The Newcastle Upon Tyne Hospitals NHS Foundation Trust

Renal Diagnoses for the Critical Care Team

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Introduction

- Poisoning
- Pigment Nephropathy
  - Rhabdomylosis
- Nephrotic Syndrome
- Nephritic Syndrome
  - Endocarditis

Not going to talk about:

Systemic conditions eg Vasculitis – Dr Baines Talk


POISON

Poisoning

Some of the big players

- Alcohols
- Theophylline
- Lithium
- Salicylates.

HD is most useful in removing toxins with the following characteristics:

- Low molecular weight (<500 daltons)
- Small volume of distribution
- Low degree of protein-binding
- High water solubility
- Low endogenous clearance
- High dialysis clearance relative to total body clearance.

Presentation - A&E

- GCS 6
- Vomitus on clothing ? Aspirated
- Hypothermic
- ABG (pH 6.9, Lactate 24)
- Intubated and taken for CT
- Transferred to ITU

Investigations

- ABG
- Imaging
- Bloods
- Urine
- Observations

Observations
BP 170/128
UO 50mls hr
100% in 15L
Apyrexial,
HR 120

ABG
PH 6.98
pCO2 3.66
pO2 59.0
Sats99%
Bic 8.3
Cl124
K 4.6
Na 145
BE 25.5
Lact 22

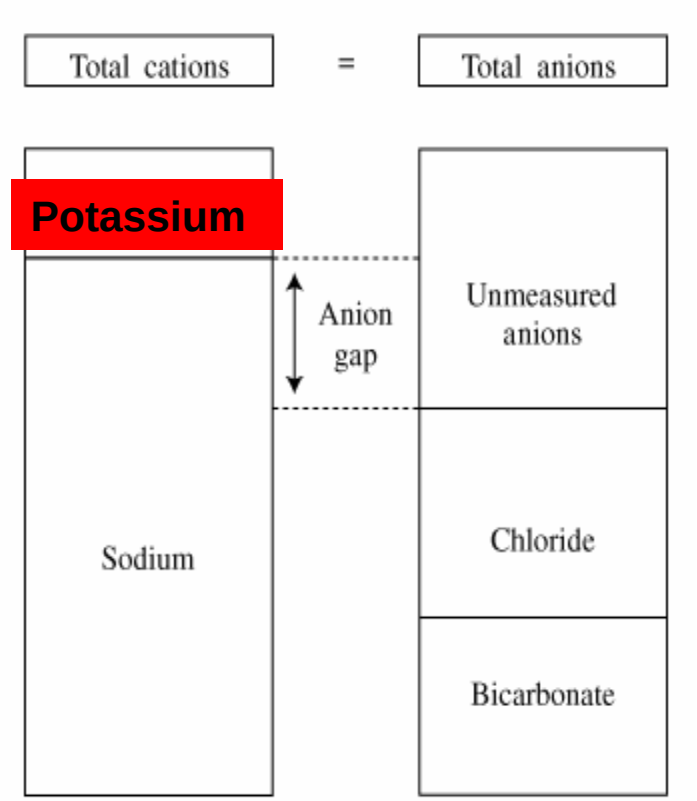
Urine

Unknown – nobody dipped it

Sodium 145 mmol/L
Potassium 4.9 mmol/L
Bicarbonate <10 mmol/L
Chloride 124
Urea 2.4 mmol/L
Creat 46 mmol/L
HB 125g/L
WCC 13.6 x109 (neutro)
PT 15.3
LFTs Normal
Calcium 2.43mmol/L
Amylase 74 mmol/L
Plasma ethanol <100mg/L
Glucose 10.7mmol/L
Serum osmolity 323mOsmol/Kg
CK 194

The Anion Gap

- Reference range is 8 to 16 mmol
- If the AG is greater than 30 mmol/l, than it invariably means that a metabolic acidosis is present.



AG = ([Na+] + [K+]) – ([Cl-] - [HCO3-])

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'Growing problem' of illegally distilled alcohol

Police are investigating whether an industrial unit where five men were killed in an explosion was being used to distil alcohol illegally.

Lincolnshire Police said chemicals found inside the "smoke-logged" unit at Broadfield Lane Industrial Estate in Boston indicated alcohol was being produced illegally.

But Supt Keith Owen, who said it was probably some sort of spirit, stressed investigations were

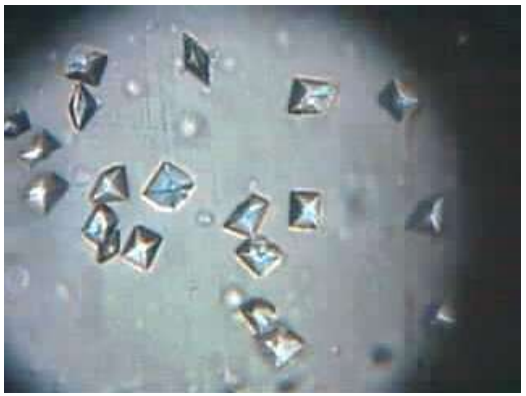
The sale of counterfeit alcohol is estimated to cost the UK £1bn a year in lost revenue

Anion Gap

- High Anion Gap metabolic Acidosis
- Due to generation of metabolites
  - Oxylate
  - Glycolate
  - Glyoxylate

