

Manual of Nephrology

Drug Therapy and Therapeutic Protocols in Renal Diseases

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*Manual of Nephrology:
Drug Therapy and Therapeutic Protocols in Renal Diseases*

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DISCLAIMER

This manual contains protocols and guidance documents assembled by the authors during many years of clinical experience in nephrology. Many are not evidence-based but we have found them useful and hope that others will do likewise. All treatments must remain at the discretion of the physician responsible for the patient's care and we can accept no responsibility for the outcomes.

The recommendations were made on the basis of clinical trials wherever possible. In the absence of relevant clinical trials, we used evidence available or our personal experience.

Our aim was to provide a manual for the treatment of the most frequent kidney diseases or disorders related to the practice of Nephrology. The information may be of use to nephrologists, general internists, general practitioners or medical students.

For more comprehensive discussions readers are referred to the more extensive textbooks, some of them were cited in the references.

GLOSSARY, ABBREVIATIONS

- ACEI: angiotensin converting enzyme inhibitor
AF: atrial fibrillation
APD: automated peritoneal dialysis
APTT: activated partial thromboplastin time
AIIRA: angiotensin II receptor antagonist
ARF: acute renal failure
BD: twice daily
BSA: body surface area
CAPD: continuous ambulatory peritoneal dialysis
COPD: chronic obstructive pulmonary disease
COX: cyclo-oxygenase
CRF: chronic renal failure
CVP: central venous pressure
D: day
DNA: deoxyribonucleic acid
DVT: deep vein thrombosis
FBC: full blood count
FFP: fresh frozen plasma
HD: haemodialysis
IM: intramuscular
INR: international normalised ratio
IP: intra-peritoneal
IV: intravenous
LFTs: liver function tests
MI: myocardial infarction
MRSA: methicillin resistant staphylococcus aureus
NSAID: non-steroidal anti-inflammatory drug
OD: once daily
PCWP: pulmonary capillary wedge pressure
PD: peritoneal dialysis

PE: pulmonary embolism
PO: per os (oral administration)
PR: per rectum
PT: prothrombin time
QDS: four times per day
RF: renal failure
RI: renal insufficiency
rHuEpo: recombinant human erythropoietin
SC: subcutaneous
TPN: total parenteral nutrition
TDS: three times per day
U: unit(s)

ACIDOSIS (METABOLIC ACIDOSIS IN CHRONIC RENAL FAILURE, CRF)

Treatment of metabolic acidosis in CRF with sodium bicarbonate is usually well tolerated, i.e. no increase in sodium retention, no oedema and no hypertension. The aim of the treatment is to maintain plasma bicarbonate > 22 mmol/l. The amount of administered sodium bicarbonate should be appropriate to the bicarbonate deficit and it can be administered as:

- Intravenously (unless fluid overload is also present), 1.26% isotonic sodium bicarbonate 500 ml or 1000 ml IV infusion (give an amount appropriate to the bicarbonate deficit).
- Orally, in chronic metabolic acidosis sodium bicarbonate can be given as 600 mg capsules or 500 mg tablets up to 3 g/d PO
- The best method to correct metabolic acidosis in patients on dialysis is to increase dialysate bicarbonate concentration up to 40 mmol/l
- In an emergency, 8.4% sodium bicarbonate solution (50 mmol) 50 ml IV over 30 min or 1 ml/kg body weight can be used, but 1.26% sodium bicarbonate is preferable because of the danger of overdosing.

ACUTELY DISTURBED PATIENT

- Haloperidol may be given orally in a range of 1.5 to 3 mg bd to tds. The IM or IV dose is 2 to 10 mg depending on the clinical manifestations and should be adjusted according to response.
- Diazepam 2 to 5 mg orally (preferably) is the alternative; it can be given parenterally up to 10 mg IM or as slow IV infusion. Parenteral use must be with caution as respiratory depression can occur. The reversal agent Flumazenil should be available.

ACUTE RENAL FAILURE (ARF)

The aetiology should be sought and if possible identified in order to apply specific treatment for prerenal hypovolemia, specific parenchymal renal disease or post renal obstruction. Ultrasound scan of kidneys and bladder may exclude acute or chronic renal failure or post renal obstruction. If intrinsic renal parenchymal disease is suspected as a cause of ARF and if the diagnosis of acute tubular necrosis is not clear from clinical presentation, renal biopsy should be done (may be urgent, and urgent transfer to a specialist renal unit should be considered). Heavy proteinuria and/or haematuria on dipstick testing of the urine suggest glomerular disease. Urgent serological tests for systemic diseases that can present with ARF should be undertaken (eg anti-neutrophil cytoplasm autoantibody, ANCA, for small vessel vasculitis; anti-glomerular basement membrane antibodies for Goodpasture's disease; anti-double stranded DNA antibodies for systemic lupus erythematosus; serum complement C3 and C4 for immune complex disease or complement deficiency). However, if clinical features are suggestive, specialist renal advice should be sought without waiting for results of these laboratory investigations.

