TUMOR LYSIS SYNDROME

SIGNS & SYMPTOMS

- Clinical: Creatinine > 1.5; Cardiac arrythmias; Seizure
- Occuring 3 days before or 7 days after chemotherapy
- Chemotherapy after rapidly growing lymphoproliferative malignancies (e.g., Burkitt's lymphoma or ALL)
- Trigered by direct tumular injury & luminal obstruction by uric acid & ca phosphate crystals

DIFFERENTIAL DIAGNOSIS:

- Prerenal azothemia (hypovolemia, NSAIDS etc) - Rhabdomyolysis - Hemolysis - Multiple myeloma - Chemotherapy-assoc thrombotic microangiopathy	- Ethylene glycol ingestion - Infection - Glomerulonephritis (RPGN) - Cardiac/ Liver problem - Vascular (Renal artery thrombosis, atheroembolism, renal vein thrombosis)

DIAGNOSIS

- CBC creatinine, na, k, icalcium, uric acid, phosphorus, mg, chloride, Liver function test, Urinalysis, UTPCR
- FeNA, Urine Na, BCR, SpGv, ABG, ECG, Chest xray, UTZ WA
- Hyperuricemia, hyperphosphatemia, hyperkalemia, hypocalcemia, Urate crystals

Table 31.12 Cairo-Bishop Definition of Tumor Lysis Syndrome

Diagnosis of Laboratory Tumor Lysis Syndrome	Diagnosis of Clinical Tumor Lysis Syndrome
Requires at least two of the following criteria achieved in the same 24-hr interval from 3 days before to 7 days after chemotherapy initiation: • Uric acid level: ≥ 8.0 mg/dL or ≥ 25% increase from baseline • Potassium level: ≥ 6.0 mmol/L or ≥ 25% increase from baseline • Phosphorus level: ≥ 4.6 mg/dL (≥6.5 mg/dL in children) or ≥ 25% increase from baseline • Calcium level: ≤ 7.0 mg/dL or ≥ 25% decrease from baseline	Laboratory tumor lysis syndrome plus at least one of the following: • Serum creatinine level ≥ 1.5 times the age-adjusted upper limit of normal • Cardiac arrhythmia/sudden death • Seizure

MANAGEMENT

- IV hydration with Isotonic crystalloid solution such as PNSS ensuing high UO (2ml/kg/hr)
- Reduce uric acid levels, control phosphate levels
- **Low-risk of TLS**
  - **Allopurinol –** inhibit uric acid formation
  - **IV hydration**
  - **NaHCO3** not recommended since systemic alkalosis can aggravate hypocalcemia, resulting in tetany & seizures; alkaline pH can precipitate phosphate nephropathy
- **Medium/high-risk of TLS**
  - **Rasburicase** – decreases both serum uric acid levels and urinary uric acid excretion
    - **Avoided** in patients w/ G6PD because hydrogen peroxide, a breakdown product of UA, can cause methemoglobinemia & in severe cases, hemolitic anemia
    - Recommend as **1st line treatment** for high risk for TLS
  - **IV hydration**
- **Supportive**:
  - Hyperkalemia (>5.5) – Calcium gluconate 10ml of 10% solution x 5 mins; D50/50+ 10 units insulin; Albuterol 10-20mg by nebulizer, K+binding resin; restric K diet
  - Met acidosis – restric dietary protein, Sodium bicarb only if Hco3 <15 or pH <7.15
  - Hyperphosphatemia- restric dietary phosphate, phosphate binders
  - Hypocalcemia- IV replacement
  - Nutrition: Caloric intake: 20-30 kcal/day; Protein intake: NonHD (0.8-1 g/kg/d); HD (1-1.5 g/kg/d); CRRT (upto 1.7 g/kg/day)
  - Enteral route; Dose adjustments of medications

HEPATO-RENAL SYNDROME

SIGNS & SYMPTOMS

- Clinical syndrome marked by irreversible AKI that develops in patients with advanced cirrhosis
- Ascites, Icteric sclera, jaundice, Anuria
- DOB, Volume overload
- Unlike pre renal AKI, HRS does not improve with aggressive expansion of intravascular space
- Peripheral vasodilation in assoc with renal vasoconstriction

DIFFERENTIAL DIAGNOSIS:

- Prerenal azothemia (hypovolemia, NSAIDS etc) - Rhabdomyolysis - Hemolysis - Vascular (Renal artery thrombosis, atheroembolism, renal vein thrombosis)	- Infection - Glomerulonephritis (RPGN) - Acute Decompensated Heart Failure

