Clinical Pathways

Oncology Patient with Fever

Andrea Orsey MD Natalie S. Bezler, MD







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 gramnegative 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

- o Strong coverage against: Streptococcus, common Gram negatives in gut (e.g., E. coli, Klebsiella)
- Limited coverage against: MSSA
- o No coverage against: MRSA, Enterococcus, Pseudomonas, anaerobes

Cefepime

- o Broadens ceftriaxone's coverage to include:
 - Gram positive: MSSA (in addition to *Streptococcus*)
 - Gram negative: Enterobacter and Pseudomonas species (including E. coli and Klebsiella)
- o No coverage against: MRSA, *Enterococcus*, anaerobes

Ceftazidime

- o Broadens ceftriaxone's coverage for Gram negatives to include *Pseudomonas*
- o 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)
- o No coverage: Gram negatives, anaerobic
- o 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)

Vancomycin



- 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

This is the Oncology Patient with Fever Clinical Pathway.

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:

III-appearing

Hx of viridans

ALL, not in

maintenanc

Relapsed ALL/

If ANC < 500:

Oncology Patient with Fever

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 CVI 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)

- ED Provider:
 STAT: Order antibiotics¹ and labs (CBC w diff, blood cultures if not done by RN) - see dosing below1
- Obtain H&P
 - (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.

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 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 Infectious Diseases (ID) to discuss proper antibiotic coverage if provider is uncertain.

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 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

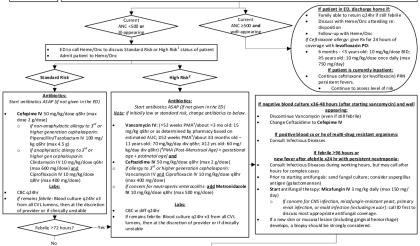
Standard Risk:

- ANC <500 (on CBC done in last 24 hours): Cefepime IV 50 mg/kg/dose q8hr (max dose 2 g/dose) Mucositis
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 - If anaphylactic allergy to 3rd or higher gen cephalosporin: Clindamycin IV 10 mg/kg/dose q6hr (max 600 mg/dose) and Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)

- Ceftazidime IV 50 mg/kg/dose q8hr (max 2 g/dose) and Vancomycin IV x1 (<52 weeks PMA¹/about <3 mo old: 15 mg/kg x1; ≥52 weeks PMA¹/about ≥3 months old − 11 years old: 17.5 mg/kg x1; ≥12 yrs old: 20 mg/kg x1) [*PMA (Post-Menstrual Age) = gestational age + postnatal age]

Concern for Neutropenic Enterocolitis/Typhlitis:

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



Discharge Criteria (1) well appearing (2) tolerating PO (3) afebrile x24 hours (4) negative blood cultures (5) APC (Absolute Phagocyte Count) >200 with rising ANC (6) outpatient follow up in place



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Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and

(2) temperature (obtained in any way) at home or in hospital $\geq 38 - 38.2^{\circ}$ C (100.4-100.9°F) sustained over an hour $\underline{or} \geq 38.3^{\circ}$ C (101°F) at any time \underline{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);

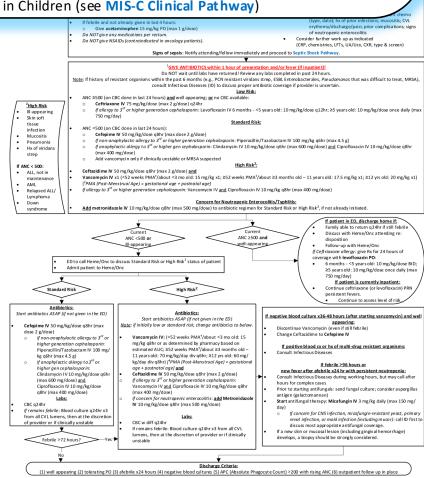
(2) Bone marrow transplant (3) Concern for Multi-System Inflammatory Syndrome in Children (see MIS-C Clinical Pathway)

