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 phosphylated 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 ± haematinics, U&Es, CRP, Ca^{2+}, PO_4^{3-}, 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

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. vasculitidies)
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 glomerulonephritits, not improving, CKD grade 4/5, previous renal transplant
- **Urologist:** urinary tract obstruction

When to dialyse

Mnemonic: **AEIOU**

Intractable….

- **A**cidosis — *pH<7.1*
- **E**lectrolyte abnormalities (hyperkalaemia, hyponatraemia, hypercalcaemia) — *K^+>6.5 or ECG changes*
- **I**ntoxicants (methanol, lithium, salicism)
- **O**verload — *Acute pulmonary oedema*
- **U**raemia — *urea>60 or pericarditis or uraemic syn*

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

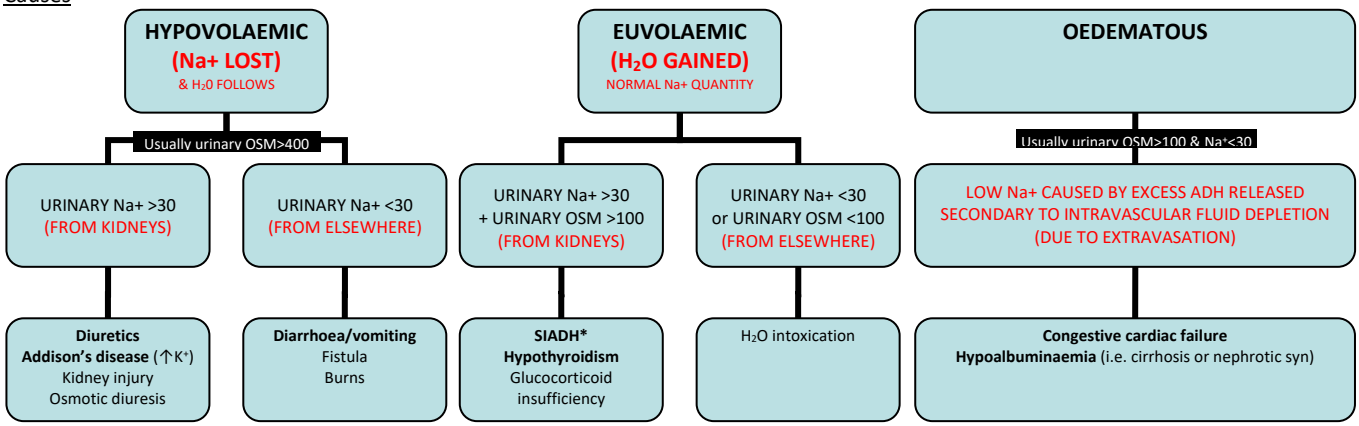
Sodium

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



*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 hyponatraema)
  - 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)

Hypernatraemia

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 dieresis (e.g. DKA) (kidneys loosing H_20 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 hypernatraemia 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 distil 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

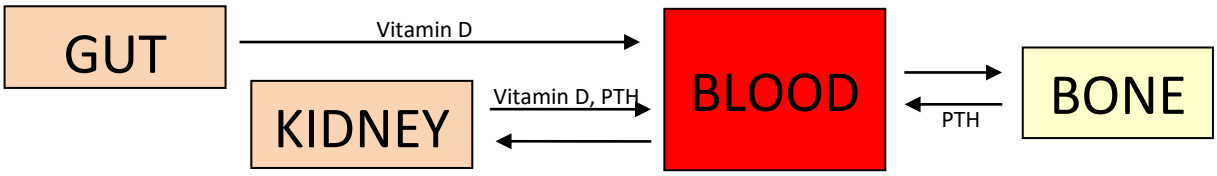
NB. may be due to pseudohyperkalaemia (haemolysis, EDTA-contaminated sample)

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 salbutmol 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 **(↑PO_4^{3-}, ↑PTH)**
  - Drugs (loop diuretics)
  - Chronic kidney disease
  - Rhabdomyolysis/tumour lysis syndrome
- PTH-related **(↑PO_4^{3-}, ↓PTH)**
  - Hypoparathyroidism
  - Hypomagnesaemia
  - Pseudohypoparathyrodism (resistance to PTH)
  - Cinacalcet
- Increased deposition/reduced uptake **(↓PO_4^{3-}, ↑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 alfacalcidol (1-α *hydroxy*colecalciferol) 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

Investigate for cause if not clear:

- 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: 5grams (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