ONCOLOGIC EMERGENCIES IN THE URGENT CARE SETTING

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Society of Pediatric Urgent Care
Weekly Webinar
March 4, 2021

CAGT
CENTER FOR CELL AND GENE THERAPY

Texas Children's Hospital

Affiliated with Baylor College of Medicine

LEARNING OBJECTIVES

1

Recognize red flags in a patient's history and physical examination that are concerning for malignancy

2

Review the diagnosis and pathophysiology of oncologic emergencies that may present in the urgent care setting

3

Discuss early management and stabilization of patients with oncologic emergencies prior to transfer to higher acuity settings

CASE #1

- 3-year-old boy presents with intermittent fevers to Tmax of 104° F for the past month, initially thought to be a viral illness, now with increased fatigue.
- Mild cough, no congestion, no rhinorrhea, no shortness of breath, difficulty breathing, no vomiting, no diarrhea, no rash
- No known sick contacts, no recent travel history
- Reports increased irritability, especially at night, sometimes awakening him from sleep, also intermittently refusing to walk (wanting to be carried)
- No night sweats but had a 5-pound weight loss over the past month

PHYSICAL EXAM

Temp 103.1° F HR 151 BP 98/71 RR 16 SpO2 98%

GEN: well-appearing, playful, in no acute distress

HEENT: normocephalic, atraumatic, EOMI, PERRL, TMs normal bilaterally, no oral ulcers, no posterior pharyngeal erythema or edema

LYMPH: diffuse cervical, axillary, and inguinal lymphadenopathy, largest measuring 2 cm in diameter, immobile, firm, and fixed

PULM: clear to auscultation bilaterally, good air entry to bases, no crackles, no wheeze

CVS: regular rhythm, no murmurs, rubs, or gallops, radial pulses 2+ bilaterally, cap refill <2 sec

ABDO: soft, non-tender, mildly distended, no rebound/guarding, bowel sounds present, hepatosplenomegaly present

GU: testes without swelling or masses

EXT: no abnormalities, no lower limb edema

SKIN: no rashes, no bruising, no jaundice, warm, well-perfused

NEURO: functionally intact, normal gait

RED FLAG SIGNS & SYMPTOMS

- Fever lasting >4 weeks
- Unexpected weight loss
- Bone pain that awakens patient from sleep
- Night sweats
- Diffuse lymphadenopathy
- Hepatosplenomegaly

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- Mild cough, no congestion, no rhinorrhea, no shortness of breath, difficulty breathing, no vomiting, no diarrhea, no rash
- No known sick contacts, no recent travel history
- Reports increased irritability, especially at night (likely bone pain), sometimes awakening him from sleep, also intermittently refusing to walk (wanting to be carried)
- No night sweats but had a 5-pound weight loss over the past month

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INITIAL WORK-UP

- CBC/diff
- Chem10
- Uric acid, LDH
- Liver panel
- Chest x-ray if respiratory symptoms
- Infectious work-up if fevers

LABS

WBC 2540 cells/µL

ANC 610

ALC 1668

Hb 8.8 g/dL

Platelets 27,000 cells/µL

Na 137
K 5.8
Cl 105
CO_2 18
Glucose 88

Ca 7.6
Mg 1.8
Ph 7.2
BUN 14
Cr 0.3

Uric acid 8.8 mg/dL
LDH 3,216 U/L

<u>Micro:</u>

Rapid flu negative

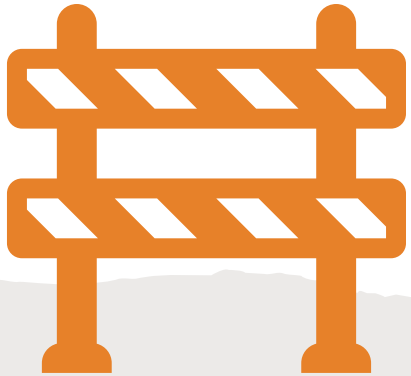
Peripheral blood cultures drawn

AST 39
ALT 35
GGT 15
Conjugated bilirubin 0.0
Unconjugated bilirubin 0.0
Albumin 4.0

ACUTE LEUKEMIA

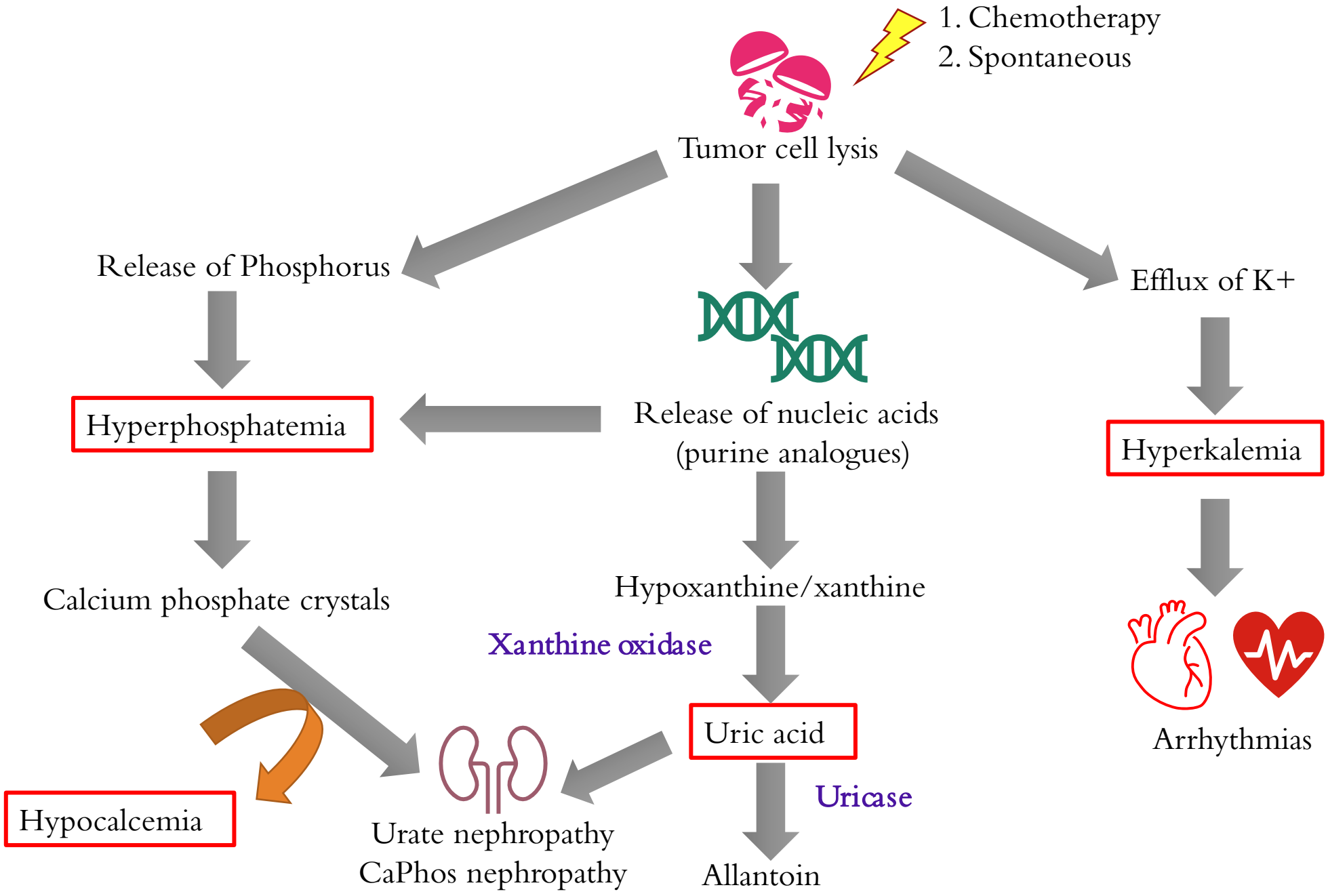
- Cancer of the white blood cells (WBCs) and their precursors (lymphoblasts, myeloblasts) that proliferate in excess within the bone marrow and other hematopoietic tissues
- Most common childhood malignancy, accounting for 29% of all cancer diagnoses in children from 0-14 years of age
  - Most common age range between 2-6 years old
- Most common leukemia = B-cell acute lymphoblastic leukemia
- Diagnosed on bone marrow aspirate and biopsy, lumbar puncture evaluating for morphology, immunologic surface markers, cytogenetic abnormalities

IF LEUKEMIA IS SUSPECTED IN A PATIENT, AVOID STARTING STEROIDS



TUMOR LYSIS SYNDROME (TLS)