Pre-renal ARF requires aggressive correction of hypovolaemia with fluid replacement. The volume of replacement fluid = previous 24 h urine output + estimated loss of fluid by diarrhoea, vomiting etc. + insensible loss (500 ml, more if febrile or in hot climate). Colloid or crystalloid solutions may be used to achieve normovolaemia confirmed by clinical signs and central venous pressure (CVP). The choice of replacement fluid should ideally be guided by information about the type(s) of fluid lost. Remember that loss of water alone is uncommon so that dextrose solutions alone are rarely adequate for replacement: some additional salt is usually required.

In patients with volume depletion begin with 500 mL of isotonic saline IV within 30 – 60 minutes. Repeat infusion of the same volume once or twice until urine output of 1 – 2 mL/min is achieved and then give IV fluid on basis of urine output. Measure central venous pressure CVP (if possible).

Diuretics do not prevent acute renal failure and the role of dopamine is very controversial. In the early phase of ARF, assuming

hypovolemia has been corrected; an oliguric patient may be given one of the diuretics:

- Frusemide bolus 40–250 mg slowly IV or 10-40 mg/hour IV infusion. This may increase urine volume to a useful extent but should not be repeated if it fails to do so.
- Bumetanide 1 mg PO/IV or
- Torasemide 5-40 mg PO.

Catheterization for assessment of hourly urine output is necessary. Take out catheter as soon as oliguria confirmed. The catheter is a source of infection.

Renal dose of dopamine 2–5 µg/kg/min IV is still controversial.

Pulmonary oedema, acidosis and/or hyperkalaemia not responsive to conservative treatment may require dialysis (see also “Hyperkalaemia”). Dialysis options are:

- One of many varieties of continuous renal replacement therapies
- Haemodialysis (daily or alternate day)
- Peritoneal dialysis

Choice of treatment is dependent upon various factors including availability, expertise of staff, haemodynamic stability of the patient, vascular access; whether the primary need is fluid removal or solute removal or both, etc.

Treatment of specific metabolic disorders are described elsewhere (See hyperkalemia, metabolic acidosis etc.).

Avoid nephrotoxic drugs: NSAIDs, aminoglycosides, ACEI. Aminoglycoside antibiotics can be used if essential, but dosage and frequency of administration should be adjusted for loss of excretory renal capacity. As a general principle, loading doses should be as normal, but maintenance doses need to be smaller and/or less frequent.

If the cause of ARF is acute interstitial nephritis, any offending medication or therapy must be discontinued. Steroids have been used (with no controlled trials) either as pulse IV methylprednisolone 500–1000 mg/d for 3–4 days or short courses of prednisolone 60 mg od PO for 2 weeks with a rapid taper (See Interstitial nephritis).

Glomerulonephritis (GN) may be isolated or part of a systemic disease. Cellular casts and/or large numbers of dysmorphic red blood cells in the urinary sediment suggest GN. Renal biopsy is required to establish the nature of the glomerular lesion (see “Glomerulonephritis”).

Treatment of post renal ARF is relief of obstruction and the prognosis depends upon the cause of the obstruction and the duration of impaired urinary drainage. Bladder outflow obstruction can be relieved by urethral or suprapubic bladder catheterization, obstruction higher up the urinary tract may require percutaneous nephrostomy and/or ureteric stents.

Proper nutrition and diet high in protein and calories must be assured, orally if possible. Gastric or jejunal feeding tube or TPN may be required.

As for other patients requiring Intensive care, consider gastric protection with proton pump inhibitor omeprazole 10-40 mg daily PO or H₂ antagonist ranitidine 150 mg bd PO, or 50 mg bd IM or 50 mg diluted in 20 ml 5% Glucose or 0.9% saline IV slowly over 2 minutes. These may reduce the risk of gastrointestinal hemorrhage.

ADULT POLYCYSTIC KIDNEY DISEASE (APCKD)

Cyst drainage

Direct reduction of cyst size by percutaneous aspiration, aspiration with sclerosis, or surgical drainage has been effectively used to relieve severe or refractory pain; there is, however, no evidence that these measures improve renal function or delay the rate of disease progression.

Hypertension in APCKD patient

Patients with hypertension and APCKD generally respond well to ACE inhibitors. In addition to lowering systemic pressures, ACE inhibitor therapy also can reverse left ventricular hypertrophy. The aim of antihypertensive therapy should be to lower the blood pressure to 130-140/80-85 mm Hg, similar to that in patients with essential hypertension.

