

# Clinical nephrological problems important to the urologist

J. PLANGE-RHULE, F.B. MICAH and J.B. EASTWOOD\*

Department of Medicine, Komfo Anokye Teaching Hospital, Kumasi, Ghana, and \*Department of Renal Medicine, St George's Hospital, London, UK

## Introduction

The renal physician and urologist should be in frequent contact, for many of their patients have clinical problems that embrace both specialities. For the renal physician the discovery that a patient's renal failure arises from urinary tract obstruction (if more than just urethral obstruction) will lead to an urgent request for assistance from the urologist. For the urologist, requests for assistance can be no less urgent. Patients in hospital for urinary tract surgery are at risk of urinary tract sepsis and when this happens loss of renal function can become the dominant clinical problem. Furthermore, there is the difficulty of assessing fluid status in patients where there is no easy access to central venous pressure measurement. Of more concern is that some patients with worsening renal failure may develop hyperkalaemia and acid-base disturbances. In the outpatient setting it is not uncommon for patients with predominantly nephrological disease to be referred to the urologist. Such problems as dysuria and frequency, and macroscopic haematuria, may have no discernible urological cause. Shared management may be important in conditions like tuberculosis of the renal tract, polycystic kidney disease, metabolic renal stone disease and many others.

## The patient with existing impairment of renal function

### *How to recognize such patients*

All patients presenting to a urologist should have a full relevant history taken, and be examined for signs of concurrent medical and surgical conditions. Points in the history that might indicate renal disease include diabetes mellitus, hypertension and previous renal disease; other possible indicators of renal disease are oedema and macroscopic haematuria. On examination, the BP and pulse should be measured, and the state of hydration and evidence of anaemia recorded. All patients should have their urine tested routinely. Proteinuria is an important indicator of intrinsic renal disease, although it may be absent when the renal failure

arises from renal arterial disease (pre-renal) or obstruction in the lower urinary tract (post-renal). Some predominantly renal conditions are typically associated with little if any proteinuria, e.g. interstitial nephritis, reflux nephropathy, adult polycystic kidney disease and congenital anatomical disorders

In the tropics, as in many developed countries, it is likely that diabetes mellitus is a leading cause of chronic renal failure; it is also likely that uncontrolled/untreated hypertension is an important cause. Other important causes are chronic glomerulonephritis, schistosomiasis, renal tuberculosis, reflux nephropathy and the sickle-cell disorders. Amyloidosis, which is a complication of both leprosy and tuberculosis, is a cause of renal failure in the tropics that is less common in the developed world. However, it is important to realize that there are currently few data on the causal factors for chronic renal failure in developing countries, and renal registries as yet exist mainly only in developed countries.

### *Implications for the urologist*

*Assessment of renal function.* In any patient undergoing a significant urological procedure, it is important to measure urea, creatinine and electrolytes. Where there is significant impairment of renal function the GFR should be assessed formally, e.g. by using creatinine clearance. In most cases it is the degree of renal dysfunction and not the specific renal diagnosis that is important.

*Hypertension.* In patients undergoing elective surgery and known to be hypertensive it is important to establish that the patient is on drugs that are both effective and well-tolerated. Patients who at the preoperative visit are found to have a BP of >140/90 mmHg should be referred and treated as appropriate.

In patients undergoing urgent surgery whose BP is unacceptably high the problem of BP control is best managed by close liaison with a physician and the anaesthetist. In such cases a calcium-channel blocker will often be an acceptable choice.  $\beta$ -blockers can cause bradycardia, which may mask acute bleeding after surgery.

*Diabetes mellitus.* The management of well-controlled diabetics undergoing minor procedures should be straightforward. In such patients it is usually sufficient to give intravenous fluids and measure the blood glucose at intervals until the patient has recovered sufficiently from the operation to take fluids by mouth. If glycaemic control is poor it is important to regain control before contemplating the operation.

