1. **Modification of Drug Doses in Renal Failure**

**General points**

- Multiple drugs have significant renal excretion of the parent drug or an active metabolite.
- A pharmacological reference such as the MIMS annual should be used where the metabolism and interactions of a new medication are unknown.
- Consultation should be considered prior to the use of known nephrotoxins (eg intravenous radiocontrast) in patients with existing renal impairment.
- Please note that most prescribing guidelines use the Cockroft Gault formula rather than eGFR to make dose adjustments.

**Glomerular Filtration Rate (ml/min)**

Males  
\[
(140 - \text{age}) \times \text{wt (kg)} \\
0.8 \times \text{s.creat (μmol/L)}
\]

Females  
\[
(140 - \text{age}) \times \text{wt (kg)} \\
\text{s.creat (μmol/L)}
\]

The following common drugs should have either a dosage modification or be avoided in patients with renal insufficiency:

**Antibiotics**

- Aminoglycosides
- Glycopeptides (eg vancomycin),
- Penicillin
- Quinolones (ciprofloxacin, norfloxacin)
Intravenous radiocontrast agents
- See guidelines for use

Opiates (especially infusions)
- Avoid
  - Pethidine
  - Morphine /codeine (pro drug of morphine)
  - Fentanyl infusions are safe.

Anti-arrhythmics
- digoxin, sotalol, ß-blockers

NSAIDs & COX-2 inhibitors (avoid in most cases)

Metformin (use with caution if eGFR<60, withhold if eGFR<30)
2. Acute Kidney Injury (AKI)

Definition
- Acute rise in serum urea or creatinine over baseline levels
- Often, not always, accompanied by oliguria (urinary output <400ml/day or persistently <30ml/hour).

Practical Points
- Can lead to life threatening fluid and electrolyte abnormalities.
- A syndrome and not a diagnosis.
- Correct management demands a correct diagnosis be made as a matter of urgency i.e. in hours and not days.
- pre-renal and post-renal causes are potentially rapidly reversible if recognised early.
  Prompt management will avoid the progression to acute tubular necrosis (ATN).

Early consultation should be considered in severe cases.

Causes of AKI: see Table 1

Assessment of patient

History
- Fluid balance, fluid intake and fluid losses.
- Recent hypotension or sepsis.
- Recent IV radiocontrast,
  particularly in patients with diabetes or myeloma.
- History of prostatic disease
- Current and recent medications
  especially NSAIDs, ACE inhibitors All-Antagonists, antibiotics, IV contrast, Cyclosporin, Tacrolimus, statins.

Physical Examination
- Complete assessment of fluid status including, thirst, oral mucosa, skin turgor, pulse, JVP, postural blood pressure, lung bases and presence or absence of peripheral oedema.
- Serial weighing is invaluable.
- Signs of low cardiac output or incipient cardiogenic shock e.g. poor tissue perfusion, gallop rhythm.
- Renal bruits particularly in the context of ACE inhibition, hypertension +/- "flash pulmonary oedema".
- Exclude the presence of an enlarged bladder. If unsure, consider “bladder scan” +/- urethral catheterisation for residual volume estimation.
- Livedo reticularis or vasculitic skin rash.

Initial investigations
- Examination of urine may help to distinguish particular causes (Table 2).
- Serum biochemistry including electrolytes, urea, creatinine, creatine kinase and uric acid.
- In the setting of suspected tubulo-interstitial nephritis or microangiopathy a full blood count including eosinophil count, blood film, reticulocyte count, lactate dehydrogenase and serum haptoglobins should be measured.
- In the appropriate setting, drug levels, serum and urinary EPG/IEPG should be measured.
- Renal ultrasound should be considered in all cases, particularly when the diagnosis is unclear. A "bladder scan" may be useful if bladder outflow obstruction
is suspected and renal U/S is not readily available.

Management of ARF

1. Treat significant metabolic derangements first, especially hyperkalaemia (see below)

2. Restore renal perfusion
   - Fluid resuscitation if hypovolaemia.
   - Consider inotropes if low cardiac output.

3. Reverse underlying cause if possible
   - Indwelling urinary catheter if lower urinary tract obstruction.
   - Urological or radiological referral if upper urinary tract obstruction.
   - Withhold or cease all potential nephrotoxins.

4. Trial of intravenous diuretic therapy
   If refractory oliguria despite adequate fluid resuscitation in prerenal AKI and patient is hypervolaemic:
   - intravenous frusemide in escalating doses
   - 0.5-1mg/kg initially
   - If no diuresis after 30 minutes, 125mg over 45 minutes
   - If no further diuresis, a final dose of 250mg over 90 minutes
   (higher rates of infusion may cause irreversible ototoxicity)

5. If refractory, renal consultation with a view to supportive management (dialysis) should be pursued
   - Perform pre-emptive serological testing for HIV, HBV and HCV

6. Beware: In the recovery phase, dehydration complicated by prerenal AKI may develop due to post-obstructive or post-ATN diuresis. Meticulous monitoring of fluid status and daily weights is imperative.
3. **Hyperkalaemia** (Causes: see Table 3)

**Severity**

depends on:
- Absolute level.
- Rate of change (e.g. rapid rise in rhabdomyolysis).
- Presence of ECG changes - peaked T waves, broadened QRS, sinus asystole, ‘sine wave pattern’, asystole/VF.
- Associated hypocalcaemia (increases cardiac sensitivity).

**can be classified as:**
- **Mild** ($K^+ < 6$mmol/L, possible peaked T waves).
- **Moderate** ($K^+ 6 - 8$mmol/L, peaked T waves).
- **Severe** ($K^+ > 8$mmol/L or significant ECG changes).

**Initial investigations** (in the absence of an obvious cause):
- Serum $K^+$ and serum osmolarity.
- Urinary $K^+$ and urinary osmolarity.
- Calculate Trans-Tubular Potassium Gradient (TTKG):
  \[
  \frac{U_{K^+}/P_{K^+}}{U_{Osm}/P_{Osm}} < 6 \Rightarrow \text{aldosterone deficiency or resistance} \\
  \frac{U_{K^+}/P_{K^+}}{U_{Osm}/P_{Osm}} > 10 \Rightarrow \text{extra-renal cause hyperkalaemia}
  \]

**Treatment**

1. **Treat cardiac toxicity first**
   - Administer 10mL 10% **Calcium Gluconate**, 
     - if $K^+ \geq 6.5$mmol/L or in the presence of ECG changes.
     - slow IV push into a patent cannula as it can cause extravasation injury.