  - More toxic than parent compound
  - Favours the production of lactate from pyruvate

Pathophysiology



Fast

Ethylene glycol

Alcohol dehydrogenase

Glycoaldehyde

Aldehyde dehydrogenase

Anion Gap metabolic acidosis

Glycolic acid

Lactate dehydrogenase and glycolic acid oxidase

Glyoxylic acid

Pyridoxine

Thiamine

Glycine

Oxalate acid

Formic acid

α – hydroxy – β - ketoadipate

Clinical Presentations

Ethylene glycol toxicity is divided into **3 distinct phases**:

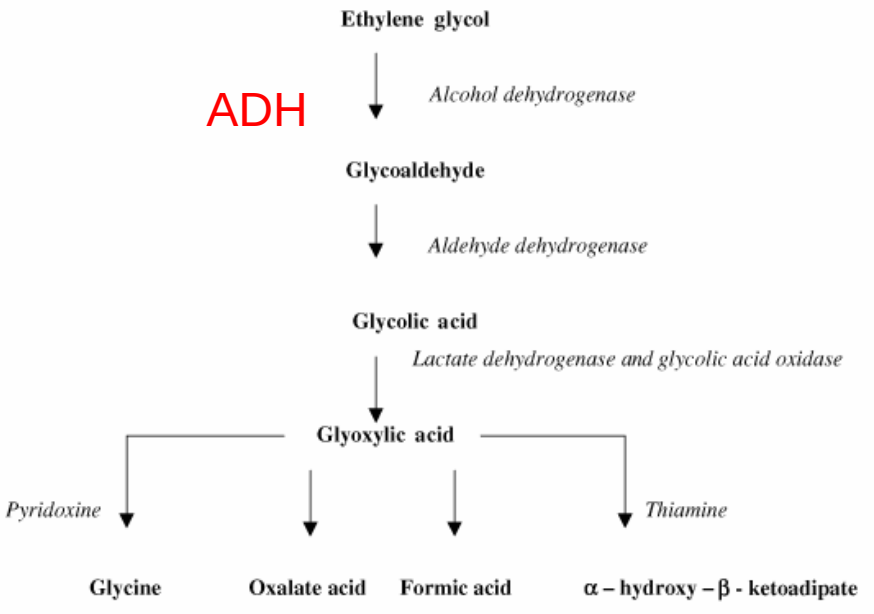
Phase 1 (Minutes – 12 hours): CNS toxicity predominates with inebriation (without odor of ethanol on the breath), coma, nystagmus, paralysis, and seizures. Nausea, vomiting, and papilledema may also occur. An elevated serum osmolarity is seen early in this phase.

- Phase 2 (12-24 hours): Cardiopulmonary symptoms predominate with mild tachycardia and hypertension. Other effects include anion gap metabolic acidosis (possibly severe) with compensatory hyperventilation, hypoxia, CHF, and ARDS.

- Phase 3 (>24 hours): This renal phase is characterized by acute tubular necrosis and renal failure. Oliguria, anuria, haematuria, and proteinuria are common.

The 4 major goals in the treatment of ethylene glycol and methanol poisonings are as follows:

1. **Inhibition (ADH) prevent toxic metabolite formation,**
2. **Correction of the acidosis with bicarbonate,**
3. **Use of specific enzymatic cofactors such as folate, thiamine and pyridoxine to modify deleterious metabolic pathways**
4. **Removal of the toxin and metabolites by haemodialysis.**