Pain in APCKD

NSAIDs (nonselective inhibitors of both COX-1 and COX-2 and selective COX-2 inhibitors) could be given for 3-5 days with good hydration, but this is controversial. Opiate analgesia may be required: start with mildest. Remember that opiate drugs and their metabolites accumulate in patients with impaired excretory renal function: this is a particular problem with pethidine, and to a lesser extent with codeine. Hydromorphone is a useful analgesic in patients with renal impairment.

Protein restriction

There are conflicting findings on the efficacy of a low protein diet (0.6 to 0.7 g/kg per day). At present, we do not recommend restriction of protein intake below 1 to 1.1 g/kg per day in patients with APCKD given the limited evidence of benefit.

Renal replacement therapy

Patients with APCKD who progress to end-stage renal disease require renal replacement therapy. In general, such patients have equivalent or perhaps better overall outcomes with any renal replacement therapy compared to non-APCKD patients. Patients are most commonly treated with hemodialysis or undergo renal transplantation. Peritoneal dialysis is less commonly performed. This is due in part to the reduced intraabdominal space available for effective peritoneal exchange in the presence of massively enlarged kidneys. Nevertheless, some centres have found that peritoneal dialysis is well tolerated and results in no specific difficulties in the patient with APCKD requiring renal replacement therapy. Some patients require pretransplant native nephrectomy to better accommodate the graft.

Urinary Tract Infection in APCKD

Patients with pyuria and positive urine cultures should be treated according to the result of antibiotic sensitivity testing. The most frequently used oral drugs are amoxicillin (250 or 500 mg tds PO); trimethoprim 200 mg bd PO (causes an artefactual rise in plasma creatinine due to inhibition of tubular secretion of creatinine); ciprofloxacin 250 or 500 mg bd PO. If parenteral antibiotic therapy is indicated an alternative is gentamicin single dose 180 mg od IM/IV over 3 min, followed by maintenance dose adjusted

according to renal function and regular measurement of gentamicin levels in blood. Treatment duration 10–14 days (see Urinary tract infections).

In complicated urinary tract infection (infected cyst) use antibiotics that penetrate cyst such as quinolones (ciprofloxacin 500 mg bd PO or 400 mg bd IV), trimethoprim (200 mg bd PO), co-trimoxazole (960 mg bd PO) or chloramphenicol 250 mg qds PO or 50 mg/kg/d IV). Chloramphenicol is reserved for treatment of life-threatening conditions.

If infection is due to streptococci or staphylococci use Vancomycin 1 g/d slow IV over 100 min, trough blood level should not be > 10 mg/dl; or Erythromycin 250 – 500 mg qds PO or 25 – 50 mg/kg/d either by continuous infusion or in divided doses every 6 h.

If infection is due to anaerobic microorganisms use Metronidazole 500 mg tds PO or in severe infection 500 mg tds IV.

Cyst infection needs treatment for at least 4–6 weeks. Surgical drainage is indicated if perinephric abscess develops.

Nephrectomy is indicated in patients with severe infection refractory to antibiotic therapy and also in some patients who will undergo renal transplantation to minimize recidivist infection during immunosuppressive therapy.

ANALGAEICS

Aspirin, enteric-coated aspirin, buffered aspirin: 75-300 mg up to 4 times/day.

In addition, low dose aspirin is often used for vascular protection (75 mg daily is convenient because of the availability of this tablet size as paediatric aspirin; even lower doses may be equally effective).

Avoid all NSAIDs when there is an increased risk of gastro-intestinal bleeding. In mild renal impairment use the lowest effective dose and monitor renal function, sodium and water retention. If used, the dosage is as follows:

Ibuprofen 1.2–2.4 g/day in 3-4 divided doses

Indomethacin 50 – 200 mg/day in 3-4 divided doses

Diclofenac (Voltarol) 75–120 mg/day in 3-4 divided doses

Others:

Paracetamol (acetaminophen) 1 g every 4-6 hours, max. 4 g daily
Co-dydramol 1-2 tablets every 4-6 hours, max. 8 tablets daily
Co-proxamol 2 tablets 3-4 times daily, max. 8 tablets daily
Co-codamol 30/500 1-2 tablets every 4 hours, max. 8 tablets daily
Codeine and its metabolites may accumulate in renal failure, so be aware of insidious onset of respiratory depression or other opiate adverse effects.
Tramadol 50 mg–100 mg, max 400 mg daily PO; 50 mg by IM or IV injection
Pethidine may accumulate in renal failure, therefore morphine is preferable. Morphine sulphate SC/IM injections 10 mg every 4 hours. For IV injection use $\frac{1}{2}$ of IM dose.
Morphine oral solutions: eg Oramorph 10 mg/5 ml. Morphine tablets: eg Sevredol tbl 10 mg every 4 hours.
Hydromorphone (Palladone) is particularly useful in patients with renal disease, including those on dialysis. Capsule sizes are 1.3 mg or 2.6 mg and the drug must be given at 4 hourly intervals. Dose can be escalated to achieve pain control.
Fentanyl patches (self-adhesive patches delivering transcutaneous drug) provide a convenient form of administration of continuous potent analgesic. Patches are available in a range of doses and typically last for 72 hours.

ANAPHYLACTIC SHOCK

Adrenaline (epinephrine) 1:1000, 0.3-0.5 ml IM is preferred route since absorption more reliable than via SC route. IV administration of adrenaline (epinephrine) 0.5–1 mL of 1:10,000 solution is reserved for dire emergencies. Adrenaline injection can be repeated every 5-10 minutes until recovered (according to pulse, BP, respiratory function).

Chlorpheniramine maleate (Piriton) 10 mg IM/IV
Hydrocortisone 200 mg IV. Dose can be repeated after 6 h.
Oxygen at 100% 12 L/hour
If patient is hypotensive/hypovolemic (BP<90 mm Hg) give IV infusion of 500 ml 0.9% saline or 500 ml colloid (eg Haemaccel) over 15 min.

ANTICOAGULATION

Many patients with renal disease are taking aspirin or anticoagulants and the general principles are similar to those in non-renal patients. Low molecular weight heparins should be used with caution in patients with impaired renal function.

Anticardiolipin antibodies

Patients with anticardiolipin antibodies who have a history of venous or arterial thrombosis should be anticoagulated for at least 12 months and preferably for life and/or the duration of antibody positivity.

Anticoagulation regimen before surgery

Risks associated with temporary cessation of anticoagulation depend upon the original reason for anticoagulation: risks are highest for patients with prosthetic heart valves in whom anticoagulation should be maintained, even at lower intensity, if possible. By contrast, anticoagulation for reasons associated with haemodialysis access patency can usually be temporarily interrupted without difficulty.

Where reversal of anticoagulation is deemed essential: if INR is 2-3, discontinue warfarin 4 days before surgery. Aim for INR less than 1.5 on the day of surgery. If one day before operation INR is >1.8 give 1 mg vitamin K SC and check INR 24 hours later. If INR is still high on the day of operation, give 3 units of fresh frozen plasma (FFP), it will have an effect that may last for 10 hours.

If patient is on IV heparin: stop heparin six hours before surgery. Delay heparin injections/infusions for 12 hours after surgery.

If patient was on warfarin, re-start warfarin as soon as possible after surgery. Administration of vitamin K renders patients more difficult to adequately re-anticoagulate so should be avoided if possible.

Heparin infusion

Check PT and APTT. Initiate therapy with 5000 u heparin IV over 5 minutes followed by heparin 1000 u/hr. Add 25,000 u heparin to 50 ml isotonic saline to have heparin 500 u/ml in a syringe pump. Start at 1000 units per hour (2 ml/h).

Check APTT 6 hours after starting heparin infusion or 6 hours after adjusting the dose. Aim for APTT ratio 1.8-2.5. Adjust the dose as follows:

<u>APTT ratio</u>	<u>Change rate u/h by</u>
5.1–7	– 500
4.1–5	– 300
3.1–4	– 100
2.6–3	– 50
1.5–2.5	0
1.2–1.4	+ 200
< 1.2	+ 400

– Means reduce the dose by....

+ Means increase the dose by....

Start warfarin the same day. Heparin therapy is overlapped with warfarin for a minimum of 5 days; heparin should be discontinued on 4th or 5th day provided that the INR is in therapeutic range (eg for venous thromboembolism INR 2.0-3.0).

Prophylactic anticoagulation

Routine prophylaxis for surgical/ medical patients: Unfractionated **heparin** SC 5000 u every 12 hours for 7 days or until patient is ambulant.

Low molecular weight heparins are as effective and safe as unfractionated heparin in the prevention of venous thromboembolism. The standard prophylactic regimen does not require monitoring. In severe renal impairment, the risk of bleeding during heparin treatment is increased and low molecular weight heparins are best avoided.

Enoxaparin (Clexane) subcutaneous injections for prophylaxis of DVT especially in *surgical patients*:

moderate risk: 20 mg (2000 units) approx. 2 hours before surgery then 20 mg (2000 units) every 24 hours for 7-10 days

high risk: 40 mg (4000 units) 12 hours before surgery then 40 mg (4000 units) every 24 hours for 7-10 days.

