Tumor Lysis Syndrome in the Hospitalized Setting

Tumor Lysis Syndrome (TLS) is a potentially life-threatening oncologic emergency caused by the rapid breakdown of cancer cells, often following cytotoxic therapy. This pamphlet provides students with a detailed guide to understand, monitor, and manage TLS, with case scenarios to apply the knowledge.

Overview and Causes

- **Definition:** TLS is a metabolic disorder resulting from the rapid lysis of malignant cells, releasing intracellular contents (potassium, phosphate, uric acid) into the bloodstream, leading to hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia. It can cause acute kidney injury (AKI), arrhythmias, seizures, and death.
- **Pathophysiology:**
  - Rapid cell turnover (spontaneous or post-therapy) → Release of potassium (hyperkalemia), phosphate (hyperphosphatemia), and nucleic acids (metabolized to uric acid → hyperuricemia).
  - Uric acid and calcium phosphate precipitation in renal tubules → AKI.
  - Hypocalcemia secondary to phosphate binding.
- **Risk Factors:**
  - **High-Risk Malignancies:**
  - **Acute Lymphoblastic Leukemia (ALL):** Especially with high WBC (>50,000/μL), bulky disease.
  - **Acute Myeloid Leukemia (AML):** High blast count, monocytic subtype (M4/M5).
  - **Burkitt Lymphoma:** High proliferation rate, bulky disease (>10 cm).
  - **Diffuse Large B-Cell Lymphoma (DLBCL):** Advanced stage, elevated LDH.
  - **Chronic Lymphocytic Leukemia (CLL):** Post-targeted therapy (e.g., venetoclax).
- **Tumor Characteristics:**
  - High tumor burden (bulky disease, organ infiltration).
  - High proliferation rate (elevated LDH, Ki-67 >80%).
  - Chemosensitivity (rapid cell death post-therapy).
- **Patient Factors:**
  - Pre-existing renal dysfunction (eGFR <60 mL/min).
  - Dehydration (urine output <80 mL/h).

- Acidic urine pH (<5.5, promotes uric acid crystallization).
- **Treatment-Related:**
  - **Chemotherapy:** Cytarabine, cisplatin, etoposide (rapid cell kill).
  - **Targeted Therapy:** Venetoclax (CLL), rituximab (lymphoma).
  - **Radiation:** Large tumor burden (e.g., mediastinal mass).
  - **Steroids:** High-dose (e.g., prednisone 60 mg/m^2/day in ALL).
- **Spontaneous TLS:** Rare, seen in Burkitt lymphoma or ALL with high tumor burden, even without therapy.

Evaluation and Diagnosis

- **Clinical Presentation:**
  - **Symptoms:** Nausea, vomiting, lethargy, muscle cramps (electrolyte imbalances), oliguria (AKI), seizures (hypocalcemia), or arrhythmias (hyperkalemia).
  - **Timing:** Typically 12-72 hours post-therapy; can be spontaneous.
- **Cairo-Bishop Criteria for TLS:**
  - **Laboratory TLS:** ≥2 of the following within 3 days before or 7 days after therapy:
    - Uric acid ≥8 mg/dL or 25% increase from baseline.
    - Potassium ≥6 mEq/L or 25% increase from baseline.
    - Phosphate ≥4.5 mg/dL (adults) or 25% increase from baseline.
    - Calcium ≤7 mg/dL or 25% decrease from baseline.
  - **Clinical TLS:** Laboratory TLS plus ≥1 of the following:
    - AKI (creatinine ≥1.5x upper limit of normal).
    - Cardiac arrhythmia or sudden death (e.g., hyperkalemia-induced VT).
    - Seizure (hypocalcemia).
- **Initial Labs:**
  - **Electrolytes:** Potassium, phosphate, calcium, uric acid, magnesium.
  - **Renal Function:** Creatinine, BUN, urine output.
  - **LDH:** Marker of tumor burden and cell turnover.
  - **CBC:** Assess for leukocytosis (leukemia), anemia, thrombocytopenia (marrow involvement).
  - **ECG:** Peaked T waves (hyperkalemia), QT prolongation (hypocalcemia).

Diagnostic Criteria Table

Category	Criteria Threshold	Notes
Laboratory TLS	Uric acid, potassium, phosphate, calcium	≥2 abnormalities within 3 days before or 7 days after therapy.

