Acute renal failure
5% hospitalised patients
20% ITU patients
Defined as a rapid reduction on renal function over hours to days, with resultant impaired excretion of nitrogenous waste products. May be associated with oliguria
Classified as pre-renal, renal (intrinsic) or post-renal:

Pre-renal (50-70%)
Pump failure
  MI
  Arrhythmia
  LVF
  Pericardial effusion
  Cardiomyopathy
Volume depletion
  Dehydration
  Haemorrhage
  Burns
  Gut losses (vomiting, fistula, diarrhoea)
  Sepsis
  Sequestration (pancreatitis, crush injury)
  Renal losses (overdiuresis)
  Hepatorenal syndrome (splanchnic vasodilatation)

Pre-renal causes exacerbation by ACE inhibitors and NSAIDS.
  ACE inhibitors – impair AT2 production, leading to efferent arteriolar vasodilatation and reduced GFR
  NSAIDS – impair cyclooxygenase inhibiting production of afferent vasodilatory eicosanoids

Renal (20-30%)
  Acute tubular necrosis (see below)
  Acute glomerulonephritis
    Type 1 – anti-GBM antibodies (Goodpasture’s disease)
    Type 2 – Immune complex deposition (SLE etc)
    Type 3 – ANCA positive (Wegeners’ granulomatosis)
  Acute interstitial nephritis
  Drugs
    NSAIDs
    Antibiotics (penicillins, cephs, cipro, sulphonamides)
  Infections
    Streptococcus
    Legionella
    Viruses

  Glomerulonephritis = proteinuria, haematuria and red cell casts
  Rapidly progressive GN characterized by disease which produces extensive extracapillary proliferation (crescents) or necrosis.
AIN characteristically associated with sterile pyuria, white cell casts, eosinophiluria, and eosinophilia (up to 75%). Rash present in 25%. Typically occurs 3-5 days after drug administration. Diagnosis = renal biopsy. Rx = drug cessation. Usually resolution in 3-7 days.

**Post-renal** (10%)
Obstructed anatomic or functioning solitary kidney
- Stone
- Tumour
- Clot
- Sloughed papilla
- Stricture

Bilateral ureteric obstruction
- RPF
- Retroperitoneal tumour or lymphadenopathy
- Cervical tumour
- Bladder tumour
- BPH with ureteric orifice distortion/obstruction

Chronic urinary retention
- BPH
- Bladder neck stenosis
- Neuropathic bladder
- Blocked catheter

Urinary fistula (urea and creatinine reabsorption)

**Urinary findings in acute renal failure**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Urinalysis</th>
<th>Urinary [Na]</th>
<th>Urine: plasma Cr</th>
<th>Fractional Na or RFI</th>
<th>Osmolality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-renal</td>
<td>Hyaline casts or normal</td>
<td>&lt;20</td>
<td>&gt;30</td>
<td>&lt;1</td>
<td>&gt;500</td>
</tr>
<tr>
<td>RPAN</td>
<td>Red cell casts, RBCs, proteinuria</td>
<td>&lt;20</td>
<td>&gt;30</td>
<td>&lt;1</td>
<td>&gt;500</td>
</tr>
<tr>
<td>ATN</td>
<td>Granular casts, tubular cells</td>
<td>&gt;40</td>
<td>&lt;20</td>
<td>&gt;1</td>
<td>&lt;400</td>
</tr>
<tr>
<td>AIN</td>
<td>White cell casts, WBCs, eosinophils</td>
<td>&gt;40</td>
<td>&lt;20</td>
<td>&gt;1</td>
<td>&lt;400</td>
</tr>
</tbody>
</table>

NB. Urea:creatinine ratio high in pre-renal failure and low in intrinsic renal disease
Acute tubular necrosis
Commonest cause of renal failure in hospital setting
Renal hypoperfusion and ischaemia commonest cause of ATN; also due to endogenous/exogenous nephrotoxins
Endogenous nephrotoxins (Few)
- Pigment nephropathy: myoglobin (rhabdo in extended lithotomy)
  haemoglobin
- Crystal nephropathy: uric acid, calcium oxalate
- Tumour lysis syndrome
Exogenous nephrotoxins (Many – commonest below)
- Contrast material
- Antibiotics (aminoglycosides and amphotericin B)
- Chemotherapeutic agents
- NSAIDs
- ACE inhibitors
Natural history
- Oliguric phase*: <24 hours - 3 weeks
  Typically 150-300 ml/day
- Diuretic phase*: SCr often continues to rise for 24-48 hours
  Severe polyuria rare
  25% of deaths seen in this phase
- Recovery phase: GFR resolution at 3 months
  *Oliguria < 400ml/day
  *Polyuria >3L day
Pathophysiology
Renal failure

