Contents

Contributors vi
Preface vii
Abbreviations viii
1 Renal function 1
   Angela Cottrell
2 Urinary tract infection 9
   Samih Al-Hayek
3 Evaluation of lower urinary tract symptoms 25
   Jay Khastgir
4 Stone disease of the urinary tract 49
   Nimalan Arumainayagam
5 Prostate cancer 63
   Kieran Jefferson, Natasha Jefferson
6 Bladder cancer 75
   Steve Williams, Merce Jorda, Murugesan Manoharan, Mark Soloway
7 Renal masses 93
   Anthony Koupparis
8 Scrotal swellings 105
   Angela Cottrell
9 Investigation of erectile dysfunction 111
   Matthew Hotston
Index 119
Contributors

Samih Al-Hayek, MD, LMSSA, LRCP(Lond), LRCS(Eng), MRCS
Specialist Registrar in Urology
Department of Urology
Weston General Hospital
Weston-Super-Mare
UK

Nimalan Arumainayagam, BMedSci, BMBS, MRCS
Clinical Research Registrar in Urology
Bristol Urological Institute
Southmead Hospital
Bristol
UK

Angela M. Cottrell, MBBS, BSc, MRCS
Clinical Research Fellow
Bristol Urological Institute
Bristol
UK

Matthew Hotston, MBChB, MRCS(Eng)
Specialist Registrar in Urology
The Royal Marsden Hospital
London
UK

Kieran Jefferson, MA, FRCS(Urol)
Consultant Urological Surgeon
University Hospital of Coventry and Warwickshire
Coventry
UK

Natasha Jefferson, MA, MRCP, FRCR
Consultant Radiologist
Horton Hospital
Banbury
UK

Merce Jorda, MD, PhD
Professor of Clinical Pathology
Medical Director, Clinical Laboratory Services
UMHC/SCCC and UM Hospital
Department of Pathology
Leonard M. Miller School of Medicine
University of Miami Hospital and Clinics
Miami, Florida
USA

Jay Khastgir, MBChB, MS, FRCSEd, FRCS(Glas), FRCS(Urol)
Consultant Urological Surgeon
Department of Urology
Morrison Hospital
Swansea
UK

Anthony Koupparis, BSc, MBChB, FRCS(Urol), MD
Specialist Registrar in Urology
Department of Urology
Cheltenham General Hospital
Cheltenham
UK

Murugesan Manoharan, MD, FRCS, FRACS
Associate Professor of Urology
Department of Urology
Leonard M. Miller School of Medicine
Miami, Florida
USA

Mark S. Soloway, MD
Professor and Chairman
Department of Urology
Leonard M. Miller School of Medicine
Miami, Florida
USA

Steve K. Williams, MD
Uro-Oncology Fellow
Department of Urology
University of Miami
Miami, Florida
USA
Preface

Urology is one of the fastest developing of specialties, but the main aim here is to provide a source reference for many of the conditions and means of investigating them that are encountered and used within the context of everyday urological practice.

One of the consultants I worked for during the early stages of my training was always keen to point out that urological problems are regularly encountered in many other specialties as a consequence of a wide variety of disease processes, not least of which is the realm of the community care and general practitioner, and it is with this thought in mind that this book has been put together.

This volume is aimed at as wide a readership interested in the discipline of urology as possible, from the medical student encountering the specialty for the first time to the expert keen for some up-to-date images of common urological conditions. The aim has been to provide a readable, user-friendly text looking at the major areas dealt with by urology as a specialty, accompanied by illustrations.

The book begins with a look at renal function – its measurement and the assessment of its impairment, before moving on to look at the investigation and diagnosis of urinary tract infection. The management of lower urinary tract symptoms or LUTS as this spectrum of presenting complaints is known, is dealt with in a separate chapter, followed by a look at the investigation of stone disease. The next section of the book looks at the presentation and investigation of common urological malignancies in chapters covering prostate, bladder and renal cancer. Testicular cancer is dealt with in the following chapter, which also takes a look at common benign scrotal conditions. Finally, the book is rounded off by a summary of the investigations and assessment techniques used in patients with erectile dysfunction.

