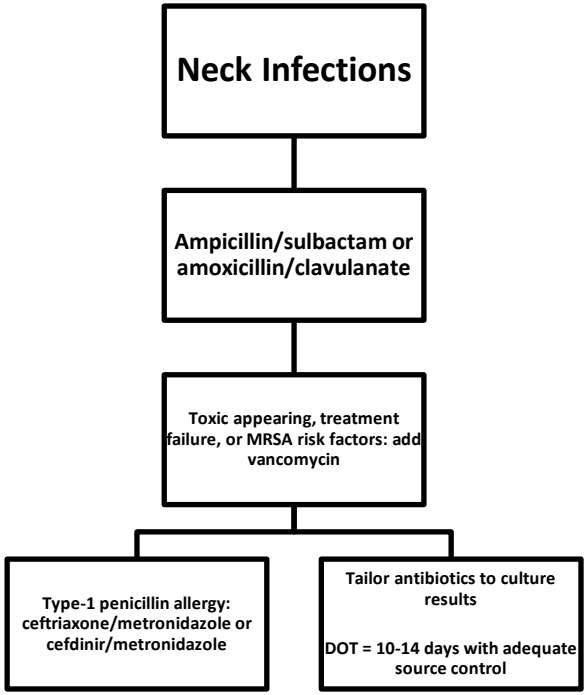
Definitions and Antibiogram

- 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) & Acute Bacterial Arthritis (ABA)

1. Definitions:

Acute hematogenous osteomyelitis (AHO): 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

Acute bacterial arthritis (ABA): Bacterial infection of synovial fluid of a joint, with associated signs of acute inflammation

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 acute bacterial 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
    - Ultrasound
        - Noninvasive imaging study can be used in evaluation of acute bacterial arthritis
    - 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

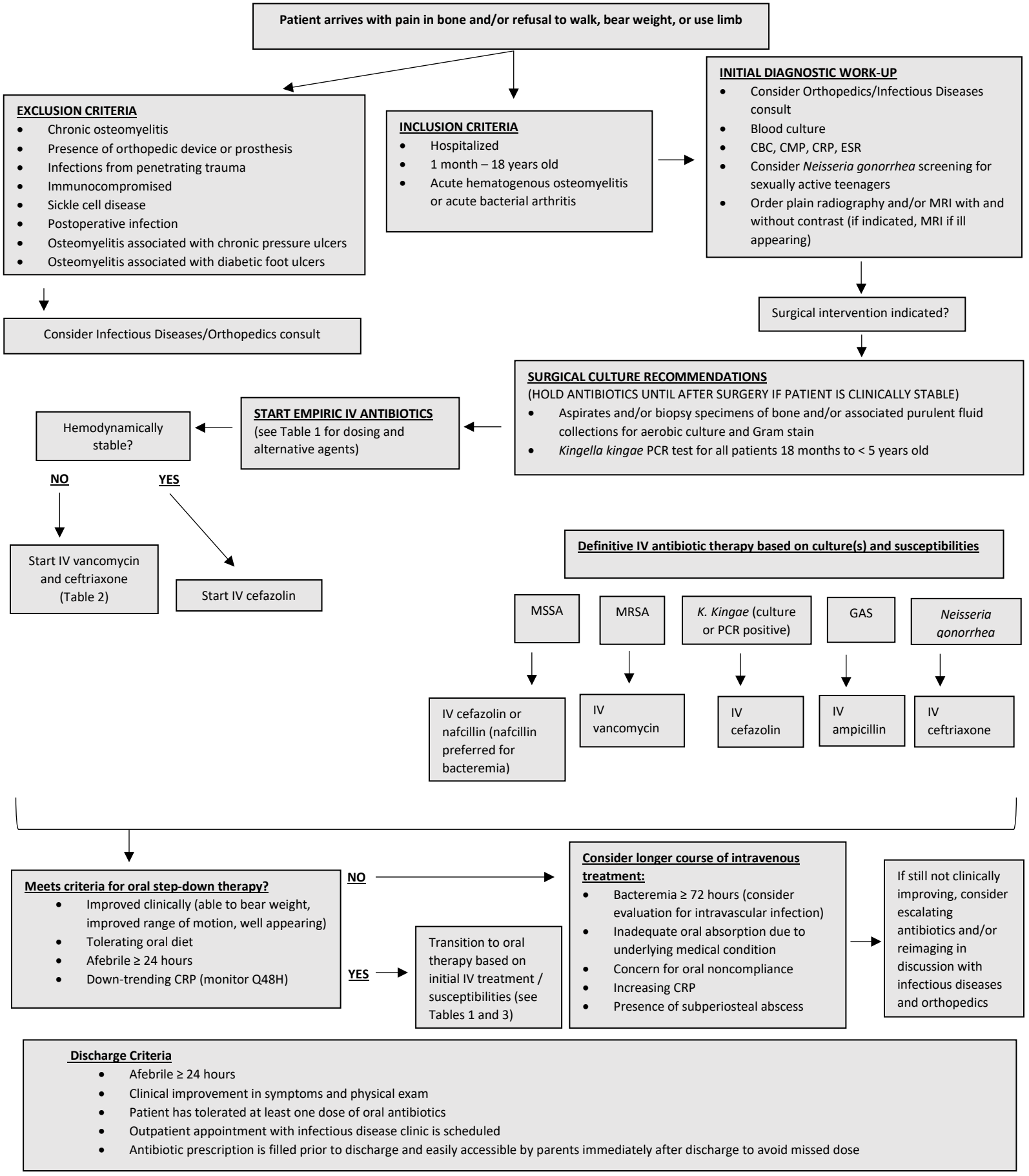


Table 1: Empiric or Culture Negative Antibiotic Therapy Recommendations		
	Intravenous Treatment	**Oral Step-Down Therapy (Culture Negative and Clinically Improving on Empiric Therapy)**
Hemodynamically stable patients **30 days - 4 years old** **Most common pathogens:** *S. aureus* *S. pyogenes* *K. 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 12-20 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 approximately 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
- Acute bacterial 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 acute bacterial arthritis

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 Central Line Associated Infections

Table of Contents

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 for Children: Antimicrobial Management in Acute Chest Syndrome

Definitions

A. Acute Chest Syndrome (ACS): a patient with sickle cell disease (SCD) presenting with new lung infiltrates accompanied by respiratory symptoms (cough, chest pain, respiratory distress, rales) and/or fever, as a result of a vaso-occlusive crisis in the lungs
B. Complicated pneumonia: presence of significant effusion (moderate to large), empyema, severe or impending respiratory failure, and/or signs/symptoms of sepsis or shock
C. Fever: core body temperature ≥ 38.3°C (101°F)
D. Type-1, IgE-mediated allergy: hives, anaphylaxis, bronchospasm, edema
E. Under-immunized: patient who has not received at least 2 Pneumococcal vaccinations
F. Un-immunized: patient who has not received any Pneumococcal vaccinations

Diagnosis – Initial Work-Up

A. CBC with differential, reticulocyte count, type & screen
B. BMP or CMP
C. Chest X-ray, 2-view
    a. Note: radiographic changes may lag behind clinical findings consistent with ACS
D. Procalcitonin
E. Blood cultures x 2
F. Pulse oximetry
G. Sputum culture (if appropriate based on patient age and ability to produce a high-quality specimen)
H. Viral PCR testing
    a. Rapid testing of RSV/influenza/COVID-19 can be performed during the respiratory viral season, without the need for sending the full BIOFIRE respiratory PCR if positive
I. Consider: blood gas

Non-Antimicrobial Considerations

A. Aggressive pain management
B. Lung expansion with incentive spirometry: goal of 10 breaths every 2 hours while awake
    a. Use noninvasive or mechanical ventilation if needed
C. Maintain O2 saturations ≥ 93% or within 3% of the patient's baseline
D. For patients with wheezing or history of asthma/reactive airway disease: follow the Arnold Palmer Hospital asthma order set/algorithm
E. Maintain euvolemia
F. Hgb goal: 9-11 g/dL
G. HbS goal: < 30%
H. Transfer to higher level of care and order a Pulmonology consult for patients with severe respiratory distress and/or concern for rapid deterioration

Empiric Antimicrobial Therapy

A. Empiric antibiotic rationale:
   a. Empiric antimicrobial coverage should include coverage of both Pneumococcus spp. as well as atypical organisms (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*)
   b. Use of narrow spectrum β -lactam therapy is recommended first line (ampicillin or amoxicillin) in combination with atypical coverage
      i. Based on our antibiogram, invasive isolates of Pneumococcus at APH are > 90% susceptible to penicillin
   c. Levofloxacin monotherapy may be used when indicated (AMT approval required)
      i. Levofloxacin has excellent coverage of both Pneumococcus and atypical organisms
   d. Patients with a history of ceftriaxone-induced hemolytic anemia:
      i. Use narrow spectrum β -lactam therapy such as ampicillin or ampicillin/sulbactam in combination with atypical coverage
      ii. Levofloxacin monotherapy may be used as an alternative (AMT approval required)
   e. Use of doxycycline for atypical coverage:
      i. Use for patients with an allergy to or intolerance of azithromycin (i.e. QTc prolongation)
      ii. May be used in any patient regardless of age

B. Empiric Antimicrobials (refer to the APH Antimicrobial Dosing Card for empiric dosing)

Treatment scenarios	Antimicrobial of choice
First line empiric therapy	Ampicillin OR Amoxicillin + Azithromycin OR Doxycycline
Second line empiric therapy Use for patients with exposure to/failure of <u>high dose</u> amoxicillin in previous 30 days and for patients who are under-immunized	Ampicillin/sulbactam OR Amoxicillin/clavulanate + Azithromycin OR Doxycycline
Third line empiric therapy Use for patients with type-1 penicillin allergy or who are un-immunized	Ceftriaxone + Azithromycin OR Doxycycline
Empiric therapy for patients with a type-1 penicillin and cephalosporin allergy or history of ceftriaxone-induced hemolytic anemia and inability to use first line therapy above	Levofloxacin **monotherapy** (AMT approval required)
Influenza positive respiratory PCR Consider adding to the empiric regimen chosen above if presenting within 3 days of symptom onset	Oseltamivir
Complicated pneumonia	Refer to the "Management of Community Acquired Pneumonia – Complicated CAP" guideline

Note: **Hold home antibiotic prophylaxis while on systemic antimicrobials**

Duration of Therapy

A. Total duration of antimicrobial therapy is dependent on agent:
    a. β -lactam therapy: 5-7 days
    b. Atypical therapy:
        i. Azithromycin: 3-5 days dependent on dosing (3-day regimen preferred)
        ii. Doxycycline: 5 days
    c. Levofloxacin: 5 days
    d. Oseltamivir: 5 days

De-escalation of Empiric Antimicrobial Therapy

A. Streamlining
    a. De-escalate based on sputum culture results/susceptibilities if applicable
    b. If respiratory PCR is negative for atypical pathogens, consider discontinuation of atypical coverage (for patients on dual β -lactam + atypical therapy)
        i. The BioFire® FilmArray Respiratory PCR Panel has high sensitivity and specificity for *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*

BioFire® FilmArray Respiratory PCR Panel Sensitivity/Specificity for Atypical Pathogens	
Sensitivity	97.1%
Specificity	99.3%

B. IV to PO stepdown
    a. Criteria: afebrile for at least 24 hours with improved clinical presentation
    b. Suggested oral stepdown options are outlined below based on initial empiric therapy used

Empiric antimicrobial	**Oral stepdown recommended**
Ampicillin	Amoxicillin
Ampicillin/sulbactam	Amoxicillin/clavulanate
Ceftriaxone	Amoxicillin/clavulanate Type-1 penicillin allergy: cefpodoxime 5 mg/kg/dose PO every 12 hours; maximum 200 mg/dose
Azithromycin, levofloxacin, and doxycycline	Same agent, 1:1 conversion

Discharge Criteria

A. Afebrile at least 24 hours
B. Clinical status improved
C. Return to baseline O2 saturations
D. Able to take PO antibiotics
E. Stable Hgb for 24 hours
F. Adequate pain control
G. Adequate oral intake

Appendix I: ACS Prevention

A. Incentive spirometry during hospitalization: goal of 10 breaths every 2 hours while awake

B. Antibiotic prophylaxis

   a. Due to functional asplenia, sickle cell patients should be initiated on antibiotic prophylaxis at diagnosis to prevent invasive Pneumococcal infections

   b. Antibiotic prophylaxis should be discontinued after 5 years of age in children who have not experienced invasive pneumococcal infection and have received all recommended pneumococcal immunizations

   c. Antibiotic options include penicillin VK (drug of choice) or amoxicillin PO, or ampicillin IV if unable to give oral therapy (NPO)

      i. Patients with a type-1 penicillin allergy may receive erythromycin for prophylaxis.