Diabetics undergoing urgent surgery will often need to be managed with intravenous insulin during the operation; this is particularly important in patients with sepsis or hypovolaemia, and in those who are jaundiced.

#### *Peri-operative management*

The goal of management of any patient with pre-existing renal dysfunction is to ensure that the GFR after surgery is as good as that measured beforehand. Nevertheless, there is little doubt that patients with pre-existing renal impairment are at greater risk peri-operatively than those without. The most important hazard is volume depletion, as individuals with renal dysfunction tend to be polyuric, and they maintain this polyuria despite a decrease in circulating blood volume. For this reason such patients can become volume-deplete quite quickly, especially in a hot climate.

For patients undergoing planned surgery it is important that the anaesthetist is involved as soon as possible. Ideally, such patients should be first on the operating list, so that potentially hazardous delays are minimized. All patients should be receiving intravenous fluid (preferably 0.9% saline), and if possible the vein used should be one that will not be needed for arteriovenous fistula formation in the future. During surgery all fluid losses should be replaced, and afterwards the patient's state of hydration must be maintained. Importantly, patients may continue to pass quantities of urine yet become volume-deplete. In this state any further volume loss may result in oliguria, a hazardous condition for a patient with renal failure in a tropical country and with no recourse to any form of dialysis. In practice, because of difficulties in recording and interpreting input-output charts, a daily record of body weight is the best method of avoiding volume depletion. For this purpose an ordinary domestic 'standing' pair of scales (accurate to 0.5 kg) will usually suffice, although more accurate 'chair' scales are generally preferable as they can accommodate patients who cannot stand. For patients admitted as an emergency the principles of maintenance of fluid balance are even more important.

*Drugs.* The drugs used for premedication, as they are used only once, are unlikely to pose any threat to the patient with renal failure. The anaesthetist will need to

consider carefully which anaesthetic agents are to be used. After surgery pain control may present particular difficulties; it is not generally realized that, while opioids are metabolized by the liver, their metabolites are excreted by the kidney. The duration of action of opioids can be considerably prolonged and have an adverse effect on ventilation soon after surgery. If such drugs are used they should be given infrequently and in small doses. Sedatives of the benzodiazepine group also have a particularly prolonged action in patients with renal failure (see 'Drugs and the kidney').

*Sepsis.* Procedures particularly prone to be associated with bacteraemia should be covered by a single dose of a suitable intravenous broad-spectrum antibacterial agent.

### **Acute impairment of renal function (acute renal failure)**

Perhaps the most important complication that occurs during the course of the urologist's work is a deterioration in GFR. The urologist will clearly want to be sure that obstruction of the urinary tract is excluded. Fortunately, ultrasonography is becoming available in more developing countries, so at present more invasive procedures can usually be avoided. In the absence of obstruction other causes should be sought.

#### *Volume status*

In hospitals with few facilities a clinical assessment is very important; the best 'bedside' sign is the jugular venous pressure. With the patient lying at 45°, and in a good light (preferably daylight), the diffuse distension of the lower neck that occurs with each expiration should be observed. If nothing can be seen, the intra-abdominal pressure can be increased by gentle pressure in the centre of the abdomen; it may then be possible to see the neck veins. Lying the patient flatter may make the neck veins stand out better, but the reference point remains the manubrio-sternal joint (angle of Louis). Once the top of the column of venous blood can be seen, the state of hydration (volume) can be estimated. If the patient is 'under-filled' then he or she will benefit from intravenous 0.9% sodium chloride solution. Other signs of fluid depletion are a low BP, a 'thready' radial pulse and a decrease in body weight. Where these signs are not present any decrease in BP while the patient is seated (or, if safe, standing), and cold extremities, should be sought.

