Diagnosis and treatment of tumour lysis syndrome in adults

Introduction:

Tumour lysis syndrome (TLS) is characterised by breakdown of tumour cells causing a release of intracellular contents into the bloodstream.

This leads to a syndrome of

- characteristic electrolyte abnormalities
- renal injury
- seizures,
- dysrhythmia
- sudden cardiac death.

Commonly occurs in the first few days after induction chemotherapy/steroids for haematological malignancies

Can occur spontaneously or after radiotherapy or treatments such as tumour embolization or radiofrequency ablation.

Clinical TLS carries a significant morbidity, with approximately **one-third of patients requiring dialysis** and an **overall mortality of approximately 15%.**

Risk factors for developing TLS

- High grade/poorly differentiated haematological malignancy (esp. ALL/AML/Burkitt's)
- High disease burden (bulky nodal disease > 10cm/WCC >100/extensive marrow involvement/ LDH > 2x ULN)
- Pre-existing renal disease
- Co-existing acute illness

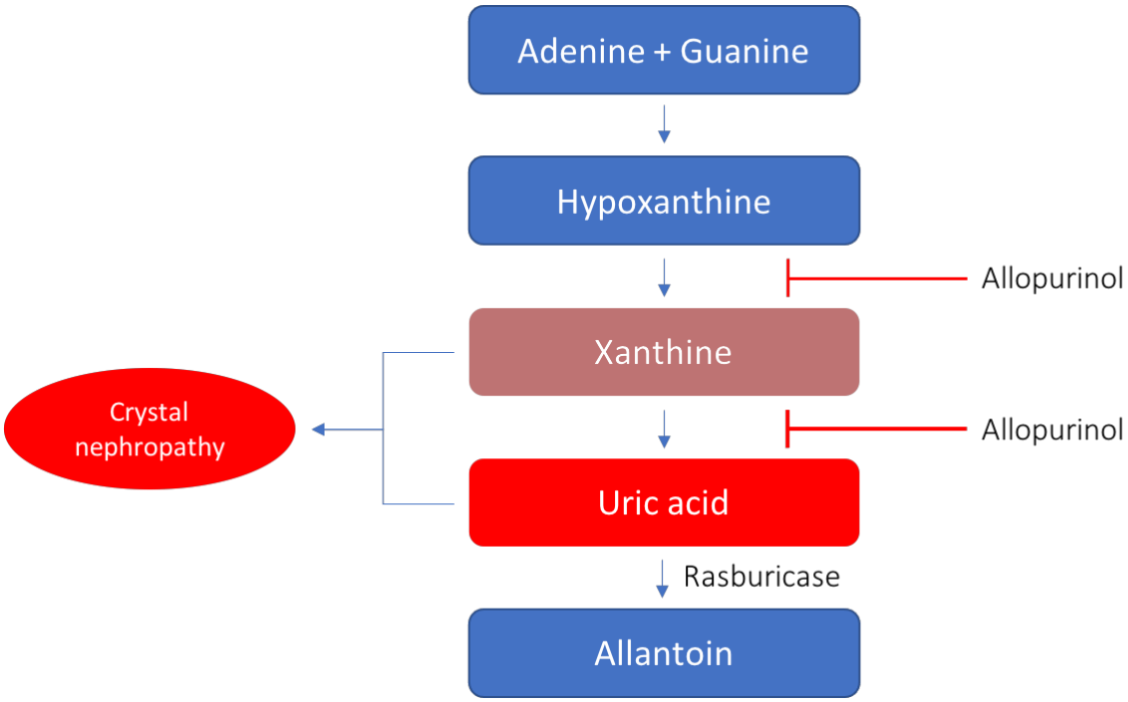
Critical care input for TLS patients may be needed for

- High-risk patients who are starting chemo/steroids
- Patients with established TLS who are deteriorating (likely to need CVVHD)
- Patients admitted for other reasons who are starting anti-cancer treatment in ICU and are at risk for developing TLS

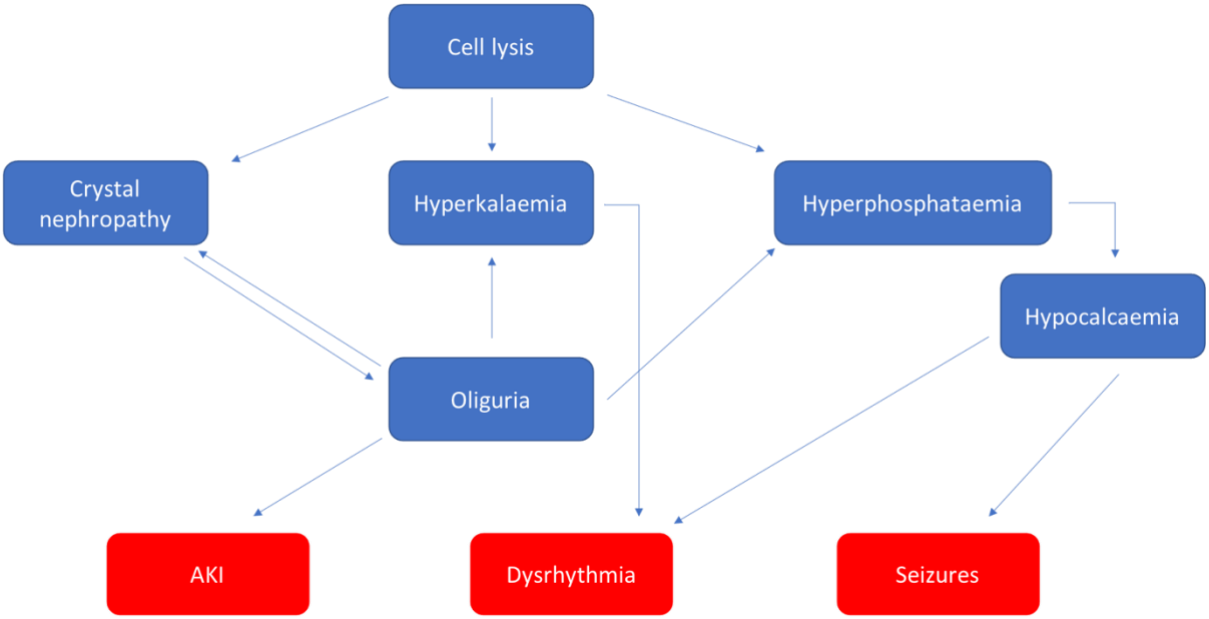
Pathophysiology:

The core concepts in TLS and the mechanism by which its clinical effects occur are:

- Purine metabolism and crystal nephropathy
- Calcium-phosphate complexes
- Potassium/cytokine release and oliguric AKI



Hyperkalaemia, acidaemia and a pro-inflammatory state result from release of potassium and intra-cellular cytokines, leading to further AKI and increasing risk of dysrhythmias.



Diagnosis and monitoring:

TLS should be suspected in any cancer patient with otherwise unexplained

- AKI
- Hyperphosphataemia
- Hypocalcaemia
- Hyperkalaemia
- Seizures
- Dysrhythmia
- Cardiac arrest

The formal definition of TLS is by Cairo-Bishop criteria

1. Presentation within the same 24-hour period on day -3 to +7 of anti-cancer therapy
2. Laboratory criteria, ≥2 of**:**
   Urate $^{\geq}$ 476 $\mu mol l^{-1}$
   K ≥ 6 $mmol l^{-1}$
   PO4 ≥ 1.45 $mmol l^{-1}$
   Ca ≤1.75 $mmol l^{-1}$
3. Clinical criteria, meeting laboratory criteria plus one of:
   AKI (sCr > 1.5 x baseline)
   Dysrhythmia
   Seizures

All patients at risk of TLS

- monitoring of their biochemistry and fluid depending on their risk factors.
- TLS blood samples must be sent immediately and on ice to avoid a falsely low urate level
- 6 hourly U&Es, Ca, PO_4, uric acid, LDH (Trak order set: "tumourlysis WGH") – can de-escalate frequency if no evidence of TLS in liaison with haematology
- If there is evidence of developing laboratory TLS,
  - escalated to the treating team,
  - increased frequency of blood sampling(?frequency)
  - close urine output monitoring
  - consideration given to critical care referral.

Patients with *laboratory TLS*

- high risk of developing clinical manifestations,
- receive continuous cardiac monitoring
- frequent blood sampling (?frequency)
- supportive care and treatment as outlined below.

Patients with *clinical TLS*

- very high-risk group
- should be managed in a critical care environment due to the risks of
  - severe electrolyte disturbances

- dysrhythmia
- possibility of requiring Renal Replacement Therapy

If TLS criteria are not met and biochemistry values remain stable

- frequency of blood sampling may be reduced (?frequency)
- monitoring and prophylaxis will be continued until the course of anti-cancer treatment is complete.

Treatment:

Following risk assessment for TLS by the haematology team, any patient at risk of TLS should be offered some degree of prophylaxis.

Urate lowering therapies

- All patients at risk of, or with established tumour lysis syndrome.

- **Allopurinol**
  - a xanthine oxidase inhibitor
  - prophylaxis in low-risk patients.

- **Rasburicase**
  - an exogenous form of the enzyme urate oxidase that is lacking in humans,
  - prophylaxis (3mg OD for high-risk patients)
  - treatment (0.2mg/kg OD, max 15mg) of TLS.
  - contraindicated in G6PD deficiency, in which case allopurinol should be used.
  - Allopurinol should be stopped if a patient is on rasburicase

Intravenous fluid resuscitation

- Goal is to achieve and maintain euvolaemia rather than fluid overload.
- Assess fluid balance
- Give isotonic crystalloid to reach euvolaemia
- Followed by a trial of IVF 100-200ml/hr to encourage renal excretion of urate/PO_4/K^+
- If urine output not keeping up with IVF rate then can try diuresis but likely to need to stop fluids and prepare for CVVHD if becoming increasingly oliguric

Calcium supplementation

- Should generally be avoided due to the risk of worsening Ca-PO_4 complex deposition

- Asymptomatic hypocalcaemia should be tolerated and monitored, even if severe.
- Calcium supplementation should be reserved for hypocalcaemic patients with symptoms attributable to low calcium (paraesthesia, tetany, seizures, dysrhythmias), or those who require cardioprotective treatment for hyperkalaemia.
- The amount of calcium given should be titrated to symptom resolution rather than a normal lab value.

Renal replacement therapy

- useful in the treatment of TLS as it directly corrects many of the underlying problems (hyperkalaemia, acidaemia, hyperuricaemia, hyperphosphataemia, AKI)
- Usual indications (refractory hyperK/hypervolaemia/acidaemia or symptomatic uraemia
- Lower threshold for commencing CVVHD for patients with TLS who are deteriorating despite medical management.

Medication review

- Any electrolyte supplementation or nephrotoxic medications suspended.
- Potassium and phosphate binding medications such as calcium resonium or Lokelma and Sevelamer respectively, may be considered for mild cases

Urinary alkalinisation with bicarbonate

- No longer recommended for TLS.

Title: Diagnosis and treatment of tumour lysis syndrome in adults – guidance for critical care	
	Authors: Dr S Talbot, Dr M Blackstock
Status Draft/Final: Final	**Approved by:** QIT editorial group
	Written: 1/9/23
Reviewed on: 15/3/24	**Next review : 15/3/26**