Treatment

- Fomepizole is competitive inhibitor of alcohol dehydrogenase

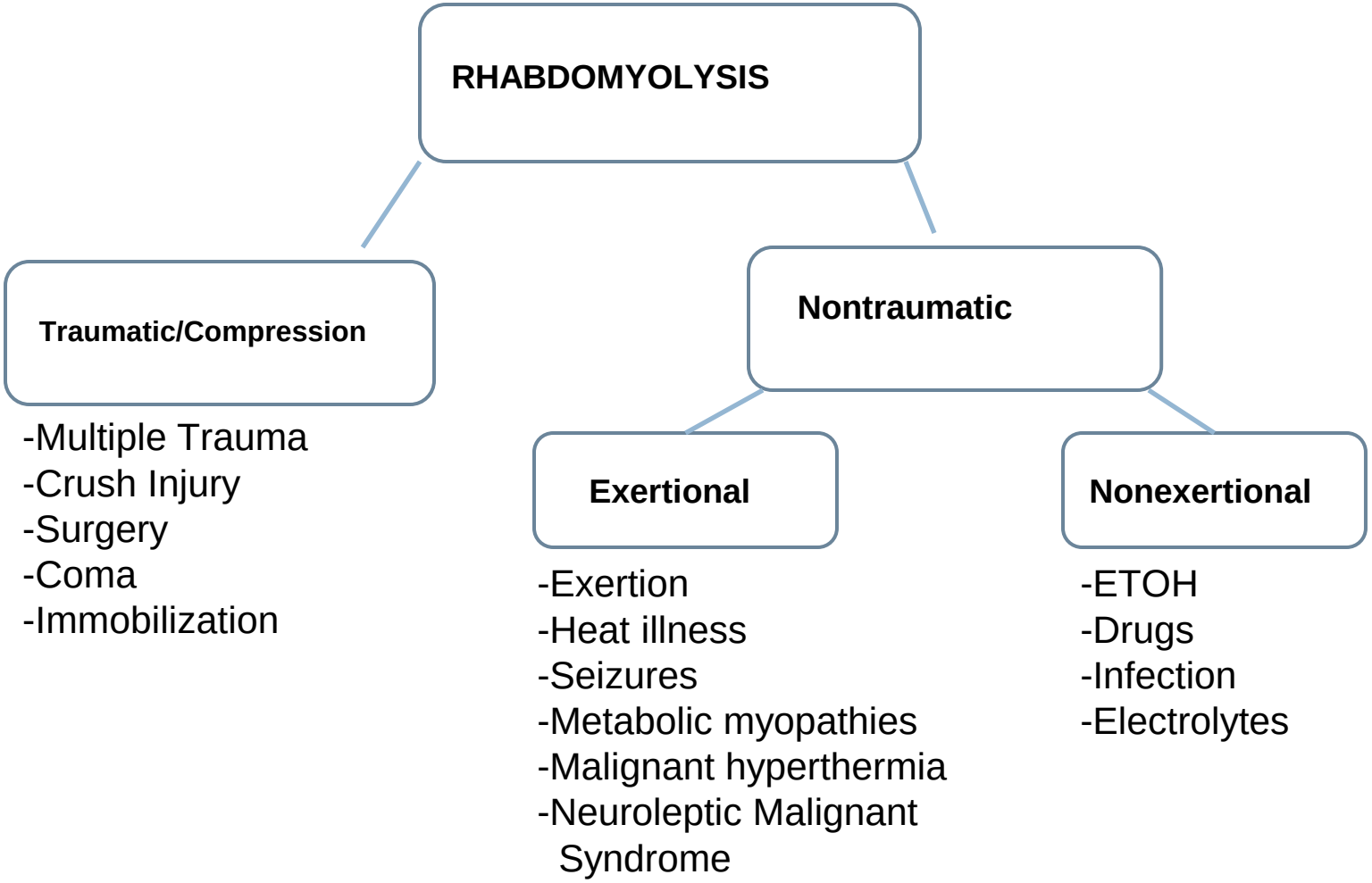
Fomepizole

- Treat both methanol and ethylene glycol poisoning.
- Fomepizole is easy to dose, easy to administer, and side effects are rare.
- Main disadvantage is its high cost.

rhabdomyolysis

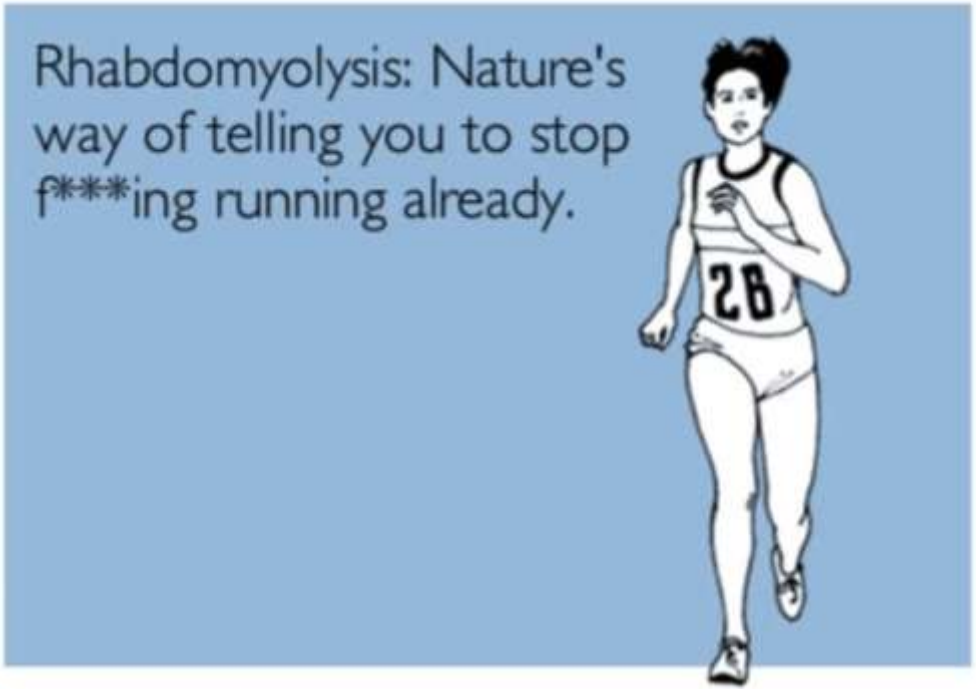
Rhabdomyolysis is a syndrome characterised by muscle necrosis and the release of intracellular muscle constituents into the circulation

