Interpretation of Urea & Electrolytes

Urea and Creatinine

Physiology

Creatinine
- Creatine, a substance produced in the liver, is an energy store for fast twitch muscle fibres
- Creatine is phosphorylated to make creatine phosphate
- Creatine phosphate can then be broken down to produce ATP (for energy) and creatinine (waste product)
- Creatinine is then transported to the kidneys where it is excreted
- Creatinine blood concentration is specific for determining kidney injury (but baseline depends on muscle mass)

Urea
- The urea cycle converts ammonia (toxic product of deamination reactions of amino acids) to urea in the liver
- Urea is then transported to the kidneys where it is excreted
- Urea blood concentration is not specific for determining kidney injury; other causes:
  - ↑urea = dehydration, GI bleed, increased protein breakdown (surgery, trauma, infection, malignancy), high protein intake, drugs
  - ↓urea = malnutrition, liver disease, pregnancy

Acute kidney injury

Acute kidney injury (AKI) = rise in serum creatinine >50% from baseline, or urine output <0.5ml/kg/h for 6 hours
Determine if it is pre-renal, renal or post-renal

All patients need:
- Urine dipstick (interpreted in context of history)
- Bloods (including FBC ± haematinsics, U&E, CRP, Ca²⁺, PO₄³⁻, PTH)
- VBG (check for: metabolic acidosis & low bicarbonate – may need weak bicarbonate infusion; and hyperkalaemia)
- Accurate fluid balance chart (requires catheterisation)
- Stopping of any renal-excreted drugs (see drugs & RF)

Pre-renal renal failure (70%)
- Causes: hypovolaemia/sepsis (most common AKI cause), renovascular disease
- Suggested by: history, hypotension, ↑urea > ↑creatinine
- Investigation:
  - Fluid volume assessment
  - Renal artery Doppler (if suspect renovascular disease)
- Treatment: IV fluid resuscitation
- Complications: acute tubular necrosis (ATN)

Intrinsic renal failure (20%)
- Causes: ATN (ischaemic or nephrotoxic), acute interstitial nephritis, acute glomerulonephritis
- Suggested by: causative drugs, renal hypoperfusion, other glomerulonephritis symptoms, haematuria & proteinuria
- Investigation:
  - Urine dipstick
    - blood +++ protein +++ in glomerulonephritis
    - in ATN, urine is usually bland
  - Urine protein-creatinine ratio (PCR; to quantify & monitor proteinuria if dipstick protein +ve; <15mg/mmol = normal; >300mg/mmol = nephrotic)
  - NB. Urine PCR (mg/mmol) X 10 = 24h protein loss (mg)
  - Possible further tests
    - Nephritic screen (if suspect glomerulonephritis): ANA, ANCA, anti-GBM, complement, RhF, hepatitis serology, anti-phospholipid Ab
    - Renal biopsy (if: unexplained AKI; glomerulonephritis suspected; positive nephritic screen; persistent ATN; suspected tubule-interstitial nephritis)
    - Urgent renal biopsy (if suspect rapidly progressive glomerulonephritis – suggested by rapid loss of kidney function & worsening severe proteinuria and haematuria & nephritic syndrome)
    - Myeloma screen (if old)
    - Creatinine kinase (if suspect rhabdomyolysis)
    - Serum bicarbonate
- Treatment:
  - Treat cause (e.g. hypoperfusion) + sodium bicarbonate (protects kidney) in ATN
  - Stop causative agent for acute interstitial nephritis
  - Immunosuppressants for glomerulonephritis
- Complications: irreversible renal damage

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Post-renal renal failure (10%)

- Causes: urinary tract obstruction (prostate, stones, structure, tumour, blood clot etc)
- Suggested by: history, ↑ urea = ↑ creatinine
- Investigate:
  - Renal tract USS
- Treatment: relieve obstruction e.g. catheterise (urinary/suprapubic) if urethral or nephrostomy if ureteric
- Complications: pyelonephritis (can progress to irreversible renal damage)

**Chronic kidney disease**

Chronic kidney disease = presence of marker of kidney damage (e.g. proteinuria) or decreased GFR for > 3 months

