OHSU Health

Heme Malignancy Emergencies for the Hospitalist

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Objectives

- Appreciate potential pitfalls in the triage of urgencies/emergencies among patients with hematologic malignancies
  - Cancer diagnosis?
  - Level of emergency?

- Review initial management of patients with a new diagnosis of leukemia

- Review common urgencies/emergencies in patients with hematologic malignancies

Disclosures

- I have no relevant financial disclosures

Triage

Cancer Triage to ICU

- 650-bed university hospital (France)
- Cancer patient hospital mortality 5%
- Closed medical ICU (Senior intensivist makes final decision)

- 206 ICU referrals over 1 year
  - 101 refused ICU
    - 54 too sick
    - 47 too well

Thiery et al. JCO 2005

Cancer Triage to ICU

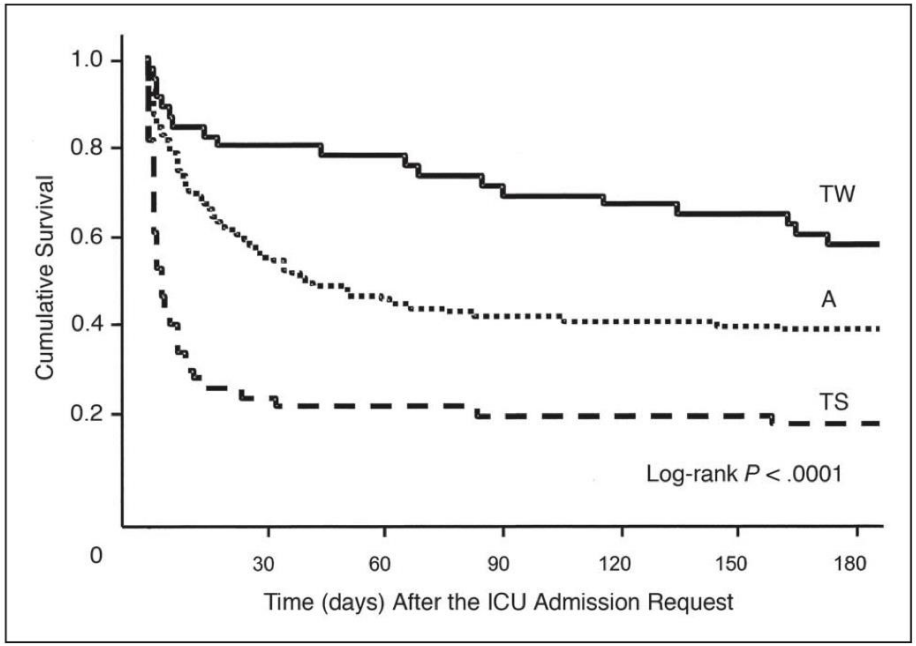


Fig 2. Survival in patients who were admitted (A; dotted line; n = 105), patients considered too sick to benefit (TS; dashed line; n = 54), and patients considered too well to benefit (TW; bolded line; n = 47). ICU, intensive care unit.

Thiery et al. JCO 2005

Triage Challenges

- Is there a cancer diagnosis?
  - Presenting with new diagnosis
  - Varied index of suspicion for cancer-related complications
  - Need to coordinate diagnostic biopsy in early management