John L. Probert
June 2008

Special acknowledgement

The publisher is very grateful to Mr Vivek Kumar for his kind assistance in supplying several of the images that appear in Chapter 4 of this book.

Vivekaandan Kumar, MBBS, MS(Gen. Surg), MD(Res), FRCS
Specialist Registrar
Department of Urology
Gloucestershire Royal Hospital
Gloucester
UK
Abbreviations

- [⁹⁹mTc]MDP: technetium-labelled methylene diphosphonate
- 5-ALA: 5-aminolaevulinic acid
- A2M: α₂-macroglobulin
- ACT: α₂-antichymotrypsin
- AFP: α-fetoprotein
- AJCC: American Joint Committee on Cancer
- ARE: androgen-responsive element
- AUA: American Urological Association
- BHD: Birt-Hogg-Dube syndrome
- BOO: bladder outlet obstruction
- BOOI: Bladder Outlet Obstruction Index
- BPE: benign prostatic enlargement
- BPH: benign prostatic hyperplasia
- BPO: benign prostatic obstruction
- BTA: bladder tumour antigen
- BVE: bladder voiding efficiency
- cGMP: cyclic guanosine monophosphate
- CIS: carcinoma in situ
- CT: computed tomography
- DMSA: dimercaptosuccinic acid
- DRE: digital rectal examination
- DTTP: diethylenetriaminepentaacetic acid
- EAU: European Association of Urology
- ED: erectile dysfunction
- EDTA: ethylenediaminetetraacetic acid
- EDV: end diastolic flow velocity volume
- eGFR: estimated glomerular filtration rate
- ELISA: enzyme-linked immunosorbent assay
- EMB: eosin-methylene blue
- FDA: Food and Drug Administration
- GFR: glomerular filtration rate
- HAL: hexyl aminolaevulinate
- H&E: haematoxylin and eosin
- HIF-α: hypoxia-inducible factor-α
- hK2: human kallikrein 2
- hK3: human kallikrein 3
- HSP: Henoch-Schönlein purpura
- HU: Hounsfield unit
- ICC: international correlation coefficient
- ICS: International Continence Society
- IgA: immunoglobulin A
- IIEF: International Index of Erectile Function
- IPSS: International Prostate Symptom Score
- IR(ME)R: ionizing radiation regulations
- ISUP: International Society of Urological Pathologists
- IVC: inferior vena cava
- IVU: intravenous urogram
- KFP: formation product
- KSP: saturation product
- KUB: kidneys, ureters and bladder (radiograph)
- LUTS: lower urinary tract symptom
- MAG3: mercaptoacetylitrigricine
- MDRD: Modification of Diet in Renal Disease
- MRHA: mannose-resistant haemagglutination
- MRI: magnetic resonance imaging
- MSU: midstream urine
- MUCP: maximum urethral closure pressure
- MUP: maximum urethral pressure
- NGU: non-gonococcal urethritis
- NIH: National Institutes of Health
- NMP-22: nuclear matrix protein 22
- NPV: negative predictive value
- NSAID: non-steroidal anti-inflammatory drug
- OAB: overactive bladder syndrome
- OIH: orthoiodohippuran
- PDE5: type 5 phosphodiesterase
- PDGF-β: platelet-derived growth factor-β
- PET-CT: positron emission tomography with CT
- PIN: prostatic intraepithelial neoplasia
- PN: Polymorphonuclear neutrophils
- PPV: positive predictive value
- PSA: prostate-specific antigen
- PSMA: prostate-specific membrane antigen
- PSV: peak systolic velocity
- PUNLMP: papillary urothelial neoplasm of low malignant potential
- Qmax: maximum flow rate
- Qave: average flow rate
- RBC: red blood cell
- RCC: renal cell carcinoma
- REM: rapid eye movement
- RFA: radiofrequency ablation
- RI: resistance index
- SCr: serum creatinine
- SLE: systemic lupus erythematosus
- SPA: suprapubic aspirate
- STD: sexually transmitted disease
- STIR: short tau inversion recovery
- TcMDP: technetium-labelled methylene diphosphonate
- TGF-α: transforming growth factor-α
- TGF-β: transforming growth factor-β
- TNM: Tumour, Nodes, Metastasis
- TRUSS: transrectal ultrasound scanning
- TURBT: transurethral resection of a bladder tumour
- TURP: transurethral resection of the prostate
- UC: urinary cytology
- UICC: International Union Against Cancer
- UPP: urethral pressure profilometry
- UTI: urinary tract infection
- VEGF: vascular endothelial growth factor
- VHL: von Hippel-Lindau
- VUDS: videodynamics
- VUR: vesicoureteric reflux
- VV: voided volume
- WBC: white blood cell
- WHO: World Health Organization
Chapter 1

