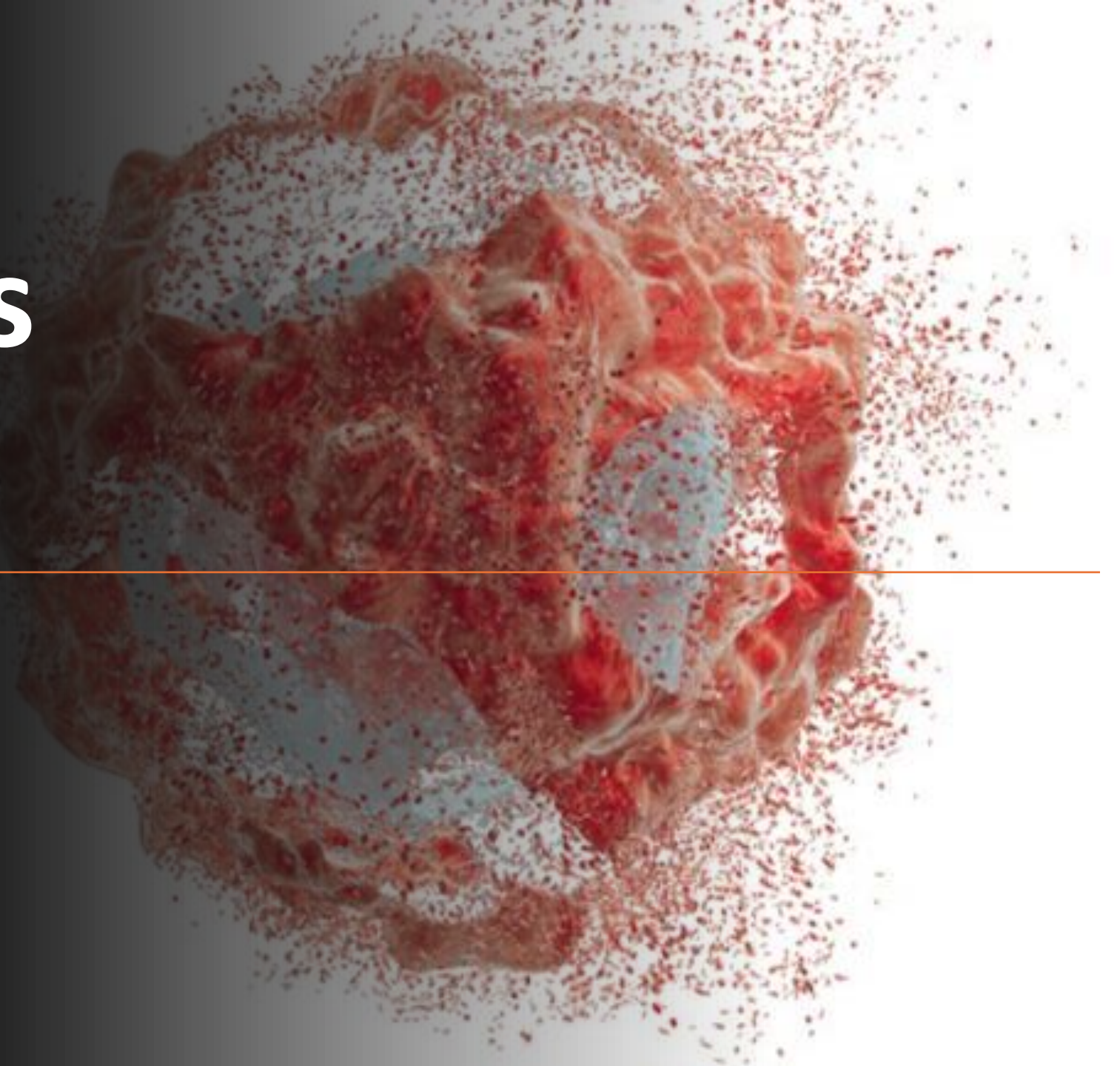

17-20 OCTOBER
2024
KONYA
Konya City Hospital

Tumor Lysis Syndrome



Khalid A. Ateyyah, MBBS. SBEM, ArBEM
Consultant Emergency Medicine & EMS
Assistant Professor, Taibah University
College of Medicine
Madinah, Saudi Arabia

Disclosure

I have no actual or potential conflict of interest in relation to this presentation



Tumor Lysis Syndrome

The Most Common Oncologic Emergency

Prevalent in Adult & Pediatric

On Chemotherapy, and Spontaneously

Tumor Lysis Syndrome - StatPearls - NCBI Bookshelf (nih.gov). Last Update: October 31, 2022.

Tumor Lysis Syndrome

Most Symptoms are related to

Massive Tumor Cell Lysis with the release of

Intracellular Chemical Substances

Tumor Lysis Syndrome - StatPearls - NCBI Bookshelf (nih.gov). Last Update: October 31, 2022.

