Hyperleukocytosis and Leukostasis

Hyperleukocytosis is commonly defined by a WBC > 100 x 10^9/L but complications can occur at lower values. It common in patients with acute myeloid leukemia (AML) and is associated with increased mortality. Leukostasis refers to evidence of tissue hypoperfusion in the presence of a very high WBC. Leukostasis is more common in AML than acute lymphoblastic leukemia (ALL) due to the larger size and poor deformability of the myeloblasts. In patients with hyperleukocytosis respiratory failure and intracranial hemorrhage are the most common causes of death, and it is frequently complicated by disseminated intravascular coagulation (DIC) or tumor lysis syndrome (TLS).

Pathophysiology

Uncontrolled blast proliferation + reduced affinity for the bone marrow → Hyperleukocytosis

Leukostasis leads to end-organ hypoperfusion through microvascular occlusion, hemorrhage, infarction, and edema at the tissue level.

Incidence and Prognosis

Hyperleukocytosis is common in acute leukemias:
- Up to 20% of patients with AML
- Up to 30% of patients with ALL

Outcomes depend on the type leukemia and presence of symptoms. Short-term mortality rates may be as high as 20-40% for patients with AML.

Clinical Presentation and Diagnosis

Leukostasis is a clinical diagnosis that can be made when the <u>WBC is > 100 x 10^9/L and there are signs of tissue hypoxia</u>. However, a high index of suspicion must be maintained in any patient with acute leukemia as it may occur at lower cell counts in some settings.

Additional important findings:
- **Arterial pO2 may be falsely low** due to cellular metabolism in vitro. Pulse oximetry may be a more reliable measure of oxygenation.
- Blast cells may release potassium as they breakdown in vitro leading to **pseudohyperkalemia**. Measure both serum and plasma potassium levels to confirm.
- **Lactic acidosis** may be due to anerobic glycolysis and lactate production by leukemic cells rather than tissue hypoxemia.

Patients may also have co-existing TLS and/or DIC.

Neurologic Manifestations	• Altered LOC, delirium, coma, headache, vision changes, focal deficits, intracranial hemorrhage
Pulmonary Manifestations	• Hypoxemia, shortness of breath, respiratory failure
Other Manifestations	• Myocardial infarction, arrhythmias, right ventricular failure, acute kidney injury, bowel or limb ischemia, priapism

Management

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<u>Emergent Cytoreductive Therapy:</u>
Contact your local hematologist as well as the closest specialized cancer centre. **Definitive Treatment = Induction Chemotherapy.** However, there are temporizing measures that are available while this is being arranged:

Hydroxyurea:
- Typically: 50-75mg/kg/day PO in 3-4 divided doses
- May be helpful if there is diagnostic uncertainty, induction chemotherapy is thought to be too high risk, or while arranging transfer to a tertiary care center.

Leukapheresis:
- Rapidly lowers WBC with a single session but has not been shown to decrease mortality or complications related to leukostasis
- Complications: Bleeding, infection, citrate toxicity, worsening thrombocytopenia
- <u>Should not be used in acute promyelocytic leukemia</u>

Some centers also use low dose cytarabine infusions for cytoreduction.

2

<u>Supportive Measures:</u>
IV fluids should be administered to all patients to reduce blood viscosity.
- Caution must be taken to avoid volume overload leading to pulmonary edema and worsening respiratory failure.

If possible, avoid therapies that may increase blood viscosity:
- Red blood cell transfusions
- Diuretics

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<u>Monitor Closely for Complications:</u>
Both spontaneous and treatment-related TLS may occur. **These patients should receive rasburicase** while following electrolytes, creatinine, and uric acid levels Q6H.

DIC is also common:
- Check CBC, INR, fibrinogen Q6H
- If DIC occurs, maintain fibrinogen > 1g/L and platelets > 20 x 10^9/L (or > 50 x 10^9/L if bleeding)
- See the acute promyelocytic leukemia summary for special considerations in these patients

These patients require **frequent reassessments** as they may **rapidly deteriorate.** If the patient is being transferred to a specialized center, caution must be taken to ensure they are adequately monitored and supported during transport.