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
  - Arrythmia
  - 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

Cause	Urinalysis	Urinary [Na]	Urine: plasma Cr	Fractional Na or RFI	Osmolality
Pre-renal	Hyaline casts or normal	<20	>30	<1	>500
RPGN	Red cell casts, RBCs, proteinuria	<20	>30	<1	>500
ATN	Granular casts, tubular cells	>40	<20	>1	<400
AIN	White cell casts, WBCs, eosinophils	>40	<20	>1	<400

NB. Urea:creatinine ratio high in pre-renal failure and low in intrinsic renal disease

$$\text{Fractional Excretion of Sodium } (FE_{Na}) = \frac{\frac{U_{Na} \times V}{U_{creat} \times V}}{P_{creat}} \times 100\%$$

$$\text{Renal Failure Index } (RFI) = \frac{U_{Na} \times P_{creat}}{U_{creat}}$$

Acute tubular necrosis

Commonest cause of renal failure in hospital setting

Renal hypoperfusion and ischaemia commonest cause of ATN; also due to endogenous/exogenous nepohrotoxins

Endogenous nephrotoxins (Few)

- Pigment nephropathy — myoglobin (rhabdo in extended lithotomy) haemogobin
- 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

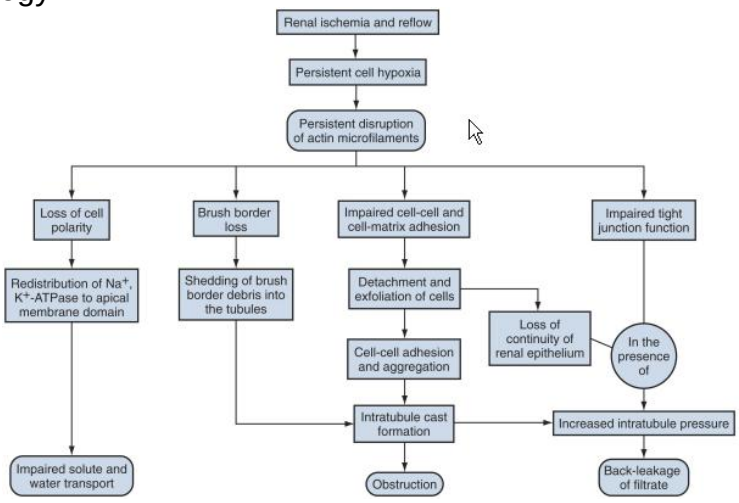
Natural history

- 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 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

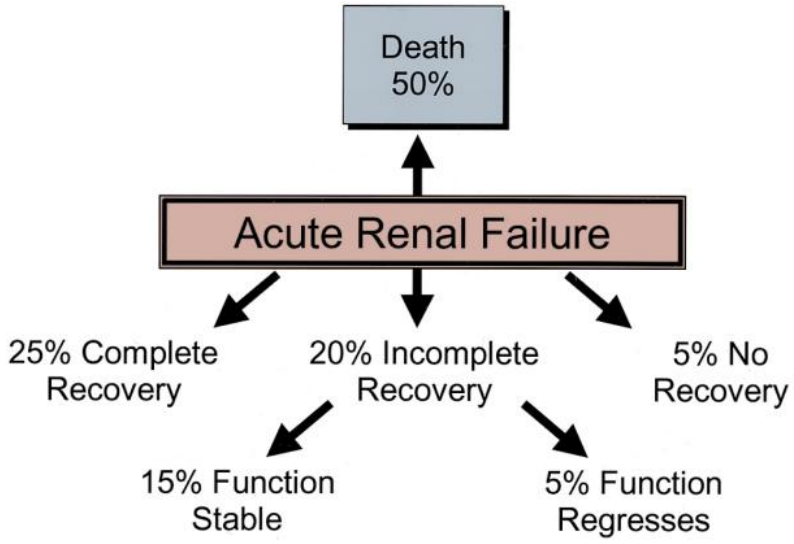
Diagnosis

- 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	JVP, hypertension, pulmonary oedema	
Electrolyte abn.	Low	sodium and calcium
	High	K, Mg, phosphate, acid (urate, H+)
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