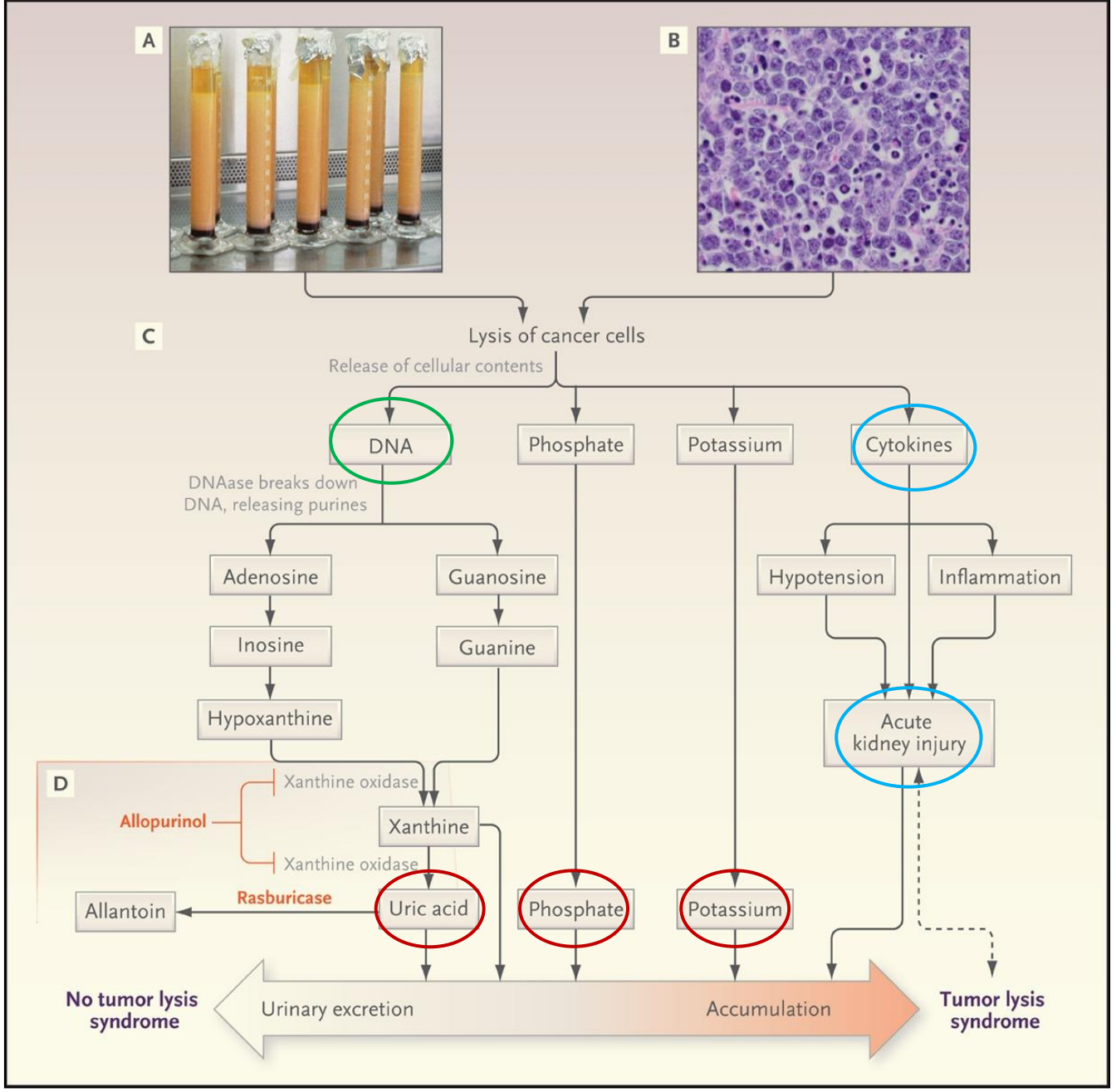
Tumor Lysis Syndrome

AKI

Fatal Arrhythmia

Death **“14 – 79%”**

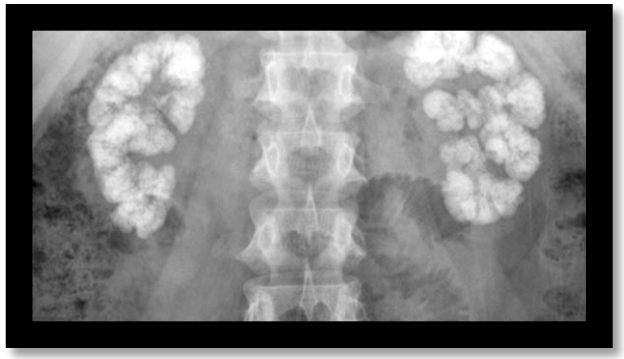
Tumor Lysis Syndrome - StatPearls - NCBI Bookshelf (nih.gov). Last Update: October 31, 2022.