Renal ischaemia = depletion of ATP = AMP accumulation = AMP metabolism to hypoxanthine, adenine and inositol (Hypoxanthine important substrate for oxygen free radical production during reperfusion). Loss of ATP results in myriad changes, the most important are seen above.

Clinical presentation and management of acute renal failure

Diagnosis

History
Clinical examination
   Careful assessment of fluid status (JVP, failure, postural BP)
   Abdominal examination (?bladder)
   Rashes
Chart review
   Hypotensive episodes (ward chart or theatre record)
   Drug frequency and dosage
Urinalysis
   See above
   Abdominal ultrasonography

Complications

Fluid overload
Electrolyte abn.
Uraemia
   a. Bleeding, anaemia
   b. Pleuritis, pulmonary oedema
   c. Pericarditis, cardiomyopathy
   d. Encephalopathy, confusion, fits, peripheral neuropathy
   g. N+V, diarrhea, GI bleed
   h. Impaired granulocyte + lymphocyte function

Prognosis

![Diagram of Acute Renal Failure Prognosis]

- Death 50%
- 25% Complete Recovery
- 20% Incomplete Recovery
- 5% No Recovery
- 15% Function Stable
- 5% Function Regresses
Management

Three principles;
- Identify and remove any precipitant
- Provide supportive therapy
- Prevent complications

Conservative medical management

*Fluid Balance*
Carefully monitor intake/output and weights.
Restrict fluids.

*Electrolytes and Acid-Base Balance*
Prevent and treat hyperkalemia.
Avoid hyponatremia.
Keep serum bicarbonate > 15 mEq/L.
Minimize hyperphosphatemia.
Treat hypocalcemia only if symptomatic or if intravenous bicarbonate is required.

*Uremia and Nutrition*
Administer protein (1.0–1.8 g/kg/day) and maintain caloric intake; consider forms of nutritional support.
Keep carbohydrate intake at least 100 g/day to minimize ketosis and endogenous protein catabolism.

*Drugs*
Review all medications.
Stop magnesium-containing medications.
Adjust dosage for renal failure; readjust with improvement of glomerular filtration rate.

Treatment of hyperkalaemia

ECG monitoring > 6mmol/l
IV injection 10ml 10% calcium gluconate lasts 30-60 mins
Inhalation of 5mg salbutamol nebuliser lasts 30-60mins
10U insulin in 50ml 20% dextrose lasts ~6 hrs
Calcium resonium 15g tds lasts 6-8 hrs

Dialysis

Indications for dialysis*
- Fluid overload unresponsive to diuretics
- Severe hyperkalaemia (K > 6.5 mmol/l)
- Severe metabolic acidosis (pH < 7.1)
- Uraemic symptoms (>30 mmol/l)
- Drug overdose with dialyzable toxin

* Vary from department to department. Values taken from Bellomo 1998 (ITU) dialysis-dependent renal injury reported due to hypotension and complement activation
CVVH associated with the least fluid shifts cf. HD or PD. – thus used in critical care setting
Conversion from oliguric to non-oliguric ARF

Controversial

Limited evidence that associated with better outcome, but ‘creates space’ allowing for easier administration of parenteral nutrition, drugs and fluids

Uncontrolled studies suggest that patients who respond to mannitol, frusemide or dopamine by producing a diuresis do better (Consentino 1995), but may simply reflect less severe disease from outset.