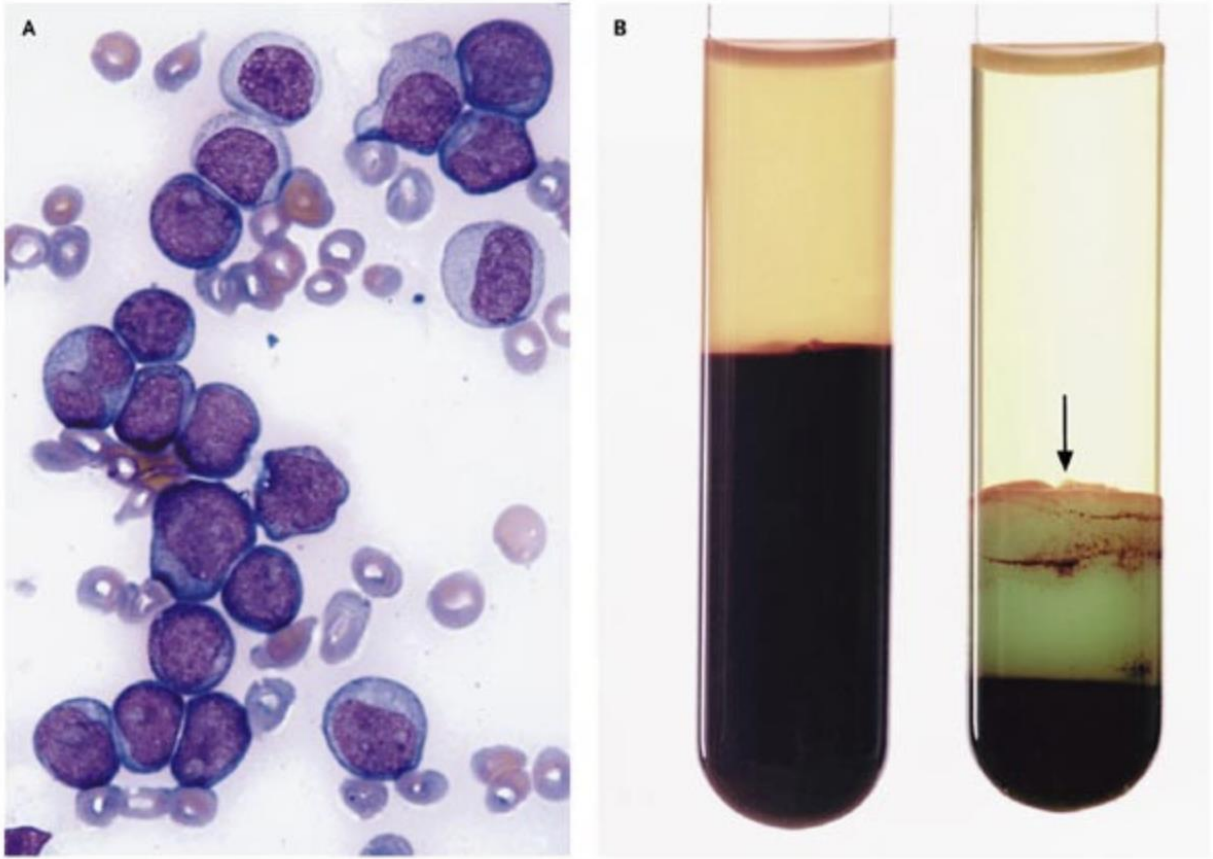
- Is this an emergency?
  - Signs/symptoms of inflammation may be muted
  - Index of suspicion required to consider or test for complications
    - Some dramatic presentations are not true emergencies
    - Some bland presentations are true emergencies

Leukemia

Case

- 26 y/o woman
- Progressive fatigue, dyspnea, blurred vision, near-syncope
- Pallor, fever, diffuse nontender lymphadenopathy, retinal hemorrhages