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 sever 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 contast 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

Cause and Frequency of End-stage Renal Disease

ADULT		PEDIATRIC	
Diabetes	34.2%	Glomerulonephritis	37.6%
Hypertension	29.4%	Congenital/other hereditary diseases	19.1%
Glomerulonephritis	14.2%	Collagen vascular diseases	9.9%
Cystic kidney diseases	3.4%	Obstructive nephropathy	6%
Interstitial nephritis	3.4%	Cystic kidney diseases	4.3%
Obstructive nephropathy	2.3%	Interstitial nephritis	4.2%
Collagen vascular diseases	2.2%	Hypertension	4.2%
Malignancies	1.3%	Diabetes	1.4%
		Malignancies	0.4%

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

Anaemia	low erythropoietin
Hypertension	sodium and water accumulation
Uraemia	peripheral neuropathy Pleurisy and pericarditis Cardiomyopathy
Renal osteodystrophy	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.
Proteinuria*	
Hyperlipidaemia	
Malnutrition	
Impaired fertility	anovulation, ED, impaired spermatogenesis
Reduced libido	
Pregnancy complication	increased preterm fetal loss (up to 16% in those with creat < 180 umol/l; more for higher values) Increased likelihood of dialysis requirement

*Proteinuria

- Degree of proteinuria predicts prognosis in patients with CKD
- Some people report CKD levels with suffix ‘p’ if significant proteinuria
- Protein/creatinine ration 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

Classification

Stage 1	Renal damage with normal GFR	**> 90 ml/min**
Stage 2	Renal damage with mildly impaired GFR	**< 90 ml/min**
Stage 3	Renal damage with moderately impaired GFR	**< 60 ml/min**
Stage 4	Renal damage with severely impaired GFR	**< 30ml/min**
Stage 5	Established ESRF	**< 15 ml/min**

Management

Focus Area	*Goal*	*Treatment*
Blood pressure control	<130/80 if proteinuria < 1 g/day	Angiotensin-converting enzyme inhibitor
	<125/75 if proteinuria > 1 g/day	Angiotensin receptor blocker
		Salt restriction
		Diuresis
Reduction in proteinuria	<0.5 g/day	Angiotensin-converting enzyme inhibitor
		Angiotensin receptor blocker
		? Aldosterone blockade
Glycemic control	HbA_{1C} < 7%	Oral hypoglycemic agents
		Diet
		Insulin
Dietary protein restriction	0.6 to 0.8 g/kg/d [*]	Dietary consult
Lipid lowering	Low-density lipoprotein level ≥ 70 mg/dL [†]	Statin [†] [‡]
		Triglyceride-lowering agent
Anemia management	Hemoglobin > 12 g/dL	Erythropoietin
		Iron
Lifestyle modifications	Ideal body weight [*]	Weight loss program (dietary counseling, su
	Smoking cessation	Antidepressants
	Exercise three times per week	
	Depression modification	
Calcium × phosphorus product	<4.5 mmol/L	Vitamin D supplementation
	<55 mg/dL	Use of dietary phosphorus restriction
	Phosphorus < 5.5 mg/dL (1.78 mmol)	Phosphate binders
	Intact parathyroid hormone level of 70 to 110 pg/mL (CKD stage 4)	
	30–70 pg/mL (CKD stage 3)	
	25(OH)vitamin D > 30 ng/mL	