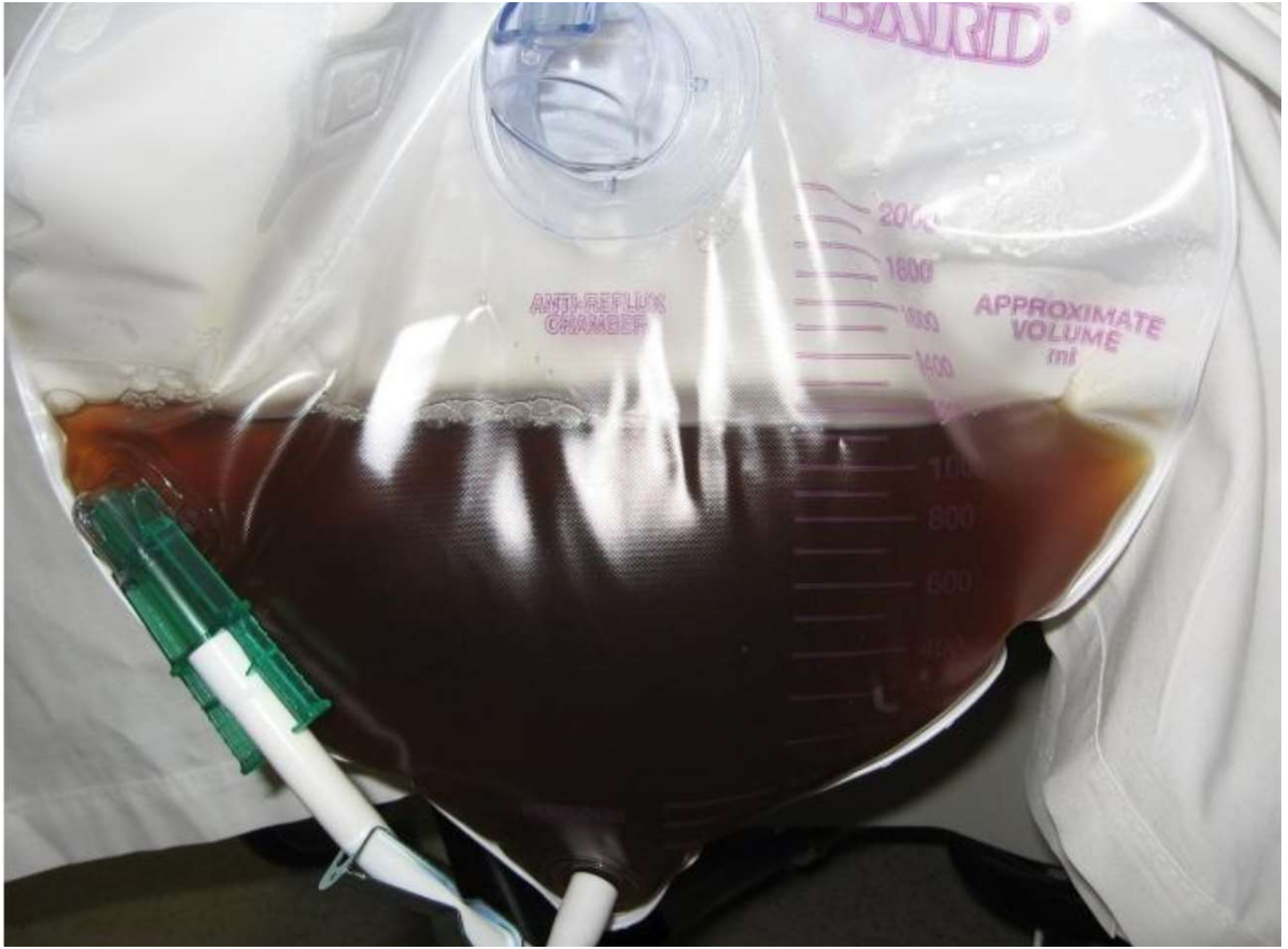
Causes (Muscle Breakdown)



Symptoms

- The characteristic triad of complaints in rhabdomyolysis is muscle pain, weakness, and dark urine .