Loop diuretics

Flushes out obstructing casts and debris; reduces work of TALH

No evidence of benefit in terms of recovery, dialysis or death in placebo controlled RCTs (Shilliday 1997; Uchino 2004)

No evidence for increased mortality (BEST data; Uchino 2004)

Mannitol

Flushes tubules; reduces hypoxic cell swelling; free-radical scavenger

Limited evidence in animal studies; appears to reduce ischaemic insult if given immediately before clamping of renal artery at time of partial nephrectomy/renal transplant (animal studies only)

Dopamine

Renal dose 0.4 – 2.0 ug.kg/min

Selective renal vasodilation, natriuresis and increased RBF (dopamine 1 receptors)

One PC-RCT showed no evidence for benefit (Belloma 2000)

Also a/w dopamine 2 receptor (CNS), alpha adrenergic (vasoconstriction) and beta-adrenergic (increased cardiac contractility) side effects, leading in some cases to severe complications in critically ill

New selective DA-1 agonist (fenoldopam) shows promise in animal studies but has not been shown to be effective in preventing contrast induced nephropathy (Stone 2003)

ANP

Renal vasodilation, increased RBF

Experimental drug

One large PC-RCT showed no overall benefit but did improve outcome in a subset of patients with oliguric ATN (Rahman 1994)

Prevention of acute renal failure

Typically in contrast-induced nephrotoxicity

High risk patients

Elderly

Diabetes

Pre-existing renal failure

Evidence

Intravenous hydration better than none (Solomon 2004)

No evidence for additional benefit of diuretics

Non-ionic contrast better than ionic contrast media (Rudnick 1995)

? N-acetylcysteine

600mg bd for 48 hours pre-treatment
Conflicting evidence from metaanalyses (Alonso 2004; Kshirsagar 2004)
However cheap, non-toxic and might work – often given
Sodium bicarbonate
Protective vs. N saline when given 1 hr pre-Ix (Merten 2004)
Chronic Renal Failure

Major impact on life expectancy: in dialysis patients;
22% die in first year
50% die within 3 yrs
67% die within 5 yrs

Primary cause of death due to cardiovascular disease; next infective complications

Complications of renal failure

<table>
<thead>
<tr>
<th>Complication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>low erythropoietin</td>
</tr>
<tr>
<td>Hypertension</td>
<td>sodium and water accumulation</td>
</tr>
<tr>
<td>Uraemia</td>
<td>peripheral neuropathy</td>
</tr>
<tr>
<td>Pleurisy and pericarditis</td>
<td>Cardiomyopathy</td>
</tr>
<tr>
<td>Renal osteodystrophy</td>
<td>reduced 1-alpha hydroxylation of vitamin D and reduced phosphate excretion = secondary hyperPTHism. Bone demineralization leads to lytic areas and #. Elevated calcium phosphate causes heterotopic calcification. Tertiary hyperPTHism may occur.</td>
</tr>
<tr>
<td>Proteinuria*</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td></td>
</tr>
<tr>
<td>Malnutrition</td>
<td></td>
</tr>
<tr>
<td>Impaired fertility</td>
<td>anovulation, ED, impaired spermatogenesis</td>
</tr>
<tr>
<td>Reduced libido</td>
<td></td>
</tr>
<tr>
<td>Pregnancy complication</td>
<td>increased preterm fetal loss (up to 16% in those with creat &lt; 180 umol/l; more for higher values) Increased likelihood of dialysis requirement</td>
</tr>
</tbody>
</table>

*Proteinuria

Degree of proteinuria predicts prognosis in patients with CKD
Some people report CKD levels with suffix ‘p’ if significant proteinuria
Protein/creatinine ratio or albumin/creatinine ratio
Protein/creatinine ratio
100 = 1 g protein over 24 hours
300 = 3 g protein over 24 hours = nephrotic range
PCR not reliable if UTI, orthostatic, fever, exercise and menstruation
Renal failure

Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Renal damage with normal GFR</th>
<th>Renal damage with mildly impaired GFR</th>
<th>Renal damage with moderately impaired GFR</th>
<th>Renal damage with severely impaired GFR</th>
<th>Established ESRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt; 90 ml/min</td>
<td>&lt; 90 ml/min</td>
<td>&lt; 60 ml/min</td>
<td>&lt; 30 ml/min</td>
<td>&lt; 15 ml/min</td>
</tr>
<tr>
<td>2</td>
<td>Renal damage with mildly impaired GFR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Renal damage with moderately impaired GFR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Renal damage with severely impaired GFR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Established ESRF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Management