PATHOPHYSIOLOGY OF TLS



RISK FACTORS FOR DEVELOPING TLS

- WBC >50,000 cells/μL
- High tumor burden (large mediastinal mass, significant hepatosplenomegaly or lymphadenopathy)
- High tumor proliferation rate (LDH ≥2x ULN)
- Presence of kidney injury (oliguria, anuria, dehydration, renal insufficiency/failure)
- Hyperuricemia
- Respiratory insufficiency

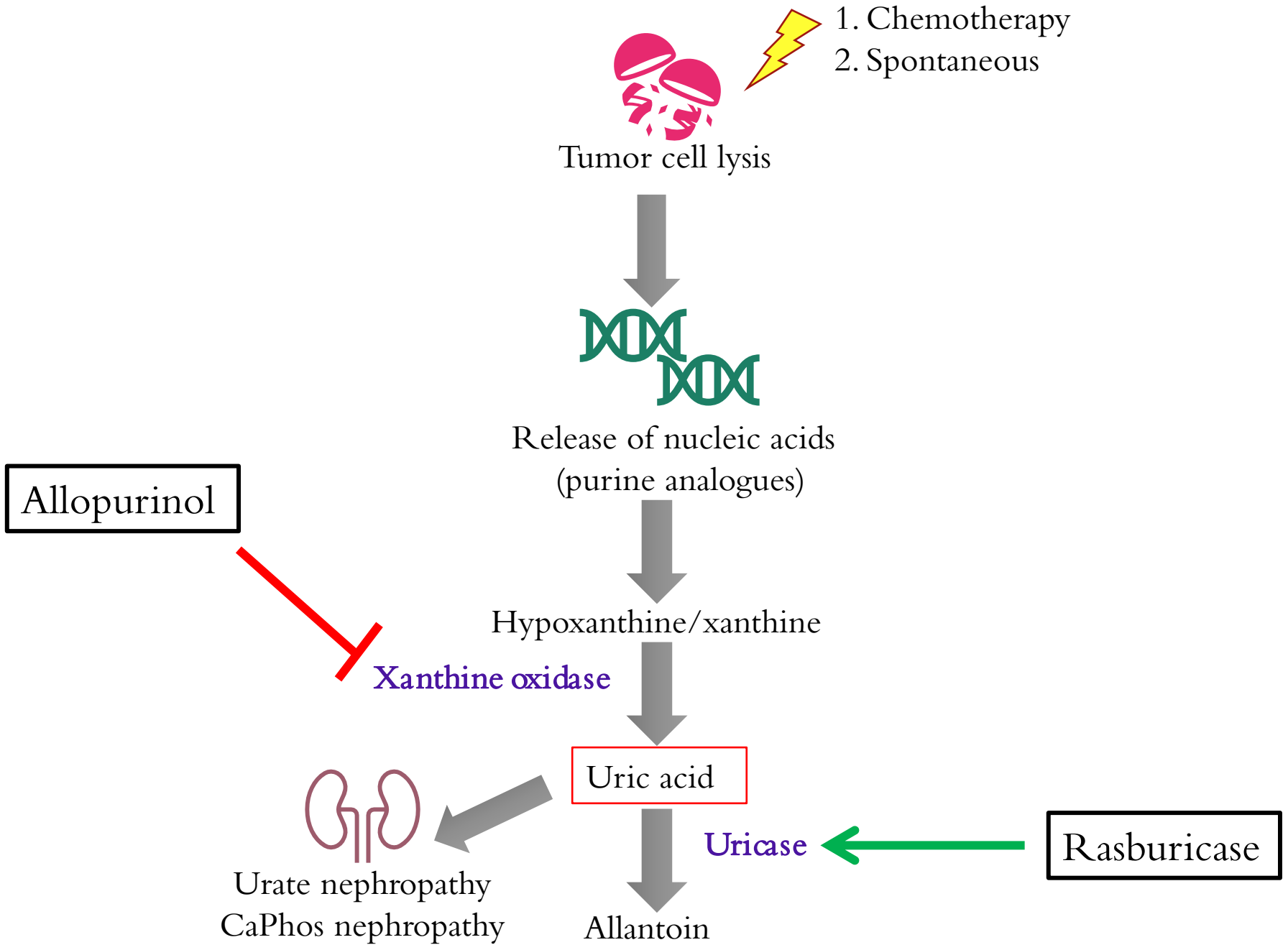
MANAGEMENT OF TLS

- Start IV fluids at 2-4x maintenance WITHOUT additives (No K, Ca, or Phosphorus)
  - Maintain intravascular volume
  - Maintain renal perfusion
  - Maintain adequate urine output ($\geq$100 mL/m^2/hr)
- Obtain EKG if hyperkalemia >6 mmol/L or symptomatic

MANAGEMENT OF ELECTROLYTE ABNORMALITIES

Electrolyte	Abnormality	Treatment
Uric Acid	≥ 8 mg/dL or 25% increase from baseline	Rasburicase Allopurinol (for uric acid <8 mg/dL)
Potassium	≥ 6 mg/dL or 25% increase from baseline	Sodium polystyrene sulfonate Furosemide Albuterol nebulizer
Phosphate	> 6.5 mg/dL or 25% increase from baseline	Sevelamer Aluminum hydroxide
Calcium	ical < 4.5 mg/dL	**ONLY TREAT IF SYMPTOMATIC** IV calcium carbonate IV calcium acetate IV calcium gluconate

PATHOPHYSIOLOGY OF TLS



INITIAL STABILIZATION & TRANSFER

- Start IV fluids (D5NS, LR) at 2x maintenance
- Monitor urine output (>100 mL/m^2/hr)
- May consider Lasix if hyperkalemic, no signs of hypovolemia, or obstructive uropathy
- Obtain EKG to evaluate for arrythmias, signs of hyperkalemia
- Initiate transfer to Emergency Center at academic medical center with Oncology service
- Can administer rasburicase and/or start allopurinol if cleared by Oncology service and if there is ability to do so

KNOWLEDGE CHECK QUESTION

Which of the following electrolyte abnormalities are observed in tumor lysis syndrome?

A. Hyperuricemia, hypokalemia, hypercalcemia, hyperphosphatemia

B. Hyperuricemia, hyperkalemia, hypercalcemia, hypophosphatemia

C. Hyperuricemia, hypokalemia, hypocalcemia, hyperphosphatemia

D. Hyperuricemia, hyperkalemia, hypocalcemia, hyperphosphatemia

CASE #2

- 12-month-old previously healthy girl presents with pallor and rash for the past 3 weeks, now with fever to Tmax of 101.5° F (axillary measurement).
- Rash developed on abdomen, raised lesions with blue hue, non-pruritic, hasn't spread to other parts of her body. Mom also noticed that her abdomen is more distended.
- Feeding well although mom recently noted that she needs to wake her up to feed
- No nausea, vomiting, diarrhea, abdominal pain, cough, congestion, shortness of breath, irritability
- Meeting developmental milestones, vaccinations up to date
- Normal birth history, no previous hospitalization or surgeries

PHYSICAL EXAM

Temp 99.2° F HR 170 BP 110/75 RR 20 SpO2 99%

GEN: Quiet, pale, in no acute distress

HEENT: normocephalic, atraumatic, EOMI, PERRL, conjunctival pallor, TMs normal bilaterally, no oral ulcers, no posterior pharyngeal erythema or edema

LYMPH: diffuse cervical, axillary, and inguinal lymphadenopathy

PULM: Clear to auscultation bilaterally, good air entry to bases, no crackles, no wheeze, no shortness of breath

