



Oncology Patient with Fever

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What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

Objectives of Pathway

- Decrease time to antibiotics
- Decrease morbidity/mortality from infection
- Improve rate of correct antibiotic coverage for neutropenic oncology patients with different risk factors
- Decrease unnecessary long-term antibiotic use and associated toxicities
- Increase rate of proper anti-fungal coverage
- Decrease unnecessary admissions for low risk patients

Why is Pathway Necessary?

- Febrile events occur in 1/3rd of neutropenic patients with cancer
- Infection is a major cause of morbidity/mortality
- Fever is often the first sign of potential infection
- Standardized protocols for fever & neutropenia have been shown to improve outcomes

Organisms Identified

- Shift towards a dominance of Gram positive organisms due to prophylactic antimicrobials and CVLs
 - Most common organisms
 - Coagulase-negative *Staph.*
 - *Strep. viridans*
 - *Staph. aureus* (including MRSA)
- Gram negative bacilli account for 1/3 to 1/2 of bacteremias
 - Most common organisms
 - *E. coli*
 - *Klebsiella*
 - *Pseudomonas*
 - *Acinetobacter*
 - *Enterobacter*

*Need for broad gram-positive and gram-negative coverage, including *Pseudomonas*, depending on level of risk*

Time to Initial Antibiotics

- Early intervention of antibiotics in septic patients has been shown to improve outcomes¹
- Early antibiotic administration is associated with higher survival rates in febrile neutropenic patients²
- Implementing a standard protocol for children with febrile neutropenic patients has been shown to decrease the time to antibiotic administration³

Initial Antibiotic Choices

- Ceftriaxone
 - Strong coverage against: *Streptococcus*, common Gram negatives in gut (e.g., *E. coli*, *Klebsiella*)
 - Limited coverage against: MSSA
 - No coverage against: MRSA, *Enterococcus*, *Pseudomonas*, anaerobes
- Cefepime
 - Broadens ceftriaxone's coverage to include:
 - Gram positive: MSSA (in addition to *Streptococcus*)
 - Gram negative: *Enterobacter* and *Pseudomonas* species (including *E. coli* and *Klebsiella*)
 - No coverage against: MRSA, *Enterococcus*, anaerobes
- Ceftazidime
 - Broadens ceftriaxone's coverage for Gram negatives to include *Pseudomonas*
 - Loses much of ceftriaxone's Gram positive activity (e.g., not reliable against *Streptococcus*, *Staphylococcus*, or *Enterococcus* species)
- Vancomycin
 - Very strong coverage against: Gram positives (*Staphylococcus*, *Streptococcus*, and *Enterococcus*)
 - No coverage: Gram negatives, anaerobic
 - Often added to ceftazidime to provide strong activity against common Gram negatives and Gram positives
- Metronidazole
 - Strong coverage: anaerobes (includes *Bacteroides*)
 - Added only if patient does **not** have strong anaerobic coverage and it is needed (e.g., add to vancomycin/ceftazidime or to cefepime monotherapy)
 - It is not needed if already receiving anaerobic coverage (e.g., with piperacillin/tazobactam, ampicillin/sulbactam, or meropenem)

- Early vancomycin treatment may reduce mortality in high risk patients
- However, judicious use of vancomycin is warranted as:
 - It can cause nephrotoxicity.
 - There has been a link between its overuse and the development of drug resistance in *Enterococcus* species and *S. aureus*.
- Recommend discontinuing use, after 36-48 hours of therapy, if susceptible species are not grown on culture⁴

CLINICAL PATHWAY: Oncology Patient with Fever

THIS PATHWAY
SERVES AS A GUIDE
AND DOES NOT
REPLACE CLINICAL
JUDGMENT.

This is the Oncology Patient with Fever Clinical Pathway.
We will be reviewing each component in the following slides.

Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and (2) temperature (obtained in any way) at home or in hospital 38 - 38.2°C (100.4-100.9°F) sustained over an hour or ≥38.3°C (101.1°F) at any time **and** the patient is ill-appearing (hypothermic/hypotensive/altered mental status)

Exclusion Criteria: (1) Patients who completely finished chemotherapy >1 month ago **and** no longer have a central venous line (CVL); (2) Bone marrow transplant (3) Concern for Multi-System Inflammatory Syndrome in Children (See MIS-C Clinical Pathway)

Initial Management:
ED Triage: Triage ESI Level 2

ED RN:

- Obtain vitals ASAP upon presentation
- Obtain vascular access and labs per Nursing Treatment Protocol
 - Access port/central line if present. Place PIV if unable to access or no CVL.
 - Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
 - CBC with auto diff
- If febrile and not already given in last 4 hours:
 - Give **acetaminophen** 15 mg/kg PO (max 1 g/dose)
- Do NOT give any medications per rectum.
- Do NOT give NSAIDs (contraindicated in oncology patients).

Signs of sepsis: Notify attending/fellow immediately and proceed to **Septic Shock Pathway**.

ED Provider:

- STAT: Order antibiotics¹ and labs (CBC w diff, blood cultures if not done by RN) – see dosing below¹
- Obtain H&P
 - Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

GIVE ANTIBIOTICS within 1 hour of presentation (and/or fever if inpatient)!
Do NOT wait until labs have returned! Review any labs completed in past 24 hours.

Note: *If on levofloxacin/ciprofloxacin prophylaxis at home, consult in Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections
If history of resistant organisms within the past 6 months (e.g., PCN resistant viridans strep, ESBL Enterobacteriales, Pseudomonas that was difficult to treat, MRSA), consult ID to discuss proper antibiotic coverage if provider uncertain.