Prophylaxis of DVT in medical patients: 40 mg (4000 units) every 24 hours for at least 6 days until patient ambulant (max.14 days).

Deltaparin sodium (Fragmin) subcutaneous injections for *prophylaxis of DVT*:

moderate risk: 2500 units 1-2 hours before surgery, then 2500 units every 24 hours for 5-7 days

high risk: 2500 units 1-2 hours before surgery; then 2500 units twice daily (or 5000 units once daily).

Compression stockings and ambulation are basic measures that complement the medication.

Pulmonary embolism (PE) and deep vein thrombosis (DVT)

In addition to specific procedures: oxygen 100% (unless COPD) and pain relief (morphine 10 mg IV), anticoagulate with standard unfractionated heparin (see above) followed by warfarin.

Patients with a single episode of DVT or PE should receive warfarin for 6 months; those with recurrent thrombosis or embolism or atrial fibrillation may require prolonged therapy and in those with prosthetic heart valves or other intravascular device, lifelong therapy is normally indicated.

Warfarin dosage

Check baseline INR before starting warfarin therapy. If normal, a suggested initiation regimen is to give 10 mg warfarin daily for two consecutive days. Commence warfarin on day 0 (and give subsequent daily doses) at 17.00 h.

Check INR the following morning and adjust the doses of warfarin:

Day	INR	Dose (mg)	Maintenance (mg)
1	<1.4	10	
2	<1.8	10	
3	<2	10	6
	2	5	5.5
	2.5	4	4.5
	2.9	3	4
	3.3	2	3.5
	3.6	0.5	3
	4.1	0	*

* Miss dose, and give the following day 1 mg; if INR >4.5 miss two doses

The daily dose of warfarin should be adjusted according to the target INR:

<u>Condition</u>	<u>INR</u>
Prevention of DVT	2–3
Treatment of DVT or PE	2–3
AF	2–3
Acute MI	3–4.5
Mechanical prosthetic heart valve	3–4.9

The dose may be altered according to clinical circumstances.

Therapy for idiopathic venous thromboembolism typically includes a 5-to-10-day course of heparin followed by 3 to 12 months of oral anticoagulation therapy with full dose warfarin, with adjustment of dose to achieve an international normalized ratio (INR) between 2.0 and 3.0.

Reversal of anticoagulation is done in patients on warfarin who are undergoing surgical procedures. If INR>1.5 give 2 units of FFP (600 mL) IV over 1 hour plus vit K 1 mg IV (if INR>3 vit K 2 mg IV stat).

ANTIPHOSPHOLIPID ANTIBODY SYNDROME (APS)

Prophylaxis of recurrent arterial/venous thrombo-embolic events includes the following:

Prophylaxis of DVT

Aspirin + heparin or warfarin.

Aspirin 75–150 mg once a day

Target INR of 2.5–3.5 for all patients with APS treated with oral anticoagulants.

Most patients with definite APS and previous thrombosis should be treated to a target INR of 3.5. The exception could be individuals with only venous events and those at high risk of bleeding, who could be considered for lower intensities of anticoagulation.

Anticoagulate with warfarin indefinitely.

Warfarin is teratogenic and it should not be used in pregnant women.

Do not give anticoagulation if platelet count is less than $50 \times 10^9/l$.

Pregnancy in association with antiphospholipid antibodies

Warfarin is teratogenic! Heparin plus low dose aspirin is more effective than aspirin alone for achieving live birth among women with antiphospholipid antibodies.

Women with history of pregnancy loss, history of thrombotic events or high titre of IgG antiphospholipid antibodies may be treated with 5000 u of unfractionated heparin twice daily. Standard heparin may be substituted for low molecular weight heparin in the treatment of pregnant women with antiphospholipid antibody syndrome:

Deltaparin 5000 – 10000 u od SC + aspirin 75–100 mg od PO.

ASCITES

Salt restriction.

Furosemide 40–120 mg/24 hours + Spironolactone 100 mg/24 hours. Repeated large-volume paracentesis (4–6 litres) with albumin infusion. Six to 8 g of albumin/litre of ascitic fluid removed is administered intravenously during or after the procedure to prevent relative hypovolemia, which usually occurs 3–6 hours later.

ATRIAL FIBRILLATION (AF)

AF is common in patients with renal disease. Short episodes may occur in haemodialysis patients due to volume shifts. Sustained or paroxysmal AF can be managed similarly to non-renal patients with the exception that digoxin is renally excreted and the maintenance dose and frequency must be reduced.