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



CONTACTS: NATALIE BEZLER, MD | ANDREA ORSEY, MD

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Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and (2) temperature (obtained in any way) at home or in hospital 238 - 38.2°C (100.4-10.9°F) sustained over an hotor or 238.3°C (101°F) at any time or

<u>Initial Management:</u>

ED Triage: Triage ESI Level 2

ED RN:

- Obtain vitals ASAP upon presentation
- Obtain vascular access and labs per Nursing Treatment Protocol
 - o Access port/central line if present. Place PIV if unable to access or no CVL.
 - o Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
 - o CBC with auto diff

Immediate evaluation is

necessary to ensure

management is initiated

quickly.

Care is outlined for nurses

and providers.

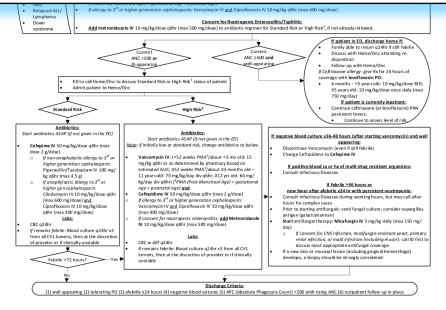
- If febrile and not already given in last 4 hours:
 - Give acetaminophen 15 mg/kg PO (max 1 g/dose)
- Do NOT give any medications per rectum.
- Do NOT give NSAIDs (contraindicated in oncology patients).

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 ***



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

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)]

High risk criteria

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and/or fever (if inpat) bs completed in past 2 p, ESBL Enterobactera ic coverage if provide

old: 10 mg/kg

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ental status)

Mucositis

Pneumonia

Hx of viridans strep

²High Risk
Ill-appearing

Skin soft tissue infection

If ANC < 500:

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

negative blood culture x36-48 hours (after starting vancomycin) and wel appearing: Discontinue Vancomycin (even if still febrile)

If positive blood cx or hx of multi-drug resistant organisms

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

Consult Infectious Diseases during working hours, but may call afthours for complex cases
Prior to starting antifungals: send fungal culture; consider a spergil antigen (galactomannan)

day)

o If concern for CNS infection, micafungin-resistant yeast, prima renal infection, or mold infection (including mucor): call ID first

renal infection, or mold infection (including mucor): call discuss most appropriate antifungal coverage. If a new skin or mucosal lesion (including gingival hemorrhage develops, a biopsy should be strongly considered.

yte Count) >200 with rising ANC (6) outpatient follow up in pla

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 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 Infectious Diseases (ID) to discuss proper antibiotic coverage if provider is 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
 - o If 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)

Standard Risk:

- ANC <500 (on CBC done in last 24 hours):
 - O Cefepime IV 50 mg/kg/dose q8hr (max dose 2 g/dose)
 - o If non-anaphylactic allergy to 3rd or higher generation cephalosporin: Piperacillin/Tazobactam IV 100 mg/kg q6hr (max 4.5 g)
 - o If anaphylactic allergy to 3rd or higher gen æphalosporin: Clindamycin IV 10 mg/kg/dose q6hr (max 600 mg/dose) and Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)
 - Add vancomycin only if clinically unstable or MRSA suspected

High Risk²:

- Ceftazidi me IV 50 mg/kg/dose q8hr (max 2 g/dose) and
- Vancomycin IV x1 (<52 weeks PMA[‡]/about <3 mo old: 15 mg/kg x1; ≥52 weeks PMA[‡]/about ≥3 months old 11 years old: 17.5 mg/kg x1; ≥12 yrs old: 20 mg/kg x1) [$^{\dagger}PMA$ (Post-Menstrual Age) = gestational age + postnatal age]
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Concern for Neutropenic Enterocolitis/Typhlitis:

Add metronidazo le 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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Consult ID for appropriate antibiotics if the provider is uncertain, particularly for patients with a hx of resistant organisms in the past 6 months.

ental status)

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(type, date): hx of prior infections: mucositis: CVL of neutropenic enterocolitis

Consider further work up as indicate (CRP, chemistries, LFTs, UA/Ucx, CXR, type &

ESBL Enterobacterales, Pseudomonas that was difficult to treat, MRS

actam IV 100 mg/kg q6hr (max 4.5 g)

ompleted in past 24 hours

verage if provider is uncertain.