BAIRD
ANTI-REFLUX CHAMBER
APPROXIMATE VOLUME
ml
1800
1400
1000
800
600

Creatine Kinase

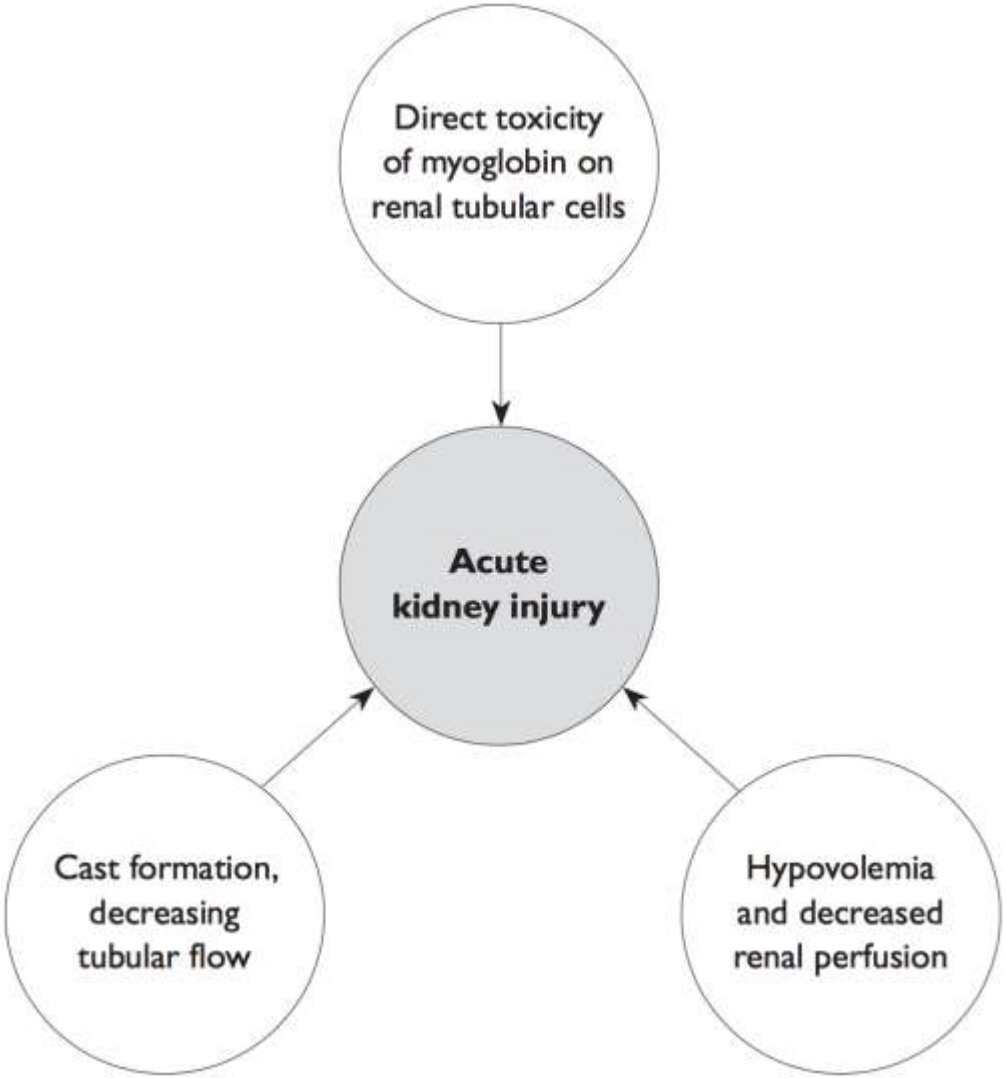
- The serum CK begins to rise within 2 to 12 hours following the onset of muscle injury and reaches its maximum within 24 to 72 hours.
- CK falls - three to five days of cessation of muscle injury.
- CK has a serum half-life of about 1.5 days and declines at constant (40 to 50% /day).
- In patients whose CK does not decline as expected, think compartment syndrome.

Breakdown of skeletal muscle

Include enzymes such as

- Creatine kinase (CK)
- Glutamic oxalacetic transaminase
- Lactate dehydrogenase
- Aldolase
- Myoglobin
- Electrolytes such as potassium and phosphates
- Purines.

Rhabdomylosis



Complications

- Acute Kidney Injury
- Disseminated intravascular coagulation
- Electrolyte and metabolic derangements
  - Hypoalbuminemia
  - Hypocalcemia
  - Hyperkalemia
  - Hypernatremia
  - Hyperphosphatemia
  - Hyperuricemia
- Cardiac dysrhythmias
- Compartment syndromes
- Shock
- Death

Fluid and electrolyte abnormalities

- Hypovolemia results from “third-spacing” due to the influx of extracellular fluid into injured muscles and increased risk AKI.
- Hyperkalemia and hyperphosphatemia from the damaged muscle cells.
- Levels of potassium may increase rapidly.

Hypocalcemia

- Can be extreme, occurs in the first few days
- Entry into damaged myocytes
- Deposition of calcium salts in damaged muscle and decreased bone responsiveness to parathyroid hormone.

Bicarbonate

Bicarbonate: Forced alkaline diuresis

- Urine pH is raised to above 6.5, may diminish the renal toxicity of haem.
- Decrease the release of free iron from myoglobin
- Decrease formation of vasoconstricting F2-isoprostanes
- Reduce the risk for tubular precipitation of uric acid
- Prevents haem-protein precipitation with Tamm-Horsfall protein, and therefore intratubular pigment cast formation.
- **No clear clinical evidence that an alkaline diuresis is more effective than a saline diuresis in preventing AKI**

Mannitol, Dialysis

Mannitol: Forced diuresis

- May minimize intratubular heme pigment deposition and cast formation, and/or by acting as a free radical scavenger, thereby minimizing cell injury[6,7].
- Net clinical benefit of remains uncertain, and, therefore, not routinely administered.

Dialysis

- Supportive
- AKI

Treatment

- The kidney is the best filter at removing myoglobin.
- No preventive kidney replacement therapy.
- However, the kidneys need a perfusion pressure and fluid volume to help them eliminate the toxin.