2. **Institute appropriate cardiac monitoring**

3. **Shift $K^+$ into cells temporarily in moderate-severe cases**
   - **Insulin/Dextrose infusion**
     - 50mL 50% Dextrose and 10 units actrapid IV
     - **Always give Dextrose first and monitor BSLs closely.**
     - Works within 30 minutes and lasts 2-4 hours.
     - Monitor blood sugar regularly for 4 hours after insulin administration
   - **Sodium Bicarbonate** (especially if acidotic.)
     - 100mL 8.4% NaHCO$_3$ IV over 30 minutes)

4. **Potassium restricted diet**

5. **Promote $K^+$ excretion and reverse underlying cause**
   - **Resonium** (calcium or sodium polystyrene resin)
     - 15-30g PO or PR.
     - Monitor effect after 4-6 hours.
     - Can be repeated 2nd hourly in more severe cases.
   - **Dialysis**
     - may be required in severe or progressive cases,
     - especially if associated with renal failure.
4. Hypokalaemia

Causes: see Table 4

Severity (depends on):
- Absolute level and chronicity.
- Rate of change.
- Presence of symptoms (weakness).
- Presence of Digoxin toxicity.
- Presence of ECG changes (U waves, VEBs, atrial tachyarrhythmias, asystole).

Initial investigations (in the absence of an obvious cause):
- Serum Na⁺, K⁺, Mg²⁺, Cl⁻, HCO₃⁻, osmolarity.
- Urinary K⁺, urinary Cl⁻, urinary osmolarity.
- Calculate anion gap
  - Na⁺ – (Cl⁻ + HCO₃⁻).
- Calculate Trans-Tubular Potassium Gradient (TTKG):
  - \( \frac{(U_K^+/P_K^+) \cdot (U_{Osm}/P_{Osm})}{< 2 } \rightarrow GI losses \)
  - \( > 4 \rightarrow \text{Renal losses/Excess aldosterone} \)

Treatment
- Establish underlying cause.
- Potassium replacement:
  - Oral - each 600mg tablet of KCl (Slow K) contains 8mmol K⁺.
  - Intravenous –
    - do not exceed 40mmol/L if given in infusion fluids.
    - do not exceed 10mmol/hour K⁺ unless given via central line with continuous ECG monitoring.
- Failure to respond to the above measures should suggest the need for concomitant Mg²⁺ replacement even in the presence of Mg²⁺ levels within the normal range.
5 Hypernatraemia

Practical points
- Severe hypernatraemia can cause confusion, coma, seizures and death.
- Over-rapid correction can result in cerebral oedema, precipitating seizures.
- Determination of the fluid state of the patient is essential for accurate diagnosis and treatment.
- Hypernatraemia only occurs in patients who are unable to control their own salt and water balance.

Causes of Hypernatraemia: see Table 5

Initial investigations (in the absence of an obvious cause):
- Serum Na⁺, K⁺, Cl⁻, osmolarity.
- Urinary Na⁺, Cl⁻, osmolarity

Treatment
If hypovolaemic/dehydrated
- Calculate ‘Free water deficit’:
  \[ 0.6 \times \text{body weight} \times \{(\text{Actual } S_{Na}/140) - 1\} \]
- Aim to correct the ‘free water deficit’ within 48-72 hours.
- Replace ‘free water deficit’ at a rate to achieve a serum sodium adjustment not exceeding 0.5mmol/L per hour e.g. 70kg man with serum sodium 165mmol/L, administer 7.5 litres Dextrose 5% over not less than 30 hours.
- Replace intravascular deficit and ongoing salt losses (if significant signs of hypovolaemia or concurrent salt loss e.g. due to diarrhoea) with additional Normal Saline or a combination of N/2 saline, or Dextrose Saline.
- Regular monitoring of fluid status, urinary output and serum electrolytes, urea and creatinine is imperative.

If normovolaemic or over-hydrated:
- Promote sodium loss with frequent loop diuretics and replace with low sodium solution.
- Haemodialysis may be required in severe cases, especially when there is neurotoxicity or associated renal failure.

6 Hyponatraemia

Practical points
- Severe hyponatraemia may cause cerebral oedema manifested by headache, confusion, coma, seizures and respiratory arrest.
- Because of the dangers inherent in rapid correction, the approach adopted to management of hyponatraemia is greatly influenced by the presence or absence of symptoms.
Severity is determined by absolute level ($\leq 120\text{mmol/L}$), the rate of decline and the presence or absence of symptoms.

Over-rapid correction can precipitate irreversible CNS damage due to central pontine myelinolysis.

Causes of hyponatraemia: see Table 6

Initial investigations
- Serum sodium, osmolarity and urinary sodium, osmolarity should be measured before any intravenous fluids or diuretics are administered.
- These measurements, in combination with assessment of the patient’s fluid balance, are critical in determining aetiology and, in particular, ruling out SIADH (Table 7).
- If diagnosis unclear: CXR, TFTs, Synacthen test, CT brain.

Management
Due to the risk of central pontine myelinolysis, rate of correction should never exceed
- $0.5 - 1\text{mmol/hr}$
- $10\text{mmol}$ in any 24 hour period

If volume depleted
- Correct fluid/saline deficit with Normal Saline.

If oedematous (complete correction is unusual in these states)
- Modest fluid restriction $\leq 1000\text{mL per day}$ should stabilise further decline.
- Salt restricted diet.
- Reverse underlying cause if possible (eg stop offending drugs).

If no apparent fluid deficit (usually SIADH) (Table 7)
- Strict fluid restriction $< 750 -1000\text{mL per day}$.
- If unsuccessful, consider initiating water excretion using:
  - Demeclocycline ($150\text{mg qid}$)
  - Oral Sodium or Urea ($10\text{gm in 100ml H}_2\text{O}$)
  - Tolvaptan (seek specialist advice as this drug is not widely available)
- In refractory cases, seek specialist assistance.

Hypertonic saline (3%) with or without Frusemide
- Only to be given for the emergency treatment of symptomatic severe hyponatraemia.
- Requires ICU/HDU monitoring and Specialist consultation.
- Calculate Sodium deficit:
  - $0.6 \times \text{body weight} (140 - \text{actual serum Na}^+)$
  - Aim for gradual correction, less than $10\text{mmol/24 hrs}$
  - Cease infusion once clinical state improves or serum Na$^+ \geq 125\text{mmol}$
7  **Hypercalcaemia**  
Must correct for serum albumin  
- add 0.02 x (40-measured albumin) to measured calcium

**Causes of hypercalcaemia:** see Table 8  
- Often asymptomatic, can cause confusion, anorexia, nausea, polyuria. May cause cardiac arrhythmia or coma if severe (greater than 4.0mmol/L).

**Initial investigations**  
- Ionised calcium, magnesium, phosphate, electrolytes, urea, creatinine, alkaline phosphatase, PTH and albumin.
- If diagnosis remains unclear, consider CXR, mammogram, serum and urine EPG/IEPG, PSA, PTHrp, isotope bone scan.