Low Risk:

- ANC ≥500 (on CBC done in last 24 hours) **and** well appearing; **or** no CBC available:
 - Ceftriaxone IV** 75 mg/kg/dose (max 2 g/dose) q24hr
 - If anaphylaxis to any cephalosporin, or if non-anaphylactic reaction to 3rd or higher generation cephalosporin:* Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
 - If clear viral process (e.g., B19 positive) and there is no CVL:* hold antibiotics based on clinical judgment

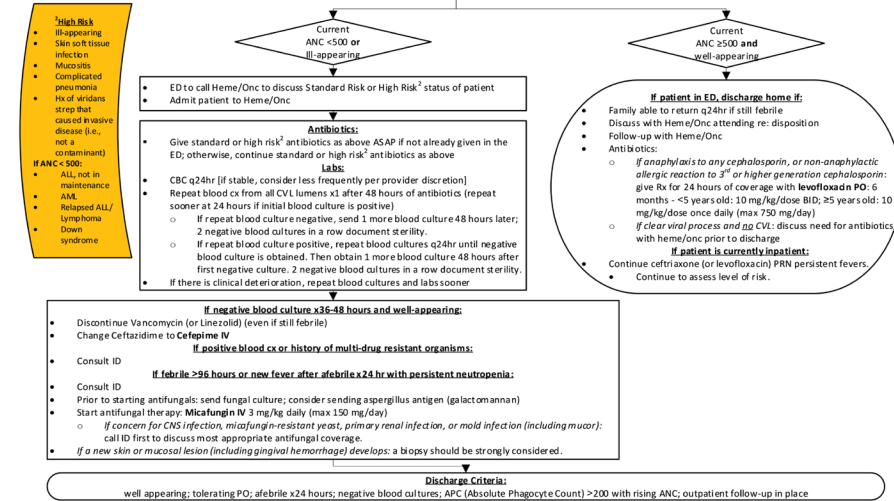
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 - Add vancomycin only if MRSA suspected

High Risk:

- Ceftazidime IV** 50 mg/kg/dose q8hr (max 2 g/dose) **and**
- Vancomycin IV** (<2 weeks PMA)/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥25 weeks PMA/about ≥3 months old – 11 years old: 70 mg/kg/day div q8hr (max 3 g/day); ≥12 yrs old: 60 mg/kg/day div q8hr (max 3 g/day) (PMA (Post-Menstrual Age) = gestational age + postnatal age)
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- If skin/soft tissue infection:* obtain skin culture ASAP (preferably before antibiotic). Consider adding "skin and soft tissue MSSA/MRSA PCR swab" (needs separate swab from wound culture)

Concern for Neutropenic Enterocolitis/Typhlitis:
Add **metronidazole IV** 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.



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Exclusion Criteria: (1) Patients who completely finished chemotherapy >1 month ago **and** no longer have a central venous line (CVL); (2) Bone marrow transplant (3) Concern for Multi-System Inflammatory Syndrome in Children (see **MIS-C Clinical Pathway**)

- Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
- CBC with auto diff
- If febrile and not already given in last 4 hours:
 - Give **acetaminophen** 15 mg/kg PO (max 1 g/dose)
 - Do NOT give any medications per rectum.
 - Do NOT give NSAIDs (contraindicated in oncology patients).
- Signs of sepsis: Notify attending/fellow immediately and proceed to **Septic Shock Pathway**.
- Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

GIVE ANTIBIOTICS within 1 hour of presentation (and/or fever if inpatient!)
Do NOT wait until labs have returned! Review any labs completed in past 24 hours.

Note: "If on levofloxacin/ciprofloxacin prophylaxis at home, consult in Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections. If history of resistant organisms within the past 6 months (e.g., PCN resistant viridans strep, ESBL Enterobacteriales, Pseudomonas that was difficult to treat, MRSA), consult ID to discuss proper antibiotic coverage if provider uncertain.

Low Risk:

- ANC ≥500 (on CBC done in last 24 hours) **and** well appearing; **or** no CBC available:
 - **Ceftriaxone IV** 75 mg/kg/dose (max 2 g/dose) Q24hr
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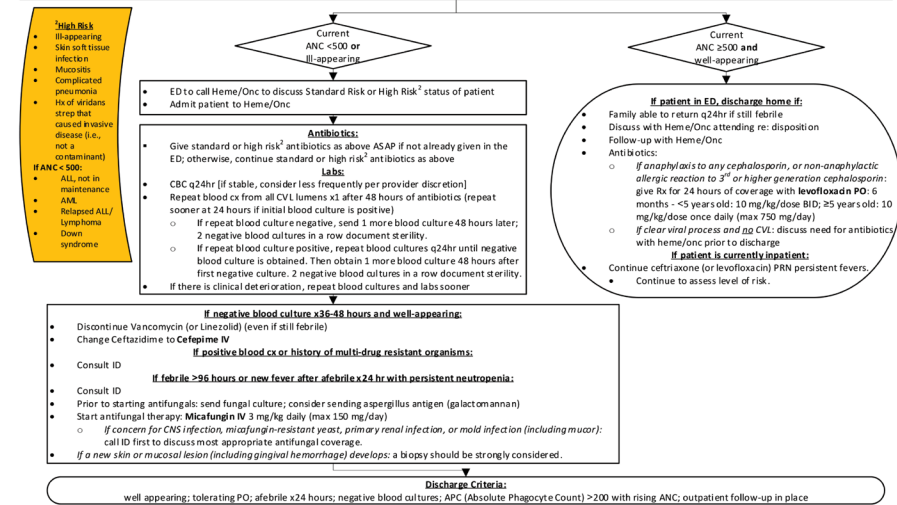
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 - Add vancomycin only if MRSA suspected

High Risk:

- **Ceftazidime IV** 50 mg/kg/dose q8hr (max 2 g/dose) **and**
- **Vancomycin IV** (<2 weeks PMA) about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA/about ≥3 months old – 11 years old: 70 mg/kg/day div q8hr (max 3 g/day); ≥12 yrs old: 60 mg/kg/day div q8hr (max 3 g/day) (PMA (Post-Menstrual Age) = gestational age + postnatal age)
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- *If skin/soft tissue infection:* obtain skin culture ASAP (preferably before antibiotic). Consider adding "skin and soft tissue MSSA/MRSA PCR swab" (needs separate swab from wound culture)

Concern for Neutropenic Enterocolitis/Typhlitis:
to antibiotic regimen for Standard Risk or High Risk*, if not already initiated.