If patient in ED, discharge home if: Family able to return a 24hr if still fehril Discuss with Heme/Onc attending re: disposition Follow-up with Heme/O

If Ceft riaxone aller gy: give Rx for 24 hours of coverage with levofloxa in PO: 6 months - <5 years old: 10 mg/kg/dose BID ≥5 years old: 10 mg/kg/dose once daily (ma

If patient is currently inpatient persistent fevers.

ative blood culture x36-48 hours (after starting vancomycin) and w appearing:

Discontinue Vancomycin (even if still febrile)

If positive blood cx or hx of multi-drug resistant organisms

new fever after afebrile x24 hr with persistent neutropen hours for complex cases

antigen (galactomannan)

renal infection, or mold infection (including mucor); call ID first If a new skin or mucosal lesion (including gingival hemorrhage)

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Chandard Diele

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 - If anaphylactic allergy to 3rd or higher gen cephalosporin: Clindamycin IV 10 mg/kg/dose q (max 400 mg/dose)
 - o Add vancomycin only if clinically unstable or MRSA suspected

High Risk²:

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- If allergy to 3rd or higher generation cephalosporin: Vancomycin IV and Ciprofloxacin IV 10 mg/kg

Concern for Neutropenic Enterocolitis/T

Add metronidazole IV 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard

Low risk = ANC ≥500 and well appearing patients

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 patient

- The antibiotic of choice is ceftriaxone.
- If there is an allergy to a 3rd generation or higher cephalosporin, use levofloxacin.

disposition Follow-up with Heme/

If patient in ED, discharge home if: Family able to return q24hr if still febril

Ceft riaxone aller av: give Rx for 24 hours of

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mental status)
no longer have a central venous line (CVL);

Standard Risk = ANC <500

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Do NO1

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 - If allergy to 3rd or higher generation ceph
 750 mg/day)

- The antibiotic of choice is cefepime.
- Piperacillin/tazobactam is no 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, clinda and cipro.
- Vancomycin coverage should only be added if the patient is clinically unstable or there is MRSA suspected.

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new fever after afebrile ≥96 hours or new fever after afebrile x24 hr with persistent neutropenia; Consult Infectious Diseases during working hours, but may call a hours for complex cases

Prior to starting antifungals: send fungal culture; consider aspergilli antigen (galactomannan) Start antifungal therapy: Micafungin IV 3 mg/kg daily (max 150 mg

 If concern for CNS infection, micafungin-resistant yeast, primar renal infection, or mold infection (including mucar): call ID first discuss most appropriate antifungal coverage.
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mental status)
no longer have a central venous line (CVL);

ED Triage: Triage ESI Level ED RN: Obtain vitals ASAP upon presentation ²High Risk High risk criteria III-appearing High risk patients are listed to the right. Skin soft tissue High risk patients are at greater risk for progression to septic shock or other adverse outcome infection These patients are either Mucositis Initially designated as high risk at admission (see High Risk criteria) Pneum onia Note: If his , MRSA) Hx of viridans Or have failed low risk therapy after 72 hours strep ANC ≥ Broader coverage should be initiated with ceftazidime and vancomycin. If ANC < 500: ALL, not in Ceftazidime broadens ceftriaxone's Gram negative coverage, but loses Gram positive dailv (max maintenance activity AML Vancomycin: good Gram positive coverage including MRSA Relapsed ALL/ ANC < Lymphoma If there is an allergy to a 3rd or higher gen cephalosporin: vancomycin and ciprofloxacin Down should be utilized. syndrome ₅e a8hr discontinue Vancomycin (even if still febrile) ancomycia only if clinically unstable or MPSA suspector f positive blood cx or hx of multi-drug resistant organisms High Risk²: Ceftazidi me IV 50 mg/kg/dose q8hr (max 2 g/dose) and Vancomycin IV x1 (<52 weeks PMA † /about <3 mo old: 15 mg/kg x1; ≥52 weeks PMA † /about ≥3 months old – 11 years old: 17.5 mg/kg x1; ≥12 yrs old: 20 mg/kg x1) [*PMA (Post-Menstrual Age) = gestational age + postnatal age] If allergy to 3rd or higher generation cephalosporin: Vancomycin IV and Ciprofloxacin IV 10 mg/kg q8hr (max 400 mg/dose) enal infection, or mold infection (including mucor); call II new skin or mucosal lesion (including gingival hemorrhage Concern for Neutropenic Enterocolitis/Typhlitis:

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(CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

(type, date): hx of prior infections: mucositis: CVL erythema/discharge/pain; prior complications; sign

cultures if not done by RN) - see dosing below

of neutropenic enterocolitis Consider further work up as indicate

Obtain H&P

Initial Management: ED Triage: Triage ESI Level 2

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 CVI
- Blood cultures from all lumens of CVL; peripheral blood cx only if PIV placed
- CRC 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

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ompleted in past 24 hours ESBL Enterobacterales, Pseudomonas that was difficult to treat, MRS overage if provider is uncertain.

old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once dailv (ma

pactam IV 100 mg/kg g6hr (max 4.5 g) 6hr (max 600 mg/dose) and Ciprofloxacin IV 10 mg/kg/dose q8h

≥3 months old - 11 years old: 17.5 mg/kg x1: ≥12 yrs old: 20 mg/kg x1

aily (max ndard Risk or High Risk² if not already initiated

If patient in ED, discharge home if: Family able to return a 24hr if still febril Discuss with Heme/Onc attending re: disposition Follow-up with Heme/O

If Ceftriaxone allergy: give Rx for 24 hours of coverage with levofloxadn PO: 6 months - <5 years old: 10 mg/kg/dose BID

≥5 years old: 10 mg/kg/dose once daily (ma If patient is currently inpatient:

persistent fevers.

gative blood culture x36-48 hours (after starting vancomycin) and we appearing:

Discontinue Vancomycin (eyen if still febrile)

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

If febrile >96 hours or

new fever after afebrile x24 hr with persistent neutropenia hours for complex cases

antigen (galactomannan)

If concern for CNS infection, micafungin-resistant yeast, primar

renal infection, or mold infection (including mucor); call ID first discuss most appropriate antifungal coverage.

If a new skin or mucosal lesion (including gingival hemorrhage)

nt) >200 with rising ANC (6) outpatient follow up in place

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 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 Infectious Diseases (ID) to discuss proper antibiotic coverage if provider is uncertain.

Low Risk:

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

(max 400 mg/dose)

ANC ≥5

ANC <5

 \circ

0

Add vancomycin only if clinically unstable or MRSA suspected

High Risk²:

- Ceftazidi me IV 50 mg/kg/dose q8hr (max 2 g/dose) and
- Vancomycin IV x1 (<52 weeks PMA † /about <3 mo old: 15 mg/kg x1; ≥52 weeks PMA † /about ≥3 months old 11 years old: 17.5 mg/kg x1; ≥12 yrs old: 20 mg/kg x1) [*PMA (Post-Menstrual Age) = gestational age + postnatal age]
- If allergy to 3rd or higher generation cephalosporin: Vancomycin IV and Ciprofloxacin IV 10 mg/kg q8hr (max 400 mg/dose)

Concern for Neutropenic Enterocolitis/Typhlitis:

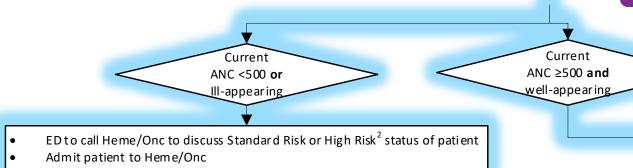
Add metronidazo le IV 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk², if not already initiated.