Category	Criteria Threshold	Notes
Clinical TLS	Laboratory TLS + clinical event	AKI: Cr ≥1.5x ULN Seizures often due to hypocalcemia. Arrhythmia: VT
High-Risk Features	Tumor burden, renal function	LDH >2x ULN Prophylaxis mandatory in high-risk patients. eGFR <60 mL/min

How to Monitor

- **Pre-Treatment (High-Risk Patients):**
  - **Baseline Labs:** Electrolytes, uric acid, creatinine, LDH (q12h for first 48h post-therapy).
  - **Hydration Status:** Urine output >100 mL/h; avoid volume overload.
  - **ECG:** Baseline for hyperkalemia or hypocalcemia changes.
- **During Treatment:**
  - **Electrolytes:** Check q6-8h for first 48-72h (potassium, phosphate, calcium, uric acid).
  - **Renal Function:** Creatinine q12h; monitor for oliguria (<0.5 mL/kg/h).
  - **Cardiac Monitoring:** Continuous telemetry if potassium >5.5 mEq/L or calcium <7 mg/dL.
  - **Urine pH:** Target 6.5-7.5 (uric acid solubility); use sodium bicarbonate if pH <6.
- **Post-Treatment:**
  - Daily labs until stable (usually 5-7 days post-therapy).
  - Monitor for delayed TLS (e.g., post-venetoclax in CLL).
- **Key Tips:**
- High-risk patients (e.g., Burkitt lymphoma, ALL with WBC >100,000/μL): Admit to ICU for monitoring.
- Avoid potassium or phosphate in IV fluids unless critically low.

Management

- **Prevention (Prophylaxis):**
  - **Hydration:** 2-3 L/m^2/day IV fluids (NS or D5W ¼ NS), goal urine output >100 mL/h.
  - **Allopurinol:** 300 mg PO daily (start 1-2 days before therapy); reduces uric acid production.
  - **Rasburicase:** 0.2 mg/kg IV daily x 1-3 days (high-risk patients: uric acid >8 mg/dL, bulky disease); contraindicated in G6PD deficiency (risk of hemolysis).

- **Urine Alkalinization:** Sodium bicarbonate 50-100 mEq/L in IV fluids (if urine pH <6.5); avoid if hyperphosphatemia (increases calcium phosphate precipitation).

- **Treatment of Established TLS:**
  - **Hyperuricemia:**
    - Rasburicase 0.2 mg/kg IV daily until uric acid <8 mg/dL (usually 1-2 doses).
    - Allopurinol 300 mg PO daily (if rasburicase contraindicated).
  - **Hyperkalemia:**
    - Potassium >6 mEq/L or ECG changes (peaked T waves, widened QRS):
    - Calcium gluconate 1 g IV (cardioprotective, repeat q4h if needed).
    - Insulin 10 units IV + D50W 50 mL IV (drives potassium into cells).
    - Lokelma (if non-urgent, removes potassium via GI tract).
    - Hemodialysis (if refractory or AKI).
  - **Hyperphosphatemia:**
    - **Phosphate >4.5 mg/dL:**
      - Aggressive hydration (NS 200 mL/h IV if tolerated).
      - Sevelamer 800 mg PO TID (phosphate binder).
      - Hemodialysis (if refractory or AKI).
  - **Hypocalcemia:**
    - Calcium <7 mg/dL or symptomatic (tetany, seizures):
    - Calcium gluconate 1 g IV (slow infusion over 10-20 min); avoid if hyperphosphatemia (risk of precipitation).

- **AKI:**
  - **Creatinine >1.5x ULN or oliguria:**
    - Aggressive hydration (NS 200 mL/h IV if no volume overload).
    - Nephrology consult; hemodialysis if refractory (e.g., uric acid >10 mg/dL, potassium >7 mEq/L).

- **Key Tips:**
  - Avoid loop diuretics (e.g., furosemide) unless volume overload (worsens uric acid deposition).
  - **Rasburicase:** Test for G6PD deficiency in at-risk patients (e.g., African, Mediterranean descent).
  - **ICU transfer:** Symptomatic electrolyte imbalances, AKI requiring dialysis, or arrhythmias.

Management Guidelines Table

Condition	Treatment Agent/Dose	Notes
Hyperuricemia	Rasburicase, allopurinol Rasburicase 0.2 mg/kg IV daily	Contraindicated in G6PD deficiency; allopurinol if rasburicase unavailable.
Hyperkalemia	Calcium gluconate, insulin Calcium gluconate 1 g IV Insulin 10 units IV	Hemodialysis if refractory; monitor ECG.
Hyperphosphatemia	Hydration, sevelamer Sevelamer 800 mg PO TID	Avoid calcium if phosphate >6 mg/dL.
AKI	Hydration, hemodialysis NS 200 mL/h IV	Nephrology consult if Cr >2x ULN.

