Student Handout: Tumor Lysis Syndrome

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> **Learning objective:** Recognize tumor lysis syndrome (TLS) as an oncologic emergency, apply Cairo-Bishop risk stratification, implement prevention protocols, and manage each metabolic derangement

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What is Tumor Lysis Syndrome?

Definition: Syndrome of severe metabolic derangements resulting from massive, rapid release of intracellular contents when malignant cells die. Occurs after chemotherapy or targeted therapy initiation in patients with rapidly dividing or bulky tumors.

Why it matters: TLS is **life-threatening** if not recognized and managed promptly. Hyperkalemia can cause fatal arrhythmias; hyperphosphatemia causes secondary hypocalcemia → tetany, seizures, cardiac dysfunction.

Epidemiology & Risk

Who Is at High Risk?

High-risk malignancies: - **Acute leukemias** (ALL, AML) — Highest risk; cells highly chemosensitive - **Lymphomas** (Burkitt, high-grade non-Hodgkin) — Especially bulky disease - **High-risk solid tumors:** Germ cell tumors, small cell lung cancer, neuroblastoma

High-risk patient factors: - Large tumor burden / High LDH (>1,500 IU/L indicates high cell turnover) - Rapidly proliferating disease - Pre-existing renal impairment (↓ ability to excrete K+, urate, phosphate) - Dehydration - Acidosis (↑ extracellular K+)

Timing

- **Peak risk:** 12–48 hours after start of chemotherapy
- **Can occur:** Up to 7 days post-initiation
- **Rapid onset:** Metabolic derangements develop quickly; clinical deterioration can be fulminant

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Cairo-Bishop Diagnostic Criteria (2004)

TLS is classified as **Laboratory TLS** or **Clinical TLS** based on objective lab parameters:

Laboratory TLS (≥2 of the following):

Parameter	Criterion
Uric acid	≥8.0 mg/dL (or 25% ↑ from baseline)
Potassium	≥6.0 mEq/L (or 25% ↑ from baseline)
Phosphate	≥4.5 mg/dL (≥6.5 if age <13) (or 25% ↑ from baseline)
Calcium	≤7.0 mg/dL (corrected) (or 25% ↓ from baseline)

Note: Hypocalcemia is secondary (reaction to ↑ phosphate), not a primary criterion. You need ≥2 of the first 4 to diagnose Lab TLS.

Clinical TLS (≥1 of the following):

Finding	Details
Seizures	Secondary to hypocalcemia, hypomagnesemia, or osmotic shifts
Arrhythmias	From severe hyperkalemia, hypocalcemia, QT prolongation
Cardiac arrest	Sudden death from electrolyte derangements
AKI	Cr ↑ ≥1.5× baseline; oliguric renal failure from urate nephropathy

Clinical TLS = Laboratory TLS + ≥1 clinical sign → Oncologic emergency

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Pathophysiology: The Metabolic Cascade

Step 1: Tumor Cell Lysis

- Chemotherapy kills cancer cells rapidly
- Intracellular contents flood into bloodstream: K+, phosphate, nucleic acids

Step 2: Hyperkalemia

- Intracellular K+ (~150 mEq/L) vastly exceeds serum (~5 mEq/L)
- Massive release → ↑ serum K+ to 6–8+ mEq/L
- **Effect on heart:** Peaked T waves → Widened QRS → Ventricular fibrillation → Cardiac arrest
- **Timeline to danger:** Can occur within hours

Step 3: Hyperuricemia

- Nucleic acids from dead cells → Purine metabolism
- ADA and XO convert purines → **Uric acid**
- Uric acid crystallizes in renal tubules → **Urate nephropathy**
- ↓ GFR → Inability to excrete K+, phosphate, uric acid → Vicious cycle
- **Threshold:** Often occurs if uric acid >8 mg/dL

Step 4: Hyperphosphatemia

- Nucleotide breakdown → ↑ serum phosphate (5–10+ mg/dL possible)
- Phosphate binds calcium → **Hypocalcemia**
- Severe hypocalcemia → Seizures, tetany, arrhythmias
- **Secondary effect:** ↑ PTH → Further K+ wasting (initially), then PTH suppression

Step 5: Acute Kidney Injury

- **Urate crystallization** (especially if acidic urine or dehydrated)
- **Phosphate precipitation** in renal tubules
- **Myoglobin deposition** (if rhabdomyolysis from lysis)
- Result: Oliguria, ↑ Cr rapidly (often within 24–48 h)

Clinical Presentation (Timeline)