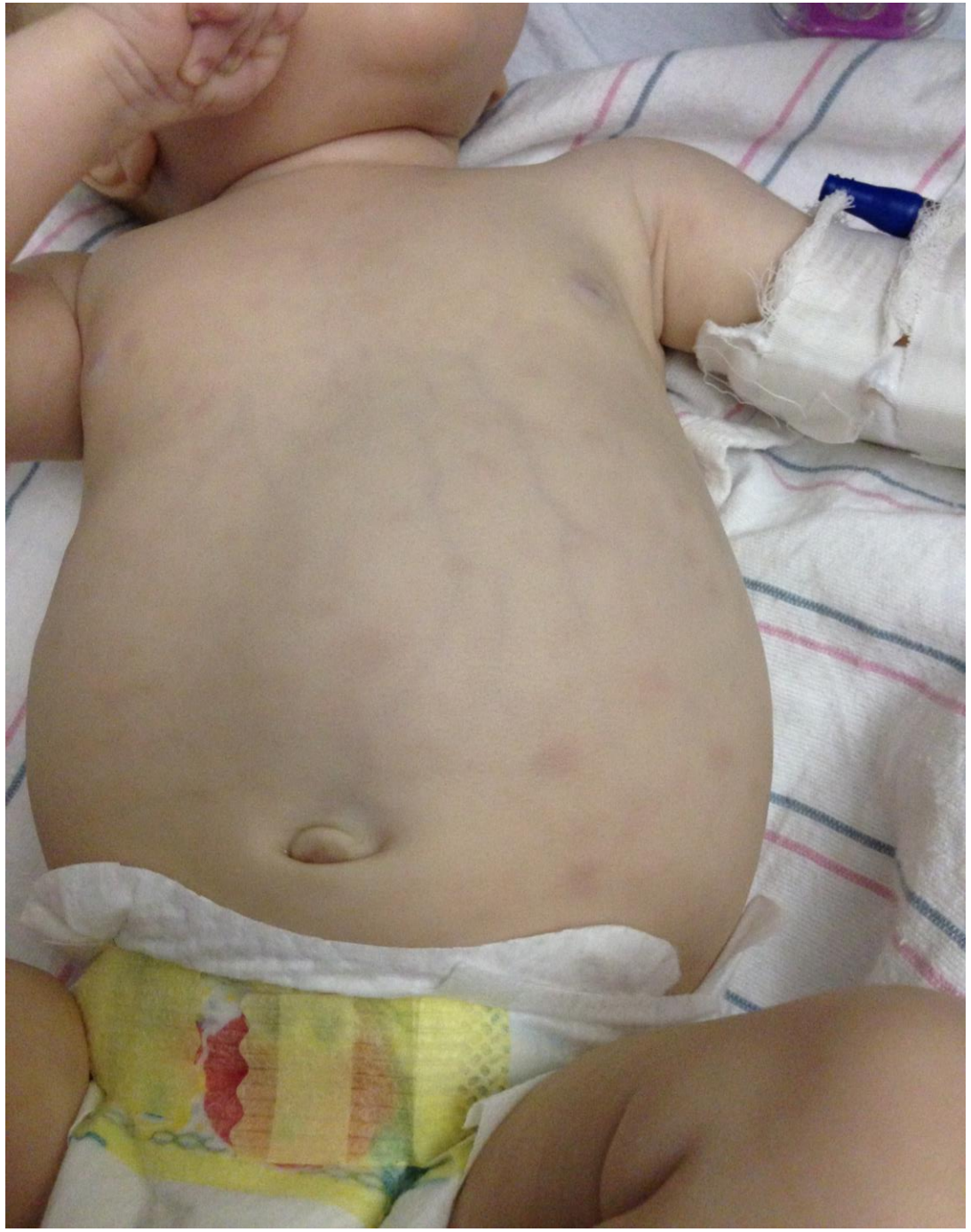
CVS: regular rhythm, no murmurs, rubs, or gallops, radial pulses 2+ bilaterally, cap refill <2 sec

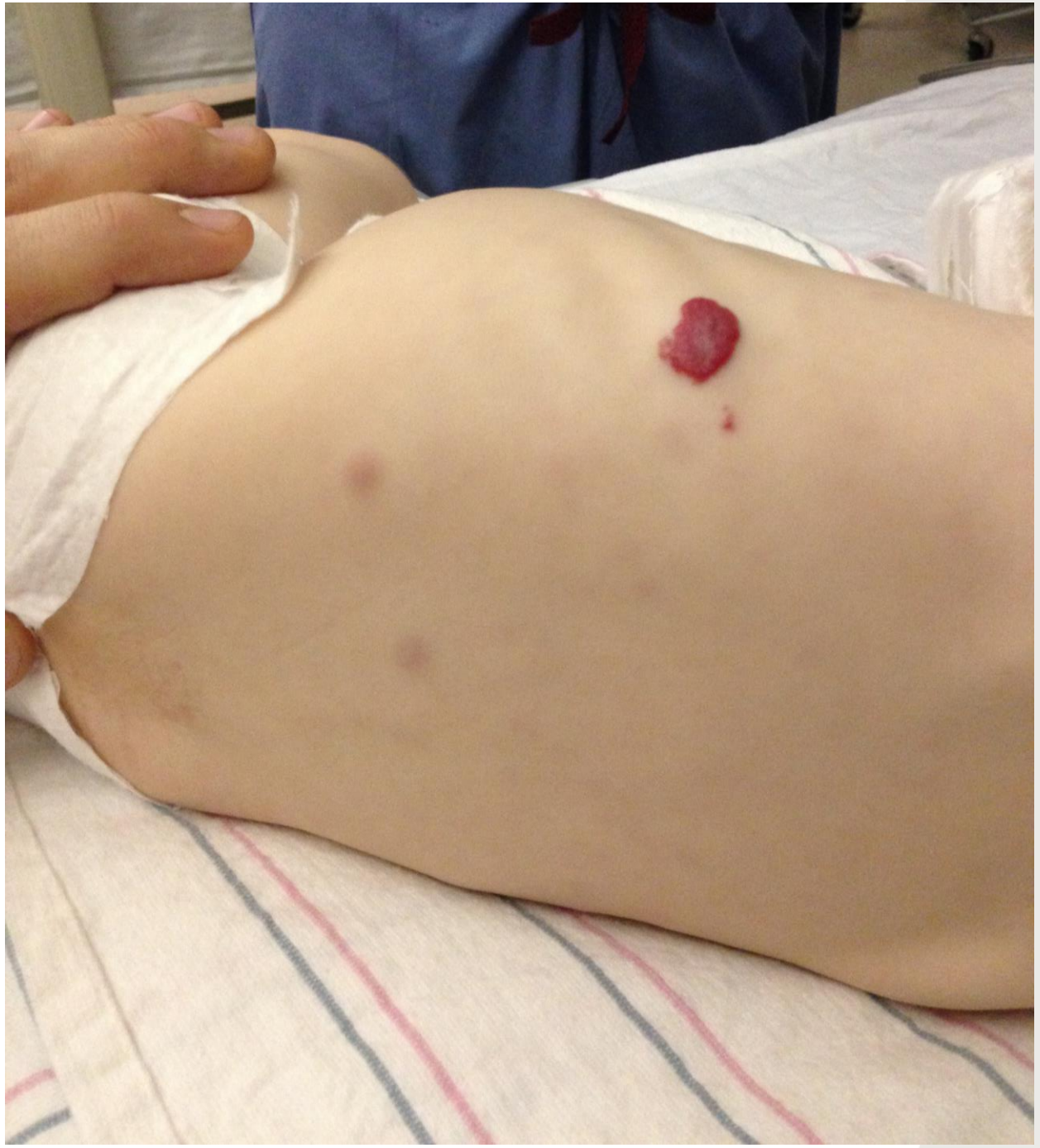
ABDO: soft, non-tender, non-distended, no rebound/guarding, bowel sounds present, hepatomegaly noted 4 cm below right costal margin, splenomegaly 6 cm below left costal margin

EXT: no abnormalities, no lower limb edema

SKIN: several macular lesions noted on abdomen with purple discoloration, no bruising, no jaundice, warm, well-perfused, hemangioma noted on left flank

NEURO: functionally intact, normal gait





LABS

WBC 372,000 cells/μL

Hb 6.8 g/dL

Platelets 44,000 cells/μL

Na 137	Ca 8.8
K 5.9	Mg 2.2
Cl 105	Ph 5.9
CO_2 18	BUN 6
Glucose 102	Cr 0.4

Uric acid 7.8 mg/dL

AST 304
ALT 20
GGT 34
Conjugated bilirubin 0.0
Unconjugated bilirubin 0.2
Albumin 4.5

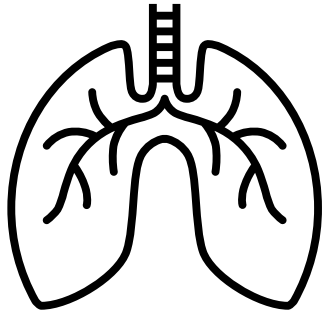
HYPERLEUKOCYTOSIS

PATHOPHYSIOLOGY OF HYPERLEUKOCYTOSIS

- Hyperleukocytosis: peripheral WBC (leukocyte) count >100,000/mm^3
- High leukocyte count leads to leukostasis: accumulation of peripheral blasts in vasculature→ increased blood viscosity→ microvascular obstruction and/or tissue hypoxia
- Clinically significant hyperleukocytosis related to size of blasts
  - In AML (larger blasts): WBC >100,000/mm^3 more likely to develop symptoms
  - In ALL (smaller blasts): WBC > 400,000/mm^3 more likely to develop symptoms
- Higher rates of early morbidity and mortality
- Poor outcome associated with higher WBC counts

