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 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
  - *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):
  - **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 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)
  - Add vancomycin only if clinically unstable or MRSA suspected

High Risk[2]:
- **Ceftazidime 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 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
- Pneumonia
- Hx of viridans strep

If ANC < 500:
- ALL, not in maintenance
- AML
- Relapsed ALL/ Lymphoma
- Down syndrome

Current ANC <500 **or** Ill-appearing

Current ANC ≥500 **and** well-appearing

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 Ceftriaxone allergy: 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 patient is currently inpatient:
- Continue ceftriaxone (or levofloxacin) PRN persistent fevers.
- Continue to assess level of risk.

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

Standard Risk

Antibiotics:
Start antibiotics ASAP (if not given in the ED)
- **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 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

Febrile >72 hours? — Yes

No

High Risk[2]

Antibiotics:
Start antibiotics ASAP (if not given in the ED)
Note: 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 and Ciprofloxacin IV 10 mg/kg/dose q8hr (max 400 mg/dose)
- *If concern for neutropenic enterocolitis*: **add Metronidazole IV** 10 mg/kg/dose q8hr (max 500 mg/dose)

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

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.

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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