Time	Finding
6–12 h post-chemo	Asymptomatic labs: ↑ K+, ↑ uric acid, ↑ phosphate
12–24 h	Patient may note weakness, palpitations; labs worsening
24–48 h	**Fulminant phase:** Severe hyperkalemia, arrhythmias, AKI oliguric; seizures if hypocalcemic
>72 h	If managed: Gradual recovery; if unmanaged: Cardiac arrest, renal failure

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Risk Stratification & Prevention Protocol

Step 1: Identify Risk at Baseline

Assess before starting chemotherapy: - Baseline uric acid, electrolytes (especially K+, PO4), creatinine - Assess tumor burden (size, LDH level) - Screen for pre-existing renal disease

Step 2: Stratify Risk & Implement Prevention

Risk Level	Example Tumors	Prevention Protocol
Low	Low-grade lymphomas, solid tumors	Standard hydration, monitor labs q 24 h
Intermediate	High-grade NHL, ALL (good ECOG)	Aggressive hydration, allopurinol, q12h labs
High	Burkitt lymphoma, blast crisis, bulky AML	**Rasburicase first-line**, aggressive hydration, q6–12h labs, ICU monitoring

Prevention Measures

Hydration

- **Goal:** Maintain urine output 200–300 mL/m²/h (or 3 L/day minimum)
- **Fluid:** 0.9% or 0.45% NaCl IV (avoid potassium-containing fluids)
- **Avoid:** Loop diuretics (↑ risk of volume depletion); some protocols use cautious loops if fluid-overloaded

Uric Acid Management

Agent	Mechanism	Use
Allopurinol	Xanthine oxidase inhibitor; converts uric acid → allantoin	Earlier standard; slower onset (24–48 h); use if rasburicase unavailable
Rasburicase	Fungal uricase; degrades uric acid → allantoin	**First-line if available** — rapid onset (30 min–2 h), reliably ↓ uric acid
Febuxostat	XO inhibitor; faster than allopurinol	Emerging option; less data in TLS

Rasburicase preferred: Onset within 4 hours; reliably reduces uric acid to <1 mg/dL. Dose: 0.2 mg/kg IV.

Electrolyte Monitoring

- **Low risk:** Baseline + q 24 h × 5 days
- **Intermediate:** Baseline + q 12–24 h × 5–7 days
- **High risk:** Baseline + q 6–12 h × 7+ days (ICU level)

Phosphate & Calcium Management

- **Avoid:** Prophylactic calcium (can precipitate in vasculature)
- **Manage:** If hypocalcemic AND symptomatic, then give calcium gluconate IV slowly with continuous cardiac monitoring
- **Phosphate binders:** Aluminum hydroxide or sevelamer (if elevated PO4)

Management of Active TLS

Hyperkalemia Management

Goal: K+ <5.5 mEq/L; urgent if K+ >6.5 with EKG changes

Intervention	Mechanism	Dose
Calcium gluconate	Cardiac membrane stabilization (not K+-lowering)	1 amp (1 g) IV slowly; repeat q 5 min if peaked T waves
Insulin + Dextrose	Shift K+ intracellularly	10 units regular insulin IV + 25 g dextrose (D50W 50 mL)
Albuterol	β-2 agonist; shift K+ into cells	10–20 mg nebulized
Sodium bicarb	Alkalinization; shift K+ intracellularly	50–100 mEq IV bolus (if acidotic)
Loop diuretic	↑ K+ excretion (if euvolemic/hypervolemic)	Furosemide 40–80 mg IV q 4–6 h
Kayexalate/patiromer	K+-binding resin (slow; not for acute)	15 g PO/PR q 4–6 h
Dialysis	Definitive removal	If K+ >7, anuria, or failed medical management

EKG findings of hyperkalemia: - Peaked T waves (earliest sign; K+ ~6.5) - Widened QRS (K+ ~7) - Loss of P waves (K+ ~7–8) - Sine wave (K+ >8) → Imminent arrest

Hyperuricemia Management

- **Rasburicase 0.2 mg/kg IV** (if not yet given)
- **Maintain vigorous hydration** (3–4 L daily if tolerated)

- **Monitor uric acid q 6–12 h** until <1 mg/dL

Hyperphosphatemia Management

- **Hydration** (dilution)
- **Phosphate binders:** Aluminum hydroxide 30 mL TID or sevelamer 800 mg TID
- **Monitor:** Repeat labs in 4–6 hours
- **Avoid calcium** unless symptomatic hypocalcemia (risk of calcification)

Hypocalcemia Management

- **Monitor:** Corrected calcium; check magnesium (often low too)
- **Symptomatic only:** If seizures, tetany, or severe arrhythmias
  - Calcium gluconate 1 amp IV in 50 mL D5W or NS over 10 minutes
  - Continuous cardiac monitoring
  - Target: Corrected Ca >6.5 mg/dL only
- **Magnesium:** Replete to >2 mg/dL