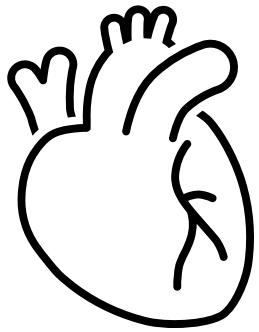
CLINICAL FEATURES OF HYPERLEUKOCYTOSIS

PULMONARY



Respiratory distress
Hypoxemia
Hemoptysis
Diffuse interstitial
or alveolar infiltrates

CARDIAC

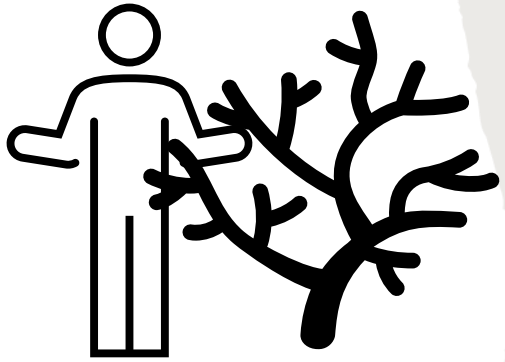


Signs of right
ventricular overload
Myocardial ischemia

NEUROLOGIC

Altered mental status
Headache
Dizziness
Seizures
Stroke
Papilledema
Visual field changes

VASCULAR



Priapism
Dactylitis
Acute limb ischemia
Bowel infarction
Renal vein thrombosis

ASYMPTOMATIC

HYPERLEUKOCYTOSIS MANAGEMENT

- Hyperhydration (≥2x maintenance IV fluids WITHOUT additives)
- Management of TLS and disseminated intravascular coagulation (maintain platelets >50,000, fibrinogen >150)
- Prompt cytoreduction
  - Chemotherapy (including steroids)
  - Leukapheresis/exchange transfusion

IMMEDIATE TRANSFER

- Once stabilized, immediately initiate transfer to Emergency Center at academic medical center with Oncology service for further management and diagnostic evaluation

CASE #3

- 14-year-old male with history of asthma presents with a 3-day history of shortness of breath and wheezing
- Last asthma exacerbation several years ago, not on controller medications, currently on the basketball team and playing well, although feels more tired after practice. No chest pain, no palpitations
- When prompted, describes night sweats that soak through his sheets several times per week, also has felt warm but didn't take his temperature, lost about 10 pounds over the past month but attributes that to increased exercise. Uses three pillows to sleep at night.
- No nausea, vomiting, abdominal pain, diarrhea, nosebleeds, gum bleeding, abnormal bruising, or rash
- Not taking any medications, no significant surgical history or hospitalizations

PHYSICAL EXAM

Temp 100.2° F HR 110 BP 110/75 RR 24 SpO2 90%

GEN: well-appearing, tired-appearing, tachypneic

HEENT: normocephalic, atraumatic, EOMI, PERRL, TMs normal bilaterally, no oral ulcers, no posterior pharyngeal erythema or edema

LYMPH: three enlarged anterior cervical lymph nodes, 5 cm in diameter, no supraclavicular, axillary, or inguinal lymphadenopathy

PULM: Mild subcostal retractions noted with occasional suprasternal tugging, decreased air entry to middle lung fields, end-expiratory wheeze noted, no crackles

CVS: regular rhythm, no murmurs, rubs, or gallops, radial pulses 2+ bilaterally, cap refill <2 sec

ABDO: soft, non-tender, non-distended, no rebound/guarding, bowel sounds present, no hepatosplenomegaly

EXT: no abnormalities, no lower limb edema

SKIN: no rashes, no bruising, no jaundice, warm, well-perfused

NEURO: functionally intact, normal gait

LABS

WBC 5660 cells/μL

ANC 3980

ALC 920

Hb 9.8 g/dL

Platelets 403,000 cells/μL

Na 140

K 4.1

Cl 102

CO_2 24

Glucose 102

Ca 8.8

Mg 2

Ph 5.5

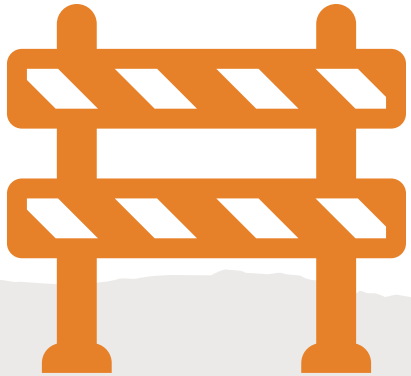
BUN 4

Cr 0.44

<u>Micro:</u>

Rapid flu negative

AVOID STARTING STEROIDS FOR ASTHMA EXACERBATION IF RED FLAGS PRESENT (OBTAIN CHEST X-RAY FIRST)



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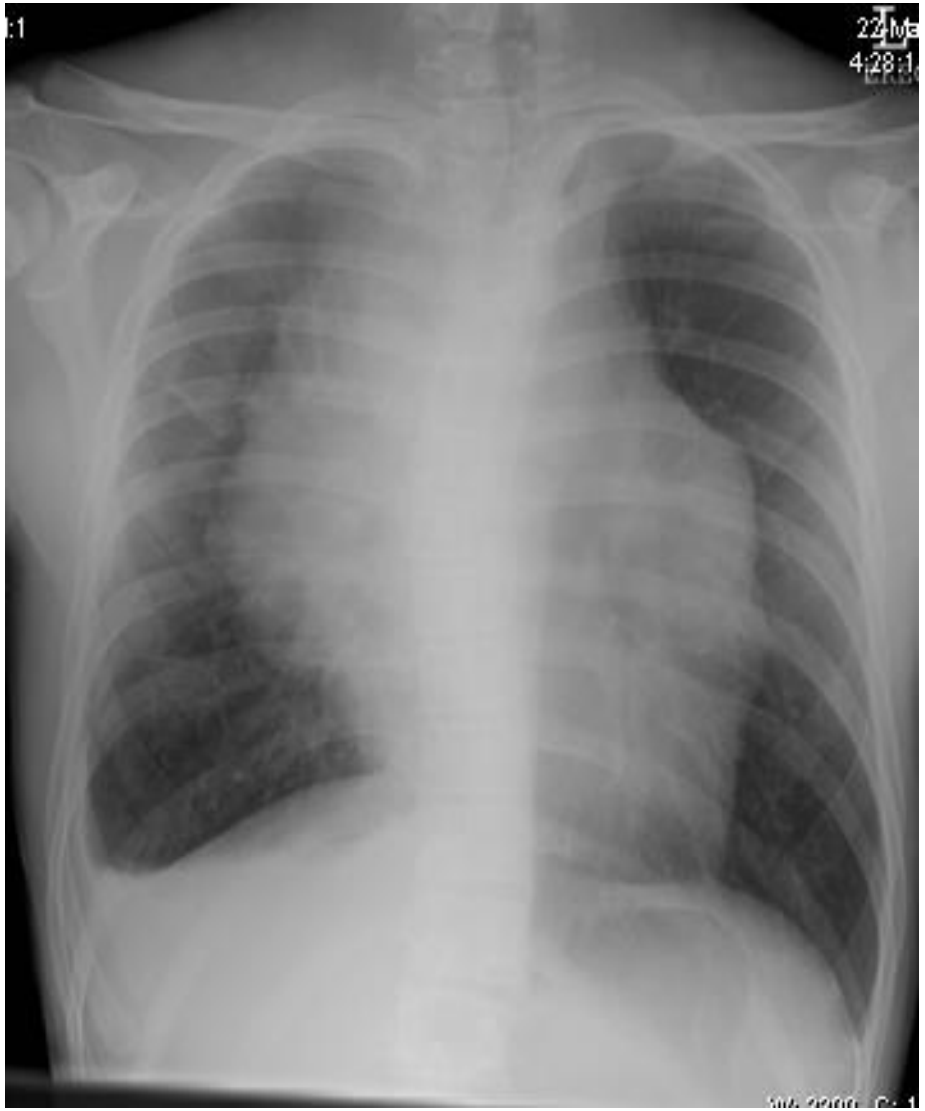
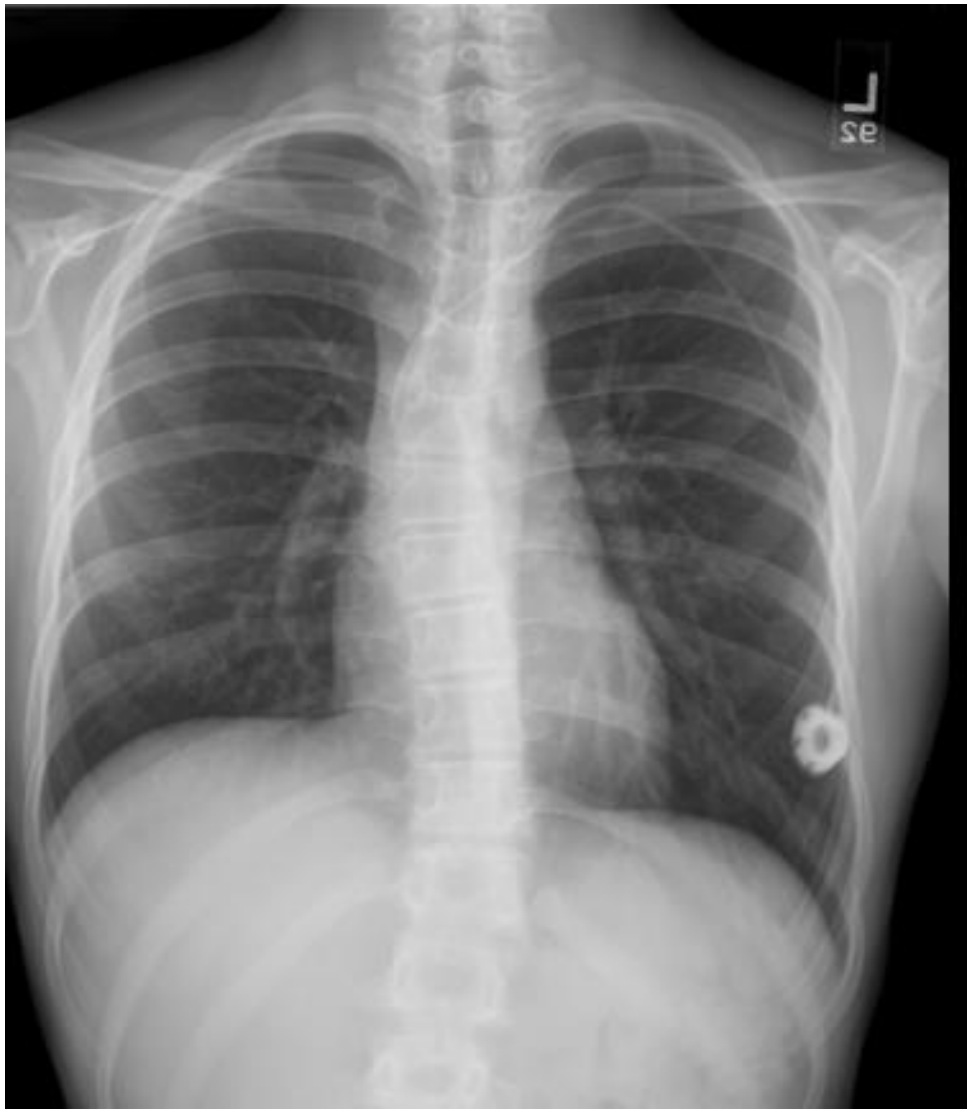
- No nausea, vomiting, abdominal pain, diarrhea, nosebleeds, gum bleeding, abnormal bruising, or rash
- Not taking any medications, no significant surgical history or hospitalizations