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CLINICAL PATHWAY: Oncology Patient with Fever

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



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

If Ceft riaxone aller gy: give Rx for 24 hours of coverage with levofloxadn 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 patient is currently inpatient:

Continue ceftriaxone (or levofloxacin) PRN persistent fevers.

Continue to assess level of risk

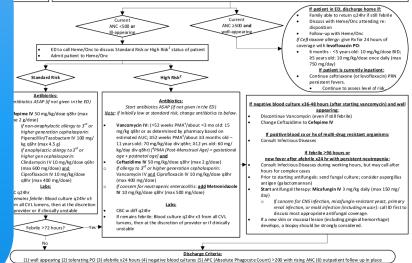
Celtasidine M 50 mg/rggrows qom (max x grows) <u>and</u>
Vancomynin M 1252 weeks PMA (blowt ≤ 30 mg/kg x1; ≥ 12 yrs old: 20 mg/kg x1

[PMA (Post-Menstruol Age) = gestational age + postnotal age)

Concern for Neutropenic Enterocolitis/Typhlitis:

Concern for Neutropenic Enterocoms/ rypnics:

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.



CONTACTS: NATALIE BEZLER, MD | ANDREA ORSEY, MD

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III-appear

Pneumonia
 Hx of viridans

ALL, not in

maintenanc

Relapsed ALL

tissue infection Mucositis



Those that are admitted with receive antibiotics based on risk status.

- Standard Risk patients will get cefepime as first line therapy
- High Risk patients will get vancomycin AND ceftazidime as first line

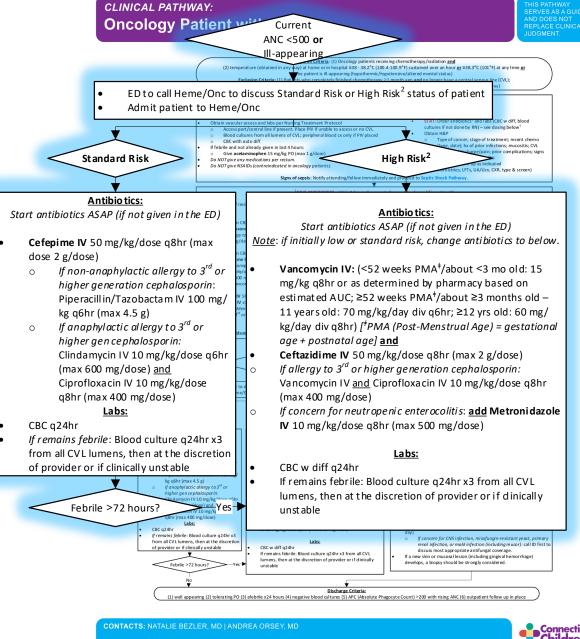
*If a Standard Risk patient remains febrile at 72 hours, proceed to the High Risk arm

²High Risk

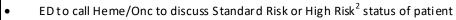
- III-appearing
- Skin soft tissue infection
- Mucositis
- Pneum onia
- Hx of viridans strep

If ANC < 500:

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







Admit patient to Heme/Onc

Standard Risk

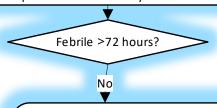
Antibio tics:

Start antibiotics ASAP (if not given in the ED)

- Cefepime IV 50 mg/kg/dose q8hr (max dose 2 g/dose)
 - If non-anaphylactic alleray to 3rd or higher generation cephalosporin: Piperacillin/Tazobactam IV 100 mg/ kg q6hr (max 4.5 g)
 - If an aphylactic allergy to 3rd or higher gen cephalosporin: Clindamycin IV 10 mg/kg/dose q6hr (max 600 mg/dose) and Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)

Labs:

- CBC q24hr
- If remains febrile: Blood culture q24hr x3 from all CVL lumens, then at the discretion of provider or if clinically unstable