In a patient who presents with AF and a rapid ventricular response rate, there needs to be an urgent assessment for underlying causes such as heart failure, pulmonary problems, hypertension, or hyperthyroidism. Treatment of these conditions may result in reversion to sinus rhythm.

Two standard approaches to converting AF to sinus rhythm are synchronized electrical DC cardioversion and pharmacological cardioversion.

DC cardioversion is indicated in patients who are haemodynamically unstable. The role for cardioversion depends

upon the duration of the arrhythmia as well as the presence of a reversible aetiological factor.

If the duration of the arrhythmia is 48 hours or less and there are no associated cardiac abnormalities (particularly mitral valve disease or significant left ventricular enlargement due to a cardiomyopathy), there is a low risk of systemic embolization and electrical or pharmacological cardioversion can be attempted after systemic heparinization. Anticoagulation is indicated for three to four weeks after cardioversion.

Patients who have been in AF for more than 48 hours should receive three to four weeks of warfarin prior to and after cardioversion with a target INR of 2.5 (range 2.0 to 3.0).

Medical control of AF and fast ventricular rate can be achieved with amiodarone, digoxin, calcium channel blocker, beta-blocker.

Amiodarone (300 mg in 5% dextrose IV over 20–120 minutes followed by 900 mg in 500 ml 5% dextrose over 24 hours, concomitantly oral 200 mg tds for week one, 200 mg bd for week two and maintenance 200 mg od) may be preferred in patients with a reduced left ventricular ejection fraction.

Digoxin is usually the preferred drug in patients with AF due to heart failure. Digoxin can also be used in patients who cannot take or who respond inadequately to beta-blockers or calcium channel blockers. The dose of digoxin: initiate with two doses of 0.5 mg PO 12 hours apart, followed by 0.25 mg 12 hourly for 2 days. Maintenance dose of digoxin is 0.0625–0.125 mg/day (reduce dose and/or frequency of administration in renal impairment).

In most other situations, a beta blocker or calcium channel blocker is preferred since, in the absence of heart failure, digoxin is less effective for rate control than beta blockers and calcium channel blockers, is less likely to control the ventricular rate during exercise (when vagal tone is low and sympathetic tone is high), has little or no ability to terminate the arrhythmia, and often does not slow the heart rate with recurrent AF.

Beta blockers (sotalol 40–80–160 mg 12 hourly or atenolol 50 mg od) and non-dihydropyridine calcium channel blockers (verapamil 40–120 mg bd PO or diltiazem 60 mg tds or diltiazem SR 60–90–120 mg bd PO) are also effective if heart failure or

hypotension is due to the rapid arrhythmia. NB Diltiazem interacts with calcineurin inhibitors (cyclosporin and tacrolimus) to cause raised cyclosporin/tacrolimus blood levels: in renal transplant recipients or other patients taking these drugs caution is required, plus increased frequency of measurement of blood levels.

Maintenance anticoagulation with warfarin is superior to aspirin. If aspirin is given the dose should be 75–300 mg/day PO.

BACTERIAL ENDOCARDITIS

Take multiple blood cultures before initiating antibiotic therapy if possible. “Blind” therapy: benzyl penicillin 1.2 g four hourly IV + gentamicin for 2 weeks followed by amoxicillin 1 g TDS for 2 weeks. Specific therapy according to the result of blood cultures. Gentamicin dose should be adjusted according to renal function and blood levels should be closely monitored. Renal toxicity can occur even if recommended therapeutic levels are not exceeded, especially if there is co-administration of loop diuretics.

BLADDER CATHETERIZATION (antibiotic prophylaxis)

Just before the intervention start prophylaxis with either: ciprofloxacin 250 mg bd PO for two days or co-trimoxazole (Septrin) 960 mg bd PO for two days.

BODY SURFACE AREA (BSA)

Appropriate dosage of some drugs used in patients with renal disease is calculated on the basis of body surface area

Body surface area = square root of [height (cm) X weight (kg)/3600]
Nowadays one can use medical calculators or internet site to simplify the calculation of BSA.

BOWEL PREPARATION IN RENAL PATIENTS

Problems with fluid load and risk of severe hyperphosphataemia make “conventional” bowel preparations, eg for colonoscopy, potentially hazardous in patients with renal disease, especially those on dialysis. Picolax (sodium picosulfate with magnesium citrate) is usually

effective. One sachet (10 mg), reconstituted in a cup of approximately 150 ml of water, is given 24 hours before procedure and a further sachet 6–8 hours later. Patients on a fluid restriction may need reassessment to compensate for fluid losses during Picolax treatment.

BRADYCARDIA

Stop beta-blockers.