- WBC 249K
- Hgb 2.9
- Plt 48k

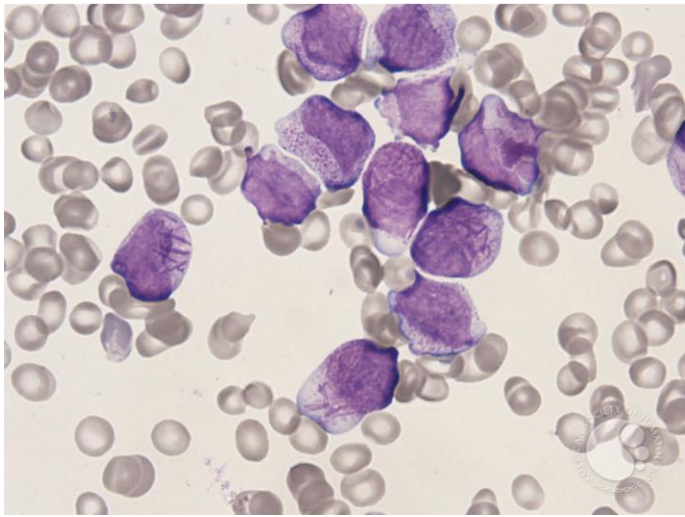


Mauro NEJM

Leukemia Classification: Flow Cytometry

- **Acute**: circulating blasts/atypical cells (>20%), new/rapid change, may have high or low WBC
  - Acute Myeloid Leukemia
    - Acute Promyelocytic Leukemia: DIC, abundant granules, Auer rods
  - Acute Lymphoblastic Leukemia

- **Chronic**: high WBC, organomegaly
  - Chronic Myeloid Leukemia: immature granulocytes, eosinophilia/basophilia
  - Chronic Lymphocytic Leukemia: lymphocytosis, "smudge" cells



ASH Image Bank

Urgency

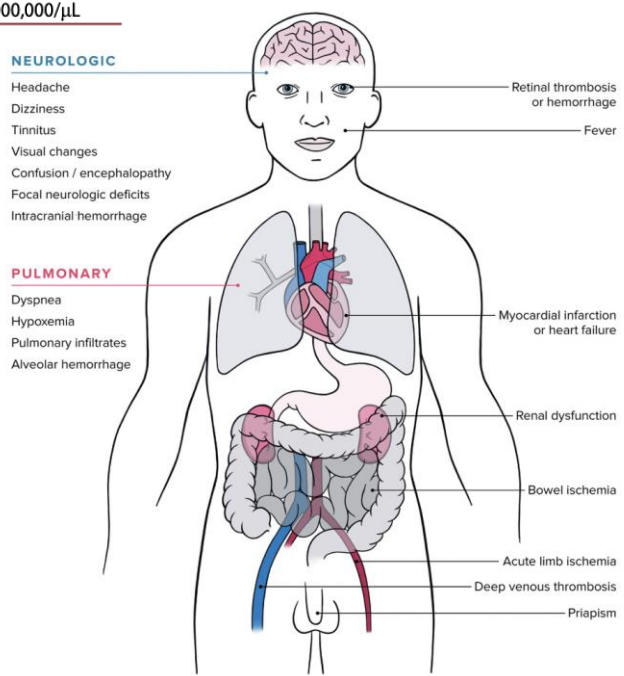
- Leukostasis
- Tumor Lysis Syndrome
- Hemostasis
  - Disseminated Intravascular Coagulopathy
  - Thrombosis
  - Bleeding

Hyperleukocytosis/Leukostasis

Table 1. Common leukemias and propensity for hyperleukocytosis and leukocytosis.

Leukemia type	Cell size/rigidity	Relative propensity for hyperleukocytosis	Relative propensity for leukostasis	Comments
Acute myeloid leukemia	Large/high	Low	High	Can occur at WBC <50,000/μL
Acute lymphocytic leukemia	Moderate/high	Moderate	Low-moderate	
Chronic myeloid leukemia	Variable/low	High	Low	
Chronic lymphocytic leukemia	Small/low	Moderate	Very low	Almost exclusively described at WBC >1,000,000/μL

- Hyperleukocytosis
  - Pseudohyperkalemia (whole blood in heparinized blood gas syringe, POC)
  - Pseudohypoxemia (pulse ox)
- Leukostasis:
  - Avoid RBC transfusion and avoid diuresis
  - Hydroxyurea/Leukapheresis
  - Definitive diagnosis/treatment