DIAGNOSIS

- CBC creatinine, na, k, icalcium, uric acid, phosphorus, mg, chloride, albumin, Urinalysis
- Liver function test (Ammonia, SGPT, TB, DB, IB)
- FeNA, Urine Na, UTPCR, BCR, SpGv, ABG, ECG, Chest xray, UTZ WA

Table 31.13 Diagnostic Criteria for Hepatorenal Syndrome

Diagnostic Criteria for Hepatorenal Syndrome

• Cirrhosis with ascites
• Serum creatinine level > 1.5 mg/dL
• No improvement of serum creatinine level (decrease to a level of ≤ 1.5 mg/dL) after at least 2 days of diuretic withdrawal and volume expansion with albumin (1 g/kg body weight per day to a maximum of 100 g/day)
• Absence of shock
• Absence of parenchymal kidney disease as indicated by:
  ◦ Proteinuria > 500 mg/day
  ◦ Microhematuria (>50 red blood cells per high-power field) and/or
  ◦ Abnormal renal ultrasonography findings

Type 1 Hepatorenal Syndrome
Rapid progressive AKI with doubling of the serum creatinine level to >2.5 mg/dL in < 2 wk
Type 2 Hepatorenal Syndrome
Moderate renal dysfunction (serum creatinine level of 1.5 to 2.5 mg/dL) with a steady or slowly progressive course

- **Type 1 HRS**
  - Develops in hospitalized patients & may be precipitated by variceal bleeding, overly rapid diuresis, the performance of paracentesis, or, most commonly, spontaneous bacterial peritonitis.
  - Fulminant course with oliguria, encephalopathy, marked hyperbilirubinemia, and death within 1 month of clinical presentation.
- **Type 2 HRS**
  - More gradual decline in renal function that develops in the setting of <u>diuretic-resistant ascites and avid sodium retention</u>
    - Prognosis is considerably better (median survival of 6 months and a 1- year survival as high as 30%)

MANAGEMENT

- Definitive treatment: **Successful liver transplantation**
- Systemic vasoconstrictions (Terlipressin) combined with albumin infusion
  - Others: norepinephrine, combination of midodrine & octreotide
- **Transjugular Intrahepatic Portosystemic Shunt (TIPS)**
- **RRT +** Molecular adsorbent recirculating system (MARS) removing albumin-bound, water-soluble vasoactive agents, toxins, and proinflammatory cytokines.
- RRT and MARS may serve as a bridge to liver transplant
- **Supportive**:
  - Hyperkalemia (>5.5) – Calcium gluconate 10ml of 10% solution x 5 mins; D50/50+ 10 units insulin; Albuterol 10-20mg by nebulizer, K+binding resin; restric K diet
  - Met acidosis – restric dietary protein, Sodium bicarb only if Hco3 <15 or pH <7.15
  - Hyperphosphatemia- restric dietary phosphate, phosphate binders
  - Hypocalcemia- IV replacement
  - Nutrition: Caloric intake: 20-30 kcal/day; Protein intake: NonHD (0.8-1 g/kg/d); HD (1-1.5 g/kg/d); CRRT (upto 1.7 g/kg/day)
  - Enteral route; Dose adjustments of medications

CONTRAST INDUCED NEPHROPATHY

SIGNS & SYMPTOMS

- **Acute decline GFR** w/in **24 to 48 hours of administration**, w/ a **peak serum creatinine conc** occurring in **3 to 5 days** & **return** to baseline **within 1 week**, although patients with moderate to advanced CKD may take somewhat longer to return to baseline.
- Combined hypoxic & toxic renal tubular damage assoc with renal endothelial dysfunction and altered microcirculation
- Mediates vasoconstriction and markedly affects renal parenchymal oxygenation especially in the outer medulla

Table 15 | CI-AKI risk-scoring model for percutaneous coronary intervention

Risk factors	Integer score (calculate)
Hypotension	5
IABP	5
CHF	5
Age >75 years	4
Anemia	3
Diabetes	3
Contrast-media volume	1 per 100 ml
SCr >1.5 mg/dl (>132.6 μmol/l)	4
or	
eGFR <60 ml/min per 1.73 m^2	2 for 40-60 4 for 20-39 6 for <20

Note: Low risk: cumulative score <5; high risk: cumulative score >16.