In some patients there will be fluid overload; this is characterized by a raised central venous pressure (again best seen at the root of the neck), pulmonary oedema manifested by fine 'crackles' at the lung bases, and sometimes oedema. In patients in bed, the oedema

is seen particularly around the thighs and buttocks (including the sacral region), and sometimes in the ankles and feet. In these patients, especially those who are anuric/oliguric, recovery of renal function depends on scrupulous attention to all aspects of management. There is no evidence that either intravenous diuretics or mannitol are effective; neither is intravenous dopamine, which indeed may be harmful as it causes arrhythmias. If there are no dialysis facilities, intravenous loop diuretics, e.g. frusemide, may increase urine volume and improve the pulmonary oedema. However, there is no evidence that there is any effect on GFR.

### *Hyperkalaemia*

In all patients with a raised plasma creatinine level or oliguria it is important to measure the plasma potassium level, which tends to increase in such patients, as the kidney is the major route of excretion. Once the plasma potassium is  $>6.0$  mmol/L there is a risk of life-threatening arrhythmia, so it must be lowered. For this reason it is advisable to establish vascular access via a large vein, and an ECG monitor should be connected. In a patient in whom the potassium is rising quickly there will be more urgency than if the level is stable.

In all patients, drugs that raise the plasma potassium (potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, NSAIDs, potassium supplements) should be stopped. Simple (but relatively slow) methods of lowering the plasma potassium are paying attention to the dietary intake of potassium, and giving ion-exchange resins, e.g. calcium polystyrene sulphonate or sodium polystyrene sulphonate (a 30 g dose can be given either orally or rectally, or both, followed by 15 g three times daily; this will often satisfactorily control plasma potassium). These methods reduce the amount of potassium absorbed by the gut. In individuals with hyperkalaemia in the presence of acidosis, these methods will be less effective as potassium will have leaked from the cells (in exchange for  $[H]^+$ ) into the bloodstream. However, oral sodium bicarbonate tablets can be effective, as they tend to increase the plasma bicarbonate and raise the plasma pH. In these circumstances potassium tends to go back into cells and  $[H]^+$  comes out. As failing kidneys are the reason for the hyperkalaemia, it is not possible to increase the excretion of potassium via the urinary tract.

To lower the plasma potassium quickly, dextrose and insulin should be administered intravenously by infusing 50 mL of 50% dextrose with 10 units of soluble human insulin over 30 min, and then continuing at 10 mL/h (10 mL contains two units of insulin). Under these circumstances it is necessary to measure frequently

the plasma glucose level. Dextrose and insulin cause redistribution of potassium (into cells) but do not lead to loss of potassium from the body.

In patients in whom there is real concern, e.g. a rapidly increasing potassium level, a potassium of  $>7$  mmol/L, or where there is cardiac irregularity, especially ventricular tachycardia or multifocal ventricular ectopics, it is important to lower the plasma potassium as a matter of urgency. Classically, the ECG shows flattening of the P-wave, widening of the QRS complex and high T-waves. To diminish the risk of life-threatening arrhythmia, i.e. to stabilize the myocyte membrane, 10 mL of 10% calcium gluconate should be given slowly and intravenously. The patient should already be on a cardiac monitor and the plasma potassium measured frequently.

### *Acidosis*

Individuals with impaired renal function are unable to excrete  $[H]^+$  so a metabolic acidosis develops; the cardinal sign of metabolic acidosis is hyperventilation. Typically, there is a low plasma pH, low bicarbonate and a low  $pCO_2$ . Sometimes there is an increased 'anion gap', where the sum of plasma  $Na^+$  and  $K^+$  is greater than the sum of  $Cl^-$  and  $HCO_3^-$  by more than the normal 10–12 mmol/L. Such an increase indicates that there are retained unmeasured anions. This situation is typical of patients with renal failure, acute or chronic. A normal anion gap in an individual with metabolic acidosis indicates that there are no retained unmeasured anions, and that the acidosis is a result of alterations in chloride and bicarbonate alone.

