CLINICAL PATHWAY:

Oncology Patient with Fever

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

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 (contraindicated in oncology patients).*

ED Provider:

- STAT: Order antibiotics[1] and labs (CBC w diff, blood cultures if not done by RN) – see dosing below[1]
- 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.

[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 Enterobacterales, *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., 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[2]:

- ***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:

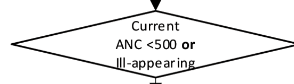
- **Add metronidazole IV** 10 mg/kg/dose q8hr (max 500 mg/dose) to antibiotic regimen for Standard Risk or High Risk[2], if not already initiated.

[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



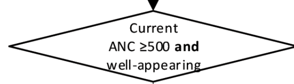
- ED to call Heme/Onc to discuss Standard Risk or High Risk[2] status of patient
- Admit patient to Heme/Onc

Antibiotics:

- Give standard or high risk[2] antibiotics as above ASAP if not already given in the ED; otherwise, continue standard or high risk[2] 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 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.

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.

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

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