         1. Note: Erythromycin is less effective at preventing invasive diseases due to higher rates of Pneumococcal resistance. Consider allergy testing and/or penicillin desensitization.

   d. Hold home antibiotic prophylaxis while on systemic antimicrobials

Patient Age	**Antibiotic Prophylaxis Regimen**
Penicillin VK	
Infants and children < 3 years of age	125 mg PO twice daily
Children ≥ 3 years of age	250 mg PO twice daily
Amoxicillin	
Infants and children ≤ 5 years of age	10 mg/kg/dose PO twice daily, max dose 125 mg *May give once daily if need for compliance
Children > 5 years of age	250 mg PO twice daily
Ampicillin IV (NPO)	
All ages	25 mg/kg/dose IV twice daily, max dose 1,000 mg
Erythromycin, Base or EES (Type 1 Penicillin Allergy)	
Infants and children 4 months to < 3 years of age	125 mg PO twice daily
Children ≥ 3 years of age	250 mg PO twice daily
Azithromycin (Type 1 Penicillin Allergy and NPO)	
All ages	5 mg/kg IV once daily, max dose 250 mg

C. Vaccinations

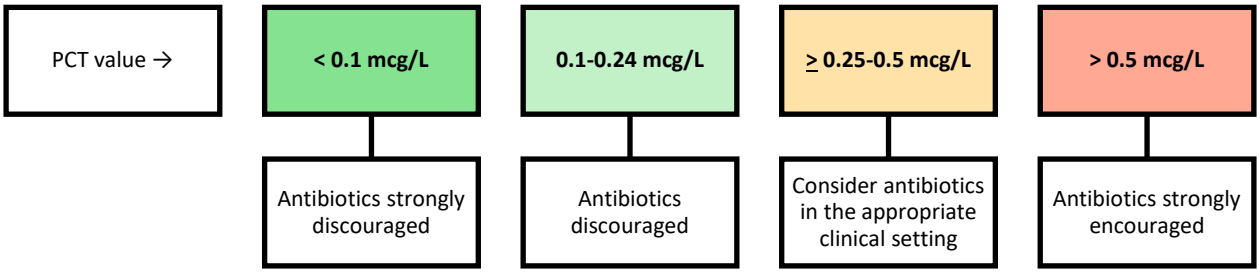
   a. Administration of age-appropriate vaccination is a cornerstone to prevention of infection

   b. Refer to the current CDC immunization schedule for recommendations on receipt of the following vaccines, including special considerations for those with asplenia:

      i. Pneumococcal (PCV15, PCV20, PCV21, and PPSV23)
      ii. Respiratory syncytial virus (RSV)
      iii. Haemophilus influenzae tybe b (Hib)
      iv. Meningococcal (MenACWY and MenB)
      v. Influenza
      vi. COVID-19

Appendix II: Procalcitonin (PCT)

A. Data is limited in children with SCD due to a lack of high-quality studies
B. Other respiratory infections like community-acquired pneumonia (CAP) and adult studies of procalcitonin in SCD suggest a benefit to using procalcitonin-guided therapy
C. PCT should not be used alone for clinical decision-making
D. PCT may be falsely elevated in patients with renal dysfunction, surgical trauma, cardiopulmonary bypass, cardiac arrest, intracranial hemorrhage, and burns
E. Recommendations:
    a. PCT values < 0.25 are suggestive of a non-bacterial diagnosis/cause of ACS
    b. Consider repeating PCT in 6-12 hours if antibiotics are not started and the patient has no clinical improvement



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

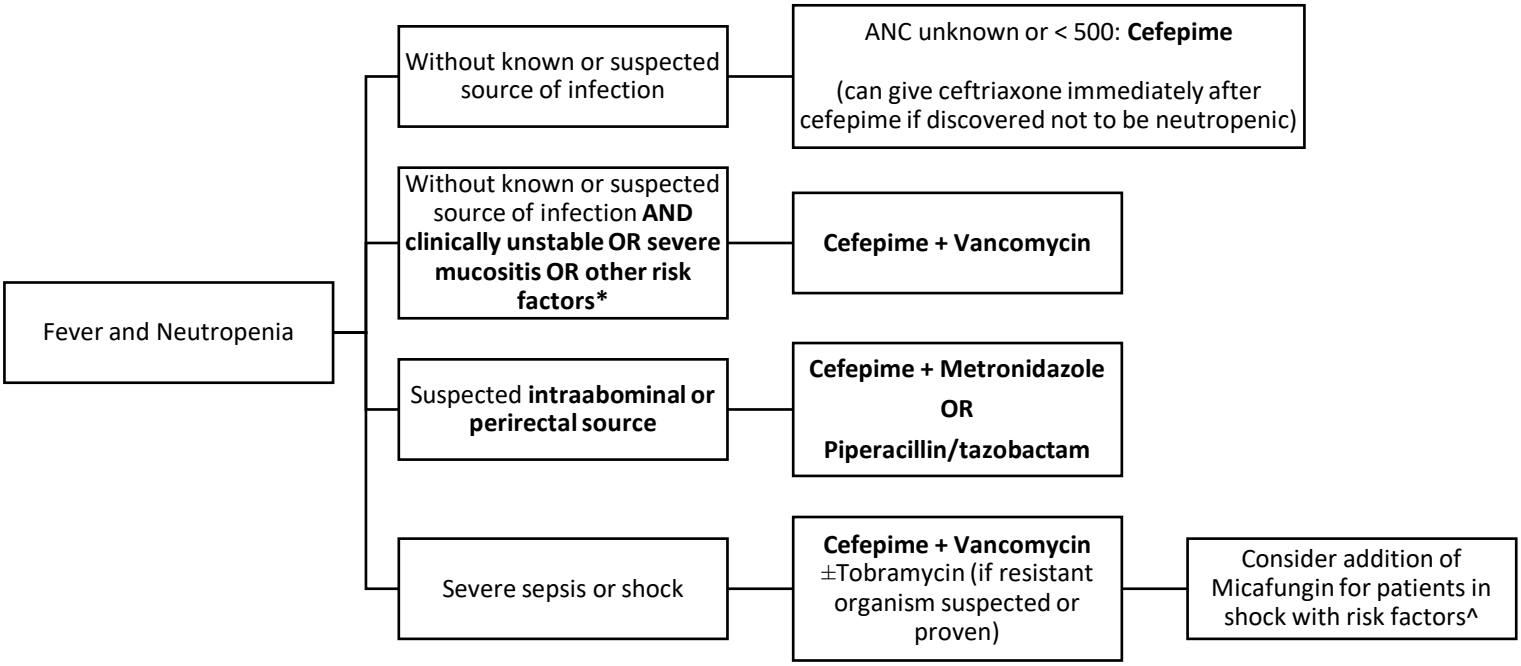
ii. LFTs > 5x ULN or known liver failure

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^:

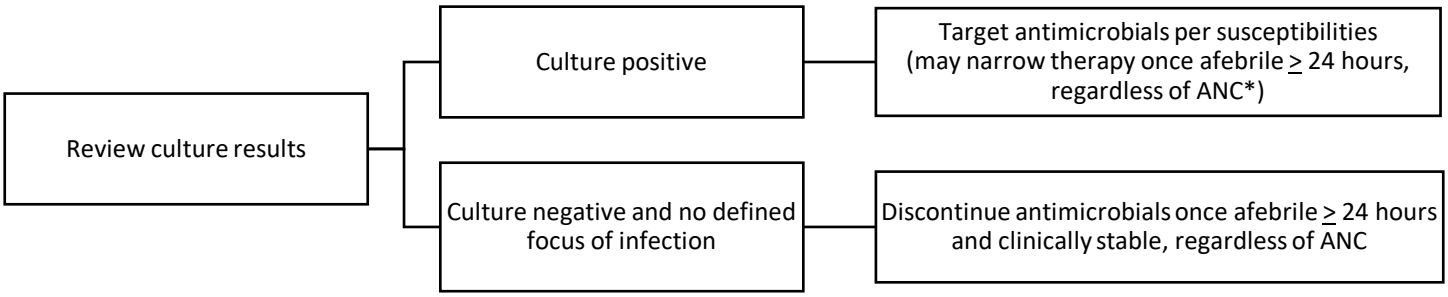
1. Exposure to broad-spectrum antibiotics for more than 7 days in last 2 weeks, recent major abdominal surgery, necrotizing pancreatitis, gastrointestinal perforation, steroid use in last 2 weeks including high doses (prednisone 2 mg/kg/day or a total dose of 20 mg/day or its equivalent) or prolonged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