Macaron et al. Leuk Lymphoma 2022

Leukapheresis for hyperleukocytosis in acute leukemia

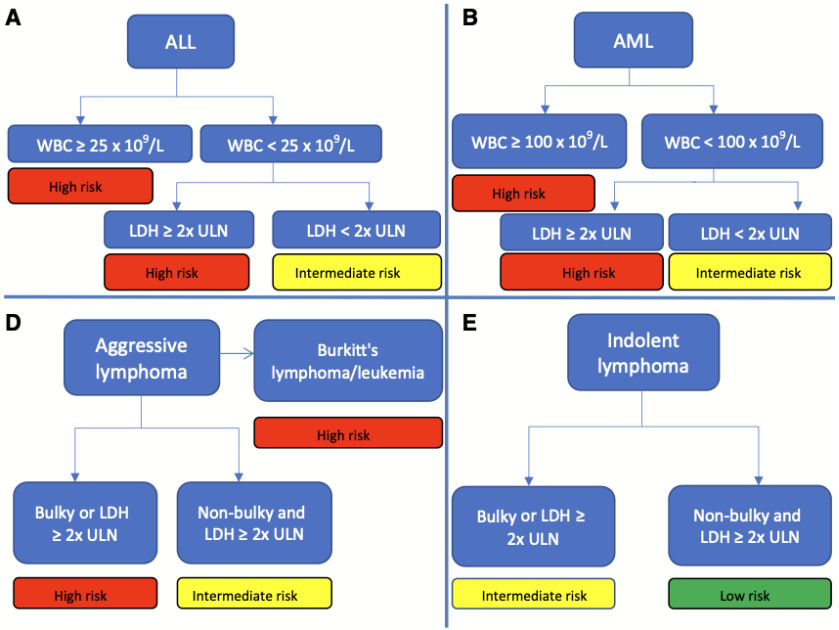
- Propensity score-matched study
  - No effect on overall survival
  - No effect on incidence of tumor lysis syndrome or DIC

- Systematic review and meta-analysis
  - 13 retrospective studies, 1743 patients
    - Patients with clinical leukostasis twice as likely to undergo leukapheresis
  - No effect on early mortality with leukapheresis (RR 0.88, CI 0.69-1.13)

Choi et al. Transfusion 2018, Bewersdorf et al. Transfusion 2020

Tumor Lysis Syndrome

- Renal Insufficiency
  - IV fluids, dialysis
- Hyperuricemia
  - Allopurinol (blocks conversion of xanthine/hypoxanthine to uric acid)
  - Rasburicase (urate oxidase)
- Hyperkalemia
  - Insulin + dextrose
  - Nebulized albuterol
  - Calcium gluconate
- Hyperphosphatemia
  - Phosphate binders
- Hypocalcemia



Durani et al. BJH 2020

Acute Promyelocytic Leukemia

- Disseminated Intravascular Coagulation (DIC)