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Inclusion criteria:

- Oncology patients who are receiving chemotherapy/radiation **AND**
- Temperature 38-38.2°C (100.4-100.9°F) sustained for an hour **OR** ≥38.3°C (101°F) at anytime **OR** ill appearing

Exclusion criteria:

- Completed chemotherapy > 1 month **AND** no longer have central lines
- Bone marrow transplants

CLINICAL PATHWAY: Oncology Patient with Fever

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Immediate evaluation is necessary to ensure management is initiated quickly. Care is outlined for nurses and providers.

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Initial Management: ED Triage: Triage ESI Level 2

ED RN:

- Obtain vitals ASAP upon presentation
- Obtain vascular access and labs per Nursing Treatment Protocol
 - Access port/central line if present. Place PIV if unable to access or no CVL.
 - Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
 - CBC with auto diff
- If febrile and not already given in last 4 hours:
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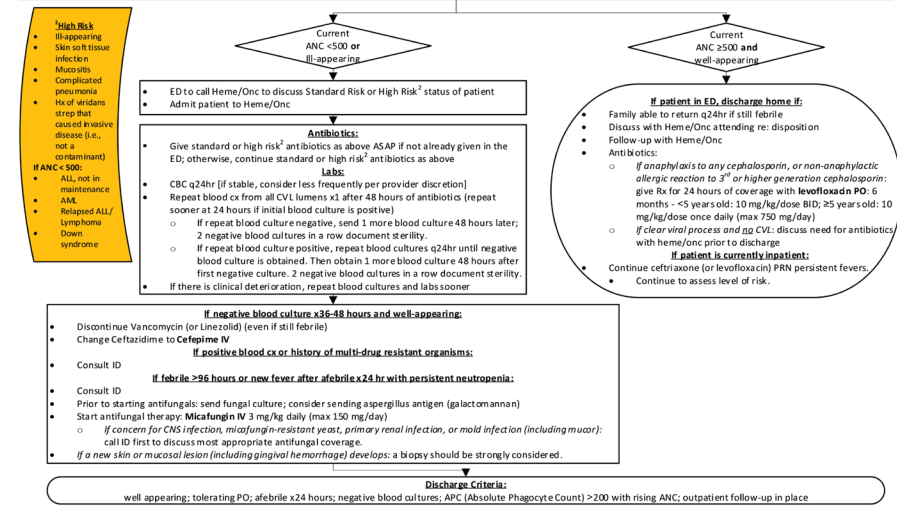
ED Provider:

- STAT:** Order antibiotics¹ and labs (CBC w diff, blood cultures if not done by RN) – see dosing below¹
- Obtain H&P
 - Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

Signs of sepsis: Notify attending/fellow immediately and proceed to **Septic Shock Pathway**.

*** If signs of septic shock are present, notify attending immediately and start the Septic Shock Pathway ***

Concern for Neutropenic Enterocolitis/Typhlitis:
Add metronidazole IV 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.



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ANTIBIOTICS SHOULD BE GIVEN WITHIN 1 HOUR OF PRESENTATION

Do not wait for labs to return!

Antibiotics are chosen based on ANC and risk factors of the patient.

$$[ANC = WBC * (\%Neutrophils + \%Bands)]$$



1 GIVE ANTIBIOTICS within 1 hour of presentation (and/or fever if inpatient)! Do NOT wait until labs have returned! Review any labs completed in past 24 hours.

Note: *If on levofloxacin/ciprofloxacin prophylaxis at home, consult Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections.

If history of resistant organisms within the past 6 months (e.g., PCN resistant viridans strep, ESBL Enterobacteriales, *Pseudomonas* that was difficult to treat, MRSA), consult ID to discuss proper antibiotic coverage if provider uncertain.

Low Risk:

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 - *If clear viral process (e.g., Biofire positive) and there is no CVL:* hold antibiotics based on clinical judgment

Standard Risk:

- ANC <500 (on CBC done in last 24 hours):
 - ***Cefepime IV** 50 mg/kg/dose q8hr (max dose 2 g/dose)
 - *If non-anaphylactic allergy to 3rd or higher generation cephalosporin:* Piperacillin/Tazobactam IV 100 mg/kg q6hr (max 4.5 g)
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High Risk²:

- ***Ceftazidime IV** 50 mg/kg/dose q8hr (max 2 g/dose) **and**
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- *If skin/soft tissue infection:* obtain skin culture ASAP (preferably before antibiotics). Consider adding “skin and soft tissue MSSA/MRSA PCR swab” (needs separate swab from wound culture)

Concern for Neutropenic Enterocolitis/Typhlitis:

- **Add metronidazole IV** 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.