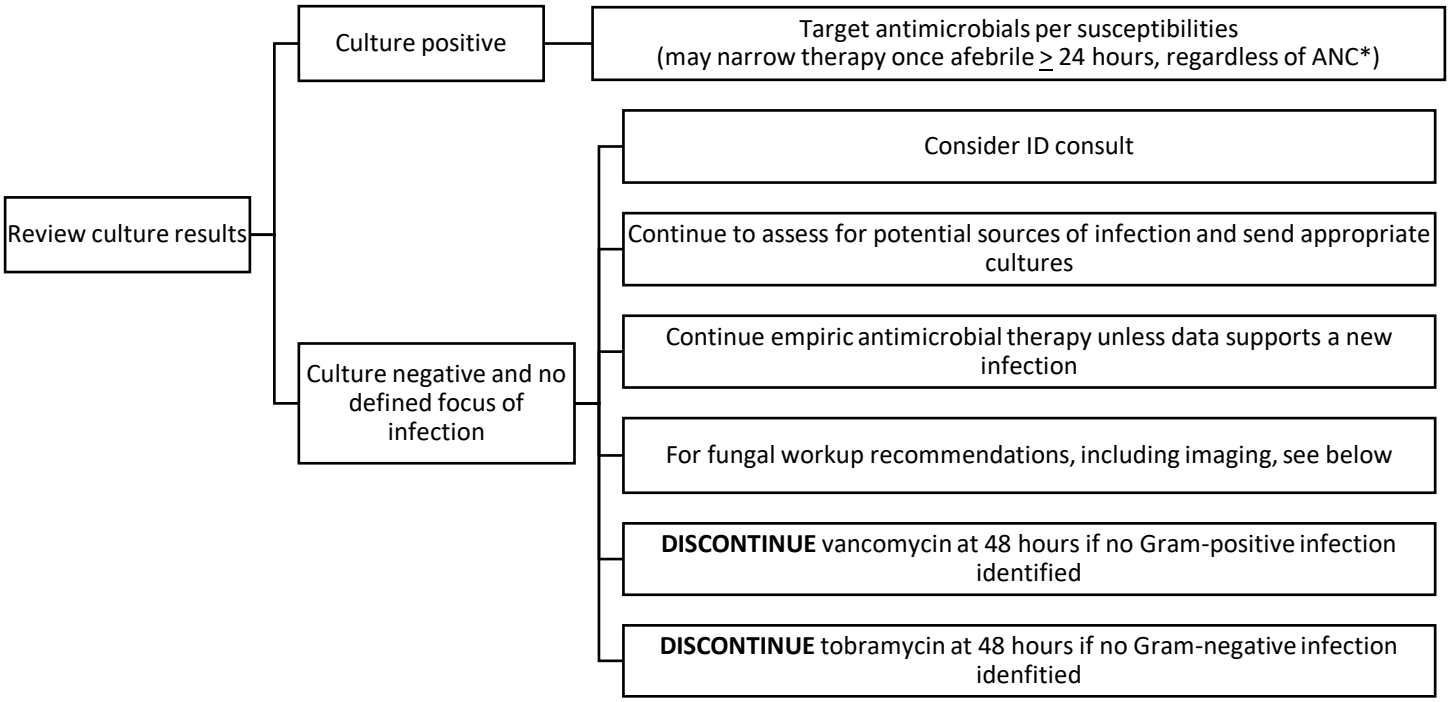
Reassessment of Antimicrobial Therapy for Febrile Neutropenia

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

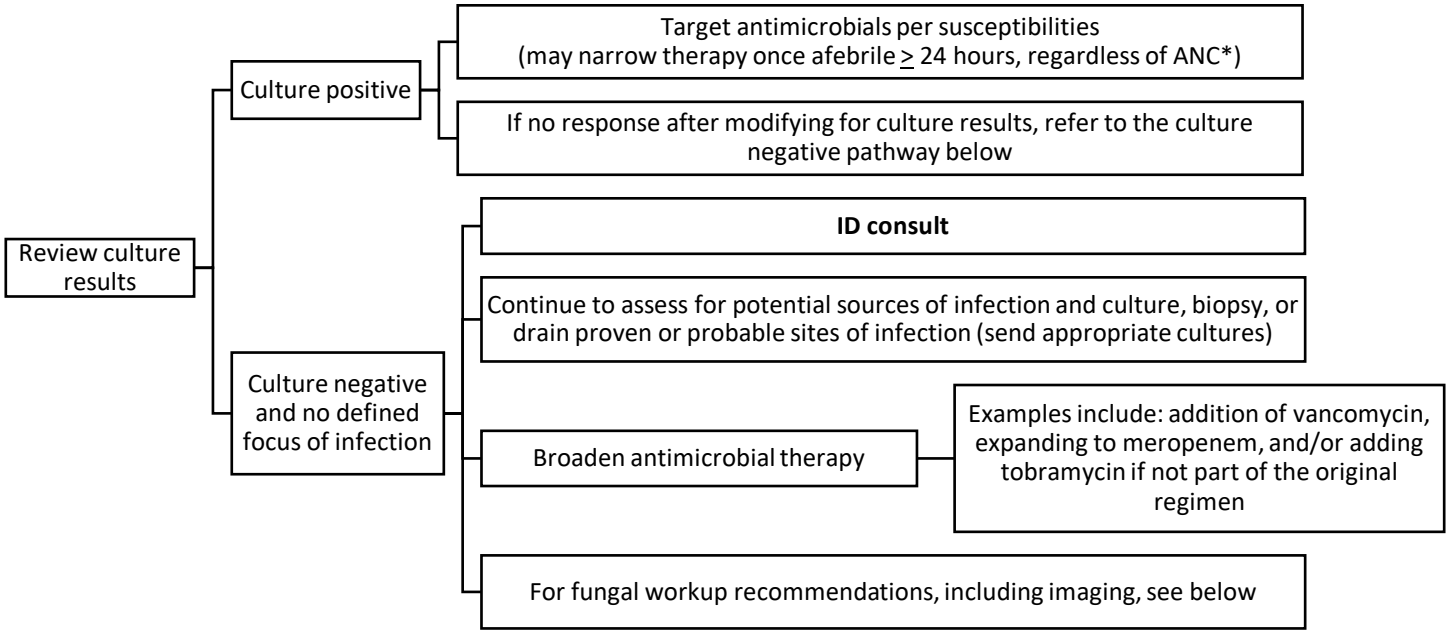
Clinical response – defervesced



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 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

Orlando Health Pediatric/Neonatal Peri-operative Antibiotic Prophylaxis Guideline

	Cefazolin	Clindamycin	Ampicillin/ Sulbactam	Gentamicin	Metronidazole	Piperacillin/ tazobactam	Vancomycin
Initial Dose Pediatric	30 mg/kg[3,4]	10 mg/kg	50 mg/kg	2.5 mg/kg[1]	10 mg/kg[2]	Infants 2-9 months: 80 mg/kg piperacillin > 9 months: 100 mg/kg piperacillin	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: 5 mg/kg Post-op: 7.5 mg/kg	80 mg/kg piperacillin	10 mg/kg
Max Dose	<120kg: 2000 mg >120kg: 3000 mg	900 mg	3000 mg amp	N/A	500 mg	3000 mg (piperacillin component)	2000 mg
Administration	3-5 min IV Push	30 min infusion	30 min infusion	30 min infusion	10 min infusion	30 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 minutes	Within 60-120 minutes
Minimum % of dose that should be administered prior to incision	100	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	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	Q2H	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]Type 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

[4]For some neurosurgical procedures: 30 mg/kg bolus, followed by 10 mg/kg/hour (max 500 mg/hr) for the duration of the procedure/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
Type I and II open bone fracture prophylaxis	Cefazolin	Clindamycin **OR** Vancomycin
Type III open bone fracture prophylaxis	Piperacillin/tazobactam **OR** Ceftriaxone^ (monotherapy)	Clindamycin **WITH** 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

^Ceftriaxone 50 mg/kg/dose; Q24H frequency when redosing is necessary

References

Prolonged Infusion of Beta-lactams In Pediatric Patients

1. Yu Y, Rüppel D, Weber W, Derendorf H. PK/PD Approaches. Drug Discovery and Evaluation: Methods in Clinical Pharmacology. Published online 2019:1-23.
2. MacVane SH, Kuti JL, Nicolau DP. Prolonging β-lactam infusion: a review of the rationale and evidence, and guidance for implementation. Int J Antimicrob Agents. 2014;43(2):105-113.
3. Onufrak NJ, Forrest A, Gonzalez D. Pharmacokinetic and Pharmacodynamic Principles of Anti-infective Dosing. Clin Ther. 2016;38(9):1930-1947.
4. Zembles TN, Kuhn EM, Thompson NE, Mitchell ML. Extended Infusion β-Lactams for the Treatment of Gram-Negative Bacteremia in Children. The journal of pediatric pharmacology and therapeutics. 2022;27(7):677-681.
5. Hong L, Downes KJ, FakhriRavari A, et al. International consensus recommendations for the use of prolonged-infusion beta-lactam antibiotics: Endorsed by the American College of Clinical Pharmacy, British Society for Antimicrobial Chemotherapy, Cystic Fibrosis Foundation, European Society of Clinical Microbiology and Infectious Diseases, Infectious Diseases Society of America, Society of Critical Care Medicine, and Society of Infectious Diseases Pharmacists. Pharmacotherapy. 2023;43(8):740-777.
6. Prescott HC, Antonelli M, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026. Crit Care Med. Published online March 23, 2026.
7. Flume PA, Mogayzel PJ, Robinson KA, et al. Cystic Fibrosis Pulmonary Guidelines. American Journal of Respiratory and Critical Care Medicine. 2009;180(9):802-808. doi:https://doi.org/10.1164/rccm.200812-1845pp
8. Imburgia TA, Kussin ML. A Review of Extended and Continuous Infusion Beta-Lactams in Pediatric Patients. 2022;27(3):214-227.
9. Briand A, Bernier L, Pincivy A, et al. Prolonged Beta-lactam Infusions in Children: A Systematic Review and Meta-analysis. The Journal of Pediatrics. 2024;275:114220-114220.
10. Burch AR, von Arx L, Hasse B, Neumeier V. Extended Infusion of Beta-Lactams and Glycopeptides: A New Era in Pediatric Care? A Systematic Review and Meta-Analysis. Antibiotics. 2024;13(2):164.
11. Kinga Anna Budai, Ágnes Eszter Tímár, Mahmoud Obeidat, et al. Extended infusion of β-lactams significantly reduces mortality and enhances microbiological eradication in paediatric patients: a systematic review and meta-analysis. EClinicalMedicine. 2023;65:102293-102293.
12. Dulhunty JM, Brett SJ, De Waele JJ, et al. Continuous vs Intermittent β-Lactam Antibiotic Infusions in Critically Ill Patients With Sepsis: The BLING III Randomized Clinical Trial. JAMA. 2024;332(8).
13. Debray A, Callot D, Hirt D, et al. Beta-lactam exposure and safety in intermittent or continuous infusion in critically ill children: an observational monocenter study. European Journal of Pediatrics. 2022;182(3):965-973.
14. Ragonnet G, Guilhaumou R, Hanafia O, et al. Continuous infusion of beta-lactam antibiotics in pediatric intensive care unit: A monocenter before/after implementation study. Anaesthesia, critical care & pain medicine. 2024;43(3):101354.
15. Lockowitz CR, Hsu AJ, Chiotos K, et al. Suggested Dosing of Select Beta-lactam Agents for the Treatment of Antimicrobial-Resistant Gram-Negative Infections in Children. *Journal of the Pediatric Infectious Diseases Society*. 2025;14(2).
16. Mirjalili M, Zand F, Karimzadeh I, et al. The clinical and paraclinical effectiveness of four-hour infusion vs. half-hour infusion of high-dose ampicillin-sulbactam in treatment of critically ill patients with sepsis or septic shock: An assessor-blinded randomized clinical trial. Journal of Critical Care. 2023;73:154170.