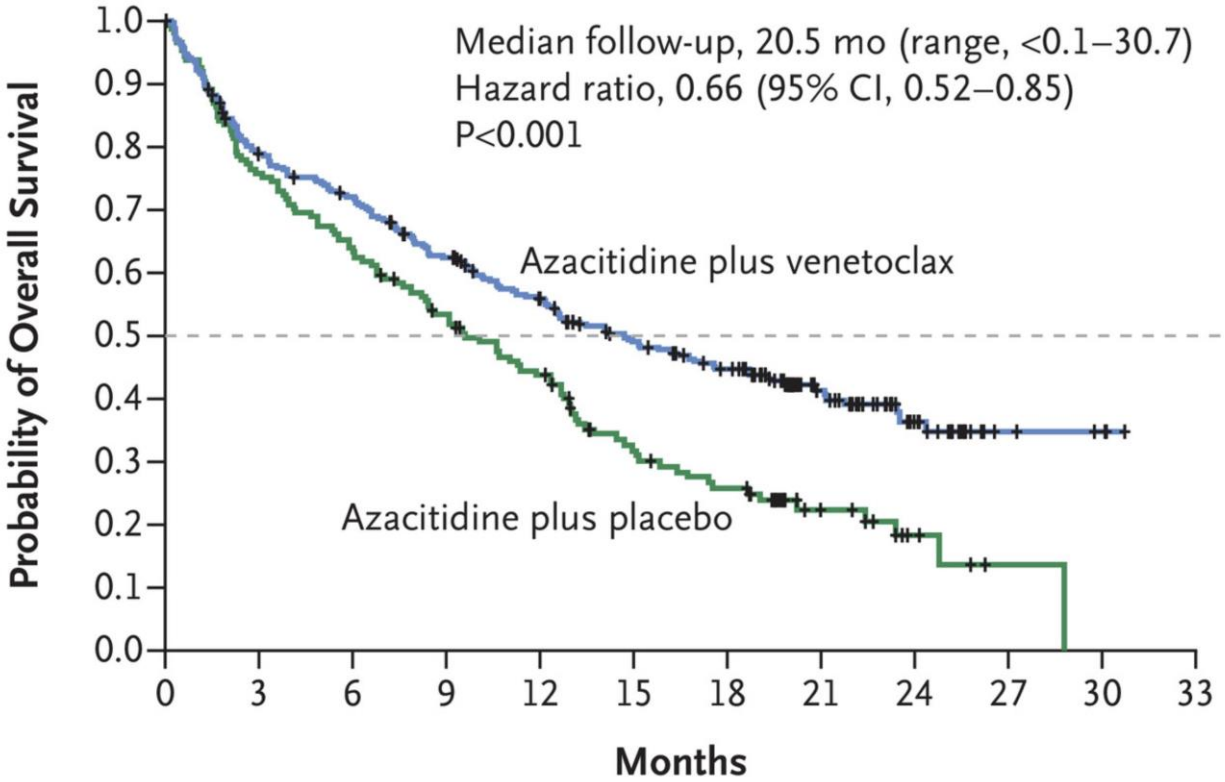
- Differentiation Syndrome
  - Associated with WBC >10k at diagnosis
    - Prophylactic steroids
    - Add hydroxyurea if WBC rising
  - Triggered by All-Trans Retinoic Acid (ATRA) treatment
    - Can be triggered by leukapheresis
  - Treat with steroids and potentially holding ATRA

AML Therapies

- “7 + 3” cytarabine and an anthracycline
  - Intensive regimen for fit patients

- Hypomethylating agents (azacitidine, decitabine)
- Azacitidine + Venetoclax
- Targeted therapies (FDA-approved, oral)
  - Glasdegib (hedgehog signaling pathway)
  - Enasidenib (*IDH2* mutated), ivosidenib. Olutasidenib (*IDH1* mutated)
  - Pegmigatinib (*FGFR1* rearrangement)
  - Gilteritinib, midostaurin, quizartinib (FLT3 mutated)
- Clinical Trials

AML: Aza/Ven (VIALE-A trial)



DiNardo et al. NEJM 2020

Other Classic Urgencies and Emergencies

Hypercalcemia

- Bones, Stones, Moans, Groans
  - Correct for serum albumin/check ionized calcium

- Saline +/- furosemide (calcinuresis)
- Bisphosphonates
- Glucocorticoids
- Calcitonin

Hyperviscosity Syndrome

- Triad
  - Neurologic abnormalities (headache, altered mental status, nystagmus, vertigo, ataxia, paresthesia, seizure)
  - Visual change (retinal vein engorgement/occlusion or hemmorhage)
  - Bleeding

- Paraproteinemia (lymphoplasmacytic lymphoma or IgM multiple myeloma)
  - Symptomatic at 5-8 gm/L

- Therapy: plasmapheresis
  - Phlebotomy as alternative

Weaver et al. Frontiers in Onc 2020

Neutropenic Fever

- IDSA definitions
  - Temp 38.3 (or 38.0 sustained over 1 hour)
  - ANC <500 (or ANC <1000 predicted to decline)

- Prior to empiric antibiotic era, **mortality 50-70%
- Broad-spectrum Gram-negative coverage including anaerobes and Pseudomonas
  - Cefepime or piperacillin/tazobactam
    - Add gentamicin if using meropenem
- Gram-positive coverage
  - Skin or suspected line infection, known colonization with MRSA
  - Consider in sepsis/severe sepsis, severe mucositis