**Commonest causes**

1. Diabetes (secondary glomerular disease)
2. Chronic hypertension
3. Chronic glomerulonephritis diseases (e.g. vasculitides)
4. Others e.g. PKD, drugs

**Determining cause**

- History
- Urine dipstick
- Renal USS
- Renal biopsy if required

**Management**

- Manage cause
- General measures: fluid restriction, reduce protein intake, ACE-inhibitor
- Treat complications: hypertension, oedema, anaemia, renal bone disease, hyperkalaemia, hyperlipidaemia
- Dialysis (when GFR <15)

**When to refer**

- ITU: refractory hyperkalaemia, refractory metabolic acidosis, pulmonary oedema, worsening uraemia
- Nephrologist: AKI ?cause, AKI grade 3/4, suspected glomerulonephritis, not improving, CKD grade 4/5, previous renal transplant
- Urologist: urinary tract obstruction

**When to dialyse**

Mnemonic: **AEIOU**

Intractable...

- Acidosis
- Electrolyte abnormalities (hyperkalaemia, hyponatraemia, hypercalcaemia)
- Intoxicants (methanol, lithium, salicilism)
- Overload
- Uraemia

$pH<7.1$

$K^+>6.5$ or ECG changes

Acute pulmonary oedema

$\text{urea}>60$ or pericarditis or uraemic sync

In chronic renal failure, regular dialysis is required when the GFR is <15ml/minute
**Sodium**

**Physiology**
- Extracellular ion
- \( H_2O \) follows solutes due to osmosis (e.g. \( Na^+ \), albumin)
- Aldosterone increases \( Na^+ \) reabsorption (& \( K^+ \) excretion) from the DCT
- ADH causes reabsorption of \( H_2O \) (alone) from the collecting duct

**Hyponatraemia**

**Causes**

- **HYPOVOLEMIC (\( Na^+ \) LOST)**
  - \( URINARY Na^+ \) >30 (FROM KIDNEYS)
  - Diuretics
  - Addison’s disease (\( K^+ \))
  - Kidney injury
  - Osmotic diuresis

- **EUVOLEMIC (\( H_2O \) GAINED)**
  - \( URINARY Na^+ \) <30 (FROM ELSEWHERE)
  - \( SIADH^* \)
  - Hypothyroidism
  - Glucocorticoid insufficiency

- **OEDEMATOUS**
  - \( LOW Na^+ \) CAUSED BY EXCESS ADH RELEASED SECONDARY TO INTRAVASCULAR FLUID DEPLETION (DUE TO EXTRAVASATION)
  - Congestive cardiac failure
  - Hypoalbuminaemia (i.e. cirrhosis or nephrotic syn)

*SIADH causes include: drugs (anti-depressants, ciprofloxacin, cyclophosphamide, carbamazepine, ecstasy), infection (abscesses, pneumonia, meningitis), neurological (brain haematomas, encephalitis, Guillain-Barre, hydrocephalus), para-neoplastic (esp SCLC)

**Investigation**

- Plasma osmolality (to confirm if true hyponatraemia)
  - Low = true
  - Normal = false (‘pseudohyponatraemia’ due to high lipids, or high glycine post-op)
  - High = dilutional (due to high glucose e.g. HHS, alcohols or mannitol)
- Urinary sodium and osmolality (to confirm if the problem is occurring in the kidneys or elsewhere)
- Specific tests to confirm specific causes e.g.
  - Addison’s disease: Synacthen (synthetic ACTH) test or 9am cortisol screening test
  - SIADH: confirmed by combination of low plasma osmolality (<275) and high urine osmolality (>100); investigate cause
  - Hypothyroidism: TFTs

**Management**

- Treat cause
- Sodium correction
  - Seizures/coma: senior could give 3% hypertonic saline (e.g. 150ml over 15mins, repeated if necessary)
  - Hypovolaemic: replace lost fluid with 0.9% saline
  - Euvolaemic: correct cause: slow 0.9% saline IV, e.g. 1L/8-10hours
  - If SIADH or oedematous: fluid restrict to 1 litre/day (excess \( H_2O \) causes dilutional hyponatraemia) and consider demeclocycline for fluid restriction-resistant SIADH