IMAGING

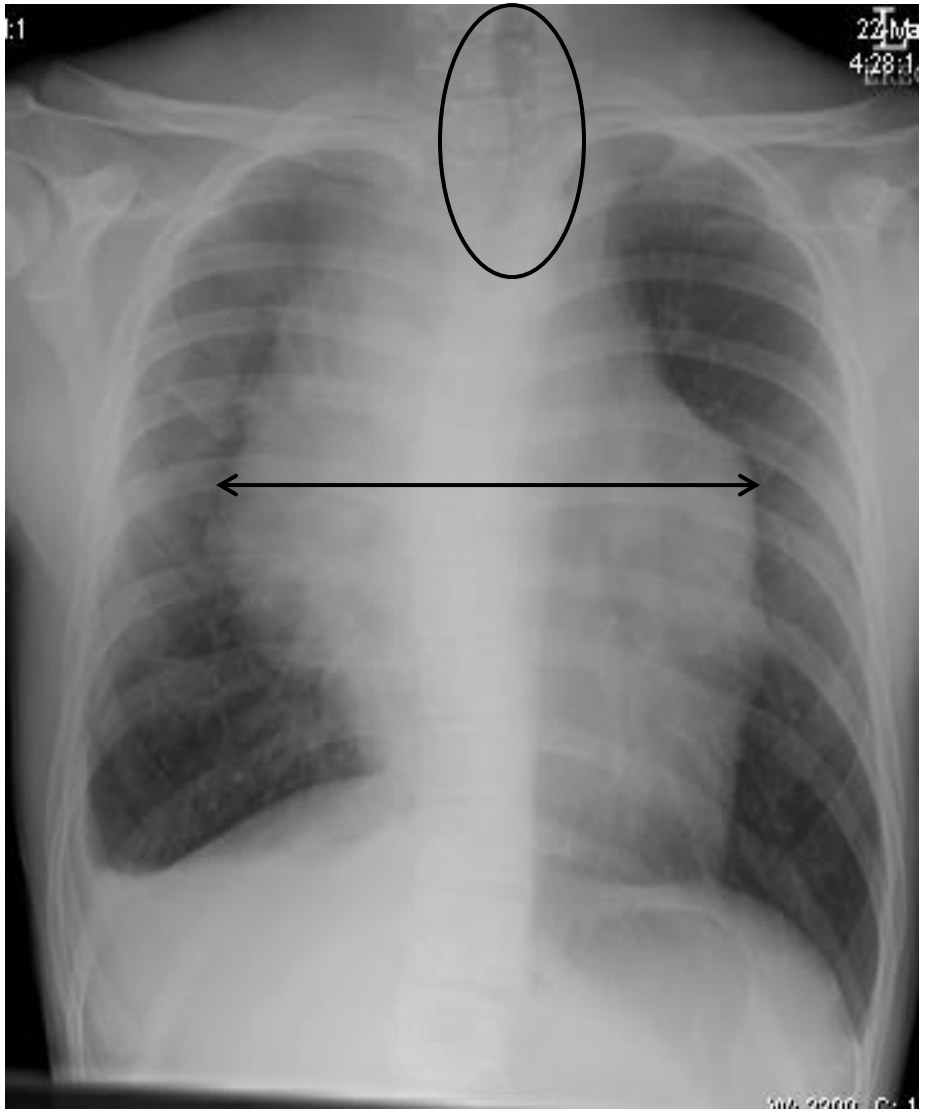


MEDIASTINAL MASS

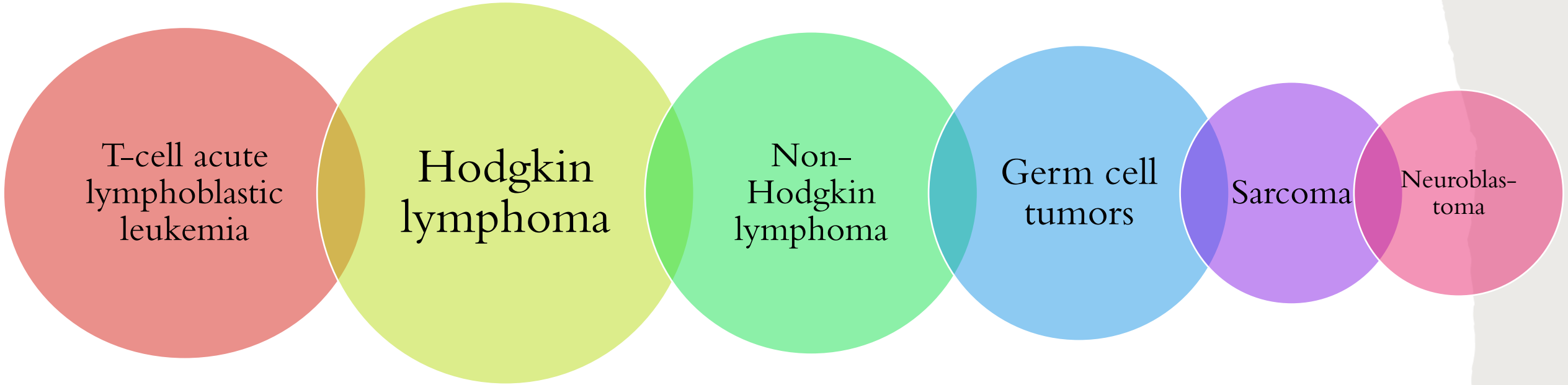
CXR one year ago



CXR today



DIAGNOSES THAT CAN PRESENT WITH MEDIASTINAL MASSES



SUPERIOR VENA CAVA SYNDROME

- Compression of mediastinal vessels and/or heart from the mass causing:
  - Prominent neck and face veins
  - Swelling or discoloration of face, neck, and upper extremities
  - Syncope
  - Chest pain
  - Shortness of breath/respiratory distress
  - Cough
  - Stridor
  - Orthopnea
  - Dyspnea