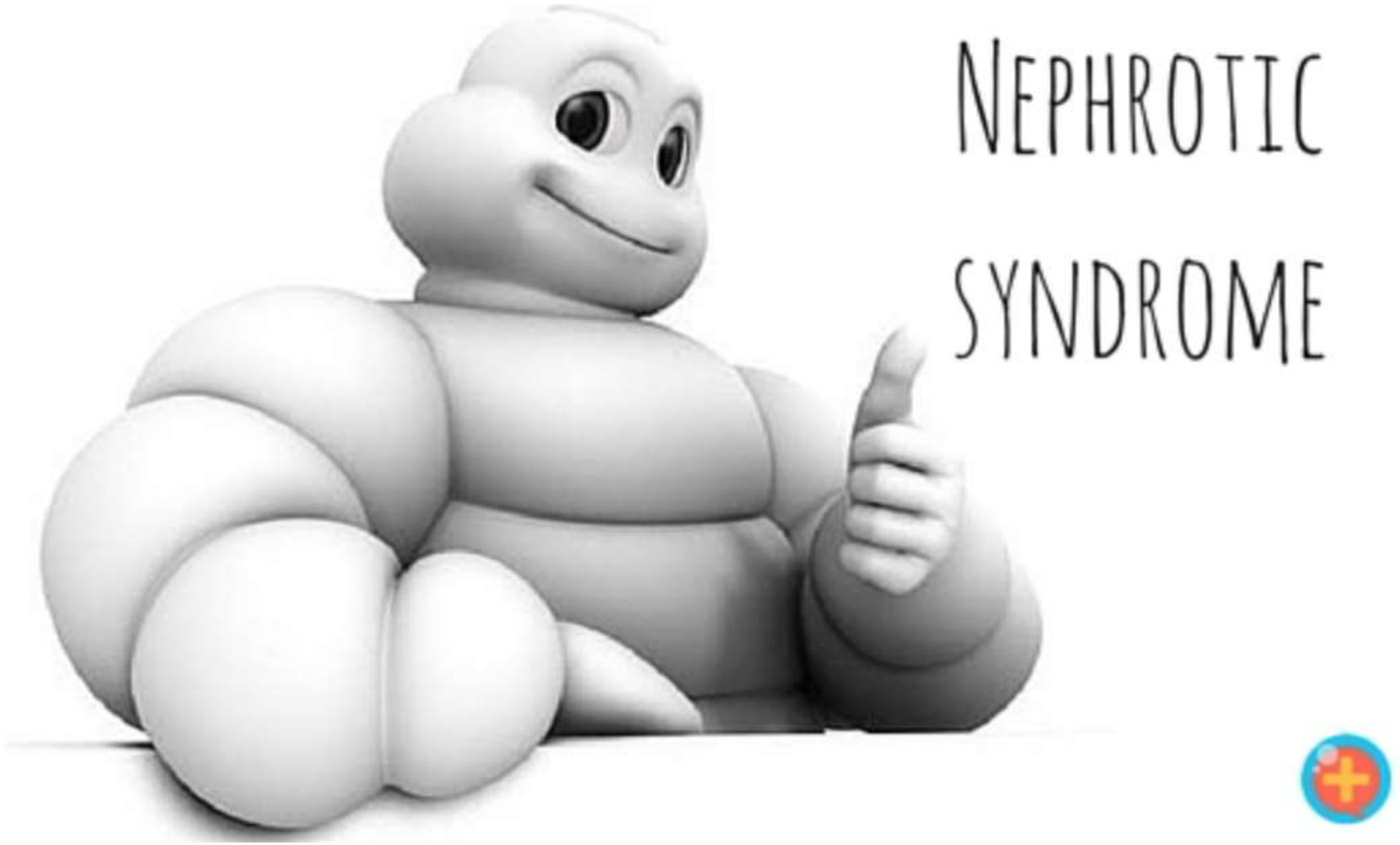
If you Need RRT - what to use?

- Intermittent HD
- Continuous therapies
- Plasma exchange

What to choose.

Classification	Molecular weight range
Small molecules e.g. **urea** (60), **creatinine** (113), phosphate (134)	**< 500**
Middle molecules e.g. **vitamin B_{12}** (1355), **vancomycin** (1448), **inulin** *5200, endotoxin fragments (1000-15,000) parathormone (9425), **ß2-m** (11,818)	**500 – 15,000**
Large molecules e.g. myoglobulin (17,000), RBP (21,000), α 1-m (26,700), EPO (30,000), **albumin** (66,000), transferrin (90,000)	**> 15,000**

Nephrotic Syndrome



What is nephrotic syndrome?

- Increased permeability of the glomerulus leading to loss of proteins into the tubules.

Nephrotic Syndrome

- Triad of:
  - **Proteinuria >3g/24hours**
    - Or spot urine protein : creatinine ratio >300-350mg/mmol
  - **Hypoalbuminaema <25g/L**
  - **Oedema**

- And often:
  - Hypercholesterolaemia/dyslipidaemia (total cholesterol >10mmol/L)

Further possible presentations...

- Oedema
- BP normal/raised
- Leukonychia
- Breathlessness:
  - Pleural effusion, fluid overload, AKI
- DVT/PE/MI
- Eruptive xanthomata/ xanthalosmata

Investigations

- Urine dipstick and send to lab (uPCR)
- Bloods – the usual ones, plus renal screen
  - Immunoglobulins, electrophoresis (myeloma screen), complement (C3, C4), Glucose.
- Renal ultrasound
- Renal biopsy

Complications

- Increased susceptibility to infection
  - 20% adult cases
  - Due to reduced serum IgG, reduced complement activity, reduced T cell function
  - Bacterial
- Thromboembolism
  - Partly due to increased clotting factors and platelet abnormalities
  - Intravascular volume depletion; the use of diuretics; immobilisation; and procoagulant diatheses (protein C and protein S deficiencies, or antiphospholipid antibodies)
- Hyperlipidaemia
  - due to hepatic lipoprotein synthesis to restore osmotic pressure

Management

- **Conservative**
  - Monitor U&E, BP, fluid balance, weight
  - Salt and fluid restriction
  - Treat underlying cause
- **Medical**
  - **Diuretics**
  - Treat hypertension
  - **Corticosteroids/immunosuppression**
  - Dialysis

Check the urine for blood and protein

Nephrotic Syndrome

Primary causes

- Minimal change Glomerulonephritis
- Focal Segmental Glomerulosclerosis
- Membranous Glomerulonephritis.