Renal Function

Angela Cottrell

The kidney has a number of functions, including:

- Maintenance of homeostasis.
- Production of erythropoietin.
- Maintenance of blood pressure.
- Hydroxylation of vitamin D.

It is the investigation of the first of these with which this chapter is concerned.

Creatinine as an indicator of renal function

One of the major roles of the kidney is the excretion of soluble waste. This is achieved by the process of glomerular filtration. Creatinine is commonly used as an indicator of the glomerular filtration rate (GFR). Creatinine is a non-toxic breakdown product of creatine, a short-term energy store found in muscle (in the form of phosphocreatine) (1.1).

Laboratory analysis of serum creatinine entails chromographic analysis of the products of the Jaffe reaction. Creatinine is mixed with alkaline picramate and an orange coloured compound is formed (1.2). The product is then analysed by a colorimeter.

Table 1.1 shows possible causes for a raised creatinine. The ‘goulash effect’ is a transient rise in serum creatinine after ingestion of large quantities of boiled meat.

1.2 Creatinine after alkaline picramate reaction.

<table>
<thead>
<tr>
<th>Table 1.1 Causes of a raised creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal impairment</td>
</tr>
<tr>
<td>Ingestion of stewed meat (‘goulash effect’)</td>
</tr>
<tr>
<td>Acute muscle necrosis</td>
</tr>
<tr>
<td>Muscular dystrophy</td>
</tr>
<tr>
<td>Starvation</td>
</tr>
<tr>
<td>Methyltestosterone therapy</td>
</tr>
<tr>
<td>Neo-bladder</td>
</tr>
</tbody>
</table>

1.1 Metabolism of phosphocreatine to creatinine.
2 Renal function

Glomerular filtration rate

Measurement of serum creatinine has its limitations. The relationship between serum creatinine and GFR is not linear, and serum creatinine level may not rise significantly until GFR is as low as 30% of normal.

GFR is an important measurement that provides clinicians with information about overall renal function. GFR can be estimated in a number of ways.

Clearance concept

GFR can be estimated by measuring clearances of a substance in which filtration by the glomerulus equals excretion in the urine. Clearance is the volume of plasma that is completely cleared of a substance by the kidneys per unit time (1.3).

1.3 Calculation of clearance in ml/min.

Calculation of creatinine clearance (1.4)

Creatinine is an endogenous substance that is present at a relatively constant level. Measurements and calculation according to the formula in figure 1.3 require 24-hour collection of urine (1.5). Therefore, patients need to be compliant for results to be accurate.

1.4 Calculation of creatinine clearance (ml/min).

Formulae to estimate GFR

Isolated measurements of serum creatinine are not accurate indicators of early renal disease. By incorporating variables such as age and weight, an estimated GFR can be derived.
Constant infusion technique

The gold standard method of measuring GFR is with inulin infusion. Inulin is a polymer of fructose that is derived from the tubers of dahlias. It is freely filtered by the glomerulus and neither secreted nor reabsorbed at the tubules. Accurate urine samples are taken following the infusion of inulin to maintain a constant concentration. This technique, although accurate, is limited to the research laboratory.