²High Risk

- Ill-appearing
- Skin soft tissue infection
- Mucositis
- Complicated pneumonia
- Hx of viridans strep that caused invasive disease (i.e., not a contaminant)

If ANC < 500:

- ALL, not in maintenance
- AML
- Relapsed ALL/ Lymphoma
- Down syndrome

If patient in ED, discharge home if: return to return q24hr if still febrile; Heme/Onc attending re: disposition with Heme/Onc; If patient is currently inpatient: if patient is currently inpatient: ceftriaxone (or levofloxacin) PRN persistent fevers. continue to assess level of risk.

ANTIBIOTICS SHOULD BE GIVEN WITHIN 1 HOUR OF PRESENTATION

Do not wait for labs to return!

Antibiotics are chosen based on ANC and risk factors of the patient.

$$[ANC = WBC * (\%Neutrophils + \%Bands)]$$

any time or the patient is ill-appearing (hypothermic/febrile); central venous line (CVL); HS-C Clinical Pathway)

ED Provider:
Order antibiotics¹ and labs (CBC w diff, blood cultures if indicated) by RN – see dosing below!
H&P
Type of cancer; stage of treatment; recent chemotherapy, date; hx of prior infections; mucositis; CVL; erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

Do NOT give any medications per rectum.
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¹GIVE ANTIBIOTICS within 1 hour of presentation (and/or fever if inpatient)!

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Note: *If on levofloxacin/ciprofloxacin prophylaxis at home, consult Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections.

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 - If clear viral process (e.g., Biofire positive) **and** there is no CVL : hold antibiotics based on clinical judgment

Consult ID for appropriate antibiotics if patient is on antibiotic prophylaxis at home, or had a hx of resistant organisms in the past 6 months.

Standard Risk:

- ANC <500 (on CBC done in last 24 hours):
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ED Provider:

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- Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

Signs of sepsis - Notify attending if low immediate and proceed to Sepsis Shock Pathway

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Note: *If on levofloxacin/ciprofloxacin prophylaxis at home, consult Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections.

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- *Cefepime IV 50 mg/kg/dose q8hr (max dose 2 g/dose)
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- If anaphylaxis to any cephalosporin, or if non-anaphylactic allergy to 3rd or higher generation cephalosporin: Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
- If renal dysfunction present: substitute vancomycin with linezolid: <12 yr old: 30 mg/kg/day div q8hr; ≥12 yrs old: 600 mg q12hr, max 600 mg/dose [Note: prolonged linezolid use can be associated with hematologic suppression]
- If skin/soft tissue infection: obtain skin culture ASAP (preferably before antibiotics). Consider adding rifampin to antibiotic regimen if culture positive.

Low risk =

ANC ≥500 and well appearing patients

- The antibiotic of choice is ceftriaxone.
- If there is an allergy, use levofloxacin.
- Can consider holding antibiotics if there is no CVL and there is a clear viral process.

Concern for Neutropenic Enterocolitis/Typhlitis:

- Add metronidazole IV 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.

ANTIBIOTICS SHOULD BE GIVEN WITHIN 1 HOUR OF PRESENTATION

any time or the patient is ill-appearing (hypothermic/... a central venous line (CVL); [2] Bone marrow transplant [3] Concern for Multi-System Inflammatory Syndrome in Children (see MIS-C Clinical Pathway)

Standard Risk = ANC <500

- The antibiotic of choice is cefepime.
- Piperacillin/tazobactam is not longer recommended as first line:
 - Viridans streptococci coverage has now improved with cefepime.
 - Broad anaerobic coverage is not needed for standard risk patients.
- If there is a non-anaphylactic allergy to 3rd or higher cephalosporins, can give pip/tazo. If there is an anaphylactic allergy, can give levofloxacin.
- Vancomycin coverage should only be added if MRSA is suspected.

Note: *If on levofloxacin/ciprofloxacin p... If history of resistant organisms within the past 6 months (e.g., P...

- ANC ≥500 (on CBC done in last 24 hours) **and** well...
 - *Ceftriaxone IV 75 mg/kg/dose (max 2 g/dose)
 - If anaphylaxis to any cephalosporin, or if non... 10 mg/kg/dose once daily (max 750 mg/day)
 - If clear viral process (e.g., Biofire positive) **and** there is no CVL, hold antibiotics based on clinical judgment

Standard Risk:

- ANC <500 (on CBC done in last 24 hours):
 - *Cefepime IV 50 mg/kg/dose q8hr (max dose 2 g/dose)
 - If non-anaphylactic allergy to 3rd or higher generation cephalosporin: Piperacillin/Tazobactam IV 100 mg/kg q6hr (max 4.5 g)
 - If anaphylactic allergy to any cephalosporin: Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
 - Add vancomycin only if MRSA suspected

High Risk:

- *Ceftazidime IV 50 mg/kg/dose q8hr (max 2 g/dose) **and**
- *Vancomycin IV (<52 weeks PMA[†]/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA[†]/about ≥3 months old – 11 years old: 70 mg/kg/day div q6hr (max 3 g/day); ≥12 yrs old: 60 mg/kg/day div q8hr (max 3 g/day)) [[†]PMA (Post-Menstrual Age) = gestational age + postnatal age]
- If anaphylaxis to any cephalosporin, or if non-anaphylactic allergy to 3rd or higher generation cephalosporin: Vancomycin IV **and** Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
- If renal dysfunction present: substitute vancomycin with linezolid: <12 yr old: 30 mg/kg/day div q8hr (max 600 mg/dose); ≥12 yrs old: 600 mg q12hr (if ≥12 yrs old and <45 kg: 20 mg/kg/day div q12hr, max 600 mg/dose) [Note: prolonged linezolid use can be associated with hematologic suppression]
- If skin/soft tissue infection: obtain skin culture ASAP (preferably before antibiotics). Consider adding “skin and soft tissue MSSA/MRSA PCR swab” (needs separate swab from wound culture)

Concern for Neutropenic Enterocolitis/Typhlitis:

- **Add metronidazole IV** 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.