CLINICAL PATHWAY: **Oncology Patient with Fever**

Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and

re (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 of 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

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 CVI
- 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 oncolo

erythema/discharge/pain; prior complications; signs of neutropenic enterocolitis

Obtain H&P

Consider further work up as indicated

(CRP, chemistries, LFTs, UA/Ucx, CXR, type & screen)

ED Provider: STAT: Order antibiotics¹ and labs (CBC w diff, blood

(type, date): hx of prior infections: mucositis: CVL

cultures if not done by RN) - see dosing below1

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

Note: 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 Infectious Diseases (ID) to discuss proper antibiotic coverage if provider is uncertain

If a standard risk patient has improvement in fevers and meets discharge criteria, they may be sent home with follow up in place.

Standard Ris

tart antibiotics ASAP (if not given in the EE

Cefepime IV 50 mg/kg/dose q8hr (max

kg q6hr (max 4.5 g)

If non-anaphylactic allergy to 3rd higher generation cephalosporin:

If anaphylactic allergy to 3rd or

Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)

If remains febrile: Blood culture q24hr x

from all CVL lumens, then at the discreti

higher gen cephalosporin:

Piperacill in/Tazobactam IV 100 mg

Clindamycin IV 10 mg/kg/dose q6h (max 600 mg/dose) and

dose 2 g/dose)

CBC q24hr

ths - <5 years old: 10 mg/kg/dose q12hr; ≥5 years old: 10 mg/kg/dose once daily (ma:

iperacillin/Tazobactam IV 100 mg/kg g6hr (max 4.5 g)

10 mg/kg/dose q6hr (max 600 mg/dose) and Ciprofloxacin IV 10 mg/kg/dose q8h

High Risk²

Start antihinties ASAP (if not given in the FD)

Vancomycin IV: (<52 weeks PMA*/about <3 mo old: 15

estimated AUC: ≥52 weeks PMA*/about ≥3 months old -

11 years old: 70 mg/kg/day div q6hr; ≥12 yrs old: 60 mg/

kg/day div q8hr) [*PMA (Post-Menstrual Age) = gestat

Ceftazidi me IV 50 mg/kg/dose q8hr (max 2 g/dose) If allergy to 3rd or higher generation cephalosporin:

If concern for neutropenic enterocolitis: add Met

IV 10 mg/kg/dose q8hr (max 500 mg/dose)

Vancomycin IV <u>and</u> Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)

If remains febrile: Blood culture g24hr x3 from all CVL

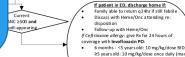
lumens, then at the discretion of provider or if dinicall

Discharge Criteria

age + postnatal age] and

CBC w diff a24hr

Note: if initially low or standard risk, change antibiotics to beld



If patient is currently inpatient:

persistent fevers.

If negative blood culture x36-48 hours (after starting vancomycin) and we appearing:

Discontinue Vancomycin (eyen if still febrile)

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

new fever after afebrile x24 hr with persistent neutropenia hours for complex cases

antigen (galactomannan)

Start antifungal therapy: Micafungin IV 3 mg/kg daily (max 150 mg

If concern for CNS infection, micafungin-resistant yeast, primar renal infection, or mold infection (including mucor); call ID first discuss most appropriate antifungal coverage.

If a new skin or mucosal lesion (including gingival hemorrhage) develops, a biopsy should be strongly considered.

Discharge Criteria: (1) well appearing (2) tolerating PO (3) afebrile x24 hours (4) negative blood cultures (5) APC (Absolute Phagocyte Count) > 200 with rising ANC (6) outpatient follow up in place



CLINICAL PATHWAY: Oncology Patient with Fever

THIS PATHWAY SERVES AS A GUIDI AND DOES NOT 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. Consider consulting ID to help determine adequate fungal coverage or further investigation and management.



Antibio tics:

Start antibiotics ASAP (if not given in the ED)

<u>Note</u>: if initially low or standard risk, change antibiotics to below.