DIFFERENTIAL DIAGNOSIS:

- Prerenal azothemia (hypovolemia, NSAIDS etc) - Hemolysis - Vascular (Renal artery thrombosis, atheroembolism, renal vein thrombosis)	- Infection - Glomerulonephritis (RPGN) - Acute Decompensated Heart Failure

DIAGNOSIS

- CBC creatinine, na, k, icalcium, uric acid, phosphorus, mg, chloride, albumin, Urinalysis
- Liver function test (Ammonia, SGPT, TB, DB, IB); ESR, CRP
- FeNA, Urine Na, UTPCR, BCR, SpGv, ABG, ECG, Chest xray, UTZ WA
- FeNA < 1%, Una <10 mmol/L, SG > 1.018

MANAGEMENT

- CPG recommend administration of IV isotonic sodium chloride or sodium bicarbonate to high-risk patients
- For **hospitalized patients**:
  - Isotonic fluids at a rate of **1 mL/kg/hr for 6 to 12 hours before and 6 to 12 hours following the procedure**
- For **outpatient**s:
  - **3 mL/kg/hr for 1 hour before the procedure followed by 6 mL/kg administered over 4 to 6 hours following the procedure**
- **NAC** at 1200 mg 2x a day (to enhanced NO-dependent vasodilation and medullary oxygenation in addition to scavenging of free radical)
- Use of **isoosmolar or low-osmolar contrast media** with lowest possible volume needed
- Withdrawal of nephrotoxic agents before & after procedure

RHABDOMYOLYSIS

SIGNS & SYMPTOMS

- Triad: muscle pain, weakness & dark urine
- Seizures, excessive exercise, alcohol or drug abuse, treatment with statins, prolonged immobilization, limb ischemia, crush injury

DIFFERENTIAL DIAGNOSIS:

- Prerenal azothemia (hypovolemia, NSAIDS etc) - Rhabdomyolysis - Hemolysis - Vascular (Renal artery thrombosis, atheroembolism, renal vein thrombosis)	- Infection - Glomerulonephritis (RPGN) - Acute Decompensated Heart Failure

DIAGNOSIS

- CBC creatinine,BUN, na, k, icalcium, uric acid, phosphorus, mg, chloride, albumin, Urinalysis
- Liver function test (Ammonia, SGPT, TB, DB, IB)
- FeNA, Urine Na, UTPCR, BCR, SpGv, ABG, ECG, Chest xray, UTZ WA
- FeNA > 1%, Una >10 mmol/L, SG = 1.01; ESR, CRP, LDH
- High Creatinine Kinase (5x UL) 1,500-100,000 IU/L; Urine supernatant test (+) for heme; Myoglobin
- Hyperkalemia, Hyperphosphatemia, Hypocalcemia, Hyperuricemia, Met Acidosis

MANAGEMENT

- Volume administration: **Isotolic solution 1-2L/hr then may titrate to maintain UO 200 – 300 mL/hr**
- **Bicarbonate infusion** for severe rhabdomyolysis (CK >5,000 & evidence of myscle injury)
  - Minimum requirement before giving:
    - Hypocalcemia is not present
    - Arterial pH is less than 7.5
    - Serum Bicarbonate is less than 30 mEq/L
  - Administration: Infuse ~130 mEq/L of Sodium Bicarbonate (150ml [3 amps] of 8.4% NaHCO3 in 1L D5W) 200ml/hr to achieve urine pH of >6.5
- Dialysis
- **Supportive**:
  - Hyperkalemia (>5.5) – Calcium gluconate 10ml of 10% solution x 5 mins; D50/50+ 10 units insulin; Albuterol 10-20mg by nebulizer, K+binding resin; restric K diet
  - Met acidosis – restric dietary protein, Sodium bicarb only if Hco3 <15 or pH <7.15
  - Hyperphosphatemia- restric dietary phosphate, phosphate binders
  - Hypocalcemia- Oral/IV replacement
  - Hyperuricemia- Allopurinol 300mg
  - Nutrition: Caloric intake: 20-30 kcal/day; Protein intake: NonHD (0.8-1 g/kg/d); HD (1-1.5 g/kg/d); CRRT (upto 1.7 g/kg/day)
  - Enteral route; Dose adjustments of medications

MULTIPLE MYELOMA/ CAST NEPHROPATHY

SIGNS & SYMPTOMS

- bone pain, fractures, anemia, infections, hypercalcemia, edema, heart failure, renal disease
- Excess light chains precipitate with Tamm-Horsfall protein secreted by the thick ascending limb of the loop of Henle & produce casts in the distal tubule
- **unexplained AKI, anemia, bone pain or fractures in an elderly patient, subnephrotic proteinuria (Bence Jones proteins)**