Freifeld et al. Clin Inf Dis 2011

Spinal Cord Compression/Cauda Equina Syndrome

- First sign/symptom of malignancy in 20%
  - Breast, prostate, lung, renal, lymphoma, myeloma
- Pain in 90%
- Progression can be rapid
  - Motor, sensory, autonomic
  - Cauda equina syndrome: urinary retention and overflow incontinence

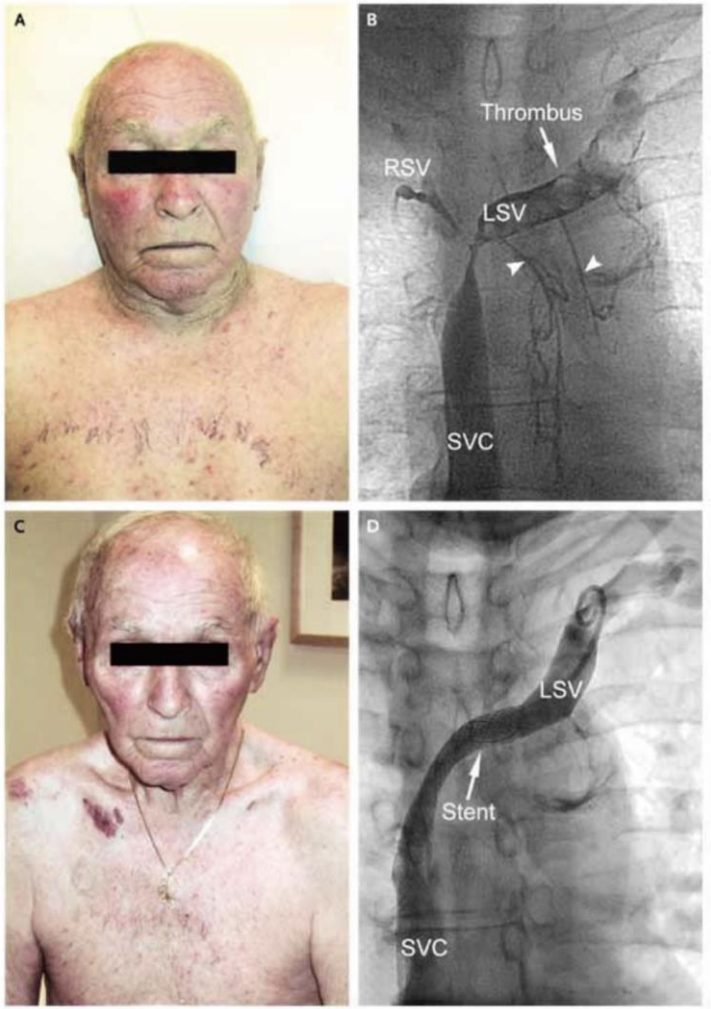
- Steroids (dexamethasone 10-100mg, then 4-24mg q 4-6hr)
- Imaging (MRI>CT)
- Consults: Surgery and Radiation
  - Indications for surgery: Column instability, prior XRT, **need diagnosis

De la Fuente et al. BJH 2020

SVC Syndrome

- Lung cancer, lymphoma
- Marked signs/symptoms: altered mental status, syncope with bending
  - Very rare cerebral edema, laryngeal/glossal edema
  - Very rarely associated with tracheal obstruction (**Emergency)

- Ligated SVC in dogs: signs/symptoms abated in 1 week
- Review of 1986 cases
  - Only 1 death: aspiration of epistaxis



Kanani et al. NEJM. Ahmann JCO

Extravasation

- Vesicants (anthracyclines, vinca alkaloids)
- Irritants (taxanes, platinums, topoisomerase inhibitors)