**Treatment (see also Oncology section)**  
- Establish and reverse underlying cause.

**Mild severity, asymptomatic hypercalcaemia (Ca\(^+\) ≤ 3mmol/L)**  
- rehydrate adequately

**Symptomatic or Ca\(^+\) > 3mmol/L**  
- Rehydrate fully with normal saline  
- Consider loop diuretic - give 20-40mg twice daily whilst monitoring fluid status, calcium, magnesium, electrolytes, urea, creatinine.

**After Specialist consultation**  
- **Calcitonin** (rapid onset of action) or **IV Pamidronate** if bone is source of hypercalcaemia.  
- Corticosteroids.  
- Cinacalcet/parathyroidectomy if hypercalcaemia is due to hyperparathyroidism.  
- Haemodialysis may be necessary if overdose or renal failure (particularly in recovery phase of rhabdomyolysis).

8  **Hypocalcaemia**

Correct measured calcium for low albumin:  
- add 0.02 x (40-measured albumin) to measured calcium

**General points**  
- Severe hypocalcaemia can be **neurotoxic** (carpo-pedal spasm, paraesthesiae, tetany, seizures) and cardiotoxic (prolonged QT interval, torsades de pointes).  
- A positive **Chvostek or Trousseau sign** is usually an indication for intravenous **Calcium**.  
- Intravenous Calcium can cause extravasation injury therefore only administer through a large bore cannula or central line.

**Causes of hypocalcaemia:** see Table 9

**Initial investigations**  
- Ionised calcium, magnesium, phosphate, electrolytes, urea, creatinine, PTH, Vitamin D and albumin.
Treatment

Mild and asymptomatic
- Oral calcium +/- oral vitamin D supplements (Ergocalciferol 1000µg daily or Calcitriol 0.25-1.0mg daily in renal impairment)

Symptomatic
- Consider intravenous Calcium Gluconate (10mL 10%) administered slowly into large vein. Avoid extravasation of this drug (causes skin necrosis)
- A calcium infusion may be necessary after consultation (especially if surgical hypoparathyroidism).
- Measure and replace Magnesium regularly during treatment.
9 **Metabolic Acidosis (reduced pH and HCO\textsubscript{3}⁻)**
(Causes: see Table 10)

**General points**
- Rarely an isolated abnormality.
- Calculate the **anion gap** (normal range 8 - 14):
  \[ \text{Na}⁺ - (\text{HCO}_3⁻ + \text{Cl}⁻) \]
- Consider intoxication if aetiology unclear (see Table 10).
- Severe prolonged acidosis can cause CVS instability.
- Calculate the **Estimated HCO₃⁻ Deficit**:
  \[ 0.5 \times \text{weight} \times (18 - \text{Actual HCO}_3⁻) \]

**Treatment**
- Identify and treat underlying cause.
- IV **Sodium Bicarbonate 8.4%** may be required if acidosis is:
  - Acute
  - Severe (HCO₃⁻ < 8mmol/L)
  - Associated with hyperkalaemia

- In severe cases: 50-100mL **Sodium Bicarbonate 8.4%** as an intravenous infusion over 30 - 60 minutes.
**Sodium Bicarbonate** therapy (IV +/- oral) carries inherent risks of:
  - Hypokalaemia
  - Hypocalcaemia complicated by tetany
  - Alkalaemia
  - Sodium overload - 100mls of 8.4% NaHCO₃ contains as much Na⁺ as 666mls of Normal Saline
  - Specialist consultation should be considered

10 **Metabolic Alkalosis**

**Aetiology**
- **Chloride responsive** (urine Cl⁻ < 10mmol/L):
  - characterised by volume loss
  - Gastric fluid loss (vomiting, lavage, drainage)
  - Diuretics
  - Rapid correction of chronic hypercapnia
  - Cystic fibrosis

- **Chloride resistant** (urine Cl⁻ > 10mmol/L):
  - Mineralocorticoid excess
  - Conn’s syndrome
  - Cushing’s
  - Exogenous
  - Liquorice
  - Profound K⁺ depletion
  - Exogenous alkali administration (drugs or diet)
  - Non-parathyroid hypercalcaemia

**Treatment**
- Replace volume deficit.
- Reverse underlying cause.
- Rarely requires specific acid treatment
• specialist consultation necessary.
• rapid correction can cause cerebral dysequilibrium.
11 Hypertensive crises

General points
- The rate of change of BP is more important than the absolute level.
- **Acute** treatment of hypertension should be considered if one of the following exists:
  - Unequivocal evidence of malignant hypertension including:
    - retinopathy
    - haemolysis
    - encephalopathy
    - renal failure
  - The patient is pregnant (see O&G section) or a child.
  - Other mitigating circumstances exist (e.g. aortic dissection, subarachnoid haemorrhage, intra- or peri-operative hypertension).
  - The diastolic BP is greater than 120mmHg.
  - The benefits of acute treatment should be balanced against the risk of a sudden drop in organ perfusion, particularly where occlusive vascular diseases exists.

**Do not lower BP acutely following a stroke without consultant advice.**
- **Parenteral** medications should only be used in a high dependency setting with appropriate monitoring.
- Asymptomatic BP elevations in chronic hypertensive patients rarely require acute treatment.

Management - see Table 11

12 Initial Antibiotic Treatment of Peritonitis in Peritoneal Dialysis (PD) Patients

Please refer to PD peritonitis protocol on the WSLHD and NBMLHD intranet. This section summarises initial therapy for PD peritonitis.

Diagnosis

- Clinical features: Cloudy PD effluent, abdominal pain, fever, nausea/vomiting/diarrhoea
- Cell count of PD dialysate shows WCC >100 x 10^6 cells/L, with 50% neutrophils
- Growth of bacteria on culture

**Note:** Other underlying pathologies (e.g. perforated diverticulum) should also be considered in a PD patient with abdominal pain.
Initial Management (0 to 48hrs)

- Send PD fluid for urgent cell count and culture. Inject 2 x 10 mls of PD effluent into a set of bectec blood culture bottles and also collect another 20 mls into a sterile (MSU) container
- Examine PD catheter exit site and tunnel for any inflammation. In the presence of a discharge from exit site, take a swab and send it for gram stain and culture.
- Commence intraperitoneal (IP) antibiotics (see Table page 3)
- Admit to Hospital if systemically unwell, severe pain and/or unable to self-care - notify the Renal Registrar or the on-call Renal CMO. If hospital admission is not needed, contact the PD nurse to arrange outpatient follow-up at the Regional Dialysis Centre, Blacktown Hospital (9881-8442 or on-call after-hours)