DIFFERENTIAL DIAGNOSIS:

- Multiple myeloma/ Ligh chain deposition disease - Prerenal azothemia (hypovolemia, NSAIDS etc) - Rhabdomyolysis - Hemolysis - Infection	- Glomerulonephritis (RPGN) - Acute Decompensated Heart Failure - Vascular (Renal artery thrombosis, atheroembolism, renal vein thrombosis)

DIAGNOSIS

- CBC creatinine,BUN, na, k, icalcium, uric acid, phosphorus, mg, chloride, albumin, Urinalysis
- Electron Gel electrophoresis
- Liver function test (Ammonia, SGPT, TB, DB, IB)
- FeNA, Urine Na, UTPCR, BCR, SpGv, ABG, ECG, Chest xray, UTZ WA
- FeNA > 1%, Una >10 mmol/L, SG = 1.01; ESR, CRP, LDH
- Hyperkalemia, Hyperphosphatemia, Hypocalcemia, Hyperuricemia, Met Acidosis
- **Biopsy**: casts are eosin positive, fractured, & waxy in apperance in LM
  - **IF:** light-chain restriction w/in the casts, although patterns may be mixed or nondiagnostic
  - **EM:** Casts have lattice-like appearance & may contain needle-shaped crystals

MANAGEMENT

- **Volume resuscitation (100 to 150 mL/hr of normal or half- normal saline)** to ensure optimum hemodynamic support & adequate UO **(≈3 L/day)** are of critical importance in the initial management
- **Loop diuretics** is **avoided** due to promotion of intratubular cast formation
- **Urinary alkalinization** not recommended

A. Chemotherapy & Stem Cell Transplantation

- Key to treating myeloma cast nephropathy is rapid reduction in FLC concentrations
- **Dexamethasone, thalidomide**, & the proteasome inhibitor **bortezomib** rapidly lower FLC concentrations **("renoprotective chemotherapy")**

B. Extracorporeal Removal of Free Light Chains

1. **High-Cutoff Hemodialysis**
   - Not known whether it offers any additional benefit over current chemotherapeutic regimens

- **Supportive**:
  - Hyperkalemia (>5.5) – Calcium gluconate 10ml of 10% solution x 5 mins; D50/50+ 10 units insulin; Albuterol 10-20mg by nebulizer, K+binding resin; restric K diet
  - Met acidosis – restric dietary protein, Sodium bicarb only if Hco3 <15 or pH <7.15
  - Hyperphosphatemia- restric dietary phosphate, phosphate binders
  - Hypocalcemia- Oral/IV replacement
  - Hyperuricemia- Allopurinol 300mg
  - Nutrition: Caloric intake: 20-30 kcal/day; Protein intake: NonHD (0.8-1 g/kg/d); HD (1-1.5 g/kg/d); CRRT (upto 1.7 g/kg/day)
  - Enteral route; Dose adjustments of medications

LEPTOSPIROSIS

SIGNS & SYMPTOMS

- Fever, Conjunctival Suffusion, Muscle Aches History of Wading In Flood Waters
  +/- Icterisia, Jaundice
-
- May span from sterile pyuria , tea colored urine, mild proteinuria to severe anuric acute renal failure.
- Commonly it may present as non- oliguric renal failure with mild hypokalemia.
- Oliguria with hyperkalemia may reflect the severity of AKI and may connote poor prognosis.
- The underlying pathology in renal leptospirosis is a combination of acute tubular damage and tubule-interstitial nephritis.
- The presence of tubular dysfunction usually predisposes the patient to hypokalemia and polyuria.

DIFFERENTIAL DIAGNOSIS:

- Prerenal azothemia (hypovolemia, NSAIDS etc) - Rhabdomyolysis - Hemolysis - Infection (Pneumonia, UTI)	- Glomerulonephritis (RPGN) - Acute Decompensated Heart Failure - Vascular (Renal artery thrombosis, atheroembolism, renal vein thrombosis)

DIAGNOSIS:

- CBC, PT, PTT, LAT igG & IgM; MAT
- Creatinine,BUN, Na, K, icalcium, uric acid, phosphorus, mg, chloride, albumin,
- Urinalysis (pyuria, casts, hematuria)
- Elevated Liver function test (Ammonia, SGPT, TB, DB, IB); lipase
- ABG, ESR, CRP, LDH, ECG, Chest xray (infiltrates/ARDS/pulmonary hemorrhage), UTZ WA,
- Neutrophilia, Thrombocytopenia, Hyponatremia, Hypokalemia