Howard SC et al. N Engl J Med 2011;364:1844-1854

Tumor Lysis Syndrome

- **Hyperphosphatemia**
  - Precipitation of Calcium-phosphate Crystals
  - **Hypocalcemia**
  - Metastatic Calcification
  - Intrarenal Calcification
  - Nephrocalcinosis
  - Nephrolithiasis
  - Obstructive Uropathy





Tumor Lysis Syndrome

Presenting Signs & Symptoms

None Specific

Cairo-Bishop Definition of Laboratory/Clinical Tumour lysis syndrome



2004

Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol. 2004 Oct;127(1):3-11.

≥ 2 Criteria 3 days before treatment & 7 days after

Uric acid	**≥8.0 mg/dL or 25% increase from baseline**
Potassium	**≥6.0 mEq/L or 25% increase from baseline**
Phosphorus	**≥6.5 mg/dL (children)** **≥4.5 mg/dL (adults)or 25% increase from baseline**
Calcium	**≤7.0 mg/dL or 25% decrease from baseline**

TLS Clinical Criteria (1)

- AKI
  - Creatinine increase by 0.3 mg/dl
  - Urine output < 0.5 ml/kg/hr
- Dysrhythmia
- Sudden Death

TLS Clinical Criteria (2)

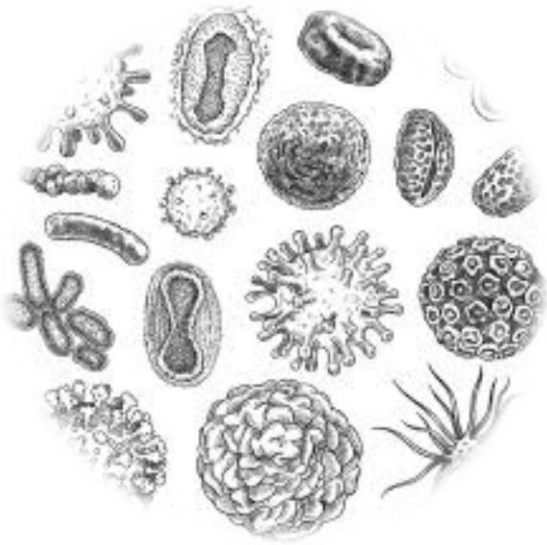
- Seizure
- Hypotension
- Heart Failure

TLS Risk Factors (4Ts)

1. Tumor related
2. Treatment related
3. Tubules related
4. Test related

TLS Risk Factors (Tumor)

- Large Tumor Burden
  - Extensive Metastasis
  - Bone marrow > 1kg cancer
  - Bulky Tumor >10 cm
  - WBC > 50K
- Organ infiltration
  - Hepato/Spleno/Nephromegaly



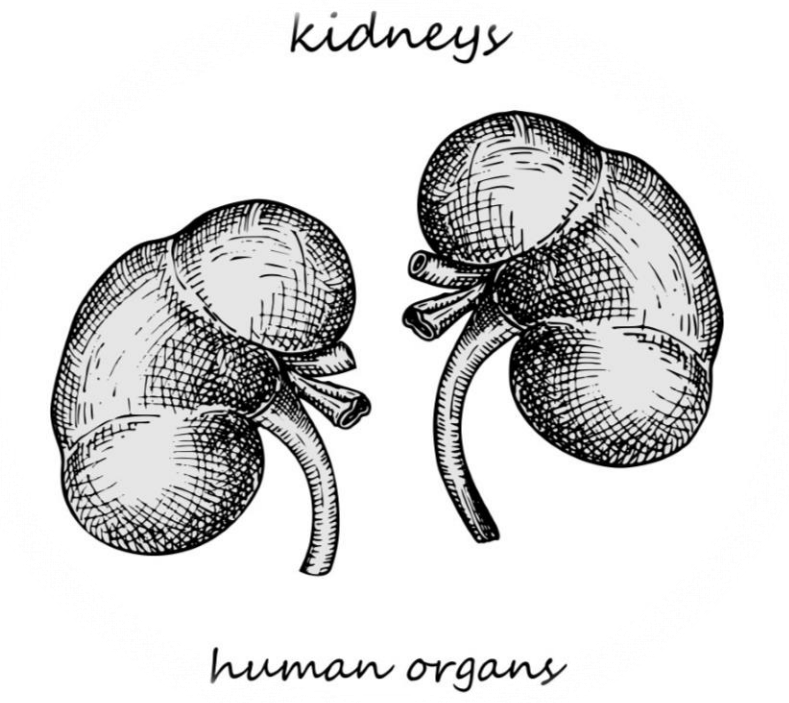
TLS Risk Factors (Treatment)

- High sensitivity to treatment
  - Cytotoxic Chemotherapy
  - Glucocorticoid Therapy
  - Cytolytic Antibody
  - Radiation therapy
- Intrathecal Chemotherapy
- Chemo-Embolization



TLS Risk Factors (Tubules)

- CKD
- Out-Flow Obstruction
- Nephrotoxic Medications
  - NSAIDs
  - Contrast
  - Vancomycin/Aminoglycoside