Initial antibiotic treatment for PD-related peritonitis pending culture results

<table>
<thead>
<tr>
<th>Standard treatment</th>
<th>Cephazolin 1.5g IP once daily&lt;sup&gt;2&lt;/sup&gt; PLUS Gentamicin 80 mg IP once daily&lt;sup&gt;3&lt;/sup&gt; PLUS Amoxycillin/clavulanate 875+125 mg orally q12h&lt;sup&gt;4&lt;/sup&gt; PLUS Tablet Nilstat 500,000 Units QID PO for the duration of treatment (at least 2 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>If any of the following are present:</td>
<td>Vancomycin at 30 mg/kg up to 2g IP once every 3 to 5 days&lt;sup&gt;3&lt;/sup&gt; PLUS Gentamicin 80 mg IP once daily&lt;sup&gt;2&lt;/sup&gt; PLUS Tablet Nilstat 500,000 Units QID PO for the duration of treatment (at least 2 weeks)</td>
</tr>
<tr>
<td>History of MRSA infection/carriage</td>
<td>Current PD exit-site infection Allergy to cephazolin</td>
</tr>
<tr>
<td>If signs of systemic sepsis (e.g. T&gt;38.5°C, rigors, hypotension)</td>
<td>Vancomycin 1g intravenously (IV) once every 3 to 5 days&lt;sup&gt;3&lt;/sup&gt; PLUS Gentamicin 80 mg IV once every 2 to 3 days&lt;sup&gt;3&lt;/sup&gt; PLUS Tablet Nilstat 500,000 Units QID PO for the duration of treatment (at least 2 weeks)</td>
</tr>
</tbody>
</table>

<sup>1</sup> IP antibiotics are given for at least 2 wks. Revise therapy when culture results are available (at 48h) – see intranet protocol for follow-up treatment of PD peritonitis.
<sup>2</sup> Antibiotics are administered into a bag of PD solution and allowed to dwell in the peritoneal cavity for 6 to 8 hours. Cephazolin/vancomycin and gentamicin can be mixed
in the same PD bag. Patients treated with automated PD usually convert to continuous ambulatory PD during antibiotic treatment

3 Measure trough gentamicin and vancomycin levels at 48h

13 Guidelines for prophylaxis against radiocontrast nephropathy (RCN)

| Prophylaxis against contrast nephropathy should be considered in all patients requiring radiocontrast with a GFR of <60mL/minute/1.73m² |

**Background**

- The incidence of RCN is 10-20% in high risk groups.
- Risk factors are:
  - Pre-existing chronic renal failure or low renal perfusion (e.g. CCF, dehydration)
  - Age >70
  - Multiple myeloma
  - Diabetes
  - Volume of contrast media used
- Optimal preparation may not be possible in all cases, particularly in the setting of an urgent test (see below)
- Although the protective effects of acetyl cysteine are equivocal, it has low toxicity and should be incorporated into a preventative approach.

**An approach to RCN prevention**

1. **Can contrast be avoided?**
   - Can the desired information be obtained from a non contrast study or other imaging modality? Note that gadolinium is associated with a risk of nephrogenic systemic fibrosis in patients with advanced renal disease and should be avoided for patients with a GFR of <30mL/minute.
   - Can an alternative contrast agent can be used (e.g. CO₂ angiography for infra- abdominal angiography)

2. **Cease medications that may increase incidence of RCN**
   - Discontinue nephrotoxic medication prior to study e.g.NSAIDS and COX 2 inhibitors for 7 days prior to the test. Metformin should be stopped for 24 hours prior to the test in all patients with a GFR <60. Diuretics should be withheld for 24 hours if possible.
   - When ceased, these medications should not be recommenced until 48 hours after the test and only if the renal function has been shown to be stable.
   - IV rehydration
   - Encourage the patients to maintain oral fluids before the procedure and not fast as is the standard ‘wisdom’ (purely to reduce the rate of the patients vomiting in the x ray department)
   - Normal saline (0.9%) given at a rate of 1mL/kg/hr, given 12 hours prior and 12 hours after contrast (unless significant fluid overload exists) is the optimal protocol. Hydration should be commences as soon as practicable for urgent procedures and ideally continued for 12 hours post procedure.
   - IV bicarbonate has theoretical benefits, however current trials reported have shown variable results. Trials reported used a non-commercially available infusion solution in a low risk population. An iso-osmolar solution of NaCl/NaHCO₃ can be made by adding 38mL of 8.4% IV NaHCO₃ to a 500mL bag of 0.45% saline.

3. **N Acetyl cysteine**
   - Give NAC orally at a dose of 600mg bd for 2 days (three doses prior and one dose after IV contrast)
• This dose is prepared in the Westmead hospital pharmacy using the Mucomyst® nebulised solution and is measured out by the patient into a diluent such as orange juice.
• NAC is not routinely recommended for prevention of contrast-induced nephropathy.

4. Contrast protocol
• Iso-osmolar non ionic contrast media (iodixanol) is associated with a lower risk of RCN compared to low-osmolality media (LOCM-iophexol or iopamidol) [9], but because of the significantly greater cost (twice the cost of LOCM), it should only be used in high risk patients after discussion with the radiologists. Low osmolality non ionic contrast (e.g. iohexol or iopamidol-standard at Westmead) should be used in all other cases.
• Where possible the contrast load should be restricted to <100mL as the dose given is an important determinant of the risk of RCN. Discuss with the radiologist performing the test if unclear of the expected contrast load.
• There is no good evidence that post-procedure haemodialysis reduces the risk of subsequent contrast-induced nephropathy, including patients on dialysis with residual renal function. Therefore special co-ordination of the timing of contrast administration with haemodialysis need not be done routinely.

14 OVERVIEW OF INTRAVENOUS IRON THERAPY

See “Guideline and Procedure for Iron Infusion in Chronic Kidney Disease (CKD) Patients of the Western Renal Services” on WSLHD/NBMLHD intranet.

Purpose of Iron Infusions
• Treatment of iron deficiency anaemia in chronic kidney disease patients
• Replacement of iron stores
• Maximise the benefits of erythropoietin therapy

Investigations and Reviews
• Investigations are needed to exclude other causes of anaemia and that treatment is appropriate to the diagnosis – eg. Haemolytic anaemia, megaloblastic anaemia, aplastic anaemia, etc
• Regular reviews of iron status (typically every 2-3 months) are needed to ensure appropriate supplementation of iron.

Contraindications
First trimester of pregnancy, haemochromatosis, active infection or sepsis

Precautions
Parenteral iron therapy is associated with a risk of ‘anaphylactoid’ (anaphylaxis-like) reactions that are potentially fatal and typically occur within the first several minutes of administration.