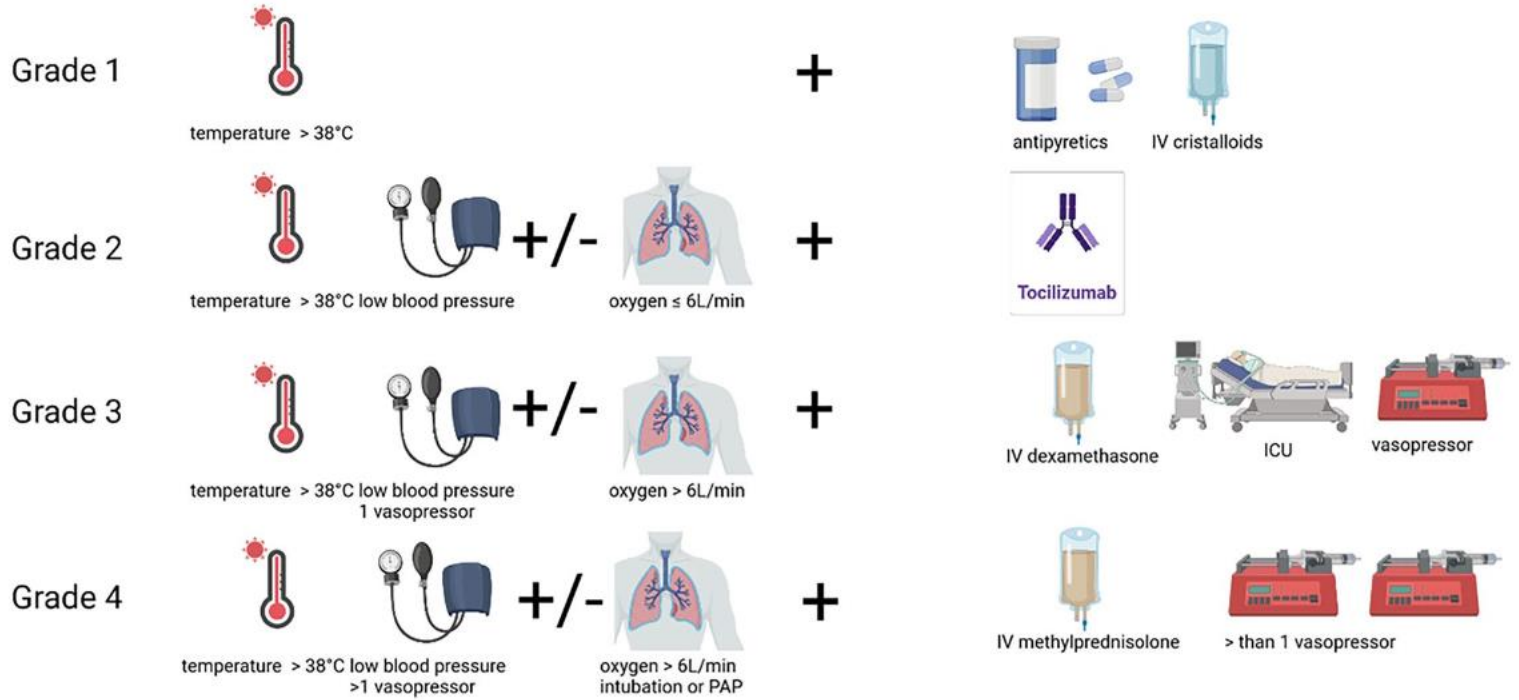
- Stop infusion
- Leave IV in place
- Consult extravastation protocol
  - Antidotes?
  - Warming?
  - Cooling?

T-cell Directed Therapy Complications

FDA-Approved T-cell Therapies

- Chimeric Antigen Receptor (CAR) T-cell therapy
  - CD19 (lymphoma/leukemia), BCMA (myeloma)
- TCR T-cell therapy
  - Gp100 (uveal melanoma)
  - MAGE-4 (synovial sarcoma)
- Tumor Infiltrating Lymphocyte (TIL) therapy
  - Melanoma
- T-cell redirecting bispecific antibodies
  - ALL, lymphoma, multiple myeloma, lung cancer…

Cytokine Release Syndrome (CRS)