TLS Risk Factors (Test)

- High LDH > 1500 IU
  - High Proliferative Rate
- Dehydration
- Hypotension



Risk Stratification

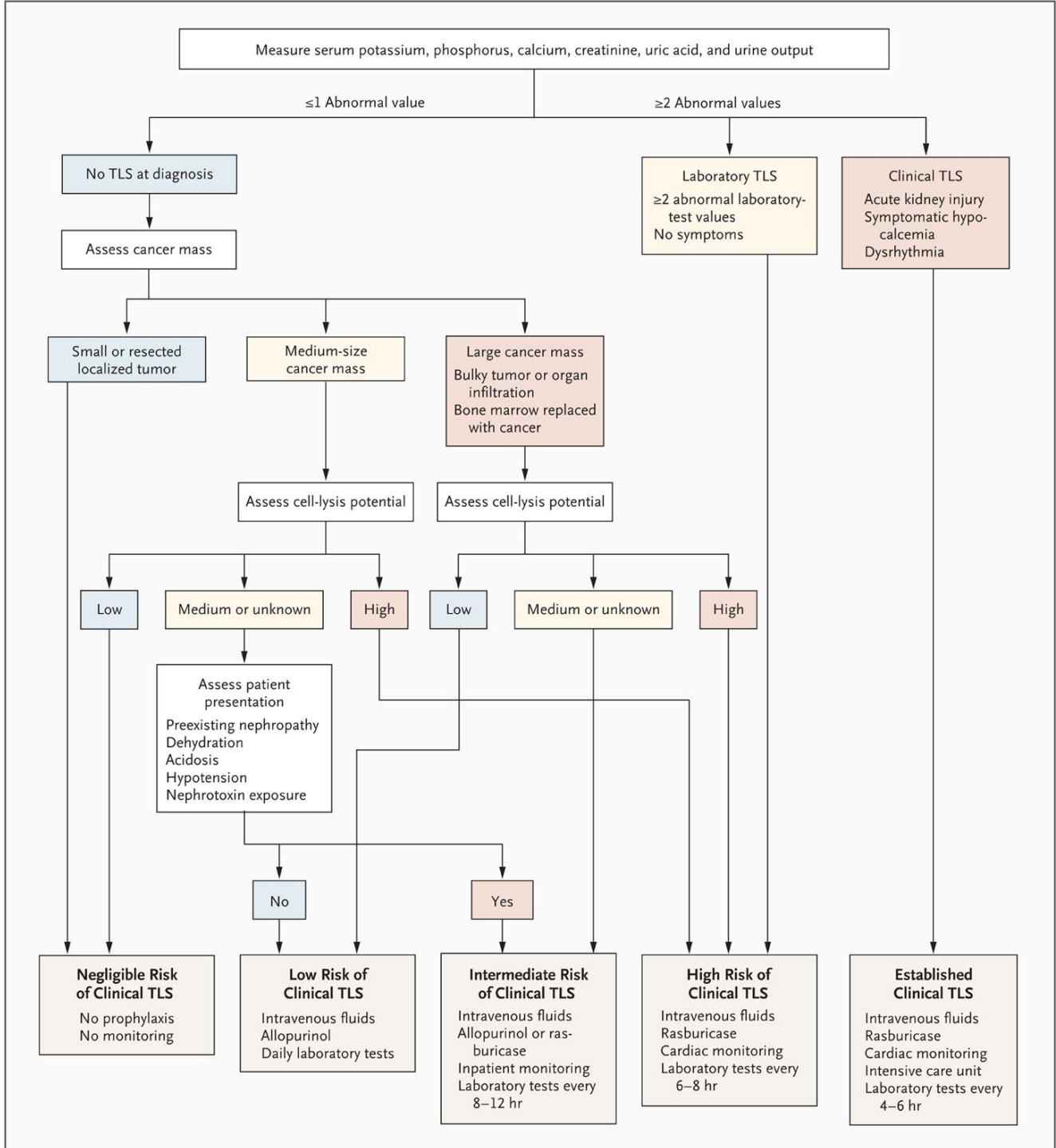
TLS Risk Stratification

	Risk group		
	Low	Intermediate	High
NHL	Indolent NHL	DLBCL	Burkitt's, lymphoblastic
ALL, WBC	$\leq$ 50,000/m^3	50,000-100,000/m^3	$\geq$ 100,000/m^3
AML, WBC	$\leq$ 10,000/m^3	10,000-50,000/m^3	$\geq$ 50,000/m^3
Other malignancies	UA < 7.5 mg/dL	Elevated LDH High tumor burden, rapid cell turnover or high chemosensitivity	UA $\geq$ 7.5 mg/dL Preexisting renal insufficiency

NHL: non-Hodgkin's lymphoma, ALL: acute lymphoblastic leukemia, WBC: white blood cell, AML: acute myeloid leukemia, UA: uric acid, DLBCL: diffuse large B-cell lymphoma, LDH: lactate dehydrogenase.