Secondary causes

- SLE
- Hep B & C
- HIV
- **Diabetes Mellitus**
- Malignancy
- & lots of others

Nephritic Syndrome

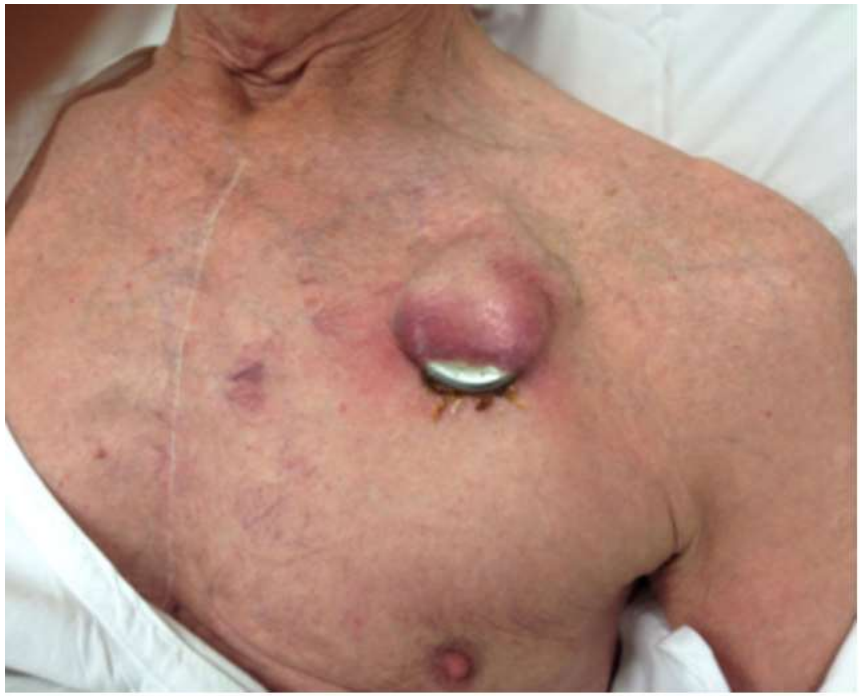
- Post streptococcal Glomerulonephritis – appears weeks after URTI
- IgA Nephropathy – appears within a day or two after URTI

Rapidly progressive Glomerulonephritis (crescentic glomerulonephritis)

- Goodpastures - anti GBM antibodies against basal membrane antigens
- Vaculitic disorder – Wegners granulomatosis, Microscopic Polyangitis, Churg Strauss disease
- Membranoproliferative Glomerulonephritis - primary or secondary to SLE, Hepatitis B/C etc
- Henoch-Schönlein purpura - systemic vasculitis – deposition of IgA in the skin & kidneys

