Acute Leukemia (AML / ALL)

The four emergencies that kill in the first 48 hours · and why APL cannot wait for confirmation

Blasts ≥ 20%
and act early

⚠ IF APL IS POSSIBLE, START ATRA NOW

Do not wait for cytogenetic confirmation. Acute promyelocytic leukemia kills by **catastrophic bleeding from DIC and hyperfibrinolysis**, and the deaths happen in the first days, before genetics return. **Suspect it with: pancytopenia, a coagulopathy out of proportion to the illness, low fibrinogen, and promyelocytes with heavy granules or Auer rods. ATRA is started on suspicion** and stopped later if the diagnosis is excluded. Support aggressively: **fibrinogen above 150, platelets above 30 to 50**, and correct with cryoprecipitate and platelets rather than waiting for a threshold to be breached.

THE DIAGNOSIS *what to send before anything is given*

Step	Detail
Define it	**≥ 20% blasts** in blood or marrow. Certain defining cytogenetic abnormalities make it AML **at any blast count**, so the number is a threshold, not the whole rule
AML or ALL	**Auer rods and myeloperoxidase point to AML.** Flow cytometry immunophenotyping decides it. **ALL needs a lumbar puncture** for CNS involvement, and AML only if symptomatic
Send with the marrow	**Cytogenetics and FISH, plus molecular testing** (FLT3, NPM1, IDH1/2 in AML; BCR-ABL in ALL). These change the drug, not just the prognosis, so send them upfront
Baseline for therapy	**Echocardiogram before anthracyclines**, hepatitis B/C and HIV serology, **fertility discussion before starting**, HLA typing if transplant is plausible

THE FOUR EMERGENCIES *each one is treatable, and each one is missed by waiting*

Emergency	Recognize	Act
Febrile neutropenia	Temp **≥ 38.3** once, or **≥ 38.0** sustained an hour, with ANC **< 500** or expected to fall below	**Broad-spectrum antipseudomonal antibiotics within 60 minutes**, after cultures but never delayed for them. Cefepime, piperacillin-tazobactam or meropenem. **Vancomycin is not routine** and needs a specific indication. **No rectal exams or suppositories**
Tumor lysis syndrome	**High potassium, phosphate and uric acid; low calcium**, with rising creatinine. Highest risk with a large blast burden and in ALL and Burkitt	**Aggressive IV fluids** plus **allopurinol** for prophylaxis or **rasburicase** for established or high-risk TLS. **Rasburicase is contraindicated in G6PD deficiency** (hemolysis). **Do not give calcium for asymptomatic hypocalcemia**: it precipitates with phosphate. Monitor labs every 6 to 8 hours
Leukostasis	**WBC above roughly 100,000** with **dyspnea, hypoxia or neurological signs**. A clinical diagnosis, far commoner in AML because blasts are large and sticky	**Urgent cytoreduction** (hydroxyurea or induction) with or without leukapheresis, plus hydration and TLS prophylaxis. **Avoid red cell transfusion until the count falls**, since it raises viscosity further. Transfuse platelets freely, which does not
DIC	Bleeding, low fibrinogen, high D-dimer, prolonged PT. **Classically APL**, but occurs in any acute leukemia	Treat the leukemia, and replace with **cryoprecipitate for fibrinogen and platelets**. In suspected APL, **start ATRA immediately** as above

DIFFERENTIATION SYNDROME *the complication of successful APL treatment*

Feature	Detail
When	Occurs in roughly **2% to 27%** of patients on ATRA or arsenic trioxide, usually **within the first weeks** of starting
What it looks like	**Fever, dyspnea, hypoxia, pulmonary infiltrates, peripheral edema, weight gain, hypotension, acute kidney injury.** It is a cytokine-release picture and is easily mistaken for pneumonia, fluid overload or sepsis in a patient who has all three on the differential
What to do	**Dexamethasone at the first suspicion**, typically 10 mg IV twice daily, and **do not wait for confirmation**. **Hold the differentiating agent if the syndrome is severe**, and restart once it resolves. Untreated, it is lethal

WHAT TREATMENT LOOKS LIKE *so you can answer the family, and anticipate the toxicity*

Disease	Backbone	What to anticipate
AML, fit for intensive therapy	**"7 + 3"**: 7 days of cytarabine with 3 days of an anthracycline. **Add midostaurin if FLT3-mutated**; gemtuzumab in selected CD33-positive favorable-risk disease	**Four weeks of profound pancytopenia.** Expect neutropenic fever in most patients. Marrow at around day 14 to confirm blast clearance
AML, unfit or older	**Venetoclax plus azacitidine** or decitabine	Far better tolerated than 7+3 and now standard for this group. **Substantial early TLS risk**: venetoclax needs a careful ramp-up with TLS prophylaxis
APL	**ATRA plus arsenic trioxide**, chemotherapy-free in low and intermediate risk	**The most curable acute leukemia**, provided the patient survives the early coagulopathy. Monitor **QTc** on arsenic, and watch for differentiation syndrome
ALL	Multi-agent chemotherapy over distinct phases, with **CNS prophylaxis by intrathecal chemotherapy in everyone**. **Add a TKI if Philadelphia-positive.** Adolescents and young adults do better on pediatric-inspired regimens	Long treatment, measured in years including maintenance. **Asparaginase brings thrombosis, pancreatitis and hepatotoxicity**. Steroid-related hyperglycemia and psychiatric effects are common

Transplant is decided by risk group and measurable residual disease, not by response alone. That is why the cytogenetics and molecular panel sent at diagnosis matter so much: they place the patient in a risk group before the first dose is given, and they determine whether the plan is chemotherapy alone or chemotherapy leading to allogeneic transplant.

PEARLS & PITFALLS

- **Steroids before a diagnosis can destroy it.** Giving steroids to an undiagnosed lymphoproliferative presentation can lyse the blasts and **make the marrow uninterpretable**, delaying definitive treatment. Get the diagnostic samples first.
- **A normal white count does not exclude acute leukemia.** Presentation may be leukopenic or aleukemic; it is the **blasts and the cytopenias** that matter, not the total count.
- **Use irradiated and leukoreduced blood products** in patients who are or may become transplant candidates, and **CMV-safe products** where indicated, to prevent transfusion-associated graft-versus-host disease.
- **Do not correct a normal-appearing calcium in TLS.** The hypocalcemia is driven by hyperphosphatemia; treat the phosphate, and give calcium only for symptoms such as tetany or arrhythmia.

References: WHO and ICC classifications of myeloid and lymphoid neoplasms · ELN recommendations for AML in adults · IDSA and ASCO febrile neutropenia guidance · published series on differentiation syndrome in APL.

Educational aid; verify against current guidance, local formulary and patient factors.