Su Kyung, Lee, Min Jung Geum. Use of Prophylactic Drugs according to Risk Classification for TLS in Patients with Hematological Malignancies. February 2023Journal of Korean Society of Health-System Pharmacists 40(1):59-71. DOI: 10.32429/jkshp.2023.40.1.002

Howard SC et al. N Engl J Med 2011;364:1844-1854



Grading

Table 2. Cairo-Bishop Grading of Clinical Tumor Lysis Syndrome for Adults

Variable	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Creatine	None	1.5 times ULN	> 1.5 - 3.0 times ULN	> 3.0 - 6.0 times ULN	> 6.0 times ULN	Death
Cardiac arrhythmia	None	Intervention not indicated	Non-urgent medical intervention indicated	Symptomatic and incompletely controlled medically or controlled with device (e.g., defibrillator)	Life-threatening (e.g., arrhythmia associated with heart failure (HF), hypotension, syncope, shock).	Death
Seizure	None	-	One brief, generalized seizure; seizure(s) well controlled by anticonvulsants or infrequent focal motor seizures not interfering with ADL	Seizure in which consciousness is altered; poorly controlled seizure disorder; with breakthrough generalized seizures despite medical intervention	Seizure of any kind which are prolonged, repetitive or difficult to control (e.g., status epilepticus, intractable epilepsy)	Death

Adapted from Cairo et al [4]. ULN: upper limit of normal.

Management

TLS Management

- High Suspicion
- Early Detection

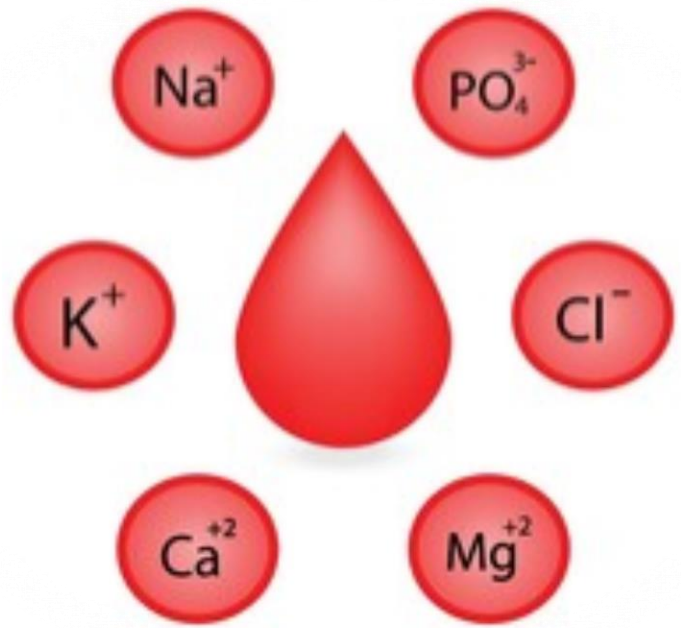
TLS Management

- Hydration
- Hydration, Hydration
- Hydration, Hydration, Hydration



TLS Management

- Electrolyte imbalances
  - Art of replacement
- Excretion
  - Uric Acid
  - Phosphate

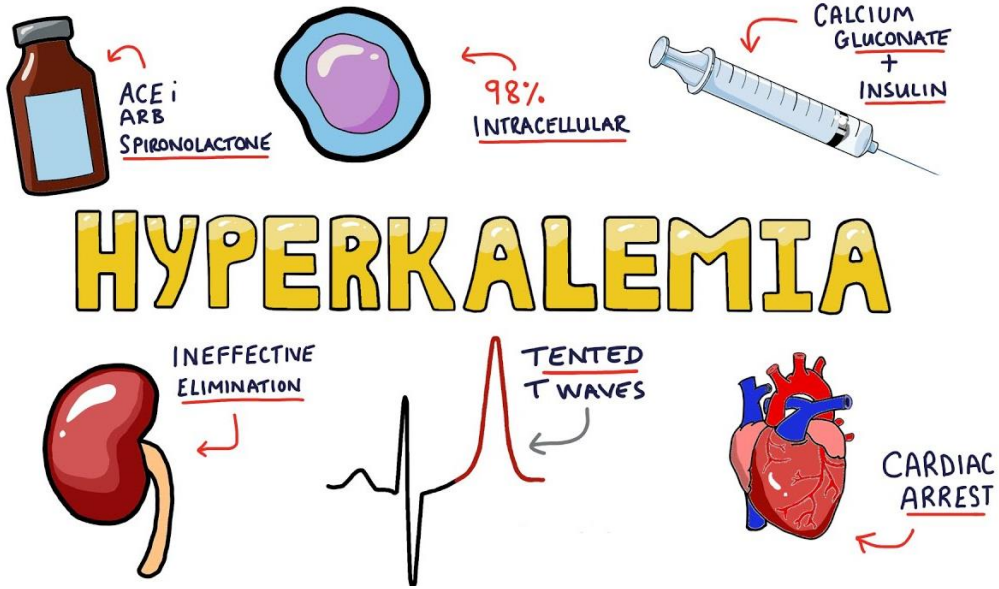


TLS Management

- Aggressive IV fluid hydration
  - 3 L/m^2 per day
  - Urine output of 2ml/kg/hr
  - Do not add potassium
    - *Urine Alkalinization*