SYMPTOMS MAY BE WORSENED IN SUPINE POSITION

STABILIZATION: AIRWAY MANAGEMENT

Avoid supine positioning

Place on oxygen supplementation if hypoxemic or for comfort

Place on continuous pulse oximetry as well as cardiac monitoring

Avoid sedating and anxiolytic medications

Make patient NPO and start on maintenance IV fluids

Avoid elective intubation for airway protection

IMMEDIATE TRANSFER

- Once stabilized, immediately initiate transfer to Emergency Center at academic medical center with Oncology service for further imaging, airway control, and biopsy to confirm diagnosis
- Continue oxygen supplementation and cardiac monitoring with continuous pulse oximetry
- Maintain sitting position during transport

KNOWLEDGE CHECK QUESTION

When stabilizing a patient with a suspected mediastinal mass, the patient should be placed on supplemental oxygen, and supine positioning, elective intubation, and sedating medications should be avoided.

True

False

CASE #4

- 5-year-old female with B-cell acute lymphoblastic leukemia currently in Maintenance therapy, presents to the closest medical care facility (an urgent care center) with fever of 101.2° F. measured orally. She is from out of town and is visiting family for the winter holidays.
- Developed cough, congestion, rhinorrhea 2 days ago without difficulty breathing, shortness of breath, fatigue, vomiting, diarrhea, or rash. Positive sick contacts. No history of prior serious infections.
- Central line removed at the beginning of Maintenance therapy
- Meds: mercaptopurine PO daily, methotrexate PO weekly, Bactrim twice weekly (PJP prophylaxis)

PHYSICAL EXAM

Temp 101.7° F HR 145 BP 105/72 RR 18 SpO2 100%

GEN: well-appearing, playful, in no acute distress

HEENT: normocephalic, atraumatic, EOMI, PERRL, TMs normal bilaterally, no oral ulcers, posterior pharynx erythematous, no tonsillar exudates

LYMPH: no cervical, axillary, or inguinal lymphadenopathy

PULM: clear to auscultation bilaterally, good air entry to bases, no crackles, no wheeze

CVS: regular rhythm, no murmurs, rubs, or gallops, radial pulses 2+ bilaterally, cap refill <2 sec

ABDO: soft, non-tender, non-distended, no rebound/guarding, bowel sounds present, no hepatosplenomegaly

EXT: no abnormalities, no lower limb edema

SKIN: no rashes, no bruising, no jaundice, warm, well-perfused

NEURO: functionally intact, normal gait

LABS

WBC 1400 cells/µL	Na 137	Mg 1.9
ANC 350	K 4.2	Ph 5.4
ALC 790	Cl 99	BUN 22
Abs Mono 260	CO_2 21	Cr 0.42
Hb 9.2 g/dL	Glucose 91	
Platelets 130,000 cells/µL	Ca 9.7	

Micro:

Rapid flu negative

Peripheral blood cultures drawn

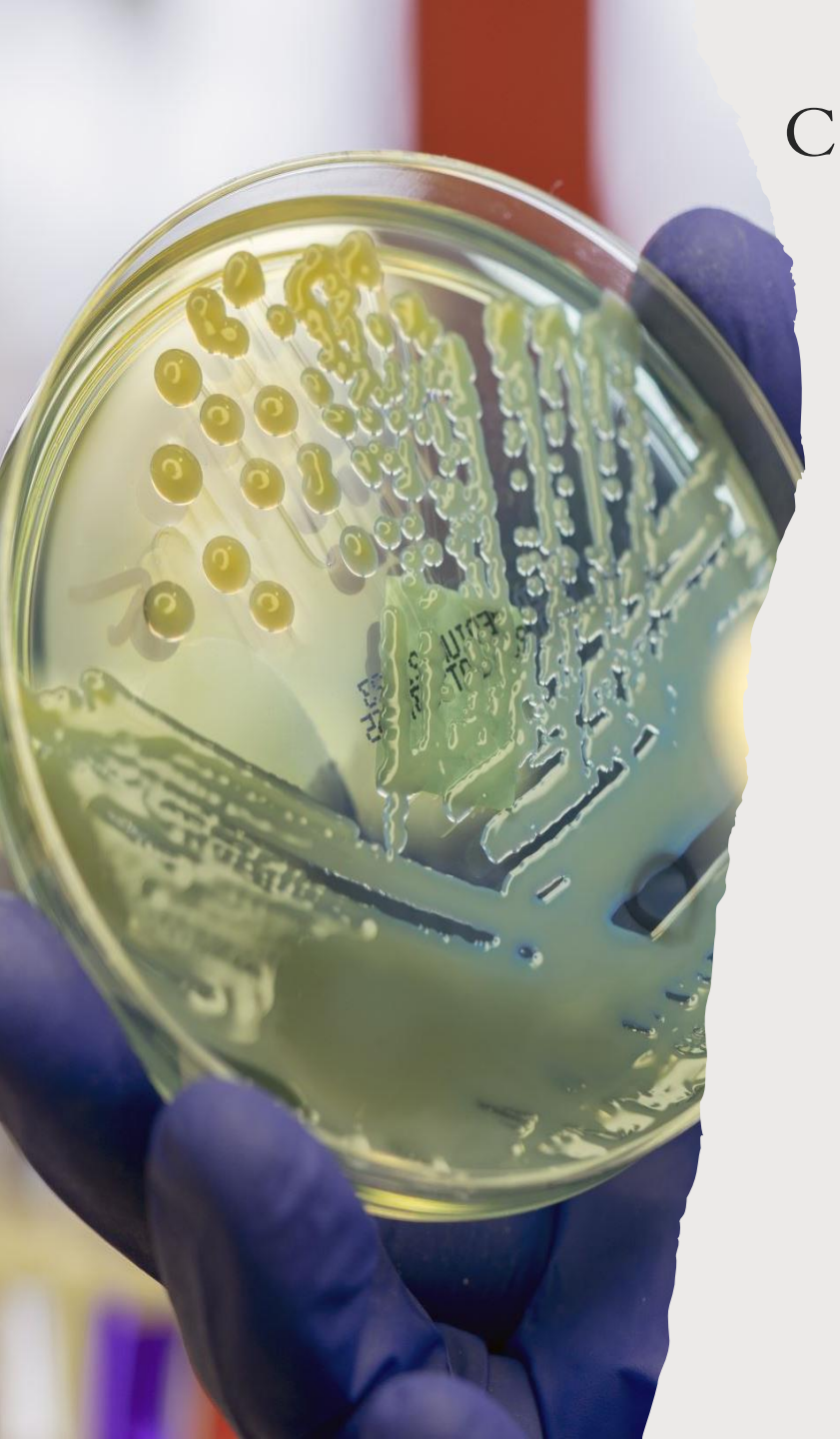
FEVER & NEUTROPENIA (F&N)

DIAGNOSIS & MANAGEMENT

- Fever of 38° C (100.4° F) x2 at least 1 hour apart OR 38.4° C (101° F)
- ANC ≤500
- Obtain history including underlying malignant diagnosis and current disease status, last chemotherapy treatment, current medications, prior serious/invasive infections
- Physical exam including vital signs, general appearance, lung, abdominal, and skin exam
- Obtain labs (CBC/diff, chemistries, renal function), blood cultures from all lumens of central catheter (if present) and peripheral culture (if possible)
- Chest x-ray only if respiratory symptoms, urine culture if symptomatic
- Administer ceftriaxone within 1 hour of presentation (while awaiting ANC to result)

SUPPORTIVE CARE

- TYLENOL for fevers
- AVOID NSAIDs or aspirin as anti-pyretics or analgesics (given thrombocytopenia)
- IV fluid bolus if tachycardic and/or hypotensive (max 20 mL/kg x3)