NB. EPO ineffective in patients with inadequate iron stores. Oral supplementation generally does raise iron levels enough? low transferring. Therefore IV iron supplementation often required

<table>
<thead>
<tr>
<th>Focus Area</th>
<th>Goal</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure control</td>
<td>&lt;130/80 if proteinuria &lt; 1 g/day</td>
<td>Angiotensin-converting enzyme inhibitor</td>
</tr>
<tr>
<td>Reduction in proteinuria</td>
<td>&lt;0.5 g/day</td>
<td>Angiotensin-converting enzyme inhibitor</td>
</tr>
<tr>
<td>Glycemic control</td>
<td>HbA1C &lt; 7%</td>
<td>Oral hypoglycemic agents</td>
</tr>
<tr>
<td>Dietary protein restriction</td>
<td>0.6 to 0.8 g/kg/day</td>
<td>Dietary consult</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>Low-density lipoprotein level ≥ 70 mg/dL</td>
<td>Statin; ni</td>
</tr>
<tr>
<td>Anemia management</td>
<td>Hemoglobin &gt; 12 g/dL</td>
<td>Erythropoietin</td>
</tr>
<tr>
<td>Calcium × phosphorus product</td>
<td>&lt;4.5 mmol/L</td>
<td>Vitamin D supplementation</td>
</tr>
<tr>
<td>Calcium × phosphorus product</td>
<td>&lt;65 mg/dL</td>
<td>Use of dietary phosphorus restriction</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&lt;150 mg/dL</td>
<td>Phosphate binders</td>
</tr>
</tbody>
</table>

Chronic renal replacement therapy

Typically indicated by creatinine clearance 10ml/min
HD, CAPD, renal transplantation
USA 60% HD; 30% functioning renal transplant; 10% CAPD
Complications

HD thrombosis, vascular access problems
CAPD catheter problems, peritonitis, constipation, poor compliance
Transplant see chapter on renal transplantation
Renal failure

Filtration AND diffusion across a semi-permeable membrane. Usually over 4 hours. Associated with relatively high fluid shifts. Cardiac function must be reasonable to accommodate these. Typically 4-5 hours.

Figure 10-5 Haemodialysis

Filtration only. Largely historical. Superceded by haemodiafiltration

Figure 10-7b VenoVenous Haemofiltration

Figure 10-8 Haemodiafiltration
Typically filtration AND fluid replacement. Runs continuously. Takes much longer than HD, but better tolerated cardiovascularly. Therefore useful in ITU and in CVS patients. Also has larger pore size – therefore may be suitable for patients with amyloidosis.

**CAPD**
Continuous ambulatory dialysis
Usually 2L bags of Dextrose into abdomen
Osmotic gradient across peritoneum
Need to get waste products out of peritoneum before dextrose absorbed and osmotic gradient reverses – different concentrations of dextrose and dwell times
- Weak (yellow) 1.36% glucose
- Medium (green) 2.27% glucose
- Strong (orange) 3.86% glucose
- Amino-acids (blue) Glucose-sparing (diabetics)
- Icodextrin (purple) Long-acting HMW molecule

Overnight bag
Common prescription = 3 yellow and overnight icodextrin

**Complications**
- Peritonitis
- Constipation
- Hernias
- Catheter complications
- Poor compliance

**Haemodialysis access**
Permanent
- Fistulae
  - Radiocephalic
  - Brachiocephalic
  - Brachiobasilic
Grafts
Tunneled lines
- Subclavian (Hickmann line)
Temporary lines
- Femoral
- Jugular

**Complications of fistulae**
- Failure
- Infection
- Thrombosis
- Steal syndrome

---

**Chronic kidney disease (CKD)**
CKD 1: GFR >90 ml/min/1.73m²
CKD 2: GFR 60–90 ml/min/1.73m²
CKD 3: GFR 30–60 ml/min/1.73m²
CKD 4: GFR 15–30 ml/min/1.73m²
CKD 5: GFR <15 ml/min/1.73m² and/or peritoneal or haemodialysis
Renal failure

Recent modification - 3 subdivided into 3a and 3b

<table>
<thead>
<tr>
<th></th>
<th>&lt;br&gt;</th>
<th>ml/min/1.73</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;90</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60-90</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>45-59</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>30-44</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td></td>
</tr>
</tbody>
</table>