- 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; ≥12 yrs old: 60 mg/kg/day div q8hr) [[†]PMA (Post-Menstrual Age) = gestational age + postnatal age] and
- Ceftazidime IV 50 mg/kg/dose q8hr (max 2 g/dose)
- If allergy to 3rd or higher generation cephalosporin: Vancomycin IV <u>and</u> Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)
- If concern for neutropenic enterocolitis: <u>add</u> Metronidazole
 IV 10 mg/kg/dose q8hr (max 500 mg/dose)

<u>Labs:</u>

- CBC w diff q24hr
- If remains febrile: Blood culture q24hr x3 from all CVL lumens, then at the discretion of provider or if dinically unstable

(2) temperature (obtained in any way) at home or in hospital 283-38.7° (LOL 10.9°F) sustained over an hour gr 283.8°C (LOL*F) at any time gr the patient is ill-appearing (hypothermic/hypotensive/altered mental status) Exclusion Criteria; (1) Patients who more in hospital add hemotherapy 7 anoth appear and not hospital hemotherapy 1 anoth appear and not already and lamens of CVI, peripheral blood cronly if PIV placed of CEC with auto diff if chiefler and not already given in last 4 hours: O NOT give NSAIDs (contraindated in anotology patients). Signs of septs: Notly attending/fellow immediately and proceed to Septic Shock Pathway.

If negative blood culture x36-48 hours (after starting vancomycin) and well appearing:

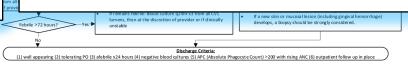
- Discontinue Vancomycin (even if still febrile)
- Change Ceftazidime to Cefepime IV

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

Consult Infectious Diseases

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

- Consult Infectious Diseases during working hours, but may call after hours for complex cases
- Prior to starting antifungals: send fungal culture; consider 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.



CONTACTS: NATALIE BEZLER, MD | ANDREA ORSEY, MD

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Inclusion Criteria: (1) Oncology patients receiving chemotherapy/radiation and 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

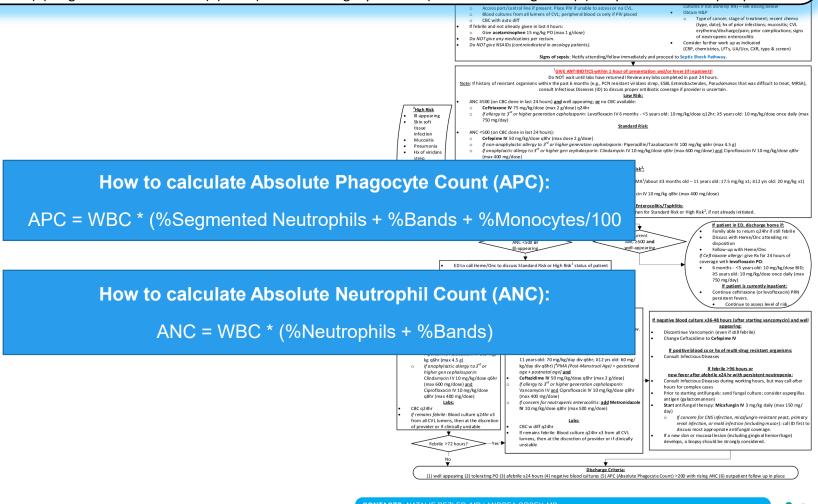
the patient is ill-appearing (hypothern

Discharge Criteria:

(1) well appearing (2) tolerating PO (3) afebrile x24 hours (4) negative blood cultures (5) APC (Absolute Phagocyte Count) >200 with rising ANC (6) 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



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Quality Metrics



- Percentage of patients with pathway order set usage
- Average time from arrival (or start of fever) to initial antibiotic order
- Average time from antibiotic order to antibiotic administration
- Average time from arrival (or start of fever) to antibiotic administration
- Percentage of patients who received the correct initial antibiotic regimen as indicated per pathway
- Percentage of patients that are appropriately changed from ceftazidime to cefepime once Vancomycin is discontinued

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.