ANTIBIOTICS SHOULD BE GIVEN WITHIN 1 HOUR OF PRESENTATION

High risk patients are listed to the right.

High risk patients are at greater risk for progression to septic shock or other adverse outcome



- 2 High Risk**
- Ill-appearing
- Skin soft tissue infection
- Mucositis
- Complicated pneumonia
- Hx of viridans strep that caused invasive disease (i.e., not a contaminant)
- If ANC < 500:**
- ALL, not in maintenance
- AML
- Relapsed ALL/ Lymphoma
- Down syndrome

- Broader coverage should be initiated with ceftazidime and vancomycin.
 - Ceftazidime broadens ceftriaxone's Gram negative coverage, but loses Gram positive activity
 - Vancomycin: good Gram positive coverage including MRSA
- If there is an allergy to a 3rd or higher gen cephalosporin: vancomycin and levofloxacin should be utilized.
- If there is an SSTI, obtaining cultures and MSSA/MRSA PCR swabs will be helpful to determine appropriate coverage.

If history

• AN

○

○

○

○

• ANC < 500 (on CBC done in last 24 hours):

○

○

○

○

Standard Risk:

- ***Cefepime IV** 50 mg/kg/dose q8hr (max dose 2 g/dose)
- *If non-anaphylactic allergy to 3rd or higher generation cephalosporin:* Piperacillin/Tazobactam IV 100 mg/kg q6hr (max 4.5 g)
- *If anaphylactic allergy to any cephalosporin:* Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
- Add vancomycin only if MRSA suspected

High Risk²:

- ***Ceftazidime IV** 50 mg/kg/dose q8hr (max 2 g/dose) and
- ***Vancomycin IV** (<52 weeks PMA[‡]/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA[‡]/about ≥3 months old – 11 years old: 70 mg/kg/day div q6hr (max 3 g/day); ≥12 yrs old: 60 mg/kg/day div q8hr (max 3 g/day)) [[‡]PMA (Post-Menstrual Age) = gestational age + postnatal age]
- *If anaphylaxis to any cephalosporin, or if non-anaphylactic allergy to 3rd or higher generation cephalosporin:* Vancomycin IV and Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
- *If renal dysfunction present:* substitute vancomycin with linezolid: <12 yr old: 30 mg/kg/day div q8hr (max 600 mg/dose); ≥12 yrs old: 600 mg q12hr (if ≥12 yrs old and <45 kg: 20 mg/kg/day div q12hr, max 600 mg/dose) [Note: prolonged linezolid use can be associated with hematologic suppression]
- *If skin/soft tissue infection:* obtain skin culture ASAP (preferably before antibiotics). Consider adding "skin and soft tissue MSSA/MRSA PCR swab" (needs separate swab from wound culture)

Concern for Neutropenic Enterocolitis/Typhlitis:

- **Add metronidazole IV** 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.



ANTIBIOTICS SHOULD BE GIVEN WITHIN 1 HOUR OF PRESENTATION

any time **or** the patient is ill-appearing (hypothermic/...)

... a central venous line (CVL);
(2) Bone marrow transplant (3) Concern for Multi-System Inflammatory Syndrome in Children (see MIS-C Clinical Pathway)

Initial Management:
ED Triage: Triage ESI Level 2

ED RN:

- Obtain vitals ASAP upon presentation
- Obtain vascular access and labs per Nursing Treatment Protocol
 - Access port/central line if present. Place PIV if unable to access or no CVL.
 - Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
 - CBC with auto diff
- If febrile and not already given in last 4 hours:
 - Give **acetaminophen** 15 mg/kg PO (max 1 g/dose)
- Do NOT give any medications per rectum.
- Do NOT give NSAIDs (contraindicated in oncology patients).

Signs of sepsis - Notify attending if low immediate and proceed to Sepsis Shock Pathway

ED Provider:

- STAT:** Order antibiotics¹ and labs (CBC w diff, blood cultures if not done by RN) – see dosing below!
- Obtain H&P
 - Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

¹GIVE ANTIBIOTICS within 1 hour of presentation (and/or fever if inpatient)!

Do NOT wait until labs have returned! Review any labs completed in past 24 hours.

Note: *If on levofloxacin/ciprofloxacin prophylaxis at home, consult Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections.

If history of resistant organisms within the past 6 months (e.g., PCN resistant viridans strep, ESBL Enterobacterales, *Pseudomonas* that was difficult to treat, MRSA), consult ID to discuss proper antibiotic coverage if provider uncertain.

Concern for neutropenic enterocolitis/typhlitis:

For standard or high risk patients, if there is a concern for neutropenic enterocolitis/typhlitis, better anaerobic coverage is needed:

- Add metronidazole to the recommended antibiotics**

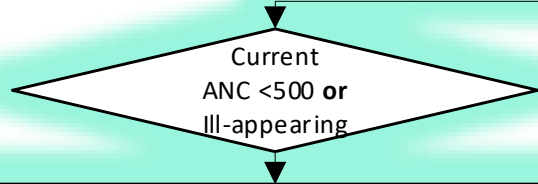
- ANC ≥500 (on C...
 - *Ceftriax...
 - If anaph...
 - 10 mg/kg
 - If clear v...
- ANC <500 (on C...
 - *Cefepime IV 50 mg/kg/dose q8hr (max dose 2 g/dose)
 - If non-anaphylactic allergy to 3rd or higher generation cephalosporin: Piperacillin/Tazobactam IV 100 mg/kg q6hr (max 4.5 g)
 - If anaphylactic allergy to any cephalosporin: Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
 - Add vancomycin only if MRSA suspected