Antimicrobial Duration of Therapy for Common Pediatric Infections

1. Bachur R, Harper MB. Reevaluation of outpatients with Streptococcus pneumoniae bacteremia. *Pediatrics*. 2000;105(3 Pt 1):502-509.
2. Baddour LM, et al. Infection endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. *Circulation*. 2015; 132(15):1435-1486.
3. Baltimore RS, et al. Infective endocarditis in childhood: 2015 update. *Circulation*. 2015; 132(15):1487-1515.
4. Bamberger DM, Boyd SE. Management of staphylococcus aureus infections. *Am Fam Physician*. 2005; 72(12):2474-2481.
5. Boulos JM, Fabre V, Dzintars K, et al. 195. Duration of Therapy for Streptococcal Bacteremia. *Open Forum Infect Dis*. 2021;8(Suppl 1):S205. Published 2021 Dec 4. doi:10.1093/ofid/ofab466.397
6. Bradley JS, et al. Nelson's Pediatric Antimicrobial Therapy. 24th ed. American Academy of Pediatrics. 2018.
7. Desai AA, et al. Safety of a new protocol decreasing antibiotic utilization after laparoscopic appendectomy for perforated appendicitis in children: a prospective observational study. *J Pediatr Surg*. 2015; 50(6):912-914.
8. Falagas ME, et al. Effectiveness and safety of short vs. long duration of antibiotic therapy for acute bacterial sinusitis: a meta-analysis of randomized trials. *Br J Clin Pharmacol*. 2009; 67(2):161-171.
9. Fraser JD, et al. A complete course of intravenous antibiotics vs a combination of intravenous and oral antibiotics for perforated appendicitis in children: a prospective, randomized trial. *J Pediatr Surg*. 2010; 45(6):1198-1202.
10. Kimberlin DW, et al. Red Book: 2018 Report of the Committee on Infectious Diseases. American Academy of Pediatrics. 2018.
11. Osmon DR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2013; 56(1):1-25.
12. Poon SHT, et al. The current management of acute uncomplicated appendicitis: should there be a change in paradigm? A systematic review of the literatures and analysis of treatment performance. *World J Emerg Surg*. 2017; 12:46.
13. Shane AL, Mody RK, Crump JA, et al. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. *Clin Infect Dis*. 2017;65(12):e45-e80.
14. Shulman ST, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012; 55(10):86-102.
15. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. *Clin Microbiol Rev*. 2014;27(1):21-47.
16. Solomkin JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2010; 50(2):133-164.
17. Tunkel AR, et al. 2017 Infectious Diseases Society of America's clinical practice guidelines for healthcare-associated ventriculitis and meningitis. *Clin Infect Dis*. 2017; 64(6):34-65.
18. Van Rossem CC, et al. Duration of antibiotic treatment after appendicectomy for acute complicated appendicitis. *Br J Surg*. 2014; 101(6):715-719.
19. Wald ER, et al. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. *Pediatrics*. 2013; 132(1):262-280.
20. Warady BA, Bakkaloglu S, Newland J, et al. Consensus guidelines for the prevention and treatment of catheter-related infections and peritonitis in pediatric patients receiving peritoneal dialysis: 2012 update. *Perit Dial Int*. 2012;32 Suppl 2(Suppl 2):S32-S86.
21. Yahav D, et al. Seven versus fourteen days of antibiotic therapy for uncomplicated gram-negative bacteremia: a non-inferiority randomized controlled trial. *Clin Infect Dis*. 2018. doi: 10.1093/cid/ciy1054. [Epub ahead of print].

Meningitis

1. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice Guidelines for the Management of Bacterial Meningitis. *Clin Infect Dis*. 2004;39:1267-84.
2. American Academy of Pediatrics: Committee on Infectious Diseases. Dexamethasone Therapy for Bacterial Meningitis in Infants and Children. *Pediatrics*. 1990;86(1):130-33.
3. Fox J. In children with bacterial meningitis, does the addition of dexamethasone to an antibiotic treatment regimen result in a better clinical outcome than the antibiotic regimen alone? Part A: Evidence-based answer and summary. *Paediatr Child Health*. 2006;11(1):33-34.
4. Kanegaye JT, Soliemanzadeh P, & Bradley JS. Lumbar Puncture in Pediatric Bacterial Meningitis: Defining the Time Interval for Recovery of Cerebrospinal Fluid Pathogens After Parenteral Antibiotic Pretreatment. *Pediatrics*. 2001;108:1169-74.
5. Swanson D. Meningitis. *Pediatr Rev*. 2015;36(12):514-26.
6. Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book 2018-2021: Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018.
7. Mongelluzzo J, Mohamad Z, Ten Have TR, Shah SS. Corticosteroids and mortality in children with bacterial meningitis. *JAMA*. 2008;299(17):2048-55.
8. van de Beek D, de Gans J, McIntyre P, Prasad K. Corticosteroids for acute bacterial meningitis. *Cochrane Database Syst Rev*. 2007;(1):CD004405. Published 2007 Jan 24.
9. Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kuppermann N, O'Leary ST, Okechukwu K, Woods CR Jr; SUBCOMMITTEE ON FEBRILE INFANTS. Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old. *Pediatrics*. 2021 Aug;148(2):e2021052228. doi: 10.1542/peds.2021-052228. Epub 2021 Jul 19. Erratum in: *Pediatrics*. 2021 Nov;148(5): PMID: 34281996.

Acute Otitis Media and Mastoiditis

1. Allan S et al. The Diagnosis and Management of Acute Otitis Media. Pediatrics March 2013; 131 (3): e964–e999. 10.1542/peds.2012-3488
2. Marchisio P, Galli L, Bortone B, et al. Updated Guidelines for the Management of Acute Otitis Media in Children by the Italian Society of Pediatrics: Treatment. Pediatr Infect Dis J. 2019;38(12S Suppl):S10-S21.
3. Emma J. Djabali et al, Antibiotic Treatment for Pediatric Acute Otitis Media and the Prevention of Serious Complications: A Meta-analysis. Pediatrics February 2022; 149 (1 Meeting Abstracts February 2022): 143.
4. Richard Kynion; Mastoiditis. Pediatr Rev May 2018; 39 (5): 267–269.
5. Kaufmann MR, et al. Management of Acute Complicated Mastoiditis: A Systematic Review and Meta-analysis. Pediatr Infect Dis J. 2022;41(4):297-301
6. Schaefer P, et al.. Acute Otitis Externa: An Update. *Am Fam Physician*. 2012;86(11):1055-1061.
7. Psarommatis IM, Voudouris C, Douros K, Giannakopoulos P, Bairamis T, Carabinos C. Algorithmic management of pediatric acute mastoiditis. *Int J Pediatr Otorhinolaryngol*. 2012;76(6):791-796. doi:10.1016/j.ijporl.2012.02.042
8. Mierzwiński J, Tyra J, Haber K, et al. Therapeutic approach to pediatric acute mastoiditis - an update. *Braz J Otorhinolaryngol*. 2019;85(6):724-732. doi:10.1016/j.bjorl.2018.06.002
9. Friesen TL, Hall M, Ramchandar N, Berry JG, Jiang W. Evolving Management of Acute Mastoiditis: Analysis of the Pediatric Health Information System Database. *Otolaryngol Head Neck Surg*. 2023;169(2):382-389. doi:10.1002/ohn.286
10. American Academy of Pediatrics. Systems-Based Treatment Table. In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book: 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics: 2021[992]
11. Gould JM, Matz PS. Otitis media. Pediatr Rev. 2010 Mar;31(3):102-16. doi: 10.1542/pir.31-3-102. PMID: 20194902.

Uncomplicated/complicated community acquired pneumonia

1. Bradley JS, Byington CL, Shah SS, et al. The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis.* 2011;53(7):e1-52.
2. Stockman et al. Procalcitonin Accurately Identifies Hospitalized Children With Low Risk of Bacterial Community-Acquired Pneumonia. *J Ped Infect Dis*. 2018;7(1):46-53.
3. Baer et al. Procalcitonin Guidance to Reduce Antibiotic Treatment of Lower Respiratory Tract Infection in Children and Adolescents (ProPAED): A Randomized Controlled Trial. *PLoS ONE*. 2013;8(8):e68419.
4. Esposito et al. Procalcitonin measurements for guiding antibiotic treatment in pediatric pneumonia. *Resp Med*. 2011;105:1939-45.
5. Christ-Crain et al. Procalcitonin Guidance of Antibiotic Therapy in Community-Acquired Pneumonia. *Am J Resp Crit Care Med*. 2006;174(1):84-93.
6. Williams DJ, Edwards KM, Self WH, et al. Effectiveness of Beta-Lactam Monotherapy vs Macrolide Combination Therapy for Children Hospitalized With Pneumonia. *JAMA Pediatr*. 2017;171(12):1184-91.
7. Blyth CC & Gerber JS. Macrolides in Children with Community-Acquired Pneumonia: Panacea or Placebo?. *J Pediatr Infect Dis*. 2018;7(1):71-7.
8. Tamma PD & Cosgrove SE. Correspondence to the editor: Duration of Antibiotic Therapy for Community-Acquired Pneumonia in Children. *Clin Infect Dis*. 2012;54(6):883-4.
9. Hazinski, M. F (2013). Nursing Care of the Critically Ill Child, 3rd ed. Elsevier, St. Louise, MO.
10. Lewis MR. *Pediatr Radiol.* 2018;48:1410-1416.
11. Islam S et al. The diagnosis and management of empyema in children: a comprehensive review from the APSA Outcomes and Clinical Trials Committee. *J Pediatr Surgery*. 2012;47:2101-10.
12. Greenberg D, Givon-Lavi N, Sadaka Y, Ben-Shimol S, Bar-Ziv J, & Dagan R. Short-course antibiotic treatment for community-acquired alveolar pneumonia in ambulatory children: a double-blind, randomized, placebo-controlled trial. *Pediatr Infect Dis J*. 2014;33(2):136-142.
13. Bielicki JA, Stöhr W, Barratt S, et al. Effect of Amoxicillin Dose and Treatment Duration on the Need for Antibiotic Re-treatment in Children With Community-Acquired Pneumonia: The CAP-IT Randomized Clinical Trial [published correction appears in JAMA. 2021 Dec 7;326(21):2208]. *JAMA*. 2021;326(17):1713-1724.
14. McCallum GB, Fong SM, Grimwood K, et al. Extended Versus Standard Antibiotic Course Duration in Children <5 Years of Age Hospitalized With Community-acquired Pneumonia in High-risk Settings: Four-week Outcomes of a Multicenter, Double-blind, Parallel, Superiority Randomized Controlled Trial. *Pediatr Infect Dis J*. 2022;41(7):549-555.
15. Williams DJ, Creech CB, Walter EB, et al. Short- vs Standard-Course Outpatient Antibiotic Therapy for Community-Acquired Pneumonia in Children: The SCOUT-CAP Randomized Clinical Trial. *JAMA Pediatr*. 2022;176(3):253-261.
16. Pernica JM, Harman S, Kam AJ, et al. Short-Course Antimicrobial Therapy for Pediatric Community-Acquired Pneumonia: The SAFER Randomized Clinical Trial. *JAMA Pediatr.* 2021;175(5):475-482.
17. Same RG, Amoah J, Hsu AJ, et al. The Association of Antibiotic Duration With Successful Treatment of Community-Acquired Pneumonia in Children. *J Pediatric Infect Dis Soc.* 2021;10(3):267-273.
18. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Prevention/management of tracheitis and ventilator associated pneumonia