**NB. correct chronic hyponatraemia slowly (risk of osmotic demyelination)**

**Hyponatraemia**

**Causes**

- **Normovolaemia** = iatrogenic (e.g. excess IV crystalloids, sodium containing drugs)
- **Hypovolaemia**
  - Producing small volumes of concentrated urine (normal response to hypovolaemia)
    - Fluid loss (i.e. diarrhoea/vomiting, burns)
  - Not producing small volumes of concentrated urine (abnormal response to hypovolaemia)
    - Diabetes insipidus (urine osmolality <750 + serum osmolality >300) (i.e. kidneys not reabsorbing any \( H_2O \))
    - Osmotic diuresis (e.g. DKA) (kidneys loosing \( H_2O \) and solutes)

**Investigation**

- Urine & serum osmolality
- Fluid deprivation test to confirm diabetes insipidus

**Management**

- Treat cause
- Sodium correction
  - Hypovolaemic (high sodium usually due to fluid loss): 0.9% saline 1L/6hours to correct hypovolaemia
  - Euvolaemic: 5% dextrose 1L/6hours

**NB. correct chronic hyponatraemia slowly (risk of osmotic demyelination)**
**Potassium**

**Physiology**
- 90% intracellular
- H+ and K+ concentrations vary together because both compete for Na+ symporter in cells and DCT
- Insulin and catecholamines increase cellular K+ uptake (by stimulating cellular Na+(in)/K+(out) pumps)
- Aldosterone increases Na+(in)/K+(out) pumps in distal convoluted tubule and therefore increases K+ excretion

**Hypokalaemia**

**Causes**
- Increased renal excretion
  - Diuretics (except potassium sparring)
  - Endocrinological (steroids, Cushing’s disease, Conn’s syndrome)
  - Renal tubular acidosis
  - Hypomagnesaemia
- Other K+ loss
  - Intestinal fluid loss (vomiting/diarrhoea)
- Increased cellular uptake
  - Salbutamol
  - Insulin
  - Alkalosis

**Management**
- >2.5mmol/L: Sando-K 2 tablets TDS x 3/7, or add 20-40mmol/L potassium chloride to IV fluids
- <2.5mmol/L: 40mmol/L potassium chloride in 1L 0.9% saline over 6 hours *(NEVER give >10mmol/h K+ outside ICU)*
- Treat cause

**Hyperkalaemia**

**Causes**
- Reduced renal excretion
  - Acute/chronic kidney injury
  - Drugs (potassium-sparring diuretics, ACE-inhibitors, NSAIDs)
  - Addison’s disease
- Excess K+ load
  - Iatrogenic
  - Massive blood transfusion
- Increased cellular release
  - Acidosis
  - Tissue breakdown e.g. rhabdomyolysis, haemolysis

NB. may be due to pseudohyperkalaemia (haemolysis, EDTA-contaminated sample)

**Management**
- Acute management
  1. ECG and 3-lead cardiac monitoring
     - Changes: low flat P waves, wide bizarre QRS, slurring into ST segment, tall tented T waves
  2. Calcium gluconate 10ml 10% IV over 5mins
     - Protects myocytes (required if ECG changes or K+ > 6.5mmol/l)
     - Works in minutes – check ECG resolved; if not, repeat dose every 10 minutes up to 50ml
     - Lasts 30-60mins
  3. Actrapid insulin 10 units in 250ml 10% dextrose IV over 30mins
     - Temporarily shifts potassium into cells
     - Check capillary glucose before, during and after
     - Gradually decreases potassium
     - Lasts 60mins
     - Check K+ decreasing at 30mins and check overall result at 2 hours (dose can be repeated)
     - Nebulised salbutamol may be used in addition for same effect – lasts 2 hours
  4. Calcium resonium
     - Works slowly
     - Only treatment that actually removes potassium from body
     - May start with this if only moderate rise e.g. K+ < 5.9mmol/L
     - Give with regular lactulose (causes constipation)
- Consider haemodialysis if above fails (also consider sodium bicarbonate in severe acidosis)
- Treat cause
Calcium

Physiology

PTH should increase in response to hypocalcaemia. Always look at the corrected calcium value (adjusted for albumin).

