

Initial management of fever (≥ 38.3 or 38.0×2) and neutropenia (ANC < 500) in children

Detailed history, physical exam and labs

- **Hx:** symptoms, exposures, phase of therapy, last IV chemo, recent procedures or transfusions, prior infectious episodes and antibiotic exposure, h/o resistant organisms (i.e. MRSA, VRE, resistant gram neg), immunizations
- **PE:** catheter site, mouth, lungs, abdomen, genital area, skin
- **Labs:** CBC with diff, 2 blood cultures (if 2 lumens of CVC, please obtain blood culture from each lumen)
 - Urine cx if dysuria or age < 1 , RVP if resp sx, *C. diff* if diarrhea
- **Imaging:** If localizable symptoms to sinuses, chest, or abdomen

Patient age	Bottle type	Blood volume per bottle
< 1 year	Pediatric aerobic	0.5 – 1 mL
1 - 8 years	Pediatric aerobic	3 mL
9 – 14 years	Adult aerobic & anaerobic	5 – 8 mL
≥ 15 years	Adult aerobic & anaerobic	10 mL

Determination of Risk

Low risk patient

Does not meet criteria for high risk

High risk patient

- AML or ALL undergoing induction
- Relapsed disease
- Clinical focus of infection other than URI (i.e., central line, pneumonia, mucositis, abd/rectal sx)
- History of resistant organisms (**discuss with ID**)

Shock regardless of risk group

Hypotension or tachycardia that cannot be explained by fever, anemia, etc.

Start empiric antimicrobial therapy (within 60 min)

- **Cefepime**
- If type I hypersensitivity, start Vancomycin + Aztreonam

Start empiric antimicrobial therapy

- **Cefepime**
- **Add Vancomycin:** cellulitis, catheter site infection, pneumonia, hypotension, AML or patient received high-dose ARA-C, h/o MRSA
- **Add Tobramycin:** h/o resistant gram neg
- **Add Metronidazole:** abd/rectal pathology

Start empiric antimicrobial therapy

- Start broad spectrum antimicrobials with **Cefepime + Tobramycin + Vancomycin**

48 hours after initiation of antimicrobial therapy

Documented infection (i.e. positive culture)- Low Risk patient

- Alter empiric regimen to best treat infection (pg. 2)
- Further antibiotics if persistent neutropenia up to discretion of oncologist

High risk patient

- Alter empiric regimen to best treat infection (pg. 2)
- Continue antibiotics until infection treated and ANC > 500 or other signs of marrow recovery

Defervescence with negative cultures- Low Risk patient

- Continue empiric therapy for 48-72 hours
- Consider discharge if clinically stable, up to discretion of oncologist (regardless of ANC)

High risk patient

- Continue empiric therapy until ANC > 500 or signs of marrow recovery, up to discretion of oncologist
- If vanc or tobra was initiated, D/C after 48h

Persistent fever but hemodynamically stable and negative cultures (High or Low Risk)

- Daily blood cultures x 3 days
- If vanc or tobra was initiated, D/C after 48 h
- Do not add antibiotics unless clinical change (i.e. new symptom or exam finding)

Persistent fever and shock (High or Low Risk)

- Continue daily blood cultures
- Alter empiric regimen to cover resistant gram positive, gram negative, and anaerobic organisms as clinically indicated
- Call ID stewardship team or consult ID

Modification of empiric regimen in setting of documented infection

Documented infection	Modification of empiric regimen
Gram positive bacteremia	Add vancomycin until susceptibilities available; Consider ethanol lock x 5 days if broviac (not port).
Gram negative bacteremia	Add tobramycin until susceptibilities available; Consider ethanol lock x 5 days if broviac (not port). Consider line removal if Pseudomonas .
Pneumonia	Consider addition of vancomycin if MRSA suspected.
Neutropenic enterocolitis	Add metronidazole.

Management of persistent fever and neutropenia (ANC <500) (lasting ≥ 5-7 days)

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Evaluation for occult fungal disease (if ANC is unlikely to recover by 10 days OR dx of AML, relapsed ALL, or highly suppressive chemotherapy)

- Obtain CT scan of chest and sinuses (age ≥ 2 years)
- Obtain CT abdomen/pelvis if positive chest CT or abdominal symptoms
- Send Aspergillus galactomannan assay
- Start empiric antifungal therapy

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Positive CT scan concerning for mold (i.e. pulmonary nodules with halo sign) or positive galactomannan

- Start **Voriconazole** if no contraindications
- Strongly consider early bronchoscopy and/or lung biopsy for definitive dx (send galactomannan from BAL)
- Obtain formal ID consult for antifungal recommendations

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Negative CT scan and galactomannan

- Start **Micafungin** as empiric therapy
- Close monitoring with weekly galactomannan

Antimicrobial dosages and monitoring parameters

Antimicrobial agent	Dose	Monitoring parameters	Trough level
Cefepime	50 mg/kg/dose IV q8h (max 2000 mg/dose)	<ul style="list-style-type: none"> CBC 	N/A
Meropenem	20 mg/kg/dose IV q8h (max 1000 mg/dose)	<ul style="list-style-type: none"> CBC 	N/A
Metronidazole	10 mg/kg/dose q8h (max 1500 mg/day)		N/A
Micafungin	1.5-3 mg/kg IV once daily (max 150 mg/dose)	<ul style="list-style-type: none"> Renal function, LFTs 	N/A
Tobramycin	2.5 mg/kg/dose Q8H <i>Note: ≥ 18 years old, consider extended interval dosing (may call pharmacy for guidance)</i>	<ul style="list-style-type: none"> Renal function 	<ul style="list-style-type: none"> Peak drawn 1 hour from start of infusion of the 3rd dose Trough drawn 30 minutes prior to 4th dose Goal peak: <u>6-8 mcg/mL</u> Goal trough: <u>0.5-1 mcg/mL</u>
Vancomycin	15 mg/kg/dose q6h (max 4000 mg/day)	<ul style="list-style-type: none"> Renal function 	<ul style="list-style-type: none"> Trough prior to 4th dose Goal trough: range is <u>10-20 mcg/mL</u> (discuss with pharmacy)
Voriconazole	<p><u>Age < 2:</u> IV: 9 mg/kg q12h PO: 9 mg/kg q12h</p> <p><u>Age 2-11:</u> IV: 9 mg/kg q12h x 2 doses, then 8 mg/kg q12h (max 350mg/dose) PO: 9 mg/kg q12h</p> <p><u>Age ≥ 12:</u> IV:</p> <ul style="list-style-type: none"> < 50kg: 9 mg/kg q12h x 2 doses, then 4 to 8 mg/kg q12h ≥ 50kg: 6 mg/kg q12h x 2 doses, then 3 to 4 mg/kg q12h <p>PO:</p> <ul style="list-style-type: none"> < 50kg: 9 mg/kg q12h (max 350mg/dose) ≥ 50kg: 200 mg q12h 	<ul style="list-style-type: none"> LFTs, renal function, electrolytes <u>AEs:</u> visual disturbances, photosensitive rash, encephalopathy 	<ul style="list-style-type: none"> Trough after 5 days Goal: <u>2-5 µg/mL</u> (trough of 1-2 may be ok) <i>Note: Intermittent therapeutic drug monitoring is warranted</i>

Selected references:

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