High Risk²:

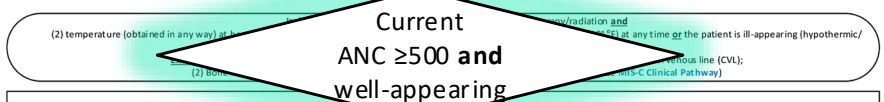
- *Ceftazidime IV 50 mg/kg/dose q8hr (max 2 g/dose) **and**
- *Vancomycin IV (<52 weeks PMA[‡]/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA[‡]/about ≥3 months old – 11 years old: 70 mg/kg/day div q6hr (max 3 g/day); ≥12 yrs old: 60 mg/kg/day div q8hr (max 3 g/day)) [[‡]PMA (Post-Menstrual Age) = gestational age + postnatal age]
- If anaphylaxis to any cephalosporin, or if non-anaphylactic allergy to 3rd or higher generation cephalosporin: Vancomycin IV **and** Levofloxacin IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
- If renal dysfunction present: substitute vancomycin with linezolid: <12 yr old: 30 mg/kg/day div q8hr (max 600 mg/dose); ≥12 yrs old: 600 mg q12hr (if ≥12 yrs old and <45 kg: 20 mg/kg/day div q12hr, max 600 mg/dose) [Note: prolonged linezolid use can be associated with hematologic suppression]
- If skin/soft tissue infection: obtain skin culture ASAP (preferably before antibiotics). Consider adding “skin and soft tissue MSSA/MRSA PCR swab” (needs separate swab from wound culture)

Concern for Neutropenic Enterocolitis/Typhlitis:

Add metronidazole IV 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.



- ED to call Heme/Onc to discuss Standard Risk or High Risk² status of patient
- Admit patient to Heme/Onc



ED RN: Obtain vitals ASAP upon presentation. Obtain vascular access and labs per Nursing Treatment Protocol. Access port/line. Blood cultures. CBC. If febrile, send blood cultures. If patient is ill-appearing, send blood cultures. ED Provider: STAT: Order antibiotics³ and labs (CBC w diff, blood cultures if not done by RN) - see dosing below!

if patient in ED, discharge home if:

- Family able to return q24hr if still febrile
- Discuss with Heme/Onc attending re: disposition
- Follow-up with Heme/Onc
- Antibiotics:
 - If anaphylaxis to any cephalosporin, or non-anaphylactic allergic reaction to 3rd or higher generation cephalosporin: give Rx for 24 hours of coverage with **levofloxacin PO**: 6 months - <5 years old: 10 mg/kg/dose BID; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
 - If clear viral process and no CVL: discuss need for antibiotics with heme/onc prior to discharge

if patient is currently inpatient:

- Continue ceftriaxone (or levofloxacin) PRN persistent fevers.
- Continue to assess level of risk.

Admission decision is made based on patient's ANC, clinical appearance, and risk factors

- ANC ≥500 and well appearing:
 - Patient will be able to be discharged home as long as they have good follow up
- ANC <500 or ill appearing:
 - Patient will likely be admitted to Heme/Onc

if patient in ED, discharge home if:

- Family able to return q24hr if still febrile
- Discuss with Heme/Onc attending re: disposition
- Follow-up with Heme/Onc
- Antibiotics:
 - If anaphylaxis to any cephalosporin, or non-anaphylactic allergic reaction to 3rd or higher generation cephalosporin: give Rx for 24 hours of coverage with **levofloxacin PO**: 6 months - <5 years old: 10 mg/kg/dose BID; ≥5 years old: 10 mg/kg/dose once daily (max 750 mg/day)
 - If clear viral process and no CVL: discuss need for antibiotics with heme/onc prior to discharge

if patient is currently inpatient:

- Continue ceftriaxone (or levofloxacin) PRN persistent fevers.
- Continue to assess level of risk.

Discharge Criteria:
well appearing; tolerating PO; afebrile x24 hours; negative blood cultures; APC (Absolute Phagocyte Count) >200 with rising ANC; outpatient follow-up in place

CLINICAL PATHWAY:
Oncology Patient with Fever

THIS PATHWAY
SERVES AS A GUIDE
AND DOES NOT
REPLACE CLINICAL
JUDGMENT.

• Those that are admitted will receive antibiotics based on risk status.

• Repeat blood cultures are not needed daily. Parameters on repeat cultures are listed here.

- ²High Risk**
- Ill-appearing
 - Skin soft tissue infection
 - Mucositis
 - Complicated pneumonia
 - Hx of viridans strep that caused invasive disease (i.e., not a contaminant)
- If ANC < 500:**
- ALL, not in maintenance
 - AML
 - Relapsed ALL/ Lymphoma
 - Down syndrome

Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and (2) temperature (obtained in any way) at home or in hospital 38 - 38.2°C (100.4-100.9°F) sustained over an hour or ≥38.3°C (101°F) at any time or the patient is ill-appearing (hypothermic/hypotensive/altered mental status)

Exclusion Criteria: (1) Patients who completely finished chemotherapy >1 month ago and no longer have a central venous line (CVL); (2) Bone marrow transplant; (3) Multi-System Inflammatory Syndrome in Children (see MIS-C Clinical Pathway)

Current ANC <500 or Ill-appearing

ED Provider:

- Order antibiotics³ and labs (CBC w diff, blood cultures if not done by RN) – see dosing below⁴
- Obtain H&P
 - Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CBC, chemistry, LFT, UA/urc, CXR, type 2 screen)

- ED to call Heme/Onc to discuss Standard Risk or High Risk² status of patient
- Admit patient to Heme/Onc

