



Tumor Lysis Syndrome

TLS · Predict it, hydrate hard, and pick the right urate-lowering drug

PREVENTION BEATS RESCUE
every time

WHO IS AT RISK *stratify before the first dose of treatment*

HIGH RISK

Burkitt lymphoma and lymphoblastic lymphoma · **ALL with WBC > 100** · **AML with WBC > 50** · bulky, rapidly proliferating, highly chemosensitive disease · **CLL starting venetoclax** · pre-existing renal impairment, dehydration, or a raised baseline uric acid.

THE BIOCHEMISTRY

Massive cell lysis dumps intracellular contents: **potassium, phosphate, and nucleic acids** (which become **uric acid**). **Calcium falls** as it binds the phosphate load. Uric acid and calcium-phosphate crystals then precipitate in the tubules and cause **acute kidney injury**.

WHEN IT HAPPENS

Usually **12–72 hours after starting treatment**, but bulky, high-turnover tumors can lyse **spontaneously before any therapy**. Do not assume you are safe because chemotherapy has not started.

DEFINE IT *Cairo-Bishop — laboratory TLS becomes clinical TLS when an organ is hit*

Category	Criteria
Laboratory TLS	Two or more of: hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia — within 3 days before to 7 days after starting treatment.
Clinical TLS	Laboratory TLS plus one of: acute kidney injury, cardiac arrhythmia, seizure, or sudden death . This is the outcome all the prophylaxis exists to prevent.
Monitoring	In high-risk patients check potassium, phosphate, calcium, uric acid, creatinine and LDH every 6–8 hours during the risk window, with continuous cardiac monitoring where potassium is rising.

PREVENT AND TREAT *fluid is the backbone; the drug depends on risk*

- Aggressive IV hydration is the single most important intervention.** Start **before** treatment in at-risk patients and aim for a high urine output, which dilutes and flushes the solute load. Watch for volume overload in cardiac or renal impairment.
- Allopurinol for low and intermediate risk**, ideally started 24–48 hours before treatment. It **blocks new uric acid formation but does nothing to existing hyperuricemia**, and it causes xanthine accumulation. Reduce the dose in renal impairment, and remember the **interaction with azathioprine and 6-mercaptopurine**.
- Rasburicase for high risk or established hyperuricemia.** Recombinant urate oxidase **rapidly degrades existing uric acid**, sharply reducing the risk of acute renal failure. This is the agent when uric acid is already up.
- Screen for G6PD deficiency before rasburicase.** It is **contraindicated in G6PD deficiency** and related disorders because it causes **severe hemolysis and methemoglobinemia** — use allopurinol and hydration instead. Send the sample on ice, since uric acid degrades ex vivo and gives falsely low readings.
- Urinary alkalization is no longer routinely recommended.** Raising urine pH improves uric acid solubility but **promotes calcium-phosphate precipitation** in the tubules, and it is largely redundant now that rasburicase is available.

MANAGE THE ELECTROLYTES *two counterintuitive rules*

POTASSIUM AND PHOSPHATE

Hyperkalemia is the immediate killer — treat aggressively with calcium for membrane stabilization, insulin-dextrose, and a binder, and monitor the ECG continuously. For **hyperphosphatemia**, use oral phosphate binders and continue hydration.

THE HYPOCALCEMIA TRAP

Do not correct asymptomatic hypocalcemia. Giving calcium into a high-phosphate environment drives **calcium-phosphate precipitation** in tissues and tubules and worsens renal injury. **Treat only symptomatic hypocalcemia** — tetany, seizures, or arrhythmia — and use the minimum effective dose.

PROPHYLAXIS BY RISK TIER *match the intensity to the risk, before treatment starts*

Risk	Typical setting	Prophylaxis
Low	Most solid tumors, indolent lymphoma, low-count chronic leukemias	Oral hydration and observation. Monitor labs after the first cycle. Routine urate-lowering therapy is not required.
Intermediate	Bulky solid tumors, some lymphomas, ALL or AML with moderate counts	IV hydration plus allopurinol , started before treatment. Laboratory monitoring every 8–12 hours for the first 24–48 hours.
High	Burkitt, lymphoblastic lymphoma, ALL with WBC > 100, AML with WBC > 50, venetoclax ramp-up, any raised baseline uric acid or renal impairment	Aggressive IV hydration plus rasburicase. Admit for cardiac monitoring , check labs every 6–8 hours , and involve nephrology early. Consider stepwise dose escalation of the trigger drug.
Established TLS	Laboratory or clinical TLS already present	Rasburicase, maximal hydration, continuous cardiac monitoring, and early renal replacement therapy for refractory hyperkalemia, oliguria, or volume overload.

THE VENETOCLAX SCENARIO *the commonest modern cause you will meet on the wards*

WHY IT IS DIFFERENT

Venetoclax in CLL produces **very rapid apoptosis**, and TLS can occur within hours of the first doses. This is why treatment uses a **gradual weekly dose ramp-up** with risk assessment based on **lymph node size and lymphocyte count** before each escalation.

WHAT THAT MEANS PRACTICALLY

Hydration and urate-lowering therapy before each dose increase, with laboratory checks at defined intervals after the dose — often at 6–8 and 24 hours. High-risk patients are **admitted for the first dose of each new level**. Do not let a patient escalate the dose at home without the prescribed monitoring.

PEARLS & PITFALLS

- Allopurinol does not lower an already high uric acid.** If the level is up, you need rasburicase, not a xanthine oxidase inhibitor.
- Check G6PD status before rasburicase** — giving it in deficiency causes severe hemolysis and methemoglobinemia.
- Do not give calcium for asymptomatic hypocalcemia;** you will precipitate calcium phosphate and worsen the kidney injury.
- TLS can occur spontaneously** in bulky, high-turnover disease before any chemotherapy is given.
- Send rasburicase-era uric acid samples on ice**, or the enzyme keeps working in the tube and the result looks falsely reassuring.
- Dialyze early** for refractory hyperkalemia, oliguric renal failure, or severe volume overload — do not wait for uremia.