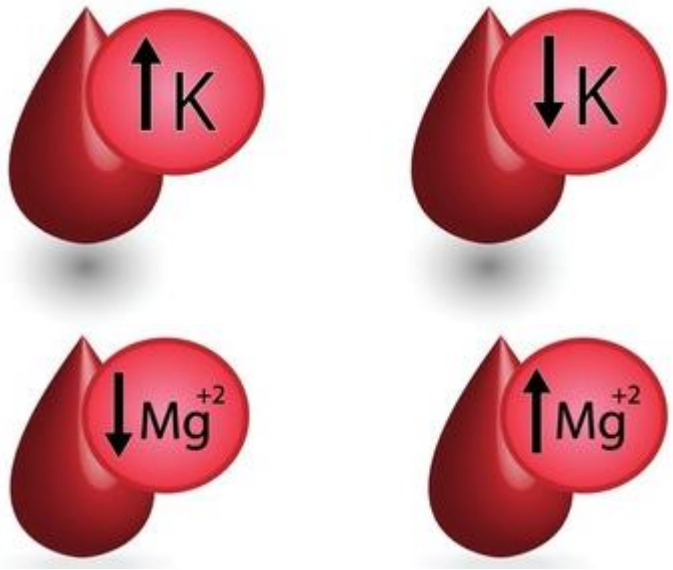
TLS Management

- Hyperkalemia:
  - Albuterol
  - Dextrose/Insulin
  - NaHCo3
  - Calcium gluconate
    - ECG changes (prolonged PR or QRS)



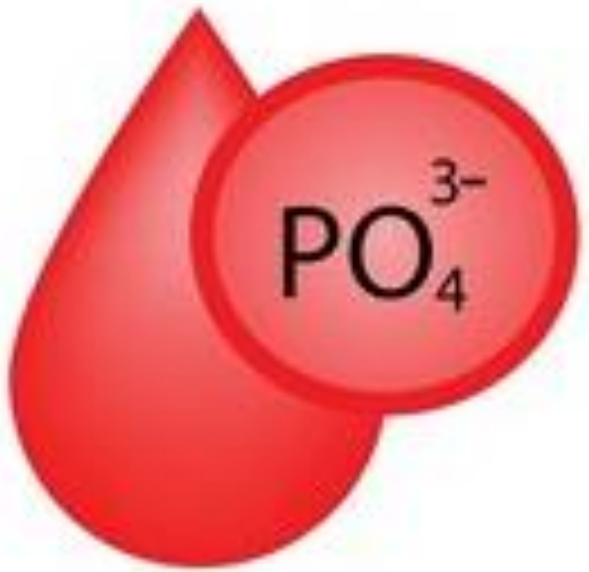
Potassium & Magnesium

- Exogenous sources to be restricted
- In case of low level
  - Treat only if symptomatic
  - **VERY CAREFUL** correction



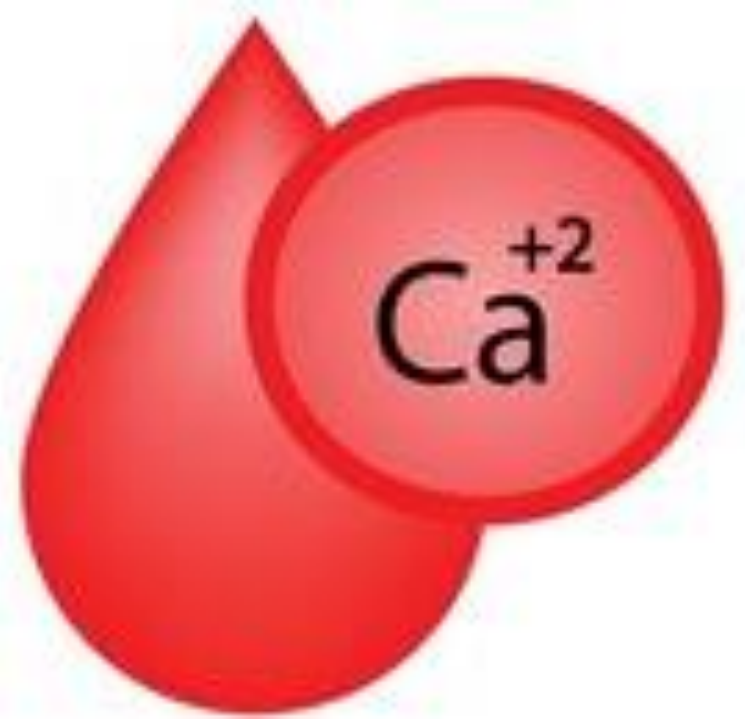
TLS Management

- Hyperphosphatemia
  - Phosphate excretion enhanced by IVF
  - Usually resolves within 6 – 12 hours
  - Hemodialysis