1. Kalil, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Disease Society of America and the American Thoracic Society. *Clin Infect Dis*. 2016.
2. Venkatachalam, et al. The diagnostic dilemma of ventilator-associated pneumonia in critically ill children. *Pediatr Crit Care Med*. 2011;12(3):286-296.
3. Wilson, et al. Pediatric ventilator-associated infections: The ventilator-associated infection study. *Pediatr Crit Care Med*. 2017;18(1):e24-e34.
4. Rosenthal VD, Rodriguez-Calderon ME, Rodriguez-Ferrer M, Singhal T, Pawar M, Sobreyra-Oropeza M, et al. Findings of the International Nosocomial Infection Control Consortium (INICC), Part II: Impact of a Multidimensional Strategy to Reduce Ventilator-Associated Pneumonia in Neonatal Intensive Care Units in 10 Developing Countries. *Infect Control Hosp Epidemiol.* 2012; 33: 704-710.
5. Sick-Samuels AC, Linz M, Bergmann J, Fackler JC, Cerenholtz SM, Ralston SL, et al. Diagnostic stewardship of endotracheal aspirate cultures in a PICU. *Pediatrics.* 2021;147(5):e20201634.
6. Muszynski JA, Sartori J, Steele L, Frost R, Wang W, Khan N, et al. Multidisciplinary Quality Improvement Initiative to Reduce Ventilator-Associated Tracheobronchitis in the PICU. *Pediatr Crit Care Med.* 2013; 14: 533-538.
7. Obeid A, Kamel R, Naous A, Merhi BA, Rajab M. Preventing ventilator-associated pneumonia in a pediatric intensive care unit using a modified ventilator-associated pneumonia bundle: Pre-interventional and post-interventional trial. *Int J Med Res.* 2014; 2: 14-19.
8. Brierley J, Highe L, Hines S, Dixon G. Reducing VAP by instituting a care bundle using improvement methodology in a UK paediatric intensive care unit. Eur J Pediatr. 2012; 171: 323-330.
9. De Cristofano A, Peuchot V, Canepari A, Franco V, Perez A, Eulmesekian P. Implementation of a ventilator-associated pneumonia prevention bundle in a single PICU. *Pediatr Crit Care Med.* 2016; 17: 451-456.
10. McBeth CL et al. Interprofessional approach to the sustained reduction in ventilator-associated pneumonia in a pediatric intensive care unit. *Crit Care Nurse.* 2018;38(6):36-46.
11. Alcan AO, Van Giersbergen MY. Pediatric ventilator bundle. *Arch Emerg Med Crit Care.* 2017;2(2):1027.
12. Brilli RJ, Shaw J, Wells D, Dent C, Ryckman S, Raake J, et al. Pediatric VAP bindle reduces VAP in PICU, NICU, CICU. *Crit Care Med.* 2006;34(12):A90.
13. Da Silva, Paulo Sérgio Lucas, Vania Euzébio de Aguiar, and Marcelo Cunio Machado Fonseca. "Does Tracheal Lidocaine Instillation Reduce Intracranial Pressure Changes After Tracheal Suctioning in Severe Head Trauma? A Prospective, Randomized Crossover Study." Pediatric Critical Care Medicine 20.4 (2019): 365-371.
14. Mathieu, Antoine, et al. "Aerosolized lidocaine during invasive mechanical ventilation: in vitro characterization and clinical efficiency to prevent systemic and cerebral hemodynamic changes induced by endotracheal suctioning in head-injured patients." Journal of neurosurgical anesthesiology 25.1 (2013): 8-15.
15. Bilotta, Federico, et al. "Endotracheal lidocaine in preventing endotracheal suctioning-induced changes in cerebral hemodynamics in patients with severe head trauma." Neurocritical Care 8.2 (2008): 241-246.
16. Yano, Masami, et al. "Effect of lidocaine on ICP response to endotracheal suctioning." Anesthesiology: The Journal of the American Society of Anesthesiologists 64.5 (1986): 651-653.
17. Rodrigues, Fernanda A., et al. "Which is safer to avoid an increase in ICP after endotracheal suctioning in severe head injury: intravenous or endotracheal lidocaine?." Journal of Neurology Research 3.2 (2013): 51-55.
18. Valles, et al. Efficacy of single-dose antibiotic against early-onset pneumonia in comatose patients who are ventilated. *CHEST*. 2103;143(5):1219-1225.
19. Lewis, et al. Influence of single-dose antibiotic prophylaxis for early-onset pneumonia in high-risk intubated patients. *Neurocrit Care*. 2018;28(3):362-369.
20. Sirvent, et al. Protective effect of intravenously administered cefuroxime against nosocomial pneumonia in patients with structural coma. *Am J Respir Crit Care Med*. 1997;155:1729-1734.
21. Acquarolo, et al. Antibiotic prophylaxis of early onset pneumonia in critically comatose patients: A randomized study. *Int Care Med.* 2005;31:510-516.
22. Mirtalaei, et al. Efficacy of antibiotic prophylaxis against ventilator-associated pneumonia. *J Hosp Infect*. 2019;101(3):272-275.
23. Foglia, et al. Ventilator-Associated Pneumonia in Neonatal and Pediatric Intensive Care Unit Patients. *Clin Microbiol Rev*. 2007;20(3):409-425.
24. Sebastian MR et al. Oral mucosal decontamination with chlorhexidine for the prevention of ventilator-associated pneumonia in children – a randomized, controlled trial. *Pediatr Crit Care Med.* 2012;13(5)e305-e310.
25. Kusahara DM et al. Oral care with 0.12% chlorhexidine for the prevention of ventilator-associated pneumnia in critically ill children: Randomized, controlled and double blind trial. *Int J Nursing Studies.* 2012;49:1354-1363.
26. Gomaa MM, et al. Pre versus post application of a 0.12% chlorhexidine based oral hygiene protocol in an Egyptian pediatric intensive care unit: Practice and effects. *The Egyptian Journal of Crit Care Med.* 2017;5:87-91.
27. Brilli RJ, Sparling KW, Lake MR, Butcher J, Myers SS, Clark MD, et al. The business case for preventing ventilator-associated pneumonia in pediatric intensive care unit patients. *Jt Comm J Qual Patient Saf.* 2008; 34: 629-638.
28. Gurskis V, Ašembergienė J, Kėvalas R, Miciulevičienė J, Pavilonis A, Valintėlienė R, et al. Reduction of nosocomial infections and mortality attributable to nosocomial infections in pediatric intensive care units in Lithuania. *Medicina (Kaunas).* 2009; 45: 203-213.
29. Bigham MT, Amato R, Bondurrant P, Fridriksson J, Krawczeski CD, Raake J, et al. Ventilator-associated pneumonia in the pediatric intensive care unit: characterizing the problem and implementing a sustainable solution. *J Pediatr.* 2009; 154: 582-587.
30. Carr AL, Daley MJ, Merkel KG, Rose DT. Clinical utility of methicillin-resistant *Staphylococcus aureus* nasal screening for antimicrobial stewardship: A review of the current literature. Carr AL et al. *Pharmacotherapy.* 2018;38(12):1216-1228.
31. Linfesty D, Manaloor J. Use of MRSA nasal swab to guide empiric antibiotic treatment of hospital acquired or community acquired pneumonia in a pediatric population. *Open Forum Infect Dis.* 2017;4(1):S502.
32. Isguder R, Ceylan G, Agin H, Gulfidan G, Ayhan Y, Devrim I. New parameters for childhood ventilator associated pneumonia diagnosis. *Pediatr Pulmonol.* 2017;52(1):119-128.
33. Sotillo-Diaz JC, Bermejo-Lopez E, Garcia-Olivares P, Peral-Gutierrez JA, Sancho-Gonzalez M, Guerrero-Sanz JE. Role of plasma procalcitonin in the diagnosis of ventilator-associated pneumonia: Systematic review and meta-analysis. *Med Intensiva.* 2014;38:337-346.
34. Wang Q, Hou D, Wang J, An K, Han C, Wang C. Procalcitonin-guided antibiotic discontinuation in ventilator-associated pneumonia: a prospective observational study. *Infect Drug Resist*. 2019;12:815-824.
35. Stolz D, Smyrnios N, Eggimann P, Pargger H, Thakkar N, Siegemund M, et al. Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study. *Eur Respir J*. 2009;34(6):1364-75.

Acute Chest Syndrome

1. Vichinsky EP, Neumayr LD, Earles AN, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group [published correction appears in N Engl J Med 2000 Sep 14;343(11):824]. N Engl J Med. 2000;342(25):1855-1865. doi:10.1056/NEJM200006223422502
2. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members [published correction appears in JAMA. 2014 Nov 12;312(18):1932] [published correction appears in JAMA. 2015 Feb 17;313(7):729]. JAMA. 2014;312(10):1033-1048. doi:10.1001/jama.2014.10517
3. Howard J, Hart N, Roberts-Harewood M, et al. Guideline on the management of acute chest syndrome in sickle cell disease. Br J Haematol. 2015;169(4):492-505. doi:10.1111/bjh.13348
4. Reagan MM, DeBaun MR, Frei-Jones MJ. Multi-modal intervention for the inpatient management of sickle cell pain significantly decreases the rate of acute chest syndrome. Pediatr Blood Cancer. 2011;56(2):262-266. doi:10.1002/pbc.22808

5. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members [published correction appears in JAMA. 2014 Nov 12;312(18):1932] [published correction appears in JAMA. 2015 Feb 17;313(7):729]. JAMA. 2014;312(10):1033-1048. doi:10.1001/jama.2014.10517
6. Ndefo UA, Maxwell AE, Nguyen H, Chiobi TL. Pharmacological management of sickle cell disease. P T. 2008;33(4):238-243.
7. Bundy DG, Richardson TE, Hall M, et al. Association of Guideline-Adherent Antibiotic Treatment With Readmission of Children With Sickle Cell Disease Hospitalized With Acute Chest Syndrome. JAMA Pediatr. 2017;171(11):1090–1099. doi:10.1001/jamapediatrics.2017.2526
8. Jain S, Bakshi N, Krishnamurti L. Acute Chest Syndrome in Children with Sickle Cell Disease. Pediatr Allergy Immunol Pulmonol. 2017;30(4):191-201. doi:10.1089/ped.2017.0814
9. Koehl JL, Koyfman A, Hayes BD, Long B. High risk and low prevalence diseases: Acute chest syndrome in sickle cell disease. Am J Emerg Med. 2022;58:235-244. doi:10.1016/j.ajem.2022.06.018
10. Buchanan GR, Yawn BP. Evidence-based management of Sickle Cell Disease: Expert Panel Report, 2014. National Heart Lung and Blood Institute. 2014.
11. Zeng L, Wang C, Jiang M, et al. Safety of ceftriaxone in paediatrics: a systematic review. Arch Dis Child. 2020;105(10):981-985. doi:10.1136/archdischild-2019-317950
12. Mckinney C, Sabus A, Ruzas C, et al. Acute chest syndrome (ACS) - children's hospital colorado. November 24, 2015.
13. The Children's Hospital of Philadelphia. Sickle cell and acute chest syndrome clinical pathway - inpatient. Sickle Cell and Acute Chest Syndrome Clinical Pathway - Inpatient. December 22, 2020.
14. Welch J. Acute Chest Syndrome in Paediatric Sickle Cell Disease. Sheffield's Children NHS. June 08, 2018.
15. Friend A, Settelmeyer T, Girzadas D. Acute chest syndrome - statpearls - NCBI bookshelf. National Library of Medicine. February 6, 2023
16. Razazi K, Gendreau S, Cuquemelle E, et al. Procalcitonin to Reduce Antibiotic Exposure during Acute Chest Syndrome in Adult Patients with Sickle-Cell Disease. J Clin Med. 2020;9(11):3718. Published 2020 Nov 19. doi:10.3390/jcm9113718
17. Schuetz P., Wirz Y., Sager R., Christ-Crain M., Stolz D., Tamm M., Bouadma L., Luyt C.E., Wolff M., Chastre J., et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: A patient level meta-analysis. Lancet Infect. Dis. 2018;18:95–107. doi: 10.1016/S1473-3099(17)30592-3.
18. Kerr S, Graue C, Broadbent K, et al. Clinical Evaluation of the BioFire ® FilmArray ® Pneumonia Panel plus. Biofire.
19. Martinez R, et al. Clinical Virology Symposium, Poster #C-368, May 2016.
20. Rogers B, et al. Arch. Path. & Lab. Med. 2015;139(5): 636-41.
21. Bellet PS, Kalinyak KA, Shukla R, Gelfand MJ, Rucknagel DL. Incentive spirometry to prevent acute pulmonary complications in sickle cell diseases. N Engl J Med. 1995;333(11):699-703. doi:10.1056/NEJM199509143331104
22. Stone E, Wenger P, Kumta J, Narang S, et al. Azithromycin Avoidance in Pediatric Patients with Sickle Cell Disease and Respiratory Infections. *Blood*. 2024;144(1):5003. https://doi.org/10.1182/blood-2024-208665.
23. Zhang Y, Kasikis S, Vanderpool S, Ogrodnik P, Spyrou N, & Hammerschlag MR. Impact of a respiratory panel on the diagnosis and management of acute chest syndrome in pediatric patients with sickle cell disease: A single-center retrospective study. *Pediatric Hematology Oncology Journal*. 2025; 10(3): 100464. https://doi.org/10.1016/j.phoj.2025.100464.
24. Kelsey Oberholtzer, Benjamin Van Tassell, Nadirah El-Amin, Cady Noda, Atypical bacteria in pediatric sickle cell patients with acute chest syndrome. *Journal of Sickle Cell Disease*. 2024; 1(1):yoae006. https://doi.org/10.1093/jscdis/yoae006.
25. Sabaté-Elabbadi A, Mekontso-Dessap A, Lionnet F, et al. Combined use of respiratory multiplex PCR and procalcitonin to reduce antibiotic exposure in sickle-cell adult patients with acute chest syndrome (The ANTIBIO-STA study): a randomised, controlled, open-label trial. *Lancet Reg Health Eur*. 2025;51:101234. Published 2025 Feb 7. doi:10.1016/j.lanepe.2025.101234.