Give atropine 500 µg IV (maximum 3 mg).

The patient may need transvenous pacing if bradycardia is persistent. In an emergency, IV injection of glucagon (50–150 micrograms/kg in 5% glucose) may be lifesaving. Precautions should be taken to protect the airway in case of vomiting.

CANDIDIASIS

Local treatment: nystatin 100,000 u/ml, 1 ml four times/day after food for 7 days, or continue therapy for 48 hours after lesions have resolved; amphotericin B lozenges 4–6 times/d. Amphotericin is preferable because it takes 30 min or so to suck the lozenges. Nystatin suspension can be used as a wash solution for false teeth.

For invasive or systemic candida infection use fluconazole as the least toxic but effective anti-fungal drug.

Mucosal candidiasis: fluconazole 50 mg/day for 14 days.

Oropharyngeal candidiasis: fluconazole day one 200 mg; then 100 mg/day for at least 14 days.

Oesophageal candidiasis: fluconazole day 200 mg on day 1; then 100 mg/day for a minimum of 21 days and for at least 14 days following resolution of symptoms.

Systemic candidiasis: fluconazole 6 mg/kg/d on first day then 3–6 mg/kg/d. For 70 kg patient this would be 400 mg PO or IV day 1, then 200 mg/daily PO or IV, continue treatment according to the response for at least 28 days.

NB Fluconazole interacts with calcineurin inhibitors (cyclosporin and tacrolimus) to cause raised cyclosporin/tacrolimus blood levels: in renal transplant recipients or other patients taking these drugs caution is required, plus increased frequency of measurement of blood levels.

Amphotericin B is the standard therapy for the treatment of severe, invasive or life-threatening systemic fungal infections. Method of administration: prepare IV infusion by dissolving amphotericin B in 5% dextrose to a final concentration 0.1 mg/mL. Give a test dose of 1 mg (10 mL of initial infusion) over 20–30 minutes, then 0.25 – 0.5 – 1.0 mg/kg (depending on the severity of infection) IV infusion over 4 to 6 hours.

The duration of therapy depends on many variables, but generally high risk patients should be treated for 10 – 14 days after disappearance of symptoms and after the last positive fungal blood culture.

Lipid (liposomal) formulations of amphotericin B are more effective and less toxic (but more expensive). Dose: Abelcet (Wyeth) 5 mg/ml, give as IV infusion, initial test dose 1 mg over 15 minutes, then 5 mg/kg daily for at least 14 days. AmBisome (NexStar) initial dose 1 mg over 10 minutes then 1 mg/kg daily as a single dose increased gradually if necessary to 3 mg/kg daily as a single dose.

Flucytosine could be used as an additional anti-fungal agent in combination with either amphotericin B or fluconazole for treatment of refractory infections. The dose of flucytosine is 25–50 mg/kg qds IV for up to 7 days.

Caspofungin is a new antifungal drug, with fungicidal activity (against Aspergillus and most Candida species). Administer as a single daily dose of either 50 or 70 mg in 200 ml 0.9% saline IV over 1-h period followed by an infusion of saline 200 ml over the next hour.

CAPD (CONTINUOUS AMBULATORY PERITONEAL DIALYSIS)

**Antibiotic prophylaxis before PD catheter insertion
(Tenckhoff catheter is most commonly used, this name tends to be used generically to mean any PD catheter)**

Vancomycin 1 g IV 12 h before the procedure and Cephalexin 0.5–1 g 3 h before the procedure

Bloody Peritoneal Dialysis (PD) fluid

Hemorrhage may be benign (retrograde menstruation, minor trauma) and will need treatment if associated with drainage problems (add heparin 500 u to each bag of CAPD fluid). More serious causes of bloody PD fluids are ruptured vessels and may require surgical exploration.

CAPD solutions

Dianeal: basic glucose/lactate based solution available in three different strengths of glucose: 1.36% (isotonic), 2.27% or 3.86%, getting more hypertonic as the % increases. Each of the three strengths are available in different volumes; the volumes frequently used are 0.5, 1, 1.5, 2, 2.5 and 3 litres.

Nutrineal: 1.1% amino acid solution. Isotonic in terms of its ultrafiltration ability. Used to increase serum albumin levels. A patient can have only one bag (2 L) per 24 hours. Patient must be adequately dialyzed before you start it as the serum urea will go up with the protein absorption. Also used for patients with diabetes mellitus to replace 1 bag a day to reduce sugar calorie load. Better biocompatibility than glucose fluid (Dianeal).