Hypocalcaemia

Causes
- Increased renal excretion (↑PO₄³⁻, ↑PTH)
  - Drugs (loop diuretics)
  - Chronic kidney disease
  - Rhabdomyolysis/tumour lysis syndrome
- PTH-related (↑PO₄³⁻, ↓PTH)
  - Hypoparathyroidism
  - Hypomagnesaemia
  - Pseudohypoparathyrodism (resistance to PTH)
  - Cinacalcet
- Increased deposition/reduced uptake (↓PO₄³⁻, ↑PTH)
  - Bisphosphonates
  - Vitamin D deficiency

Investigation
- Initial tests
  - Renal function
  - PTH
  - Phosphate, magnesium

Management
- Severe (<1.9mmol/L or symptomatic): calcium gluconate 10ml 10% IV over 30mins – should be diluted: 1ml 10% calcium gluconate to 4ml normal saline or 5% dextrose – may be repeated until asymptomatic and can be followed by an infusion if required (100ml 10% calcium gluconate in 1L dextrose or saline at 50-100ml/h)
- Mild (>1.9mmol/L and asymptomatic): calcium supplements (e.g. sandocal or calceos) 1000mg BD
- Treat cause e.g. in severe vitamin D deficiency, load with 50,000 units colecalciferol once weekly for 8 weeks; in mild vitamin D deficiency, give 800 units once daily long-term, or, if calcium and vitamin D deficient, give Adcal-D3 long-term; in CKD-associated vitamin D deficiency, use alfalcacidol (1-α hydroxycalciferol) instead because the terminal hydroxylation required for vitamin D synthesis which occurs in the kidney is deficient

Hypercalcaemia

Causes
- Decreased renal excretion
  - Drugs (thiazide diuretics)
- Increased release from bones
  - Bony metastasis (↑ALP)
  - Myeloma (normal ALP)
  - Sarcoidosis
  - Thyrotoxicosis
- Excess PTH
  - Primary hyperparathyroidism (↑PTH) or tertiary hyperparathyroidism (↑↑PTH)
- Excess vitamin D
  - Excessive vitamin D intake

N.B. Dehydration (urea and albumin raised) is also a common cause

Investigation
- Initial tests: renal function, ALP, PTH, phosphate
- Myeloma screen/ Bence-Jones protein (If suspect myeloma)
- Serum ACE (If suspect sarcoidosis)
- Isotope bone scan (If suspect bony metastasis)

Management
- Treat cause
- Replace fluid deficit and keep patient very well hydrated (continuous 0.9% saline at 1L/4-6h)
- If severe (≥3.5mmol/L or symptomatic – a medical emergency): also bisphosphonate e.g. pamidronate 30-90mg IV depending on severity (one off dose)
**Magnesium**

**Hypomagnesemia**

**Causes**
- Excess loss
  - Diuretics
  - Severe diarrhoea
  - DKA
- Poor nutrition / alcoholism
- Most in bone and cells, therefore tends to reduce if calcium or potassium are low

**Management**
- PO: magnesium aspartate 1 sachet (10mmol) BD x 3/7
- IV: 5 grams (20mmol) magnesium in 500ml 0.9% saline over 5 hours
- Dealing with concurrent electrolyte abnormalities
  - Correct hypomagnesemia before concurrent hypokalaemia, hypophosphatemia and hypocalcaemia if possible
  - Do not give IV magnesium and IV phosphate at the same time (can precipitate as magnesium phosphate)

**Phosphate**

**Hypophosphatemia**

**Causes**
- Vitamin D deficiency
- Refeeding syndrome
- Primary hyperparathyroidism
- Poor nutrition / alcoholism

**Management**
- PO: phosphate-sandoz 2 tablets TDS x 3/7
- IV: sodium glycerophosphate 10mmol in 500ml over 12 hours
- Do not give if hypercalcaemic or oliguric