Clostridioides difficile

1. McDonald, L.C. *et al.* Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis.*2018:66(7):e1-e48.
2. Martin, J., Mawer, D., & Wilcox, M.H. Clostridium difficile: biological therapies. *Current opinion in infectious diseases*. 2013(26):454-460.
3. Schutze GE, Willoughby RE. *Clostridium difficile* infection in infants and children. *Pediatrics*. 2013;131(1):196-200.
4. O'gorman MA, Michaels MG, Kaplan SL, et al. Safety and Pharmacokinetic Study of Fidaxomicin in Children With *Clostridium difficile*-Associated Diarrhea: A Phase 2a Multicenter Clinical Trial. *J Pediatric Infect Dis Soc*. 2017.
5. Wilcox MH, Gerding DN, Poxton IR, et al. Bezlotoxumab for Prevention of Recurrent *Clostridium difficile* Infection. *N Engl J Med*. 2017;376(4):305-317.
6. Isaac S, Scher JU, Djukovic A, et al. Short- and long-term effects of oral vancomycin on the human intestinal microbiota. *J Antimicrob Chemother*. 2017;72(1):128-136.
7. Dominguez SR, Dolan SA, West K, et al. High colonization rate and prolonged shedding of *Clostridium difficile* in pediatric oncology patients. *Clin Infect Dis*. 2014;59(3):401-3.
8. Van hise NW, Bryant AM, Hennessey EK, Crannage AJ, Khoury JA, Manian FA. Efficacy of Oral Vancomycin in Preventing Recurrent *Clostridium difficile* Infection in Patients Treated With Systemic Antimicrobial Agents. *Clin Infect Dis*. 2016.
9. Carignan A, Poulin S, Martin P, et al. Efficacy of Secondary Prophylaxis With Vancomycin for Preventing Recurrent *Clostridium difficile* Infections. *Am J Gastroenterol*. 2016.
10. Johnson SW, Brown SV, & Priest DH. Effectiveness of Oral Vancomycin for Prevention of Healthcare Facility-Onset *Clostridioides difficile* Infection in Targeted Patients During Systemic Antibiotic Exposure. *Clin Infect Dis*. 2020;71:1133-9.
11. Stevens VW, Khader K, Echevarria K, et al. Use of Oral Vancomycin for *Clostridioides difficile* Infection and the Risk of Vancomycin-Resistant Enterococci. *Clin Infect Dis.* 2020;71:645-51.
12. Ganetsky A, Han JH, Hughes ME, et al. Oral Vancomycin Prophylaxis Is Highly Effective in Preventing *Clostridium difficile* Infection in Allogeneic Hematopoietic Cell Transplant Recipients. *Clin Infect Dis*. 2019;68(12):2003-9.
13. Morrisette T, Van Matre AG, Miller MA, et al. Oral Vancomycin Prophylaxis as Secondary Prevention Against *Clostridioides difficile* Infection in the Hematopoietic Stem Cell Transplantation and Hematologic Malignancy Population. *Biol Blood Marrow Transplant*. 2019;25(10):2091-7.
14. Wolf J, Kalocsai K, Fortuny C, Lazar S, Bosis S, Korczowski B, Petit A, Bradford D, Croos-Dabrera R, Incera E, Melis J, van Maanen R. Safety and efficacy of fidaxomicin and vancomycin in children and adolescents with Clostridioides (Clostridium) difficile infection: a phase 3, multicenter, randomized, single-blind clinical trial (SUNSHINE). *Clin Infect Dis*. 2019 Nov 27:ciz1149. doi: 10.1093/cid/ciz1149.
15. Knight EM, Schiller DS, Fulman MK, & Rastogi R. Long-Term Efficacy of Oral Vancomycin Prophylaxis for the Prevention of Clostridium difficile Recurrence. *J Pharm Pract*. 2020;33(5):633-9.

Urinary tract infections (UTIs)

1. National Institute for Health and Care Excellence (NICE). Urinary Tract Infections in Under 16s: Diagnosis and Management. NICE Guidelines. 2022. https://www.nice.org.uk/guidance/ng224.
2. Lewis-de los Angeles WW, Thurm C, Hersh AL, et al. Trends in Intravenous Antibiotic Duration for Urinary Tract Infections in Young Infants. *Pediatrics*. 2017;140(6): e20171021
3. Roberts KB. Urinary tract infection: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics*. 2011;128(3):595-610. doi:10.1542/peds.2011-1330.
4. Roberts KB, Downs SM, Finnell SM, et al. Reaffirmation of AAP clinical practice guideline: The diagnosis and management of the initial urinary tract infection in febrile infants and young children 2–24 months of age. *Pediatrics*. 2016;138(6). doi:10.1542/peds.2016-3026.
5. Arshad M, Seed PC. Urinary tract infections in the infant. *Clinics in Perinatology*. 2015;42(1):17-28. doi:10.1016/j.clp.2014.10.003.
6. Mattoo TK, Shaikh N, Nelson CP. Contemporary management of Urinary Tract Infection in children. *Pediatrics*. 2021;147(2). doi:10.1542/peds.2020-012138.
7. Robinson JL, Finlay JC, Lang ME, Bortolussi R. Urinary tract infections in infants and children: Diagnosis and management. *Paediatrics & Child Health*. 2014;19(6):315-319. doi:10.1093/pch/19.6.315.
8. Claeys KC, Trautner BW, Leekha S, et al. Optimal Urine Culture Diagnostic Stewardship Practice – Results from an Expert Modified-Delphi Procedure. *Clin Infect Dis*. 2022;75(3):382-9.
9. Fernandez M, Merkel KG, Ortiz JD, & Quick RD. Oral Narrow-Spectrum Antibiotics for the Treatment of Urinary Tract Infection in Infants Younger than 60 Days. *J Ped Infect Dis Soc*. 2020;9(3):378-81.
10. Fox MT, Amoah J, Hsu A, et al. Comparative Effectiveness of Antibiotic Treatment Duration in Children with Pyelonephritis. *JAMA Open Net*. 2020;3(5):e203951.
11. Poole NM, Kronman MP, Rutman L, et al. Improving Antibiotic Prescribing for Children With Urinary Tract Infection in Emergency and Urgent Care Settings. *Pediatr Emer Care*. 2020;36(6):e332-339.
12. Chaudhari PP, Monuteaux MC, & Bachur RG. Emergency Department Revisits After an Initial Parenteral Antibiotic Dose for UTI. *Pediatrics*. 2018;142(3):e20180900.
13. Brady PW, Conway PH, & Goudie A. Length of Intravenous Antibiotic Therapy and Treatment Failure in Infants With Urinary Tract Infections. *Pediatrics*. 2010;126:196-203.
14. Gupta K, Hooton TM, Naber KG, et al. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):e103-20.
15. Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2019;68(10):e83-e110.
16. Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50(5):625-663.
17. Goodlet KJ, Benhalima FZ, Nailor MD. A systematic review of single-dose aminoglycoside therapy for urinary tract infection: is it time to resurrect an old strategy?. *Antimicrob Agents Chemother*. 2018;63(1):e02165-18.
18. Khan AJ, Kumar K, Evans HE. Single-dose gentamicin therapy of recurrent urinary tract infection in patients with normal urinary tracts. *J Pediatr*. 1987;110(1):131-135.
19. Varese LA, Grazioli F, Viretto A, Antoniola P. Single-dose (bolus) therapy with gentamicin in management of urinary tract infection. *International Journal of Pediatric Nephrology*. 1980;1(2):104-105.
20. Nelson Z, Aslan AT, Beahm NP, et al. Guidelines for the Prevention, Diagnosis, and Management of Urinary Tract Infections in Pediatrics and Adults: A WikiGuidelines Group Consensus Statement. *JAMA Netw Open.* 2024;7(11):e2444495.
21. Trautner BW, Cortés-Penfield NW, Gupta K, Hirsch EB, Horstman M, Moran GJ, Colgan R, O'Horo JC, Ashraf MS, Connolly S, Drekonja D, Grigoryan L, Huttner A, Lazenby GB, Nicolle L, Schaeffer A, Yawetz S, Lavergne V. Clinical practice guideline by Infectious Diseases Society of America (IDSA): 2025 guideline on management and treatment of complicated urinary tract infections: selection of antibiotic therapy for complicated UTI. *Clinical Infectious Diseases*. 2025;ciaf460. doi:10.1093/cid/ciaf460

Skin and soft tissue infections

1. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014; 59(2):e10-52.
2. Kimberlin DW, Brady MT, Jackson MA, Long SS, Bernstein HH, & Meissner HC, eds. *Red Book: 2018 Report of the Committee on Infectious* Diseases. Itasca, IL: American Academy of Pediatrics; 2018. Accessed online.
3. Bradley JS, Nelson JD, Barnett ED, et al, eds. *Nelson's Pediatric Antimicrobial Therapy*. 23rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017.
4. Schuler CL, Courter JD, Conneely SE, et al. Decreasing Duration of Antibiotic Prescribing for Uncomplicated Skin and Soft Tissue Infections. *Pediatrics*. 2016; 137(2):e20151223.
5. Moran GJ, Krishnadasan A, Mower WR, et al. Effect of Cephalexin Plus Trimethoprim-Sulfamethoxazole vs Cephalexin Alone on Clinical Cure of Uncomplicated Cellulitis: A Randomized Clinical Trial. *JAMA*. 2017; 317(20):2088-96.
6. Gottlieb M, DeMott JM, Hallock M, & Peksa GD. Systemic Antibiotics for the Treatment of Skin and Soft Tissue Abscesses: A Systematic Review and Meta-Analysis. *Ann Emerg Med*. 2019; 73(1):8-16.
7. Chen AE, Carroll KC, Diener-West M, et al. Randomized controlled trial of cephalexin versus clindamycin for uncomplicated pediatric skin infections. *Pediatrics*. 2011; 127(3):e573-80.
8. Duong M, Markwell S, Peter J, & Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. *Ann Emerg Med*. 2010; 55(5):401-7.
9. Pulia MS, Schwei RJ, Patterson BW, Repplinger MD, Smith MA, & Shah MN. Effectiveness of Outpatient Antibiotics After Surgical Drainage of Abscesses in Reducing Treatment Failure. *J Emerg Med*. 2018; 55(4):512-21.
10. Williams DJ, Cooper WO, Kaltenbach LA, et al. Comparative Effectiveness of Antibiotic Treatment Strategies for Pediatric Skin and Soft-Tissue Infections. *Pediatrics*. 2011; 128(3):3479-87.
11. Elliot DJ, Zaoutis TE, Troxel AB, Loh A, & Keren R. Empiric Antimicrobial Therapy for Pediatric Skin and Soft-Tissue Infections in the Era of Methicillin-Resistant *Staphylococcus aureus*. *Pediatrics*. 2009; 123(6):e959-66.