COMMON SOURCES OF INFECTION

- Central line (contamination leading to bloodstream infection)
- Skin/mucosal breakdown
- Respiratory illnesses (viral/bacterial)
- Translocation of gut flora

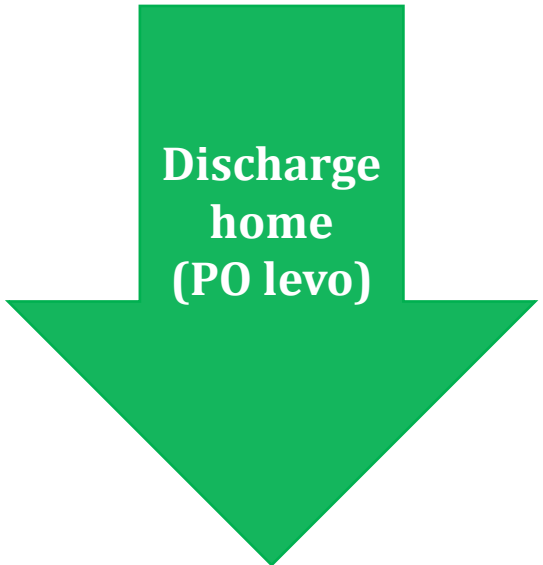
B-ALL TREATMENT AT-A-GLANCE

Induction (4 weeks)	• 3-4 chemotherapy drugs (including steroids) • **Significantly increased risk of infection**
Consolidation (8 weeks)	• 5 chemotherapy drugs (PO+IV) • Lumbar punctures (LP) with intrathecal (IT) chemo
Interim Maintenance-1 (8 weeks)	• 3 chemotherapy drugs (PO+IV)/LP+IT chemo • Hospital admission for chemotherapy (MTX)
Delayed Intensification (8 weeks)	• 5 chemotherapy drugs (PO+IV)/LP+IT chemo • **Significantly increased risk of infection**
Interim Maintenance-2 (8 weeks)	• 3 chemotherapy drugs (IV)/LP+IT chemo
Maintenance (12 week cycles)	• 4 chemotherapy drugs (mostly PO, including steroids q4wks) • 2-year total duration from start of IM-1 (~7 cycles)

DISCHARGE OR TRANSFER?

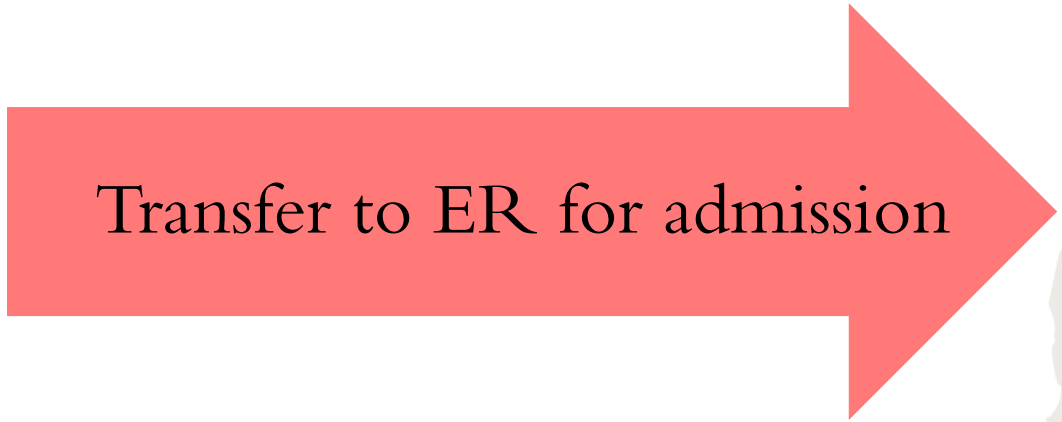
LOW-RISK

- ALL patient in Maintenance therapy
- Solid tumor patients (e.g. brain tumors, Ewing sarcoma, osteosarcoma)
- Ability to tolerate PO antibiotics (not allergic to levofloxacin)
- Ability for close follow-up

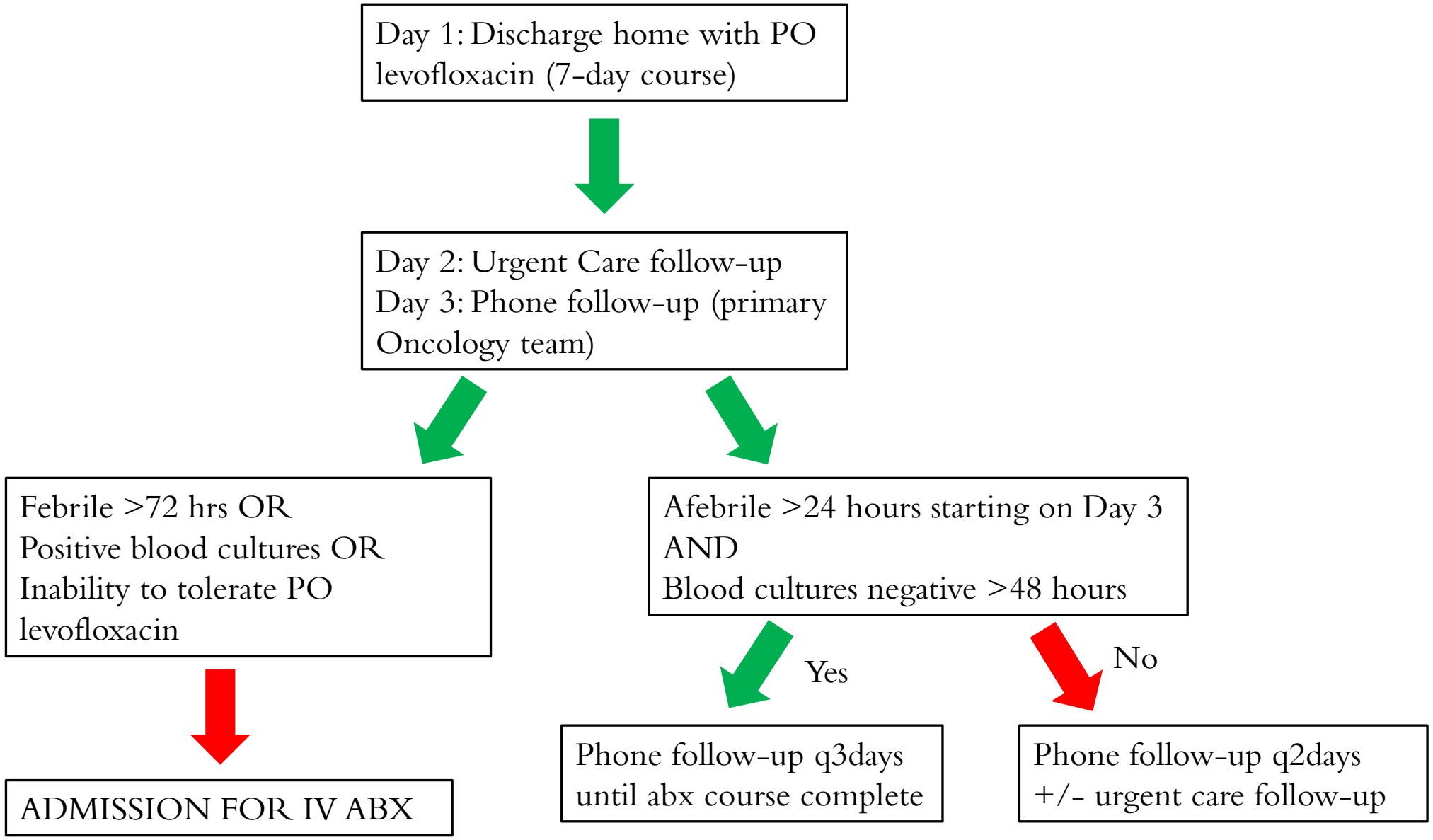


HIGH-RISK

- Any other oncologic diagnosis
- Requiring >2 boluses
- Any sign of sepsis or localizing infection