Acute Kidney Injury Management

- **Oliguria** → RRT (hemodialysis or CRRT) if K+ >6.5, uric acid >8, or fluid overloaded
- **Non-oliguric:** Continue aggressive hydration, frequent electrolyte checks
- **Expected course:** Most AKI resolves within 3–7 days if TLS managed appropriately
- **Dialysis indications:**
  - ☐ K+ >7 or peaked T waves despite medical management
  - ☐ Uric acid >8 mg/dL with AKI (urate nephropathy)
  - ☐ Pulmonary edema, hypervolemia
  - ☐ Symptomatic hypocalcemia unresponsive to calcium

Prevention of Recurrence

As cells continue to die (days 2–7): - Maintain hydration - Continue rasburicase (may re-dose if uric acid ↑ again) - Frequent lab monitoring (q 12–24 h) - Manage electrolytes proactively - Consider chemotherapy dose reduction or delay if TLS severe

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Monitoring Checklist

At baseline (before chemo): - ☐ Uric acid, BMP (K, PO4, Cr, Ca), LDH - ☐ Assess tumor burden & risk - ☐ Ensure IV access for hydration & drug administration

During TLS risk window (first 7 days): - ☐ Daily or q 12 h labs: K+, uric acid, PO4, Cr, Ca - ☐ Daily weights & I/Os - ☐ EKG if K+ >6 or EKG changes - ☐ Daily exam: mental status, seizure precautions, volume status

Post-acute phase (days 7–14): - ☐ Labs q 24–48 h - ☐ Continue rasburicase if uric acid elevated - ☐ Taper hydration as renal function recovers

Key Clinical Pearls

☐ **TLS is preventable** — Identify high risk, give rasburicase, hydrate aggressively ☐ **Rasburicase >Allopurinol** — Faster, more reliable; use if available ☐ **Hyperkalemia kills fast** — Peaked T waves = oncologic emergency; stabilize with calcium + shift K+ intracellularly ☐ **Dialysis is your friend** — Don't hesitate; TLS patients often need RRT ☐ **Hypocalcemia is secondary** — Don't give prophylactic calcium; avoid calcification ☐ **Peak risk: 24–48 hours** — Most intensive monitoring needed first 2–3 days

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Clinical Decision Tree

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Patient starting chemo for high-risk malignancy?

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├─→ YES → Stratify risk (low/intermediate/high)
│         │
│         ├─ LOW: Standard hydration, allopurinol, q24h labs
│         ├─ INTERMEDIATE: Aggressive hydration, rasburicase, q12h labs
│         └─ HIGH: Rasburicase, aggressive hydration, q6h labs, ICU monitoring
│
└─→ NO → Routine monitoring

During chemo (48–72 h window):
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├─ Lab TLS (↑ K, ↑ uric acid, ↑ PO4, ↓ Ca) → Escalate hydration, rasburicase, monitoring
├─ K+ >6.5 or EKG changes → STAT calcium gluconate + insulin + dextrose + dialysis if refractory
├─ Oliguria + AKI → Consider CRRT/hemodialysis
└─ Seizures/arrhythmias → ICU admission, continuous monitoring
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Related Content

Onconephrology Hub: - Tumor Lysis Syndrome Comprehensive Review — Detailed pathophysiology and advanced management - Cancer Electrolyte Emergencies — Related metabolic complications

Student Resources: - Student Handout: AKI Staging — Framework for acute kidney injury assessment - Hyperkalemia Management Guide — Detailed electrolyte management

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References

- **Cairo MS, Bishop M.** Tumour Lysis Syndrome: New Perspectives and Classification. Lancet Oncology. 2004;5(6):307–314.

- **Howard SC, et al.** Tumor Lysis Syndrome in the Era of Novel Cancer Therapies. Nature Reviews Nephrology. 2016;12(9):513–523.
- **Jeha S.** Tumor Lysis Syndrome. Seminars in Hematology. 2019;56(3):214–221.
- **NCCN Guidelines.** Tumor Lysis Syndrome (Version 2.2024). National Comprehensive Cancer Network.

Study Tips: - **Memorize Cairo-Bishop criteria** — 2 of 4 labs = Lab TLS - **Know the EKG progression** — Peaked T waves → Widened QRS → Sine wave - **Rasburicase is your drug** — Reliable, fast onset, reliably reduces uric acid - **Calcium + Insulin first** — Stabilize heart, then shift K+ into cells - **Dialysis threshold:** K+ >7 + anuria = Time for RRT

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