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

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

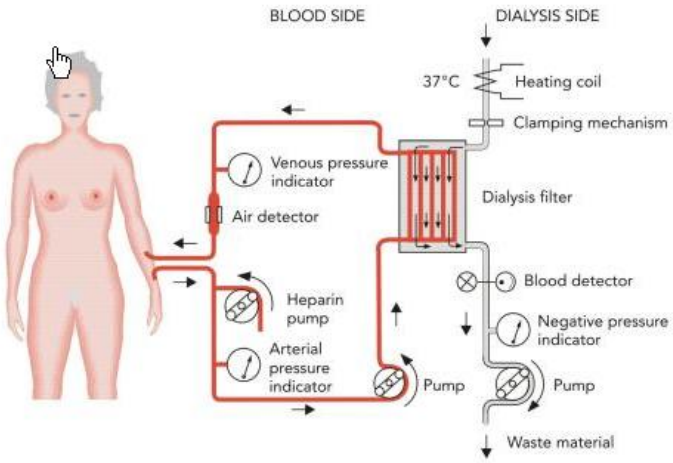


Figure 10-5 Haemodialysis

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.

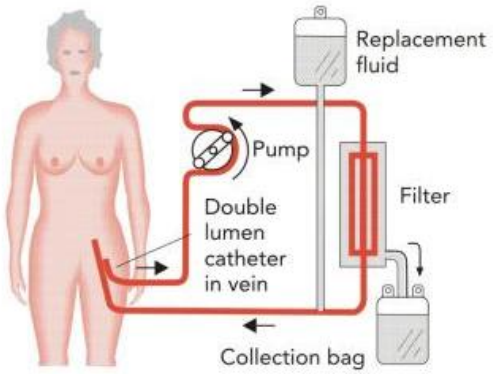


Figure 10-7b VenoVenous Haemofiltration

Filtration only. Largely historical. Superceded by haemodiafiltration

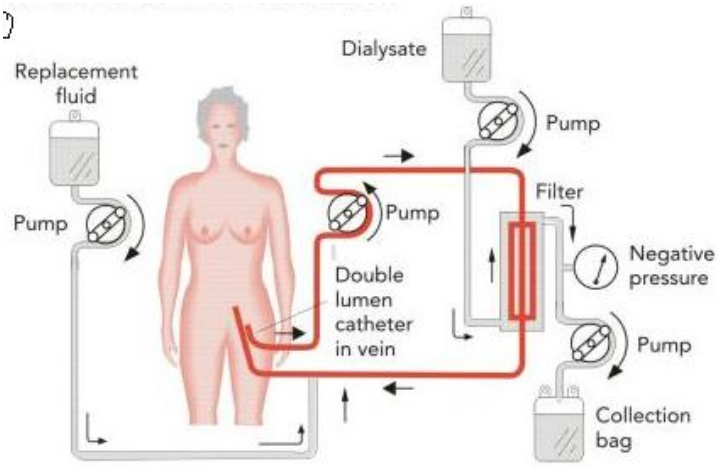


Figure 10-8 Haemodiafiltration

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

<u>Haemodialysis access</u>

Permanent
- Fistulae
  - Radiocephalic
  - Brachiocephalic
  - Brachiobasilic
- Grafts

Tunnelled lines
- Subclavian (Hickmann line)

Temporary lines
- Femoral
- Jugular

<u>Complications of fistulae</u>
- Failure
- Infection
- Thrombosis
- Steal syndrome

Chronic kidney disease (CKD)

CKD 1: GFR >90 ml/min/1.73m^2
CKD 2: GFR 60–90 ml/min/1.73m^2
CKD 3: GFR 30–60 ml/min/1.73m^2
CKD 4: GFR 15–30 ml/min/1.73m^2
CKD 5: GFR <15 ml/min/1.73m^2 and/or peritoneal or haemodialysis

Recent modification - 3 subdivided into 3a and 3b

1	>90	ml/min/1.73
2	60-90	ml/min/1.73
3a	45-59	ml/min/1.73
3b	30-44	ml/min/1.73
4	15-29	ml/min/1.73
5	<15	ml/min/1.73