An anaphylactoid reaction is characterized by any of the following:
bronchospasm acute urticaria
dyspnoea angioedema
wheezing hypotension
tachycardia abdominal cramping

If an anaphylactoid reaction occurs stop the infusion. Immediate medical review is required and appropriate drugs administered dependent on patient’s symptoms. Drugs
commonly used include adrenaline, nebulised salbutamol, antihistamines, hydrocortisone, oxygen or intravenous fluids.

**For this reason parenteral iron therapy should only be administered where trained staff and facilities for cardiopulmonary resuscitation are available.**

Premedication with hydrocortisone 100mg IV should be considered for individuals at high risk for anaphylactoid reactions (i.e. those with a history of allergies, asthma, active inflammatory disease, active rheumatoid arthritis or systemic lupus erythematosus).  

**ADVERSE REACTIONS**
Headache, nausea, vomiting, joint and muscle pains, dizziness, syncope, tachycardia, flushing, sweating, circulatory collapse, sensation of stiffness in arms, legs or face, chills, fever, rash, arthralgia, angioneurotic oedema, generalized lymphadenopathy. Local phlebitis may occur at the site of infusion.

Patients should be informed of the reason for iron, possible adverse reactions and asked to state any known allergies before the infusion.

**PLEASE NOTE:**
- Elemental iron doses using different iron complexes are not directly comparable.  
- **Mixing the infusion with acidic substances or reducing substances may liberate toxic iron ions from the iron supplement. Iron infusions should not be given with any other drugs to avoid the risk of precipitation and/or interaction.**  

1. **PROTOCOL FOR IRON POLYMALTOSE (Ferrum H or Ferrosig®)**

**Presentation**
Iron polymaltose 318mg = 100mg of iron (III) per 2mL ampoule. The aqueous colloidal solution is sterile and pyrogen free and approximates the pH and tonicity of the tissues. Dosages are calculated and prescribed based on iron (III) content.

**Observations to be taken during iron polymaltose infusion**
- Blood pressure  
- Temperature  
- Pulse  
- Respiratory rate

**Typical dosing for Haemodialysis Patients**
100-200mg as an infusion into the venous limb of the dialysis circuit once monthly. The frequency of repeat doses (usually weekly or monthly) is determined by the patients iron status and whether the iron is being given for the purpose of restoring or maintaining iron stores (see Appendix 1).

The **First Dose** is given as 100mg in 20mL 0.9% sodium chloride, infused over 2 hours via dialysis machine. Observations should be done prior to commencing the infusion then every 5 minutes for the first 15 minutes then every 30 minutes until the completion of infusion. Commence infusion at least an hour after the start of dialysis to ensure reaction is not dialysis related. A medical officer must be present or on close call for the initial 15 minutes.

Subsequent doses can be given as 100mg in 20mL 0.9% sodium chloride over 60 minutes via dialysis machine. Observations should be done prior to the infusion then every 30 minutes until the completion of infusion.
Typical Dosing for Peritoneal Dialysis and Other CKD Patients

For iron deficient patients, 500mg of iron polymaltose is usually given as a single infusion. The frequency of repeat dosing is dependant upon subsequent reassessment of iron stores.

The First Dose is given as 500mg in 250mL 0.9% sodium chloride infused at 20mL/hour for the first 50mL then if there are no adverse reactions, the infusion rate may be increased to 120mL/hour. This rate will continue until the completion of the infusion (approximately over 4 hours). Observations should be done prior to commencing the infusion then every 15 minutes for first hour then hourly until finished. A medical officer must be present or on close call for the initial 15 minutes.

Subsequent doses can be given as 500mg in 250mL 0.9% sodium chloride infused at 125mL/hour over 2 hours. Observations should be done prior to and at the end of the infusion.

Notes:
- Infusions <250mg may be put into 50mL and infused at 20ml/hour over 2.5 hours.
- In some cases, higher iron doses may be used (See Ferrosig product information)

Adverse Reactions
- Infusions are stopped immediately if a reaction occurs. Patient to be assessed and treated by a medical officer.
- Iron may be recommenced for non life-threatening reactions at half the rate when symptoms subside. First dose observation times should continue for the first 3 doses if any reaction has occurred.
- Use of iron sucrose may be considered as an alternative for non life-threatening reactions to iron polymaltose.
- FACILITIES FOR THE TREATMENT OF ANAPHYLAXIS SHOULD BE READILY AVAILABLE DURING IRON POLYMALTOSE INFUSION.

2. PROTOCOL FOR IRON SUCROSE (VENOFER®)

General Notes
More expensive than iron polymaltose however associated with a lower incidence of systemic adverse reactions. Therefore typically used for patients who have experienced a significant adverse effect following infusion of iron polymaltose.

Presentation
Each 5mL ampoule contains 20mg/mL of elemental iron as iron (III)-hydroxide sucrose complex. Also contains sodium hydroxide for pH adjustment.

Typical Dosing for Haemodialysis Patients
100-200mg as a bolus over 5-10 minutes via the venous limb of the dialysis line once weekly.

Typical Dosing for Peritoneal Dialysis and Other CKD Patients
- For patients not previously treated with iron sucrose a test dose of 20mg (=1mL) diluted in a maximum of 20mL sodium chloride 0.9% should be given over 15 minutes. For normal dosing dilute one ampoule in a maximum of 100mL of sodium
chloride 0.9% immediately prior to administration. Infuse at a rate of 100mg iron (one ampoule) over at least 15 minutes.

- Doses of 300mg infused over 1.5 hours or 400mg infused over 2.5 hours in 250mL 0.9% sodium chloride given 14 days apart are reported in the literature.
- Only limited data on doses up to 500mg in 250mL 0.9% sodium chloride infused over 3.5 to 4 hours is available.

**LIMITED REPORTS OF IRON SUCROSE INFUSIONS ABOVE 300MG/DAY ARE AVAILABLE. SINGLE DOSES OF GREATER THAN 500MG ARE NOT RECOMMENDED**

**Observations:**
- Blood pressure
- Temperature
- Pulse
- Respiratory rate

Observations should be done prior to each infusion and 15 minutes after the completion of the infusion.

**Adverse Reactions**
- A medical officer must be present for the first 15 minutes of the first infusion. **Infusions are stopped immediately if a reaction occurs. Patient to be assessed and treated by a medical officer.**
- Hypotension has been reported in haemodialysis patients receiving intravenous iron. This may be related to the rate of administration or the total dose administered.
- Extravasation must be avoided because leakage may cause pain, inflammation, tissue necrosis, sterile abscess and brown discoloration of the skin. Ice may be applied to cause local vasoconstriction and decrease fluid absorption. Massage of the area should be avoided.
- **FACILITIES FOR THE TREATMENT OF ANAPHYLAXIS SHOULD BE READILY AVAILABLE DURING IRON INFUSIONS.**

Note: Iron sucrose is strongly alkaline & must not be given subcutaneously or intramuscularly.
3. **FERRIC CARBOXYMALTOSE (Ferinject®)**

Ferinject has the advantage of quick administration < 1 hour but is much more expensive than iron polymaltose. Therefore, this formulation should generally be reserved for outpatients with supply through community pharmacy from a PBS prescription.
**Presentation**
Each 10mL ampoule contains 500mg of elemental iron as ferric carboxymaltose. Also contains sodium hydroxide and hydrochloric acid for pH adjustment.