- Antibiotics:**
- Give standard or high risk² antibiotics as above ASAP if not already given in the ED; otherwise, continue standard or high risk² antibiotics as above
- Labs:**
- CBC q24hr [if stable, consider less frequently per provider discretion]
 - Repeat blood cx from all CVL lumens x1 after 48 hours of antibiotics (repeat sooner at 24 hours if initial blood culture is positive)
 - If repeat blood culture negative, send 1 more blood culture 48 hours later; 2 negative blood cultures in a row document sterility.
 - If repeat blood culture positive, repeat blood cultures q24hr until negative blood culture is obtained. Then obtain 1 more blood culture 48 hours after first negative culture. 2 negative blood cultures in a row document sterility.
 - If there is clinical deterioration, repeat blood cultures and labs sooner

If patient is currently inpatient:

- Continue ceftriaxone (or levofloxacin) PRN persistent fevers.
- Continue to assess level of risk.

- If negative blood culture x36-48 hours and well-appearing:**
- Discontinue Vancomycin (or Linezolid) (even if still febrile)
 - Change Cefazidime to Cefepime IV
- If positive blood cx or history of multi-drug resistant organisms:**
- Consult ID
- If febrile >96 hours or new fever after afebrile x24 hr with persistent neutropenia:**
- Consult ID
 - Prior to starting antifungals: send fungal culture; consider sending aspergillus antigen (galactomannan)
 - Start antifungal therapy: Micafungin IV 3 mg/kg daily (max 150 mg/day)
 - If concern for CNS infection, micafungin-resistant yeast, primary renal infection, or mold infection (including mucor): call ID first to discuss most appropriate antifungal coverage.
 - If a new skin or mucosal lesion (including gingival hemorrhage) develops: a biopsy should be strongly considered.

Discharge Criteria:

well appearing; tolerating PO; afebrile x24 hours; negative blood cultures; APC (Absolute Phagocyte Count) >200 with rising ANC; outpatient follow-up in place

CONTACTS: NATALIE BEZLER, MD | ANDREA ORSEY, MD

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CLINICAL PATHWAY:
Oncology Patient with Fever

THIS PATHWAY
SERVES AS A GUIDE
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REPLACE CLINICAL
JUDGMENT.

If negative blood culture x 36-48hrs and well appearing:

- Discontinue vancomycin
 - Prolonged use of vancomycin can increase rates of resistance
- Ceftazidime doesn't have reliable Gram positive coverage. So without vancomycin, ceftazidime should be changed to cefepime to better cover Gram positives.

If there is a positive blood culture, or there is a history of MDRO:

- Consult ID to help choose the most appropriate antibiotic coverage.

If the patient remains febrile >96 hours, OR there is a new fever after being afebrile for 24 hours with persistent neutropenia:

- There is a risk that a fungal infection is not being treated. Send fungal studies and start micafungin.
- Consult ID to help determine adequate fungal coverage or further investigation and management.

Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and (2) temperature (obtained in any way) at home or in hospital 38 - 38.2°C (100.4-100.9°F) sustained over an hour or ≥38.3°C (101°F) at any time or the patient is ill-appearing (hypothermic/hypotensive/altered mental status)

Exclusion Criteria: (1) Patients who completely finished chemotherapy >1 month ago and no longer have a central venous line (CVL); (2) Bone marrow transplant (3) Concern for Multi-System Inflammatory Syndrome in Children (see MIS-C Clinical Pathway)

Initial Management:
ED Triage: Triage ESI Level 2

ED RN:

- Obtain vitals ASAP upon presentation
- Obtain vascular access and labs per Nursing Treatment Protocol
 - Access port/central line if present. Place PIV if unable to access or no CVL.
 - Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
 - CBC with auto diff
 - If febrile and not already given in last 4 hours:
 - Give acetaminophen 15 mg/kg PO (max 1 g/dose)
 - Do NOT give any medications per rectum.
 - Do NOT give NSAIDs (as indicated in oncology patients)

ED Provider:

- STAT: Order antibiotics¹ and labs (CBC w diff, blood cultures if not done by RN) – see dosing below¹
- Obtain H&P
 - Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CRP, chemistries, LFT, UA/Uric, CXR, bone marrow)

If negative blood culture x36-48 hours and well-appearing:

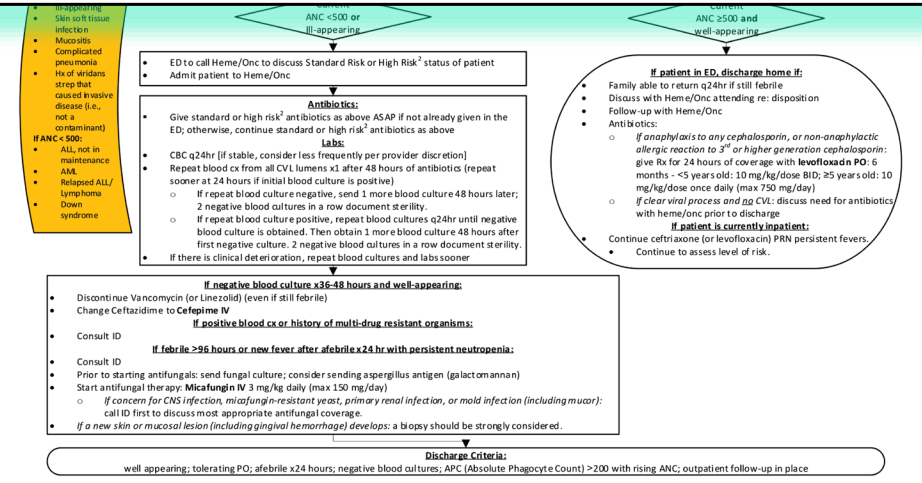
- Discontinue Vancomycin (or Linezolid) (even if still febrile)
- Change Ceftazidime to **Cefepime IV**

If positive blood cx or history of multi-drug resistant organisms:

- Consult ID

If febrile >96 hours or new fever after afebrile x24 hr with persistent neutropenia:

- Consult ID
- Prior to starting antifungals: send fungal culture; consider sending aspergillus antigen (galactomannan)
- Start antifungal therapy: **Micafungin IV** 3 mg/kg daily (max 150 mg/day)
 - If concern for CNS infection, micafungin-resistant yeast, primary renal infection, or mold infection (including mucor): call ID first to discuss most appropriate antifungal coverage.
- If a new skin or mucosal lesion (including gingival hemorrhage) develops: a biopsy should be strongly considered.



