# Oncologic Metabolic Emergencies

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**KEYWORDS**

• Cancer • Metabolic emergency • Emergency medicine • Treatment
• Tumor lysis syndrome • Hypercalcemia of malignancy

**KEY POINTS**

- Tumor lysis syndrome (TLS) and hypercalcemia of malignancy can present insidiously, but both result in significant morbidity.
- Emergency providers (EPs) should have a high index of suspicion for patients with a history of malignancy, those undergoing treatment, and those with signs and symptoms suggesting an undiagnosed cancer.
- Although hypercalcemia of malignancy typically occurs in patients with advanced disease, TLS can occur in those with curable disorders.
- When considering its increasing incidence and the importance of instituting therapy early in the disease process, the prompt and proper diagnosis and management of TLS is paramount to the EP.

## TUMOR LYSIS SYNDROME

### *Introduction*

Tumor lysis syndrome (TLS) is a metabolic emergency resulting from massive cytolysis leading to the release of tumor cellular contents into the systemic circulation. The subsequent metabolic abnormalities that result include hyperkalemia, hyperuricemia, hyperphosphatemia, and hypocalcemia. Acute renal failure, seizures, cardiac dysrhythmias, acidosis, azotemia, and potentially sudden death may result as a consequence of these metabolic abnormalities. TLS occurs most commonly after treatment with cytotoxic chemotherapy, but it can also occur spontaneously in patients as a result of cell death in highly proliferative tumors.[1,2]

TLS is one of the few oncologic emergencies that accounts for significant morbidity and mortality if not recognized early and treated appropriately.[3,4] With the use of newer and more aggressive cytotoxic therapies, the incidence of TLS has also

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increased. When considering its increasing incidence and the importance of instituting therapy early in the disease process, the prompt and proper diagnosis and management of TLS is paramount to the emergency department (ED) provider.

### *Definition*

As a set of metabolic complications that can arise from massive tumor cell death, there is a general agreement on a broad definition of TLS as a syndrome that may include hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia. However, there have been few attempts to define what encompasses this syndrome and to classify severity of disease. The 2 most complete and accepted classification systems are by Hande and Garrow[5] (1993) and Cairo and Bishop (2004).[6] Both systems distinguish between laboratory TLS (LTLS) and clinical TLS (CTLS); however, the Cairo-Bishop system is more encompassing in that it includes those patients who develop TLS beyond day 4 of treatment and those who have clinically relevant TLS at time of presentation; both are excluded in the Hande-Garrow system.[5,6] In oncology, the Cairo-Bishop classification is the most widely accepted system and therefore it is discussed here.[2]

#### *Cairo-Bishop classification*

The most current version of the Cairo-Bishop classification system (2004) defines tumor lysis syndrome as LTLS or CTLS (**Table 1**).[6]

The diagnosis of LTLS is present when 2 or more of the following metabolic abnormalities occur within 3 days before, or up to 7 days after, the initiation of therapy: hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia. Some investigators have argued that the required abnormalities need to be present simultaneously to warrant a diagnosis of LTLS; however, the Cairo-Bishop system does not explicitly state this.[4]

CTLS diagnosis requires the presence of LTLS plus one or more of the following that cannot be directly or probably attributable to a therapeutic agent: renal insufficiency (defined as creatinine $\geq$1.5 times the institutional upper limit of normal), cardiac arrhythmias/sudden death, and/or seizures (see **Table 1**).[6]

**Table 1**
**Cairo-Bishop definition of LTLS and CTLS**

| | |
|---|---|
| LTLS[a] | |
| Potassium | $\geq$6 mEq/L or 25% increase from baseline |
| Uric acid | $\geq$8 mg/dL or 25% increase from baseline |
| Phosphorous | $\geq$6.5 mg/dL (children), $\geq$4.5 mg/dL (adults), or 25% increase from baseline |
| Calcium | $\leq$7 mg/dL or 25% decrease from baseline |
| CTLS[b] | |
| Renal involvement | Creatinine $\geq$1.5 $\times$ ULN |
| Cardiac involvement | Arrhythmia/sudden death |
| Neurologic involvement | Seizure |

*Abbreviation:* ULN, upper limit of normal.

[a] LTLS requires 2 or more laboratory abnormalities within 3 days before or 7 days after cytotoxic therapy.

[b] CTLS requires the presence of LTLS plus one or more of the clinical consequences mentioned earlier.

*Adapted from* Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol 2004;127:5; with permission.