**Observations**
Observations to be taken during ferric carboxymaltose administration
- Blood pressure
- Temperature
- Pulse
- Respiratory rate

**Dosing**
- For haemodialysis patients who are iron deficient, give 500mg IV via the venous limb of the dialysis line once a month. Refer to the “Recommended Schedule for Iron Administration in HD patients” section above for the administration schedule.

- Dilution of ferric carboxymaltose for intravenous infusion:

<table>
<thead>
<tr>
<th>Ferric carboxymaltose (Ferinject®)</th>
<th>Elemental iron</th>
<th>Volume of 0.9% sodium chloride</th>
</tr>
</thead>
<tbody>
<tr>
<td>2mL to 4mL</td>
<td>100mg to 200mg</td>
<td>50mL</td>
</tr>
<tr>
<td>Greater than 4mL to 10mL</td>
<td>Greater than 200mg to 500mg</td>
<td>100mL</td>
</tr>
<tr>
<td>Greater than 10mL to 20mL</td>
<td>Greater than 500mg to 1000mg</td>
<td>250mL</td>
</tr>
</tbody>
</table>

- Infuse over at least 15 minutes.

**Notes**
- Patients should be closely monitored when single doses of ferric carboxymaltose greater than 200mg of elemental iron are administered since the safety data are limited.

- Patients with a haemoglobin of less than 100g/L may be given up to a maximum of 20mg of elemental iron per kg of body weight. **However, not more than 1000mg of elemental iron should be given per week.** Please refer the Ferinject® production information on more information on calculations and administration of the cumulative dose.

- **Infusions are stopped immediately if an adverse reaction occurs and the patient assessed and treated by a medical officer.**
- Hypotension has been reported in haemodialysis patients receiving intravenous iron. This may be related to the rate of administration or the total dose administered.
- Extravasation must be avoided because leakage may cause pain, inflammation, tissue necrosis, sterile abscess and brown discolouration of the skin. Ice may be applied to cause local vasoconstriction and decrease fluid absorption. Massage of the area should be avoided.
- **Facilities for the treatment of anaphylaxis should be readily available during iron infusions.**
References:
1. Ferrosig injection product information, MIMS online, last updated, 07/06/2006, viewed 14/01/2008
2. Venofer injection product information, MIMS online, last updated, 03/09/2004, viewed 05/2007
5. Iron Sucrose, Martindale, 35th edition
6. Basic Clinical Dialysis – Edited by David Harris, Grahame Elder, Lukas Kairaitis, Gopala Rangan, 2005
10. Protocol for Iron Polymaltose Infusion, Department of Pharmacy, Westmead Hospital, 1993
APPENDIX 1 - IRON MANAGEMENT IN HAEMODIALYSIS (HD) PATIENTS

Background
- Adequate iron stores are necessary for normal erythropoiesis as well as normal muscle function and cellular energetics
- Inadequate iron stores may result in anaemia or the use of excessive doses of erythropoietic agents (ESA's). Maintaining adequate iron stores in HD patients significantly simplifies the administration of ESA's.
- Most patients on haemodialysis are unable to maintain adequate iron stores without intravenous iron supplementation, as requirements for iron are greater than the maximum absorption possible from the gut.

Assessment of Iron Stores
- Iron studies are performed every 2 months in satellite HD patients for monitoring and dose adjustment for iron replacement in the satellite haemodialysis.
- Both transferrin saturation and ferritin levels are used as an indicator of iron stores. Levels indicating absolute and relative iron deficiency in HD patients are different to those of the general population.
- Both ferritin and transferrin saturation are falsely elevated in patients who have been given recent intravenous iron. Iron studies should therefore be measured prior to the mid-week dialysis session and intravenous iron either given during the middle or last dialysis session for the week. Ferritin levels may also be elevated transiently in the setting of acute infection.

Interpretation of Iron Studies in HD Patients
- Target values for HD patients are a ferritin of 200-500ug/L and transferrin saturation of 30-40% (see table)

<table>
<thead>
<tr>
<th>Transferrin saturation</th>
<th>Absolute or relative iron deficiency</th>
<th>Iron replete</th>
<th>Iron overload</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin (µg/L)</td>
<td>&lt;30% OR &lt;200</td>
<td>30-40% AND 200-500</td>
<td>&gt;40% OR &gt;500</td>
</tr>
</tbody>
</table>

Recommended Schedule for Iron Administration in HD Patients
- Intravenous iron should be administered at either the mid week or last weekly dialysis session in order to avoid misinterpretation of iron studies (which are routinely collected prior to the mid-week dialysis treatment).
- Intravenous iron should be withheld in patients with an active bacterial infection

<table>
<thead>
<tr>
<th>Iron status</th>
<th>Iron administration*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute or relative deficiency</td>
<td>100mg/week X 8</td>
</tr>
<tr>
<td>Iron replete</td>
<td>100mg/month</td>
</tr>
<tr>
<td>Iron overload</td>
<td>Withhold until next iron status assessment</td>
</tr>
</tbody>
</table>