OUTPATIENT LOW-RISK F&N MANAGEMENT



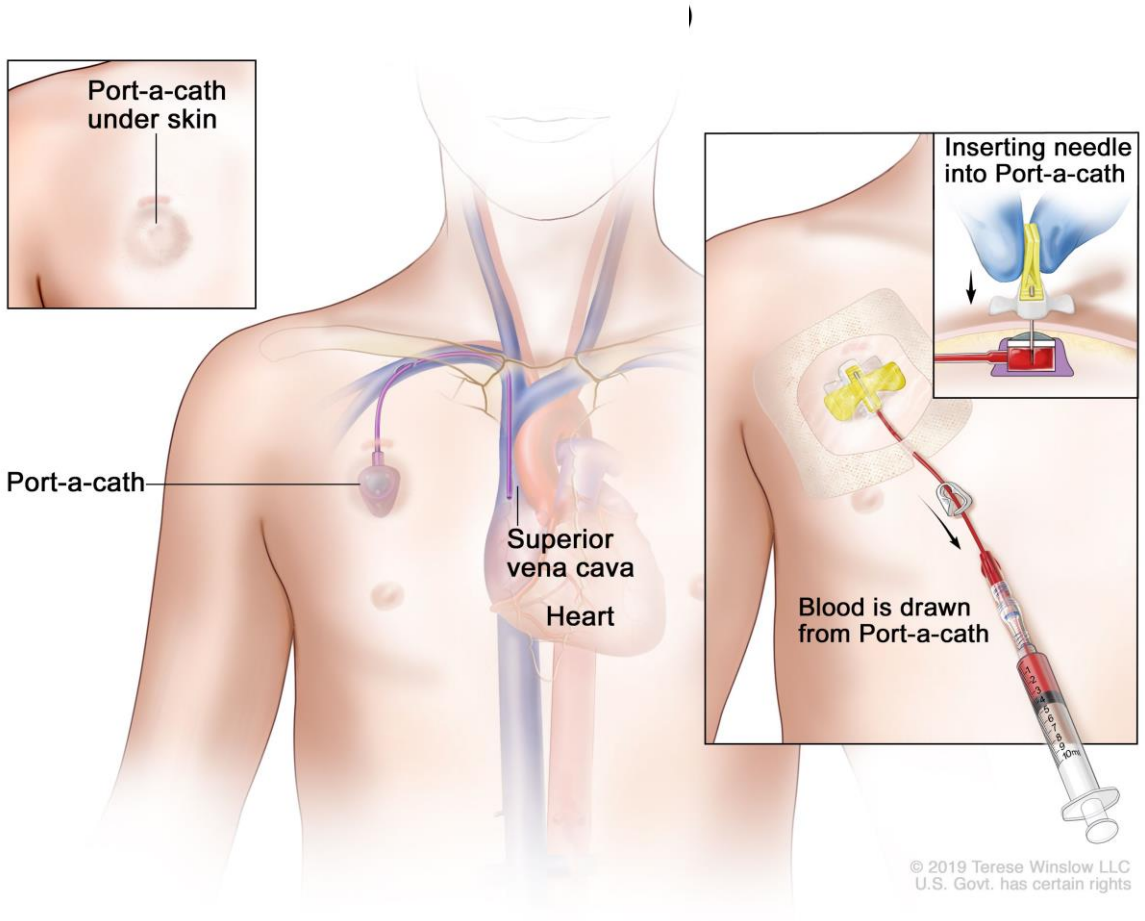
SCENARIO #2: CENTRAL LINE

CASE #4.1

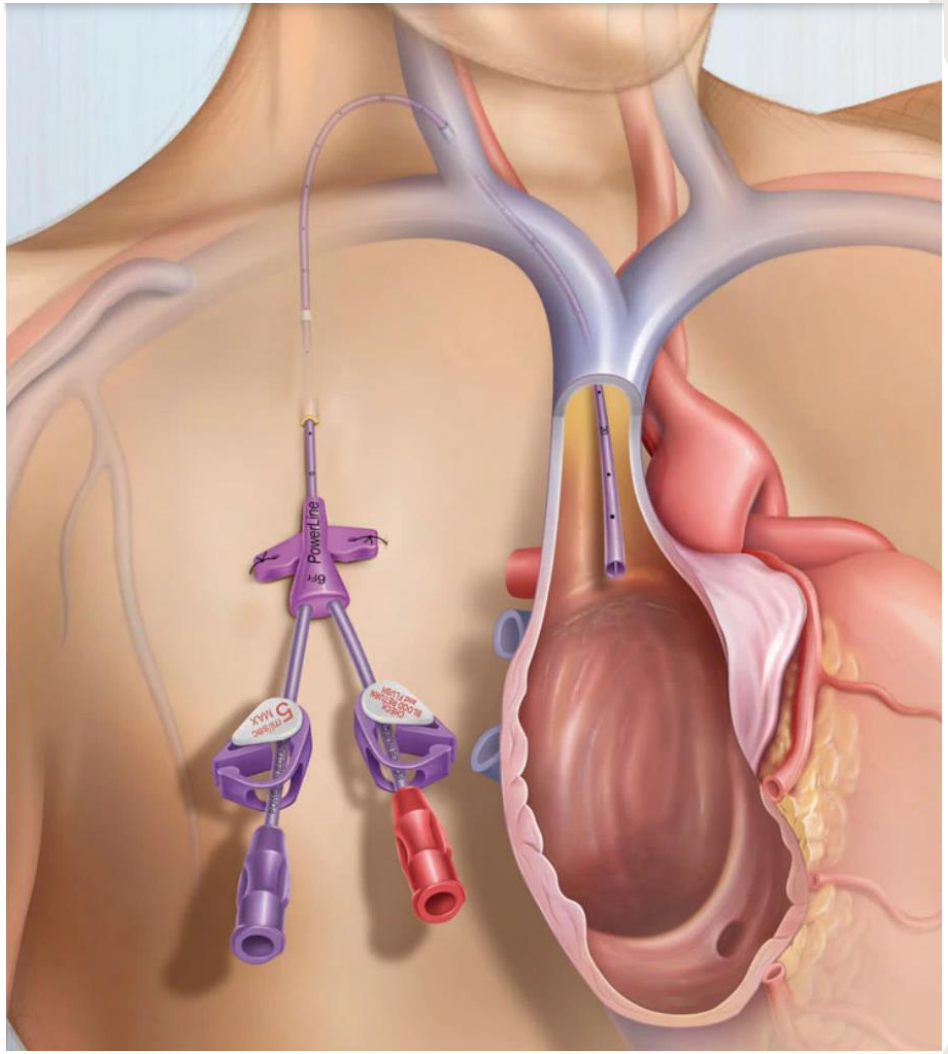
- 5-year-old female with B-cell acute lymphoblastic leukemia currently in Maintenance therapy, presents to the closest medical care facility (an urgent care center) with fever of 101.2° F. measured orally. She is from out of town and is visiting family for the holidays.
- Developed cough, congestion, rhinorrhea 2 days ago without difficulty breathing, shortness of breath, fatigue, vomiting, diarrhea, or rash. Positive sick contacts.
- Presence of central line (port-a-cath) in right chest
- Meds: mercaptopurine PO daily, methotrexate PO weekly, Bactrim twice weekly (PJP prophylaxis)

CENTRAL LINES

PORT-A-CATH (PORT)



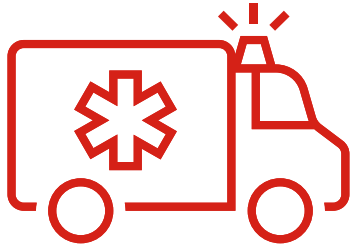
Double Lumen Central Venous Catheter



https://www.cancer.gov/publications/dictionaries/cancer-terms/def/port-a-cath
https://www.bd.com/en-us/offerings/capabilities/vascular-access/vascular-iv-catheters/central-iv-catheters/powerline-central-venous-catheter

BROAD SPECTRUM ANTIBIOTIC COVERAGE

- Obtain CBC/diff, blood cultures from all lumens of central line (in addition to peripheral blood cultures)
- Administer ceftriaxone within one hour of presentation
- Once CBC/diff results and neutropenia (ANC <500) noted, broaden antibiotic coverage to antipseudomonal 4th generation cephalosporin (e.g., cefepime), or carbapenem (e.g., meropenem)
- If unable to provide Pseudomonal coverage, transfer to closest Emergency Center for IV antibiotic administration
  - Can still qualify for low-risk criteria if all other parameters are met



KNOWLEDGE CHECK QUESTION

In which scenario would it be appropriate to discharge a febrile neutropenic oncology patient home with PO levofloxacin?

A. Solid tumor patient, required 3 IV fluid boluses, otherwise well-appearing, able to tolerate PO medications, has appropriate follow-up

B. B-ALL patient in interim maintenance therapy, required 1 IV fluid bolus, otherwise well-appearing, able to tolerate PO medication

C. B-ALL patient in maintenance therapy, otherwise well-appearing, with good follow-up, able to tolerate PO medication

D. Acute myeloid leukemia patient, otherwise well-appearing, able to tolerate PO medications, has appropriate follow-up

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QUESTIONS?