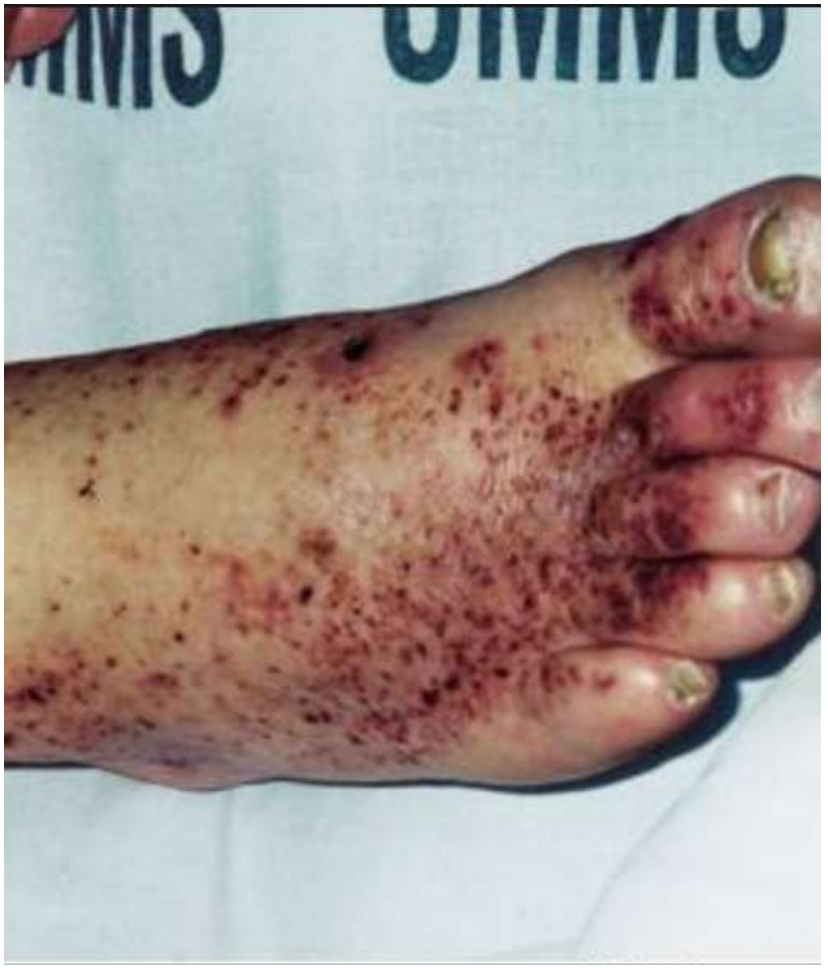
Infectious Causes

- Erroded pacemaker
- Pyrexial
- Hypotensive
- Rash
- Oedematous
- Oligoanuric



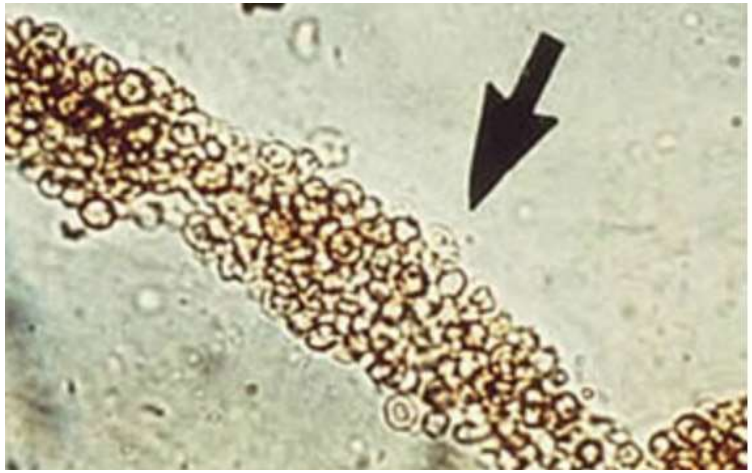
Rash

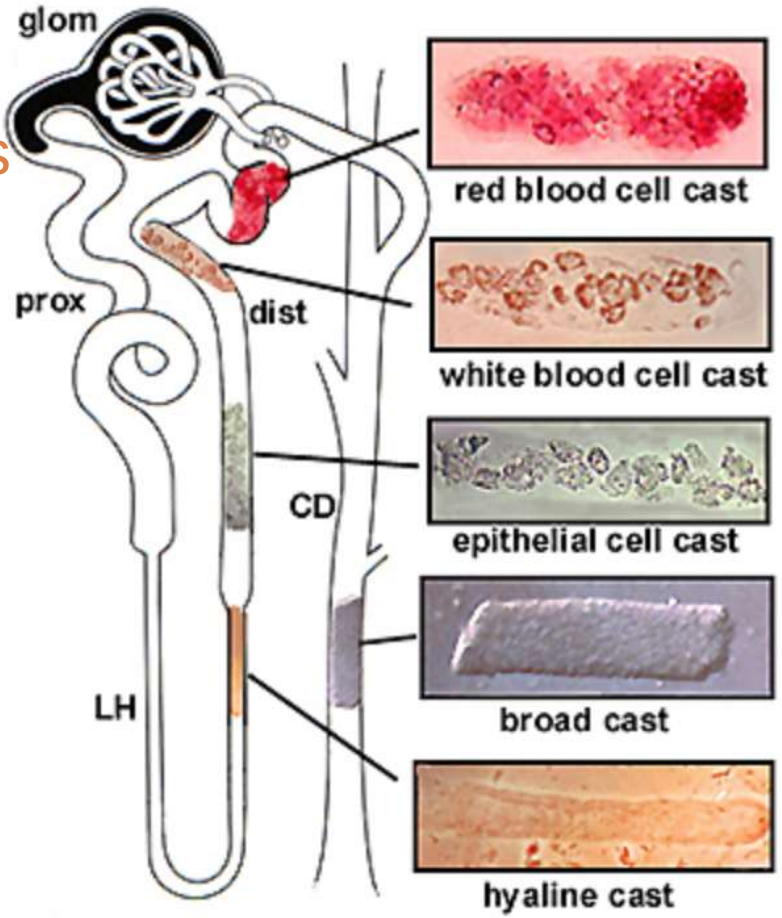
- S Aureus in Blood culture
- Permanent pacemaker removed
- Temporary inserted.
- Worsening renal function.
- Rash on lower limbs



Red Cell Cast

- always pathological
- strongly indicative of glomerular damage,
  - ANCA vasculitis, systemic lupus erythematosus
  - Post-streptococcal glomerulonephritis
  - Goodpasture's syndrome





Complement

Low complement GN:

- Systemic: *SLE, endocarditis, cryoglobulinemia, shunt nephritis*
- Isolated renal: *post-infectious GN, MPGN*

Normal complement GN:

- Systemic: *HSP, ANCA-associted (Wegener's, PAN), Goodpasture's syndrome,*
- Isolated renal: *IgA nephropathy, anti-GBM disease, RPGN*

Bacterial infection-related immune complex-mediated glomerulonephritis

- A variety of organisms may be involved in patients developing glomerulonephritis.
  - Staphylococcus aureus in acute infective endocarditis (IE)
  - Streptococcus viridans in subacute IE
  - Staphylococcus epidermidis in shunt nephritis.

- The plasma C3 & C4 levels are typically reduced

Treatment

- Supportive
- Treat underlying cause
- Try to avoid other renal insults
  - Drug-induced acute interstitial nephritis as a result of antibiotic therapy
  - Acute kidney injury (due to acute tubular necrosis)
  - Thromboembolic disease

Q&A

Any questions