### *Urea and creatinine*

In patients with acute renal failure both urea and creatinine levels are increased; sometimes there is a disproportionate rise in urea compared with creatinine. This usually occurs when there is a low urine flow and indeed the patient is sometimes fluid-deplete. This phenomenon is most commonly seen after urological operations, particularly prostatectomy.

The explanation for the disturbed urea:creatinine ratio is that under conditions of low urine flow, urea leaks back through the renal tubular wall and re-enters the circulation. A normal creatinine clearance is 80–120 mL/min; a normal urea clearance is 50–80 mL/min. Under conditions of fluid deprivation, while the creatinine clearance might not change, that of urea may decrease considerably. As might be expected, this would result in a plasma urea that is increased out of proportion to that of creatinine (Table 1).

**Table 1** Causes of a disturbed urea : creatinine ratio

<i>Increased</i>	<i>Reduced</i>
<b>Raised urea</b>	<b>Reduced urea</b>
Hypovolaemia	Inadequate intake
Corticosteroids	Reduced liver manufacture
Tetracyclines*	
<b>Reduced creatinine</b>	<b>Raised creatinine</b>
Muscle mass low	Muscle mass high
	Rhabdomyolysis

\*All drugs of the tetracycline group other than doxycycline and minocycline raise the blood urea and should be avoided. However, doxycycline and minocycline can be given in normal doses.

*Sepsis*

A common contributory factor in the development of acute oliguria is sepsis. In a urological setting the urinary tract is a likely source of infection and commonly Gram-negative organisms are responsible. Patients with sepsis tend to be more unwell than expected, and may have a fever and tachycardia. There may be focal symptoms and signs in the chest or urinary tract, or significant infection of a surgical wound. Another possible source is the skin, sometimes because of pre-existing skin ulceration, but also sometimes because of infection at an intravenous cannula site.

Important investigations include blood culture, haemoglobin level, white-cell count and the differential, and, as a marker of bacterial infection, C-reactive protein. Cultures should also be taken of sputum, any wound, urine (if available) and any obvious skin lesions.

*Peri-operative factors*

Surgery that is associated with a general anaesthetic can often be associated with volume depletion. Such patients are usually required to be 'nil by mouth', and this applies to both emergency and scheduled operations. There can sometimes be delays and, especially when the operation is minor, giving intravenous fluids might not have been contemplated. After surgery there may be nausea and sometimes vomiting, so patients may not drink any fluid for some days. Therefore, in the tropics there is a particular risk of volume depletion.

*Management*

*Volume status.* In oliguric patients, whether or not associated with surgery, the first priority is to establish volume status. The central venous pressure, as judged by the jugular veins in the neck, must be established if at all possible, whether by simple observation of the neck veins at 45°, by changing the position of the patient, or using abdominal pressure, etc. Provided that

it is certain that a patient is not overloaded with fluid, it is safe to replenish extracellular volume. The fluid used should normally be 0.9% sodium chloride solution, but in the presence of acidosis sodium bicarbonate is more logical. In the presence of volume overload such filling is not possible and, if the patient is oliguric, dialysis will need to be considered.

*Potassium.* See above.

*Acidosis.* In patients who are volume-overloaded there is little scope for correcting acidosis. In those who are volume-deplete it is clearly preferable to give bicarbonate rather than chloride. The most appropriate solution is 1.26% sodium bicarbonate, which is the equivalent of isotonic sodium chloride, and contains 150 mmol of both sodium and bicarbonate. The molar solution (8.4%, i.e. 1000 mmol/L) is unsuitable, as there is usually a need for both electrolytes and water. This molar solution should be reserved for emergency use, e.g. during cardiopulmonary resuscitation.

*Further management.* After optimizing the volume, plasma potassium and acid-base status, and prescribing appropriate antibiotics, it is important to consider what further management is necessary. The usual observations of temperature, BP and pulse should be recorded, and the patient should be weighed every day. By having a cumulative record of body weight it is possible to forestall any dangerous changes of volume.