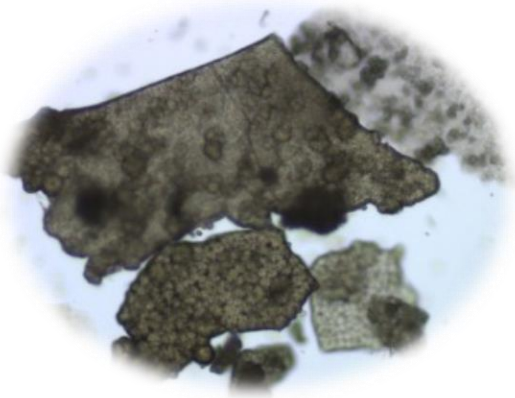
TLS Management

- Hypocalcemia
  - Lowest dose possible
  - Only symptomatic patients
    - Seizures, Arrhythmias, Tetany
  - Correct hyperphosphatemia first



TLS Management

- **Allopurinol**
  - Mainly as a prophylaxis
  - Xanthine level can be elevated
    - Can crystallize in the renal tubules



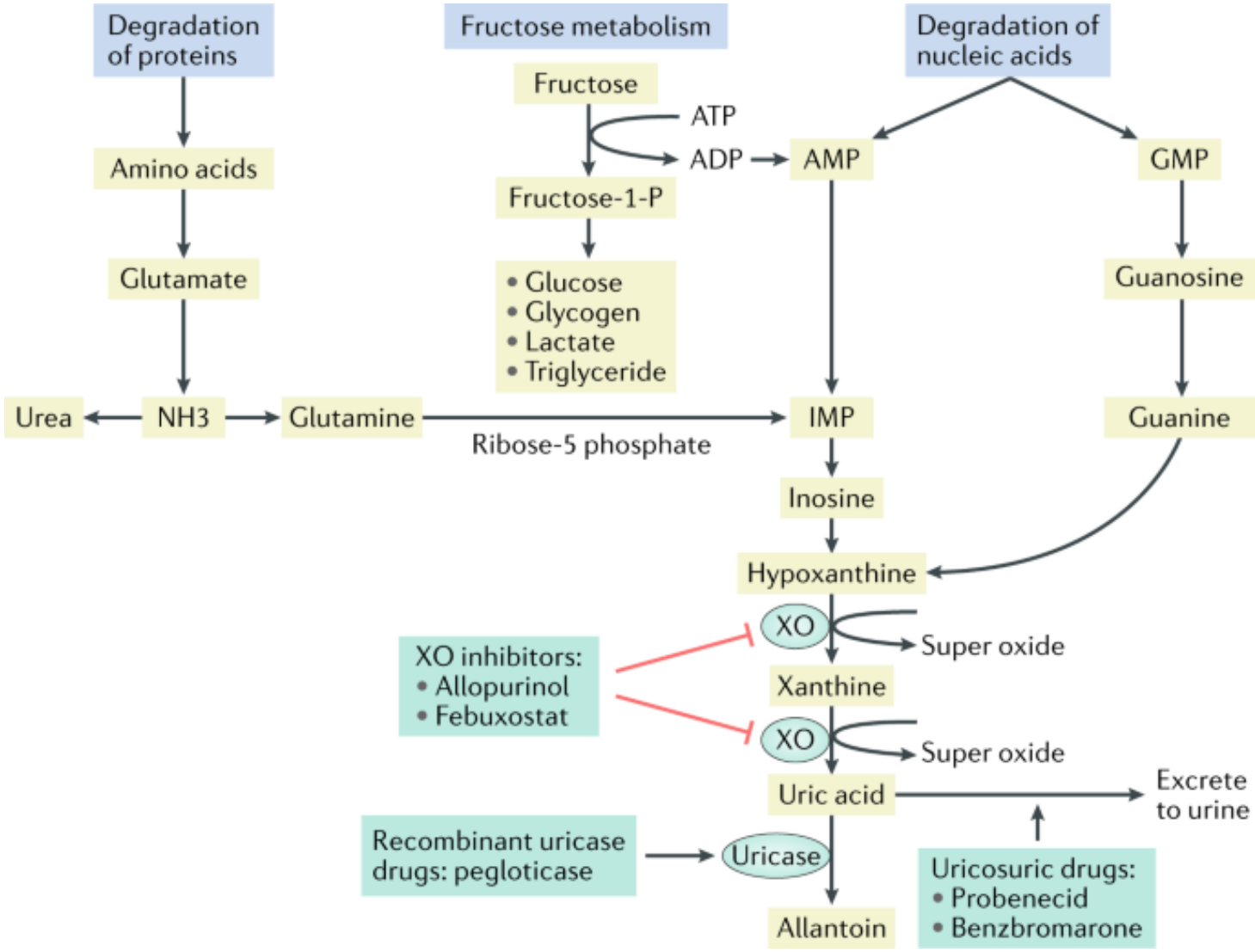
TLS Management

- Rasburicase; Elitek® / Fasturtec®

  “Catalyzes the oxidation of uric acid into soluble allantoin”