References:
### Table 1: Major Causes of AKI

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
</table>
| **1. Pre-Renal Failure**       | - Hypovolaemic shock - dehydration, fluid or blood loss, peri-operative hypotension, third space sequestration (e.g. pancreatitis), low effective blood volume (cirrhosis, nephrotic syndrome).  
- Low cardiac output (cardiogenic shock) - myocardial or valvular disease, tamponade, pulmonary embolus, cardiac arrhythmia.  
- Septic shock  
- Anaphylactic shock  
- Impaired arterial supply - thrombosis, embolism, dissection (unlikely to be rapidly reversible). |
| **2. Post-Renal Failure (obstruction)** | - Ureteric - bilateral obstruction (unilateral if lone kidney or asymmetrical function) caused by clot, calculus, sloughed papilla, cancer, external compression.  
- Bladder Neck – prostatic enlargement, blocked IDC, blood clot.  
- Urethra - stricture, urethral valve, phimosis. |
| **3. Intrinsic Renal Failure**  | - Acute Tubular Necrosis (ATN)  
  - Prolonged pre-renal failure.  
  - Toxic ATN – aminoglycosides, intravenous radiocontrast, rhabdomyolysis, urate nephropathy, ethylene glycol.  
- Diseases of glomeruli and microvasculature - glomerulonephritis, vasculitis, thrombotic microangiopathy (e.g. HUS, TTP, DIC), toxaemia, accelerated hypertension, scleroderma.  
- Tubulo-interstitial nephritis - antibiotics, NSAIDs, diuretics, anti-convulsants, Allopurinol, Cimetidine, PPIs. |
<table>
<thead>
<tr>
<th>Test</th>
<th>Interpretation</th>
<th>Supplementary note to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Culture (U+C)</td>
<td>ID, urine, GN, myoglobin, flexicure positive</td>
<td>Cysininuria (urine, myoglobin, GN, or vascular)</td>
</tr>
<tr>
<td>Urine Protein</td>
<td>Protein</td>
<td></td>
</tr>
<tr>
<td>Urine Microscopy (Amid)</td>
<td>Peritoneal ARF or peritoneal ARF, ATN, GN or vascular (especially if RBC casts)</td>
<td>Possible urea misclassification</td>
</tr>
<tr>
<td></td>
<td>Urine Sodium (may be difficult to interpret, if not distant NS)</td>
<td></td>
</tr>
<tr>
<td>Urine Sodium</td>
<td>FENa &gt;0.15, FET &lt;0.45, FET &gt;0.15, FENa &lt;0.45</td>
<td>Positive significant glomerulosclerosis</td>
</tr>
<tr>
<td>Urine myoglobin</td>
<td>FENa &lt;0.05, FET &gt;0.15, FET &lt;0.15, FENa &gt;0.15</td>
<td>Creatine is high when creatinine is increased, but no RBCs on microscopy</td>
</tr>
</tbody>
</table>
Table 3: Causes of Hyperkalaemia

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
</table>
| **A. Factitious/Spurious** |  - Haemolysed sample  
  - Prolonged tourniquet application  
  - Neutrophilia or thrombophilia |
| **B. Cellular redistribution** |  - Acidosis  
  - Drugs -  
    - ß-blockers  
    - Succinylcholine  
    - Digoxin toxicity  
  - Hyperkalaemic periodic paralysis |
| **C. Extra-renal causes** |  (GFR reduced & \( U_k^+ > 40 \text{mmol/L} \))  
  - Excess oral or intravenous supplements |
| **D. Renal causes (\( U_k^+ < 20 \text{mmol/L} \))** |  **Endogenous source** |
|  |  - Gastrointestinal bleed  
  - Haemolysis  
  - Rhabdomyolysis  
  - Tumour lysis syndrome |
|  **Hyper-reninaemic hypoaldosteronism** |  - Addison's disease  
  - ACE inhibitors or A-II-Antagonists  
  - Anti-coagulation with heparin |
|  **Hypo-reninaemic hypoaldosteronism** |  - Type IV RTA  
  - Diabetes mellitus  
  - Analgesic nephropathy/NSAIDs  
  - Lead toxicity  
  - Elderly  
  - Lupus nephritis  
  - Obstructive nephropathy  
  - Transplant nephropathy  
  - Amyloidosis  
  - HIV  
  - Sickle cell disease |
|  **Pseudohypoaldosteronism** |  - Spironolactone  
  - Triamterene, Amiloride, Trimethoprim |
Table 4: Hypokalaemia

A. Cellular redistribution
- Catecholamine excess.
- β₂ agonists.
- α₁ antagonists.
- Insulin effect.
- Alkalosis/Sodium bicarbonate.
- Treatment of megaloblastic anaemia.
- Treatment of neutropenia with GM-CSF.
- Hypokalaemic periodic paralysis.

B. Extra-renal losses (Uₖ⁺ < 30mmol/L)

<table>
<thead>
<tr>
<th>Low pH</th>
<th>Normal pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diarrhoea</td>
<td>• Poor K⁺ intake</td>
</tr>
<tr>
<td>• Fistula</td>
<td>• Cutaneous loss eg burns</td>
</tr>
<tr>
<td>• Laxatives/Laxative abuse</td>
<td>• Villous adenoma</td>
</tr>
</tbody>
</table>

C. Renal losses (Uₖ⁺ > 30mmol/L)

<table>
<thead>
<tr>
<th>Low pH (Normal anion gap)</th>
<th>Normal pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Type I RTA</td>
<td>• Post-ATN diuresis</td>
</tr>
<tr>
<td>• Type II RTA</td>
<td>• Post-obstructive diuresis</td>
</tr>
<tr>
<td>• Acetazolamide</td>
<td>• Cisplatin therapy</td>
</tr>
<tr>
<td>• Ureterosigmoidostomy</td>
<td>• Mg²⁺ depletion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(Increased anion gap)</th>
<th>High pH (Low urinary Cl⁻ &lt; 10mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diabetic ketoacidosis</td>
<td>• Vomiting</td>
</tr>
<tr>
<td>• Alcoholic ketoacidosis</td>
<td>• Nasogastric losses</td>
</tr>
</tbody>
</table>

...cont'd
Table 4: Hypokalaemia cont'd
(High urinary Cl⁻ > 30mmol/L)
- Type I RTA
- Type II RTA
- Acetazolamide
- Diarrhoea
- Spironolactone
- Triamterene, Amiloride, Trimethoprim

Disorders
- Gastrointestinal (urine K⁺ < 25mmol/L)
  - Deficient dietary intake
  - Vomiting, diarrhoea, villous adenoma, fistulae.
- Renal (urine K⁺ > 25mmol/L)*
  - Diuretics.
  - Mineralocorticoid excess-
    - Primary aldosteronism.
    - Secondary aldosteronism.
    - Liquorice ingestion.
  - Glucocorticoid excess
    - Exogenous
    - Endogenous
  - Renal tubular disorders
    - renal tubular acidosis
    - leukaemia
    - antibiotics
  - Magnesium depletion

* Prolonged vomiting with chloride depletion can result in an inappropriately high urine K⁺, resulting in further K⁺ depletion
Table 5: Hypernatraemia

**Loss of total body water**
- Extrarenal (e.g. diarrhoea)
- Renal e.g. diabetes insipidus (see Endocrinology)

**Increased administration of salt**
- Usually iatrogenic e.g. excess Normal Saline crystalloid solutions
  and/or
  - Impaired excretion e.g. ARF.