General measures are also important; the patient should be fed a nutritious diet but avoiding potassium. It is important to keep the patient mobile as much as possible; if confined to bed, physiotherapy to the limbs and chest must be continued. If the patient's clinical condition improves, i.e. the sepsis is brought under control and the patient begins to eat, it is possible that the oliguria will be relatively brief. In these circumstances it may be possible to avoid dialysis altogether. In very sick patients it may be obvious early on that dialysis is inevitable; in these cases dialysis should be started sooner rather than later.

*Renal biopsy*

In the context of acute renal failure renal biopsy is not usually indicated. Histologically the vast majority of patients show no microscopic abnormality, i.e. they have 'acute tubular necrosis'. In some cases myoglobin or haemoglobin may be seen in tubules, and there may be some necrosis of tubules.

Rarely, a patient presents to the urologist with, perhaps, macroscopic haematuria, and renal function deteriorates rapidly. Occasionally such a patient will be found to have microscopic polyangiitis, or even more rarely Goodpasture's disease. Sometimes acute renal

failure can be the result of interstitial nephritis. Only in these unusual cases is renal biopsy likely to influence management.

#### *Indications for dialysis*

As indicated above, the main indications for dialysis are (i) volume overload in the presence of oliguria, (ii) a high potassium that cannot be lowered and (iii) worsening acidosis despite attempts at correction.

Plasma urea and creatinine levels alone are not usually critically important when deciding whether or not to begin dialysis. In an oliguric septic patient (in whom the oliguria is likely to persist for days or weeks) dialysis should not be delayed simply because the urea and creatinine have not reached certain levels. In such cases dialysis should be started without delay.

### Renal replacement therapy

The need for renal replacement therapy in urological patients is mainly in the context of acute renal failure, as described above. However, in some developing countries there is also a significant incidence of renal failure as a result of ureteric and bladder disease, particularly bilharzia. There are major foci of *Schistosoma haematobium* in the Nile basin and in many parts of sub-Saharan Africa. Unfortunately, in many of the areas where bilharzia is endemic, haemodialysis and peritoneal dialysis are not available for chronic, or even acute, renal failure. This is especially true of sub-Saharan Africa, where it is unusual for suitably trained medical and nursing staff to be available. A second problem is the expense and unavailability of suitable equipment. Finally, for haemodialysis it is essential that water and electricity are readily available. The water also should be of suitable quality and at the correct pressure for the machines.

#### *Haemodialysis and peritoneal dialysis*

Haemodialysis is the most appropriate form of dialysis for acute renal failure and for most patients peritoneal dialysis is unsuitable. Indeed, in hypercatabolic patients (who are often septic) peritoneal dialysis is sometimes unable to lower adequately the rapidly rising urea. The factors influencing choice of modality are given below (Table 2).

#### *Transplantation*

Renal transplantation is unusual in sub-Saharan Africa and is unlikely to be an option in most renal centres for

**Table 2** The requirements for dialysis

<i>Requirements</i>	<i>Haemodialysis</i>	<i>Peritoneal dialysis</i>
Absolute	Central venous access	Suitable peritoneum
Drugs	Heparin	None
Highly trained staff?	Yes	Less so
Suitable for hyperacute renal failure	Yes	No
Able to remove fluid quickly?	Yes	No
Infection risk?	Line sepsis	Peritonitis
Set-up cost of service	High	Low
Maintenance cost	Moderate	High

many years. While the operation is relatively straightforward, both achieving an appropriate standard of care at the time of surgery and having adequate expertise to safely provide follow-up are unlikely to be within the capabilities of any but the most modern hospitals. Furthermore, renal transplantation is for many years likely to remain low on the list of priorities of most African health systems.

### Drugs and the kidney

Significantly many of the drugs commonly used by urologists are metabolized/excreted by the kidney; others have a deleterious effect on renal function. Below are summarized those most important to the urologist; the local formulary should be consulted for drugs not covered here.