  - 2 mg/kg/day
  - 30-min infusion
  - Electrolyte monitoring
  - Daily for three to seven days
  - Mind G6PD

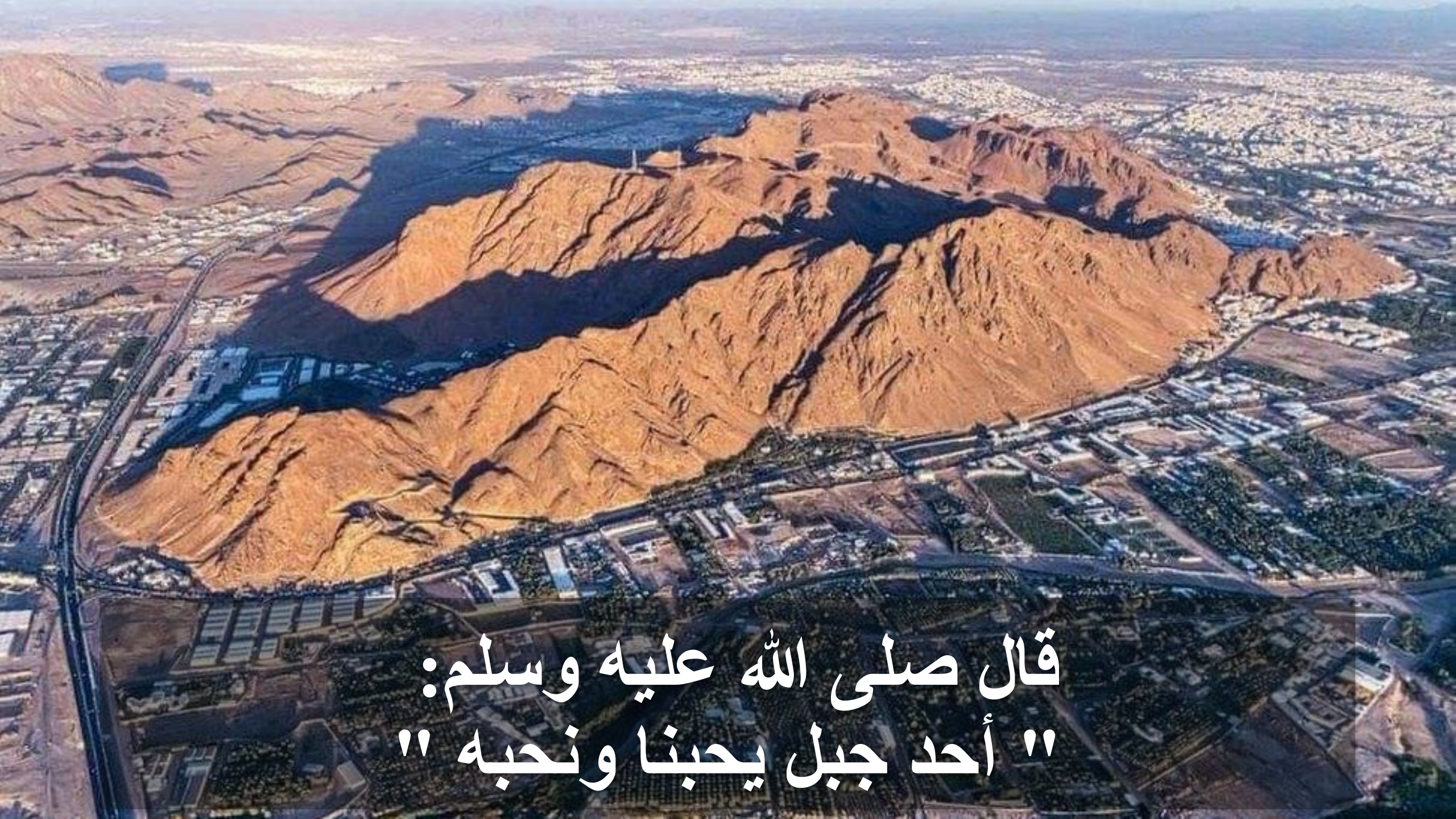
Sato Y, Feig DI, Stack AG, et al. The case for uric acid-lowering treatment in patients with hyperuricaemia and CKD. Nat Rev Nephrol. 2019 Dec;15(12):767-775. doi: 10.1038/s41581-019-0174-z. Epub 2019 Jul 11. PMID: 31296965.



TLS Management

- Hemodialysis
  - Severe AKI
  - Fluid overload
  - Persistent hyperkalemia
  - Calcium-phosphate product $\geq 70\ mg^2/dL^2$
  - Hyperphosphatemia with symptomatic hypocalcemia




قال صلى الله عليه وسلم:
" أحد جبل يحبنا ونحبه "