MANAGEMENT:

- Start Penicillin-G at 1.5million units IV every 6 hrs OR Ceftriaxone 1gram IV OD x 7 days

Hydration		
HYPERVOLEMIC	**EUVOLEMIC**	**HYPERVOLEMIC**
▪ **MAP ≤ 65** • Balanced soln/Nss 20ml/kg or 500ml over 15 mins • Non responsive: Norepinephrin ▪ **MAP > 65** • Balanced soln/Nss 20ml/kh or 500ml over 1hr	▪ **Crea < 3** • Hydration 25-30 ml/kg/day ▪ **Crea >3** • Dialysis	▪ **Crea >3** • Dialysis ▪ **Crea <3** • IV furosemide 1mg/kg → no response → Dialysis

INDICATIONS FOR RRT/DIALYSIS
Any ONE of the following: • Uremic symptoms- nausea, vomiting, altered mental status, seizure, coma • pH <7.2 • Fluid overload • Oliguria despite adequate hydration (GRADE: high- *KDIGO AKI*) • Serum crea >3 mg/dl • Serum K >5 meq in an oliguric patient • ARDS, pulmonary hemorrhage (GRADE: moderate)
INDICATIONS FOR PULSE THERAPY
• Why pulse? There is increasing evidence for an immunologic mechanism mediating renal failure and pulmonary hemorrhagic complications in leptospirosis via an exaggerated host immune response • Administration of **methylprednisolone 500 mg IV for 3 days** • **Cyclophosphamide 1gm** on the 3rd dose of MPPT or episode of hemoptysis

Acute Kidney Injury PLUS Any **ONE** of the following:

- Platelet count <100,000*
- Mean arterial pressure (MAP) <65
- Requires inotropes
- Lung infiltrates on chest xray*
- Prolonged PT and PTT

A.Recommended post-exposure prophylaxis for Leptospirosis for adults

- **LOW-RISK EXPOSURE** (single history of wading in flood or contaminated water without wounds, cuts or open lesions of the skin)
  - **Doxycycline 200 mg single dose within 24 to 72 hours from exposure**
- **MODERATE-RISK EXPOSURE** (single history of wading in flood or contaminated water & presence of wounds, cuts, or open lesions of the skin, OR accidental ingestion of contaminated water)
  - **Doxycycline 200 mg once daily for 3-5 days to be started immediately within 24 to 72 hours from exposure**
- **HIGH-RISK EXPOSURE** (continuous exposure [those having more than a single exposure or several days such as those residing in flooded areas, rescuers and relief workers] of wading in flood or contaminated water with or without wounds, cuts or open lesions of the skin)
  - **Doxycycline 200 mg once weekly until the end of exposure**

COVID 19

SIGNS & SYMPTOMS

- History of exposure to a known COVID patient, or place with known transmission
- Symptoms: Fever, Cough, shortness of breath, fatigue, anosmia, loss of taste (ageusia)

DIFFERENTIAL DIAGNOSIS

- Pneumonia - UTI - Leptospirosis	- Glomerulonephritis (RPGN) - PTB

DIAGNOSIS

- Complete Blood Count (CBC)
- Metabolic panel: creatinine, LFTs, sodium, potassium, magnesium,calcium, albumin
- Inflammatory markers: LDH, CRP, and procalcitonin, ferritin, Prothrombin and D-Dimer
- ABG, Blood cultures if concomitant bacterial infection is suspected
- Respiratory tract specimen for influenza testing
- Sputum, endotracheal aspirate (ETA), or bronchoalveolar lavage fluid culture and sensitivity
- Chest x-ray, High resolution chest CT scan plain; ECG
- RT-PCR swabtest

MANAGEMENT

- Antiviral agent
  - **Remdesivir** for hospitalized patients w/ severe COVID-19
    - Dosing: 200mg IV loading on D1 followed by 100mg IV for 5-10 days
  - **Favipiravir** for OPD
    - Dosing: 1,800mg 2x/day loading dose then 800mg 2x/day for 13 days
- Immunomodulator
  - **Tocilizumab & other IL-6 inhibitor**
- **Convalescent Plasma (CP)**
- **Hemoperfusion**
- Supportive mgt
  - Supplemental O2 (for severe pneumonia, hypoxemia, & target O2 >92%)
  - Conservative fluid mgt
  - Empiric antimicrobrials
  - Dexamethasone 6mg/day x 10 days (for o2 requiring patients)