*Analgesics.* Paracetamol is the analgesic of choice in patients with renal failure but commonly it is inadequate for pain relief. NSAIDs and opioids are better than paracetamol for pain relief, but both groups of drugs are hazardous in patients with renal impairment. There are three significant problems with NSAIDs; gastric irritation, inhibition of PG synthesis and nephrotoxicity. The gastric irritation is a particular problem in patients with advanced renal failure because of platelet malfunction and an increased tendency to bleed. The effect on PG synthesis causes salt and water retention and hyperkalaemia. The direct nephrotoxic effect may produce a rise in plasma creatinine.

On the other hand, opioids have none of the hazards of NSAIDs but they do have the problem that their metabolites accumulate in patients with renal failure. This causes a worrying prolongation of their effect and can give rise to considerable over-sedation. There is a particular problem with pethidine in that its metabolite, nor-pethidinic acid, which accumulates in renal failure, can cause seizures.

*Antibiotics.* Urological procedures involving instrumentation, especially when the urine is infected, are sometimes associated with bacteraemia. A single dose of an appropriate antibiotic can be given as indicated. Antibiotic dosage is only an issue for potentially toxic drugs for which the mode of excretion involves the kidney. Thus aminoglycosides, e.g. gentamicin and streptomycin, are best avoided where possible. For treating urinary infection, trimethoprim, ciprofloxacin, cephalosporins and penicillins are generally acceptable, but the dose should be modified in patients with severe renal failure.

*Anti-hypertensives and diuretics.* Provided that the control of BP is good, it is best to leave drug treatment unchanged. However, angiotensin-converting enzyme inhibitors and angiotensin II blockers should be stopped if the potassium is at or above the upper limit of normal. Patients on  $\beta$ -blockers will not show the normal tachycardia if they become volume-deplete.

Patients with renal impairment should not be on potassium-sparing diuretics, and any such patient who is should have their potassium measured and the drug withheld until the risk of hyperkalaemia has passed. Loop diuretics and thiazides should also be withheld until well after surgery. Any potassium supplements should also be stopped.

*Mood-altering drugs.* For most anxiolytics the dose should be reduced. Benzodiazepines accumulate in patients with renal failure and so should be avoided as much as possible, to prevent over-sedation. A particular problem is lithium, which is wholly dependent on the kidney for its excretion. Any worsening of GFR will be associated with rising lithium levels. There is a relatively narrow therapeutic window and toxic levels can be associated with considerable morbidity.

*Other drugs.* Digoxin, ethambutol and most tetracyclines (see above) are excreted by the kidney, and are

toxic when blood levels are high. Great care should be taken when prescribing these drugs.

## Conclusions

In developing countries the patterns of referral to hospital are sufficiently varied that it is inevitable that urological conditions will be referred to the nephrologist (if there is one), and vice versa. Therefore, both urologists and nephrologists must be as conversant with their sister speciality as possible, and have robust channels of referral.

For nephrologists in developing countries, in many of which there is no access to urinary tract ultrasonography, there is the constant concern that a patient may be treated conservatively but who has remediable obstruction of the urinary tract. For the urologist there is the concern that a patient may lose renal function needlessly because it has been assumed that the fall in GFR is the result of urological disease when other causes, especially drugs, both prescribed and self-prescribed, have not been considered. For both specialities there are many traps for the unwary. These concerns underline the need for urologists and nephrologists to work closely together and have a low threshold for inter-referral.

## Authors

J. Plange-Rhule, BSc, mBCLB, PhD, mRCP, mWACP.

F.B. Micah, BSc, mBChB.

J.B. Eastwood, MD, FRCP.

Correspondence: J.B. Eastwood, St George's Hospital, Blackshaw Road, Tooting, London SW17 0QT, UK.

e-mail: jbeastwood@compuserve.com