Extraneal: synonym Icodextrin 7.5%. This solution is used for sustained ultrafiltration to control fluid balance. Needs long dwell in usually 8–10 hours, but 6 hours as absolute minimum. Good for “high transporters” who retain fluid badly on long dwells otherwise. Good for patients with diabetes mellitus as can not absorb any glucose load since it is a glucose polymer and the molecule is too big to go through the membrane. If a patient is on insulin and already on CAPD and then a bag is swapped to Extraneal, you have to reduce the insulin that covers that dwell as there is then no glucose absorption where there was before. Only one bag per 24 hours (get maltose build up as a breakdown product).

Physoneal: bicarbonate based fluid in same strengths as Dianeal. Better biocompatibility as no GDP (glucose degradation products) from heat sterilizing as the bag is in 2 compartments until about to be run in to the patient. Also referred as AGE's (advanced glycosylation end products) which do the damage to the peritoneal membrane long term.

Catheter blockage or poor drainage of CAPD fluid

Check X – ray plain film of the abdomen to see whether the catheter is malpositioned.

If catheter is flipped in upper abdominal quadrants administer laxatives: senna 2–4 tbl od PO usually at night or lactulose 15 ml od PO. If the catheter does not flip to lower abdominal quadrant give more potent laxative eg sodium picosulfate one sachet of 10 mg od PO. Finally, if all these measures are without effect, and if there is an expertise - try various guide wire techniques. If all of these procedures fail, there may be a need for surgical repositioning, laparoscopic if possible.

If the blockage is due to fibrin use urokinase either 25,000 U in 2 ml saline, leave in the catheter for 2–4 hours or make up to 50 ml with isotonic saline and infuse into catheter via a pump at 2 ml/min for 24 h. Alternative is heparin 5,000 u plus urokinase 5,000 u made up to 50 ml with isotonic saline.

Colonoscopy in CAPD patient

Drain the dialysate before the procedure. After the procedure inject gentamicin into the bag and leave for 6 hours, the dose of gentamicin is dependent on the body weight (see below).

Contamination protocol for peritoneal dialysis

(Split patient line or Tenckhoff; titanium connector pulled out or disconnected; hole in PD fluid bag or lines; touch contamination followed by PD fluid flow)

Vancomycin 500 mg, distilled water for injection 10 ml, 10 ml syringe, green or orange needle. Connect 10 ml syringe and green needle. Draw up 10 ml of distilled water and add to vancomycin powder. Shake gently to mix and withdraw all 10 ml into the same syringe. Change to orange needle. Inject into new PD bag. Mix well. Drain in dialysis fluid and leave for 6 hours. Continue dialysis as normal.

The other alternative is gentamicin. Gentamicin dose dependent on the weight of patient:

Patient weight (kg)	dose of gentamicin (mg)
20–40	40
41–60	60
61–100	80
101 or more	120

You need: vials of gentamicin; 5 ml syringe; green and orange needle. Connect 5 ml syringe and green needle. Draw up appropriate dose into syringe. Change to orange needle. Inject into a new PD bag. Mix well. Drain in dialysis fluid and leave for at least 6 hours. Continue dialysis as normal.

Cefazolin 1 g IP can be used to avoid vancomycin and gentamicin.

Exit site infection

Take swab for culture and sensitivity testing prior to starting antibiotics. Flucloxacillin 500 mg qds PO for 2 weeks, followed by 250 mg qds PO for 1 week, and if refractory *Staphylococcus aureus* isolated add Rifampicin 450 mg od PO for the first 2 weeks.

If the patient is penicillin allergic:

Erythromycin 500 mg qds PO for 2 weeks followed by 250 mg qds PO, for 1 week + Fucidin 500 mg tds for the first two weeks. Fucidin is often poorly tolerated.

If infection is due to Gram negative bacteria:

Ciprofloxacin 500 mg bd PO or 400 mg bd IV for 3–4 weeks.

Recurrent or refractory infections with *Staphylococcus aureus*:

Rifampicin 300 mg bd PO, duration of treatment 12 weeks. Consider catheter removal.

Vancomycin (for gram-positive microorganisms) and gentamicin (for gram-negative microorganism) are still widely used in the treatment of exit site infections (for the doses see Peritonitis below)

Local mupirocin (Bactroban) treatment during routine exit site care in all patients on PD and specially in patients who are known *staphylococcus aureus* carriers, who have had an exit site infection, tunnel infection or peritonitis with *staphylococcus aureus*.

The use of mupirocin should be continued indefinitely.

Exit site infections are often persistent and may only be cured by removal of catheter. This is especially true if a tunnel infection develops.

Intra-peritoneal insulin

Patients with diabetes mellitus can administer insulin via the intra-peritoneal route to minimise number of subcutaneous injections. Short-acting soluble insulin should be used (eg Actrapid). PD fluids