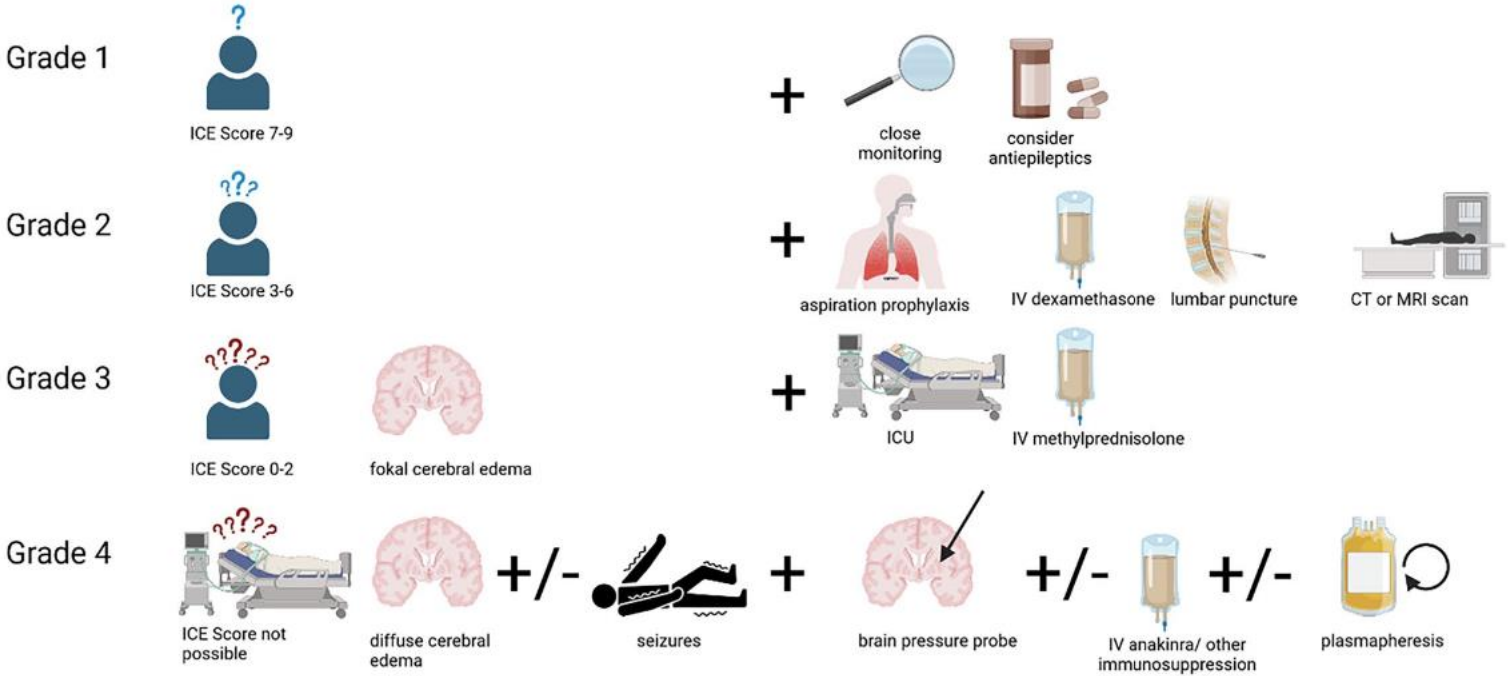


Schroeder et al. Intensive Care Med 2024

Immune Effector cell Encephalopathy (ICE) score

ICE
Orientation: Time (year, month), place (city, hospital): 4 points **Naming:** Ability to name 3 objects (eg, point to clock, pen, chair): 3 points **Writing:** Ability to write a standard sentence (eg, "our national bird is the bald eagle"): 1 point **Attention:** Ability to count backwards from 100 by 10: 1 point **Following commands:** Ability to follow simple commands (eg, "Show me 2 fingers" or "Close your eyes and stick out your tongue"): 1 point
Total: 10 points

Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS)



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- Spring and Munshi. Hematology Emergencies in Adults With Critical Illness: Malignant Hematology. Chest. 2022 Jul;162(1):120-131.

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Thank you