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Discharge Criteria:
well appearing; tolerating PO; afebrile x24 hours; negative blood cultures; APC (Absolute Phagocyte Count) >200 with rising ANC; outpatient follow-up in place

- ### Discharge Criteria
- Well appearing
 - Tolerating PO
 - Afebrile for 24 hours
 - Negative blood cultures
 - APC >200 and rising ANC
 - Follow-up in place

How to calculate Absolute Phagocyte Count (APC):

$$APC = WBC * (\%Segmented\ Neutrophils + \%Bands + \%Monocytes/100)$$

How to calculate Absolute Neutrophil Count (ANC):

$$ANC = WBC * (\%Neutrophils + \%Bands)$$

ED RN:

- Obtain vitals ASAP upon presentation
- Obtain vascular access and labs per Nursing Treatment Protocol
 - Access port/central line if present. Place PIV if unable to access or no CVL.
 - Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
 - CBC with auto diff
- If febrile and not already given in last 4 hours:
 - Give **acetaminophen** 15 mg/kg PO (max 1 g/dose)
- Do NOT give any medications per rectum.
- Do NOT give NSAIDs (contraindicated in oncology patients).

Signs of sepsis: Notify attending/fellow immediately and proceed to **Septic Shock Pathway**.

ED Provider:

- STAT: Order antibiotics¹ and labs (CBC w diff, blood cultures if not done by RN) – see dosing below²
- Obtain H&P
 - Type of cancer; stage of treatment; recent chemo (type, date); hx of prior infections; mucositis; CVL erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis
- Consider further work up as indicated (CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

¹GIVE ANTIBIOTICS within 1 hour of presentation (and/or fever if inpatient!)
Do NOT wait until labs have returned! Review any labs completed in past 24 hours.

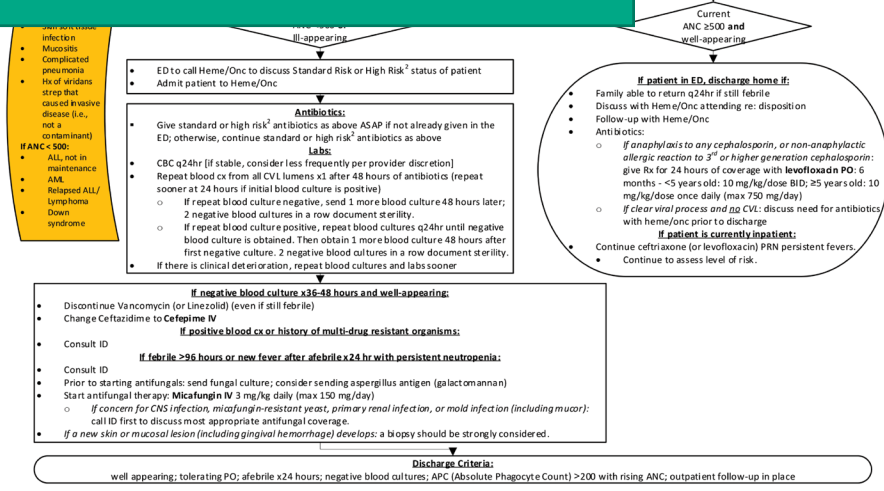
Note: *If on levofloxacin/ciprofloxacin prophylaxis at home, consult Infectious Diseases (ID) to discuss alternative antibiotics due to risk of acquired fluoroquinolone resistant infections
*If ID to discuss proper antibiotic coverage if provider uncertain.

High Risk²:

- Add vancomycin only if MRSA suspected
- *Ceftazidime IV 50 mg/kg/dose q8hr (max 2 g/dose) and
- *Vancomycin IV (<52 weeks PMA)³ about <3 mo old: 15 mg/kg q8hr or as determined by pharm svc based on estimated AUC; ≥52 weeks PMA⁴ about ≥3 months old – 11 years old: 70 mg/kg/day

Dosing:

- <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 20 mg/kg/dose q12hr
- once daily (max 750 mg/day)
- IV 6 months - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 20 mg/kg/dose q12hr (if ≥12 yrs old and <45 kg: 20 mg/kg/day div q12hr)
- "swab" (needs separate swab from wound culture)



Quality Metrics

- % Patients with pathway order set
- % Patients receiving correct initial antibiotic regimen per pathway
- % Patients changed from Ceftaz to Cefepime once Vanco is discontinued
- Average time from arrival (or start of fever) to initial antibiotic order
- Average time from antibiotic order to administration
- Average time from arrival (or start of fever) to antibiotic administration
- Pathway bundle: % Patients with correct antibiotic and arrival to abx administration \leq 60 minutes

Pathway Contacts

- Andrea Orsey, MD
 - Hematology/Oncology
- Natalie Bezler, MD
 - Hematology/Oncology

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Thank You!



About Connecticut Children's Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.