Acute hematogenous osteomyelitis and acute bacterial arthritis

1. Woods CR, Bradley JS, Chatterjee A, Copley LA, Robinson J, Kronman MP, Arrieta A, Fowler SL, Harrison C, Carrillo-Marquez MA, Arnold SR, Eppes SC, Stadler LP, Allen CH, Mazur LJ, Creech CB, Shah SS, Zaoutis T, Feldman DS, Lavergne V. Clinical Practice Guideline by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America: 2021 Guideline on Diagnosis and Management of Acute Hematogenous Osteomyelitis in Pediatrics. *J Pediatric Infect Dis Soc*. 2021 Aug 5:piab027. doi: 10.1093/jpids/piab027. Epub ahead of print. PMID: 34350458.
2. Ceroni D., Cherkaoui A., Ferey S., Kaelin A., Schrenzel J. 2010. Kingella kingae osteoarticular infections in young children: clinical features and contribution of a new specific real-time PCR assay to the diagnosis. *J. Pediatr. Orthop*. 30:301–304
3. Yagupsky P. Antibiotic susceptibility of kingella kingae isolates from children with skeletal system infections. *Pediatr Infect Dis J* 2012;31(2):212
4. Erkilinc, Mehmet MD; Gilmore, Allison MD; Weber, Morgan MD; Mistovich, R. Justin MD, MBA *Current Concepts in Pediatric Septic Arthritis, Journal of the American Academy of Orthopaedic Surgeons*: March 1, 2021 - Volume 29 - Issue 5 - p 196-206 doi: 10.5435/JAAOS-D-20-00835
5. Wheeler AM, Heizer HR, Todd JK. Influence of Culture Results on Management and Outcome of Pediatric Osteomyelitis and/or Septic Arthritis. *JJ Ped Infect Dis* 2012;1(2):152-156
6. Peltola H, Paakkonen M, Kallio P, et al. Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood: prospective, randomized trial on 131 culture-positive cases. *Pediatr Infect Dis J* 2010;29(12):1123-28.
7. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clinical infectious diseases*: an official publication of the Infectious Diseases Society of America 2011;52:e18-55
8. Bachur R, Pagon Z. Success of short-course parenteral antibiotic therapy for acute osteomyelitis of childhood. *Clinical Pediatrics* 2007;46:30-5
9. Zaoutis T, Localio AR, Leckerman K, Saddlemire S, Bertoch D, Keren R. Prolonged intravenous therapy versus early transition to oral antimicrobial therapy for acute osteomyelitis in children. *Pediatrics* 2009;123:636-42.
10. van der Merwe M, Rooks K, Crawford H, et al. The effect of antibiotic timing on culture yield in paediatric osteoarticular infection. *J Child Orthop* 2019; 13:114–9
11. Castellazzi, Luca et al. "Update on the Management of Pediatric Acute Osteomyelitis and Septic Arthritis." *International journal of molecular sciences* vol. 17,6 855. 1 Jun. 2016, doi:10.3390/ijms17060855
12. Howard-Jones AR, Isaacs D. Systematic review of duration and choice of systemic antibiotic therapy for acute haematogenous bacterial osteomyelitis in children. *J Paediatr Child Health*. 2013 Sep;49(9):760-768. doi: 10.1111/jpc.12251.
13. Thakolkaran, Nimmy, and Avinash K Shetty. "Acute Hematogenous Osteomyelitis in Children." *The Ochsner Journal* vol. 19,2 (2019): 116-122. doi:10.31486/toj.18.0138
14. Olijve L, Amarasena L, Best E, Blyth C, van den Boom M, Bowen A, Bryant PA, Buttery J, Dobinson HC, Davis J, Francis J, Goldsmith H, Griffiths E, Hung TY, Huynh J, Kesson A, Meehan A, McMullan B, Nourse C, Palasanthiran P, Penumarthy R, Pilkington K, Searle J, Stephenson A, Webb R, Williman J, Walls T. The role of Kingella kingae in pre-school aged children with bone and joint infections. *J Infect*. 2021 Jul 12:S0163-4453(21)00324-8. doi: 10.1016/j.jinf.2021.06.028. Epub ahead of print. PMID: 34265316.
15. Truelove JJ, House SA. Reducing PICC Placement in Pediatric Osteomyelitis: A Diamond in the Deimplementation Rough? *Hosp Pediatr*. 2021 Jun 29:hpeds.2021-006029. doi: 10.1542/hpeds.2021-006029. Epub ahead of print. PMID: 34187790.
16. Shaikh N, Umscheid J, Rizvi S, Bhatt P, Vasudeva R, Yagnik P, Bhatt N, Donda K, Dapaah-Siakwan F. National Trends of Acute Osteomyelitis and Peripherally Inserted Central Catheters in Children. *Hosp Pediatr*. 2021 Jun 29:hpeds.2020-005794. doi: 10.1542/hpeds.2020-005794. Epub ahead of print. PMID: 34187789.
17. Bryson YJ, Connor JD, LeClerc M, Giammona ST. High-dose oral dicloxacillin treatment of acute staphylococcal osteomyelitis in children. *J Pediatr*. 1979 Apr;94(4):673-5. doi: 10.1016/s0022-3476(79)80049-9. PMID: 430319.
18. Yagupsky P, Erlich Y, Ariela S, Trefler R, Porat N. Outbreak of Kingella kingae skeletal system infections in children in daycare. *Pediatr Infect Dis J*. 2006 Jun;25(6):526-32. doi: 10.1097/01.inf.0000215243.42501.4f. PMID: 16732151.
19. Tran Quang V, Bidet P, Birgy A, Caseris M, Basmaci R, Bonacorsi S. Susceptibility testing of Kingella kingae to cefazolin. *Clin Microbiol Infect*. 2018 Mar;24(3):312-313. doi: 10.1016/j.cmi.2017.10.003. Epub 2017 Oct 12. PMID: 29031788.
20. Dubnov-Raz G, Scheuerman O, Chodick G, Finkelstein Y, Samra Z, Garty BZ. Invasive Kingella kingae infections in children: clinical and laboratory characteristics. *Pediatrics*. 2008 Dec;122(6):1305-9. doi: 10.1542/peds.2007-3070. PMID: 19047250.
21. Messina AF, Namtu K, Guild M, Dumois JA, Berman DM. Trimethoprim-sulfamethoxazole therapy for children with acute osteomyelitis. *Pediatr Infect Dis J*. 2011 Dec;30(12):1019-21. doi: 10.1097/INF.0b013e31822db658. PMID: 21817950.
22. Bradley JS, Arrieta AC, Digtyar VA, et al. Daptomycin for pediatric Gram-positive acute hematogenous osteomyelitis. *Pediatr Infect Dis J*. 2020; 39:814–23.
23. Gjika E, Beaulieu JY, Vakalopoulos K, Gauthier M, Bouvet C, Gonzalez A, Morello V, Steiger C, Hirsiger S, Lipsky BA, Uçkay I. Two weeks versus four weeks of antibiotic therapy after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. *Ann Rheum Dis*. 2019 Aug;78(8):1114-1121. doi: 10.1136/annrheumdis-2019-215116. Epub 2019 Apr 16. PMID: 30992295; PMCID: PMC6691865.
24. Erkilinc, Mehmet MD; Gilmore, Allison MD; Weber, Morgan MD; Mistovich, R. Justin MD, MBA Current Concepts in Pediatric Septic Arthritis, *Journal of the American Academy of Orthopaedic Surgeons*: March 1, 2021 - Volume 29 - Issue 5 - p 196-206 doi: 10.5435/JAAOS-D-20-00835
25. Woods CR, Bradley JS, Chatterjee A, et al. Clinical Practice Guideline by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America: 2021 Guideline on Diagnosis and Management of Acute Hematogenous Osteomyelitis in Pediatrics. *J Pediatric Infect Dis Soc*. 2021;10(8):801-844. doi:10.1093/jpids/piab027

Central line associated infections

1. Mermel LA, Allon M, Bouza E, et al. Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2009;49:1-45.
2. Daneman N, Downing M, & Zagorski BM. How long should peripherally inserted central catheterization be delayed in the context of recently documented bloodstream infection?. *J Vasc Interv Radiol*. 2012 Jan;23(1):123-5.
3. Stewart JD & Runnegar N. Early use of peripherally inserted central catheters is safe in Staphylococcus aureus bacteraemia. *Intern Med J*. 2018 Jan;48(1):44-49.
4. Ogle AM, Wright MO, Kasparian L, Peterson LR, & Robicsek A. Line insertion in proximity to bacteremia: does timing matter?. *Am J Infect Control*. 2008;36(5):e201-2. DOI: 10.1016/j.ajic.2008.04.237
5. Hecht SM, Ardura MI, Yildiz VO, & Ouellette CP. Central Venous Catheter Management in High-Risk Children With Bloodstream Infections. *Pediatr Infect Dis J*. 2020 Jan;39(1):17-22.
6. Yahav D, Franceschini E, Koppel F, et al. Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial. *Clin Infect Dis*. 2019 Sep 13;69(7):1091-1098.
7. Fabre V, Amoah J, Cosgrove SE, & Tamma PD. Antibiotic Therapy for Pseudomonas aeruginosa Bloodstream Infections: How Long Is Long Enough?. *Clin Infect Dis*. 2019 Nov 13;69(11):2011-2014.
8. Tansarli GS, Andreatos N, Pliakos EE, & Mylonakis E. A Systematic Review and Meta-analysis of Antibiotic Treatment Duration for Bacteremia Due to *Enterobacteriaceae*. *Antimicrob Agents Chemother*. 2019 May; 63(5): e02495-18. DOI: 10.1128/AAC.02495-18
9. Park SH, Milstone AM, Diener-West M, Nussenblatt V, Cosgrove SE, & Tamma PD. Short versus prolonged courses of antibiotic therapy for children with uncomplicated Gram-negative bacteremia. *J Antimicrob Chemother*. 2014;69:770-85.
10. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62(4):e1-50. DOI: 10.1093/cid/civ933
11. Weiss SL, Peters MJ, Alhazzani W, et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. *Pediatr Crit Care Med*. 2020;21(2):e52-e106. DOI:10.1097/PCC.0000000000002198

Prevention/management of infection in pediatric oncology and bone marrow transplant patients

1. Lehrnbecher T, Robinson P, Fisher B, et al. Guideline for the Management of Fever and Neutropenia in Children with Cancer and Hematopoietic Stem-Cell Transplantation Recipients: 2017 Update. *J Clin Oncol*. 2017; 35(18):2082-94.

2. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America. *Clin Inf Dis*. 2011; 52(4): e56-e93.
3. Mermel LA, Allon M, Bouza E, et al. Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009; 49: 1-45.
4. Robinson PD, Lehrnbecher T, Phillips R, Dupuis LL, & Sung L. Strategies for Empiric Management of Pediatric Fever and Neutropenia in Patients With Cancer and Hematopoietic Stem-Cell Transplantation Recipients: A Systematic Review of Randomized Trials. *J Clin Oncol*. 2016; 34(17):2054-60.
5. Hodgson-Viden H, Grundy PE, & Robinson JL. Early discontinuation of intravenous antimicrobial therapy in pediatric oncology patients with febrile neutropenia. *BMC Pediatrics*. 2005. DOI:10.1186/1471-2431-5-10
6. Snyder M, Pasikhova Y, Baluch A. Early Antimicrobial De-escalation and Stewardship in Adult Hematopoietic Stem Cell Transplantation Recipients: Retrospective Review. *OFID*. 2017. DOI: 10.1093/ofid/ofx226
7. Averbuch D, Orasch C, Cordonnier C, et al. European guidelines for empirical antibacterial therapy for febrile neutropenic patients in the era of growing resistance: summary of the 2011 4th European Conference on Infections in Leukemia. *Haematologica*. 2013;98(12):1826-35.
8. Lehrnbecher T, Stanescu A, & Kühl J. Short Courses of Intravenous Empirical Antibiotic Treatment in Selected Febrile Neutropenic Children with Cancer. *Infection*. 2002;30:17-21.
9. Aguilar-Guisado M, Espigado I, Martin-Peña A, et al. Optimization of empirical antimicrobial therapy in patients with haematologic malignancies and febrile neutropenia (How Long study): an open-label, randomized, controlled phase 4 trial. *Lancet Haematol*. 2017;4:e573-83.
10. Le Clech L, Talarmin JP, Couturier MA, et al. Early discontinuation of empirical antibacterial therapy in febrile neutropenia: the ANTIBIOSTOP study. *Infect Dis*. 2018;50(7):539-49.
11. la Martire G, Robin C, Oubaya N, et al. De-escalation and discontinuation strategies in high-risk neutropenic patients: an interrupted time series analyses of antimicrobial consumption and impact on outcome. *Eur J Clin Microbiol Infect Dis*. 2018; Jul 26. doi: 10.1007/s10096-018-3328-1. [Epub ahead of print].
12. Alexander et al. Effect of Levofloxacin Prophylaxis on Bacteremia in Children With Acute Leukemia or Undergoing Hematopoietic Stem Cell Transplantation: A Randomized Trial. *JAMA*. 2018.
13. Wolf et al. Levofloxacin Prophylaxis During Induction Therapy for Pediatric Acute Lymphoblastic Leukemia. *Clin Infect Dis*. 2017.
14. Gafter-Gvili et al. Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy. *Cochrane Database Syst Rev*. 2012.
15. Owattanapanich et al. Efficacy of levofloxacin as an antibacterial prophylaxis for acute leukemia patients receiving intensive chemotherapy: a systematic review and meta-analysis. *Hematology*. 2019.
16. Mikulska. Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines. *J Infect*. 2018.
17. McCormick et al. Cost-effectiveness of levofloxacin prophylaxis against bacterial infection in pediatric patients with acute myeloid leukemia. *Pediatr Blood Cancer*. 2020.
18. Maser et al. Levofloxacin prophylaxis in hospitalized children with leukemia: A cost-utility analysis. *Pediatr Blood Cancer*. 2020.
19. Lehrnbecher et al. Guideline for Antibacterial Prophylaxis Administration in Pediatric Cancer and Hematopoietic Stem Cell Transplantation. *Clin Infect Dis*. 2019.
20. Lehrnbecher T, Fisher BT, Phillips B, et al. Clinical Practice Guideline for Systemic Antifungal Prophylaxis in Pediatric Patients With Cancer and Hematopoietic Stem-Cell Transplantation Recipients. *J Clin Oncol*. 2020;38(27):3205-3216. doi: 10.1200/JCO.20.00158.
21. Taplitz RA, Kennedy EB, Bow EJ, et al. Antimicrobial Prophylaxis for Adult Patients With Cancer-Related Immunosuppression: ASCO and IDSA Clinical Practice Guideline Update. *J Clin Oncol*. 2018;36(30):3043-3054. doi:10.1200/JCO.18.00374.
22. Fleming S, Yannakou CK, Haeusler GM, et al. Consensus guidelines for antifungal prophylaxis in haematological malignancy and haemopoietic stem cell transplantation, 2014. *Intern Med J*. 2014;44(12b):1283-1297. doi:10.1111/imj.12595.
23. McNeil JC, Campbell JR, & Crews JD. Infection Prevention in Pediatric Oncology and Hematopoietic Stem Cell Transplant Recipients. *Healthcare-Associated Infections in Children*. 2018;16:281-99. doi: 10.1007/978-3-319-98122-2_16.
24. Ramos JT, Romero CA, Belda S, et al. Clinical practice update of antifungal prophylaxis in immunocompromised children. *Rev Esp Quimioter*. 2019;32(5):410-425.
25. Rodrigues FG, Dasilva G, Wexner SD. Neutropenic enterocolitis. *World J Gastroenterol*. 2017;23(1):42-47. doi:10.3748/wjg.v23.i1.42.
26. Nesher L, Rolston KV. Neutropenic enterocolitis, a growing concern in the era of widespread use of aggressive chemotherapy. *Clin Infect Dis*. 2013;56(5):711-717. doi:10.1093/cid/cis998.

Pneumocystis jirovecii Pneumonia (PJP) Prophylaxis (Non-Oncologic Indications)

1. Clemente Garulo D, Núñez-Cuadros E, Camacho Lovillo M, et al. Position statement on infection screening, prophylaxis, and vaccination in pediatric patients with rheumatic diseases and immunosuppressive therapies, part 2: infection prophylaxis. Eur J Pediatr. 2023;182(9):4271-4284. doi:10.1007/s00431-023-05080-3
2. Fragoulis GE, Nikiphorou E, Dey M, et al. 2022 EULAR recommendations for screening and prophylaxis of chronic and opportunistic infections in adults with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis. 2023;82(6):742-753. doi:10.1136/ard-2022-223335
3. Kucharzik T, Ellul P, Greuter T, et al. ECCO Guidelines on the Prevention, Diagnosis, and Management of Infections in Inflammatory Bowel Disease [published correction appears in J Crohns Colitis. 2023 Jan 27;17(1):149. doi: 10.1093/ecco-jcc/jjac104]. J Crohns Colitis. 2021;15(6):879-913. doi:10.1093/ecco-jcc/jjab052
4. Malpica L, Moll S. Practical approach to monitoring and prevention of infectious complications associated with systemic corticosteroids, antimetabolites, cyclosporine, and cyclophosphamide in nonmalignant hematologic diseases. Hematology Am Soc Hematol Educ Program. 2020 Dec 4;2020(1):319-327. doi: 10.1182/hematology.2020000116. PMID: 33275674; PMCID: PMC7727566.
5. Park JW, Curtis JR, Moon J, Song YW, Kim S, Lee EB. Prophylactic effect of trimethoprim-sulfamethoxazole for pneumocystis pneumonia in patients with rheumatic diseases exposed to prolonged high-dose glucocorticoids. Ann Rheum Dis. 2018;77(5):644-649. Doi:10.1136/annrheumdis-2017-211796

Febrile infants <u>≤</u> 60 days old clinical pathway

1. Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kuppermann N, O'Leary ST, Okechukwu K, Woods CR Jr; SUBCOMMITTEE ON FEBRILE INFANTS. Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old. *Pediatrics*. 2021 Aug;148(2):e2021052228. doi: 10.1542/peds.2021-052228. Epub 2021 Jul 19. Erratum in: *Pediatrics*. 2021 Nov;148(5): PMID: 34281996.
2. Alpern ER, et al. Time to Positive Blood and Cerebrospinal Fluid Cultures in Febrile Infants ≤60 Days of Age. *Hosp Pediatr*. 2020 Sep;10(9):719-727. doi: 10.1542/hpeds.2020-0045. PMID: 32868377; PMCID: PMC7446544.
3. Van Reempts PJ, Van Overmeire B, Mahieu LM, Vanacker KJ. Clinical experience with ceftriaxone treatment in the neonate. *Chemotherapy*. 1995 Jul-Aug;41(4):316-22. doi: 10.1159/000239361. PMID: 7555213.
4. Meyers RS, Thackray J, Matson KL, McPherson C, Lubsch L, Hellinga RC, Hoff DS. *K*ey Potentially *I*nappropriate *D*rugs in Pediatrics: The KIDs List. *J Pediatr Pharmacol Ther*. 2020;25(3):175-191. doi: 10.5863/1551-6776-25.3.175. PMID: 32265601; PMCID: PMC7134587.
5. Nigrovic LE, Malley R, Agrawal D, Kuppermann N; Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Low risk of bacterial meningitis in children with a positive enteroviral polymerase chain reaction test result. *Clin Infect Dis*. 2010;51(10):1221–1222
6. King RL, Lorch SA, Cohen DM, Hodinka RL, Cohn KA, Shah SS. Routine cerebrospinal fluid enterovirus polymerase chain reaction testing reduces hospitalization and antibiotic use for infants 90 days of age or younger. *Pediatrics*. 2007;120(3):489–496
7. Kimberlin DW, Baley J; Committee on infectious diseases; Committee on fetus and newborn. Guidance on management of asymptomatic neonates born to women with active genital herpes lesions. *Pediatrics*. 2013 Feb;131(2):e635-46. doi: 10.1542/peds.2012-3216. Epub 2013 Jan 28. PMID: 23359576; PMCID: PMC3557411.
8. Mahajan P, et al. Serious Bacterial Infections in Young Febrile Infants With Positive Urinalysis Results. *Pediatrics*. 2022 Oct 1;150(4):e2021055633. doi: 10.1542/peds.2021-055633. PMID: 36097858; PMCID: PMC9648158.
9. Kuppermann N, et al. A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections. *JAMA Pediatr*. 2019 Apr 1;173(4):342-351. doi: 10.1001/jamapediatrics.2018.5501. PMID: 30776077; PMCID: PMC6450281.
10. Thomson J, et al. Cerebrospinal Fluid Reference Values for Young Infants Undergoing Lumbar Puncture. *Pediatrics*. 2018 Mar;141(3):e20173405. doi: 10.1542/peds.2017-3405. Epub 2018 Feb 2. PMID: 29437883.
11. Milcent K, et al. Use of Procalcitonin Assays to Predict Serious Bacterial Infection in Young Febrile Infants. *JAMA Pediatr*. 2016 Jan;170(1):62-9. doi: 10.1001/jamapediatrics.2015.3210. Erratum in: *JAMA Pediatr*. 2016 Jun 1;170(6):624. PMID: 26595253.
12. Mahajan P, et al. Risk of Bacterial Coinfections in Febrile Infants 60 Days Old and Younger with Documented Viral Infections. *J Pediatr*. 2018 Dec;203:86-91.e2. doi: 10.1016/j.jpeds.2018.07.073. Epub 2018 Sep 6. PMID: 30195552; PMCID: PMC7094460.