Complications

- **Acute:**
  - **AKI:** 20-30% of TLS cases; dialysis required in 5-10% (uric acid nephropathy, calcium phosphate deposition).
  - **Arrhythmias:** Hyperkalemia (VT, asystole), hypocalcemia (QT prolongation).
  - **Seizures:** Hypocalcemia (calcium <6 mg/dL), uremia (AKI).
- **Chronic:**
  - **Chronic Kidney Disease:** Post-AKI, especially if dialysis-dependent.
  - **Recurrent TLS:** With subsequent chemotherapy cycles (e.g., AML relapse).
  - **Underlying Disease:**
  - **Malignancy Progression:** Delayed therapy due to TLS complications.
  - **Infection:** Neutropenia post-chemotherapy, AKI-related immune suppression.

Key Pearls

- **Identify high-risk patients:** Bulky disease (Burkitt lymphoma, ALL), high LDH, renal dysfunction—start prophylaxis early.
- **Cairo-Bishop Criteria:** Laboratory TLS (≥2 metabolic abnormalities); clinical TLS (AKI, arrhythmia, seizure).
- **Monitor q6-8h:** Potassium, phosphate, uric acid, creatinine in first 48-72h post-therapy.
- **Rasburicase:** First-line for hyperuricemia in high-risk patients; avoid in G6PD deficiency.

- **Hyperkalemia:** Treat urgently if >6 mEq/L or ECG changes (calcium gluconate, insulin).
- **AKI:** Aggressive hydration; hemodialysis if refractory or severe electrolyte imbalances.

References

- **UpToDate:** “Tumor Lysis Syndrome: Prevention and Treatment” (2025).
- **NCCN:** “Guidelines for Management of Tumor Lysis Syndrome” (2024).
- **NEJM:** “Tumor Lysis Syndrome: Pathophysiology and Management” (2023).
- **JCO:** “Rasburicase in the Management of TLS” (2024).

Case Scenarios

Case 1: A 60-Year-Old Male with AML

- **Presentation:** A 60-year-old male with AML (WBC 80,000/µL, LDH 3x ULN) starts induction chemotherapy (cytarabine + daunorubicin). On day 2, he develops nausea, oliguria (urine output 40 mL/h), and muscle cramps.
- **Labs:** Potassium 6.2 mEq/L, uric acid 9.5 mg/dL, phosphate 5.8 mg/dL, calcium 6.5 mg/dL, creatinine 2.1 mg/dL (baseline 1.0). ECG: Peaked T waves.
- **Diagnosis:** Clinical TLS → Laboratory TLS (hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia) + AKI (Cr >1.5x ULN).
- **Management:** ICU transfer for telemetry. Calcium gluconate 1 g IV for hyperkalemia. Rasburicase 0.2 mg/kg IV daily x 2 days (uric acid to 5 mg/dL). Hydration with NS 200 mL/h IV. Sevelamer 800 mg PO TID for hyperphosphatemia. Monitor electrolytes q6h. Nephrology consult for possible hemodialysis if AKI worsens.

Case 2: A 45-Year-Old Female with Burkitt Lymphoma

- **Presentation:** A 45-year-old female with Burkitt lymphoma (bulky abdominal mass 12 cm, LDH 4x ULN) is admitted for chemotherapy (R-CHOP). Pre-treatment labs show uric acid 7.8 mg/dL, creatinine 1.2 mg/dL. She is dehydrated (urine output 60 mL/h).
- **Diagnosis:** High-risk for TLS → Bulky disease, high LDH, chemosensitive tumor.
- **Management:** Prophylaxis: Hydration with NS 3 L/m^2/day IV (goal urine output >100 mL/h). Rasburicase 0.2 mg/kg IV daily x 1 (uric acid to 4 mg/dL). Allopurinol 300 mg PO daily. Monitor electrolytes q8h for 72h. Urine pH 6.8 (no alkalinization needed). Chemotherapy started after 24h of prophylaxis; no TLS developed.

Case 3: A 55-Year-Old Male with CLL Post-Venetoclax

- **Presentation:** A 55-year-old male with CLL, 48h post-venetoclax initiation, presents with lethargy and irregular heartbeat. Exam shows HR 110 bpm, BP 100/60 mmHg, no fever.
- **Labs:** Potassium 6.8 mEq/L, uric acid 10 mg/dL, phosphate 6.2 mg/dL, calcium 6.8 mg/dL, creatinine 1.8 mg/dL (baseline 0.9). ECG: Widened QRS.
- **Diagnosis:** Clinical TLS → Laboratory TLS (hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia) + arrhythmia (hyperkalemia-induced).
- **Management:** Emergency: Calcium gluconate 1 g IV, insulin 10 units IV + D50W 50 mL IV for hyperkalemia. Rasburicase 0.2 mg/kg IV daily x 2 days. Hydration with NS 200 mL/h IV. Sevelamer 800 mg PO TID. Nephrology consult—initiate hemodialysis (refractory hyperkalemia, AKI). Hold venetoclax until TLS resolves.

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