Table 6: Hyponatraemia

**Factitious**
- Hyperglycaemia
- Hyperlipidaemia
- Hyperproteinaemia

**Total body water decreased**
- Extrarenal fluid losses e.g. vomiting, diarrhoea
- Renal fluid losses
- Diuretics (especially thiazides)
- Osmotic (hyperglycaemia, mannitol)
- Post-obstructive diuresis

**Total body water increased (oedema states)** - rarely requires emergency treatment
- Exogenous fluids
- Congestive cardiac failure
- Nephrosis
- Cirrhosis

**No apparent fluid deficit**
- Syndrome of inappropriate ADH (SIADH)
  - suspect if serum Osm < 270 < Uosm
  - urine Na+ >20mmol/L
- **Causes:** See Table 9
- Psychogenic polydipsia
- Endocrine (hypothyroidism, glucocorticoid deficiency)
  Acute and chronic renal failure (impaired water excretion)
Table 7: Causes of SIADH

<table>
<thead>
<tr>
<th>Malignancy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Small cell Ca lung</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td></td>
</tr>
<tr>
<td>Ca pancreas/ duodenum</td>
<td></td>
</tr>
<tr>
<td>Thymoma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CNS Disease</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Head trauma</td>
<td></td>
</tr>
<tr>
<td>SDH</td>
<td></td>
</tr>
<tr>
<td>SAH</td>
<td></td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td></td>
</tr>
<tr>
<td>Encephalitis</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td></td>
</tr>
<tr>
<td>AIP</td>
<td></td>
</tr>
<tr>
<td>Guillain-Barré</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary Disease</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Empyema</td>
<td></td>
</tr>
<tr>
<td>CAL</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td></td>
</tr>
<tr>
<td>Tricyclics</td>
<td></td>
</tr>
<tr>
<td>Chlorpropamide</td>
<td></td>
</tr>
<tr>
<td>Vincristine / Vinblastine</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td></td>
</tr>
<tr>
<td>Clofibrate</td>
<td></td>
</tr>
<tr>
<td>Oxytocin</td>
<td></td>
</tr>
<tr>
<td>Narcotics</td>
<td></td>
</tr>
<tr>
<td>General Anaesthesia</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td></td>
</tr>
<tr>
<td>Usually elderly ?underlying lung/brain disease</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td></td>
</tr>
<tr>
<td>Positive pressure ventilation</td>
<td></td>
</tr>
<tr>
<td>Pain (especially post-operative)</td>
<td></td>
</tr>
</tbody>
</table>
# Table 8: Hypercalcaemia

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artefactual</td>
<td>• Prolonged stasis of collected blood</td>
</tr>
<tr>
<td></td>
<td>• Hyperproteinaemia</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>– primary or tertiary</td>
</tr>
<tr>
<td>Malignancy</td>
<td>• Bony metastases eg myeloma, lung</td>
</tr>
<tr>
<td></td>
<td>• Overproduction of PTH related protein</td>
</tr>
<tr>
<td></td>
<td>SCC of lung, breast</td>
</tr>
<tr>
<td></td>
<td>• Vitamin D overproduction (lymphoma)</td>
</tr>
<tr>
<td>Calcium/Vitamin D intoxication</td>
<td>• Inadvertent or deliberate excess/overdose of</td>
</tr>
<tr>
<td></td>
<td>• Calcium supplements</td>
</tr>
<tr>
<td></td>
<td>• Vitamin D</td>
</tr>
<tr>
<td></td>
<td>• High calcium containing foods (milk-alkali syndrome)</td>
</tr>
<tr>
<td>Granulomatous diseases</td>
<td>e.g. sarcoidosis, TB</td>
</tr>
<tr>
<td>Drugs</td>
<td>• Thiazides</td>
</tr>
<tr>
<td></td>
<td>• Vitamin A</td>
</tr>
<tr>
<td></td>
<td>• Vitamin D (see above)</td>
</tr>
<tr>
<td>Immobilisation</td>
<td>(especially elderly with Pagets disease)</td>
</tr>
<tr>
<td>Other</td>
<td>e.g. hyperthyroidism</td>
</tr>
</tbody>
</table>
### Table 9: Hypocalcaemia

#### Hypocalcaemia with normal/low phosphate
- Vitamin D deficiency (dietary)
- Renal failure (↓ 1, 25-dihydroxyvitamin D)
- Liver disease (↓ 25-hydroxyvitamin D)
- Anticonvulsants (↓ 25-hydroxyvitamin D)
- Acute pancreatitis
- Magnesium deficiency

#### Hypocalcaemia with high plasma phosphate
- Idiopathic/sporadic hypoparathyroidism
- Post-operative hypoparathyroidism
- Acute rhabdomyolysis
- Recovery phase tumour lysis syndrome
- Advanced chronic renal failure
- Oliguric acute renal failure
<table>
<thead>
<tr>
<th>Normal Adjust Gap (&lt;14mmol/L)</th>
<th>Increased Acid Gap</th>
<th>Increased Acid Gap</th>
<th>Increased Acid Gap</th>
<th>Increased Acid Gap</th>
<th>Increased Acid Gap</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HCO₃ Loss</td>
<td>Hyperlostatic</td>
<td>Hyperkalemic</td>
<td>Hypercloriduric</td>
<td>Hyperparathyroid</td>
</tr>
<tr>
<td>1.</td>
<td>Gastric intestinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 10: Metabolic Acidosis
<table>
<thead>
<tr>
<th>ORAL</th>
<th>Route</th>
<th>Dose</th>
<th>Onset</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>PO</td>
<td>6.25mg</td>
<td>15 minutes</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>PO</td>
<td>10 - 20mg</td>
<td>15 minutes</td>
<td></td>
</tr>
<tr>
<td>Prazosin</td>
<td>PO</td>
<td>0.5 - 2mg</td>
<td>15 - 30 minutes</td>
<td>May cause first dose hypertension especially in elderly patients</td>
</tr>
<tr>
<td>Labetalol</td>
<td>PO</td>
<td>200mg</td>
<td>2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PARENTERAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td>IV, IM, SC</td>
<td>75µg bolus q3h</td>
<td>10 minutes</td>
<td>Initial pressor phase may occur</td>
</tr>
<tr>
<td>Labetalol</td>
<td>IV</td>
<td>20mg bolus</td>
<td>5 minutes</td>
<td>Rpt q10min, max 80mg</td>
</tr>
<tr>
<td>Hyralazine</td>
<td>IV</td>
<td>2mg/min infusion</td>
<td>10 - 20 minutes</td>
<td>Rpt every 20 minutes if necessary</td>
</tr>
<tr>
<td>GTN</td>
<td>IV</td>
<td>5 - 10µg/min (infusion)</td>
<td>1 - 2 minutes</td>
<td>May be beneficial if ischaemic CCF</td>
</tr>
<tr>
<td>Sodium Nitroprusside</td>
<td>IV</td>
<td>1 - 6µg/min (infusion)</td>
<td>secords</td>
<td>Extremely potent vasodilator</td>
</tr>
</tbody>
</table>