Radioisotope measurement of GFR

Ethylenediaminetetraacetic acid (EDTA) is added to many commercial beers to stabilize foaming and when chelated with copper it produces a blue colour used in shampoo. Chromium-labelled EDTA may also be used in the laboratory as a method of measuring GFR as it is cleared by glomerular filtration. Following injection of the substance, blood samples are taken and a rate of decay of the sample is plotted to enable calculation of GFR.

Radioisotope scans

Injection of radioisotopes that are handled by the kidney can provide useful information in the diagnosis and management of renal disease. Radioisotope imaging may be described as static or dynamic, depending on whether or not the radioisotope is freely filtered through the kidney and excreted, or taken up and bound to live renal tubules.

Static imaging

The commonest biological molecule used in static renography is technetium-labelled DMSA (dimercaptosuccinic acid). This is filtered by the glomerulus and binds to the renal tubules, where it can be detected using a gamma camera 2–3 hours after injection (1.8). DMSA scans are useful in providing anatomical information, assessing the degree of any renal scarring that may be present, and in determining split renal function (1.9, 1.10).

| Table 1.2 Classification of chronic kidney disease |
|---------------------------------|--------------------------------------------|
| Stage                          | Description                                |
| 1 Normal GFR                   | >90 ml/min/1.73 m² with other evidence of chronic kidney disease |
| 2 Mild impairment              | 60–89 ml/min/1.73 m² with other evidence of chronic kidney disease |
| 3 Moderate impairment          | 30–59 ml/min/1.73 m²                        |
| 4 Severe impairment            | 15–29 ml/min/1.73 m²                        |
| 5 Established renal failure    | 15 ml/min/1.73 m² or on dialysis            |

The full table may be found at: http://www.renal.org/CKDguide/full/Conciseguid141205.pdf
4 Renal function

Dynamic imaging (renography)

Dynamic renography is used primarily in the assessment of pelviureteric junction obstruction. As the injected radioisotopes are freely filtered by the glomerulus and excreted by the kidney, information can also be provided about glomerular filtration. Following isotope injection, gamma camera images are taken and the results are plotted over time. The commonest isotopes used are technetium-labelled diethyleneetriaminepentaacetic acid (DTPA) and mercaptoacetyltriglycine (MAG3). Orthoiodohippuran (OIH) may also be used but it is more expensive (1.11).

Before renography, the patient should be well hydrated and, to minimize any effects from a full bladder, the bladder either catheterized or emptied beforehand. This is particularly important in cases such as neuropathic bladder or vesicoureteric reflux. Dehydration and bladder effect may lead to equivocal results. In current practice, furosemide is given 15 minutes prior to isotope injection (typically 0.5 mg/kg of furosemide). The flow of urine across the pelviureteric junction can be assessed.
Renal function

junction is maximal at 15 minutes after injection of furosemide. The number of otherwise equivocal scans that might be obtained can be reduced by performing the renogram at the time of maximal diuresis (F-15 renogram).

In analysing renograms three distinct phases are described. The first phase is 'uptake'. This corresponds to the speed of injection of the radioisotope and the blood supply to the kidney. An abnormal uptake phase may be due to impaired renal function. The second phase is that of renal 'handling', determined by the transfer of isotope across the tubule cell. The third phase is that of 'washout' or drainage, and this is determined by the rate of excretion of tracer in the urine. An abnormal uptake phase may be due to impaired renal function (1.12).

Analysis of the washout phase of the renogram will indicate the degree and nature of obstruction. In certain cases an equivocal result may be obtained, where a brisk 'washout effect' is not observed but the pattern of the curve is not diagnostic of obstruction either. Diuresis renography can help interpret such cases. Traditionally, furosemide is given 20 minutes after the injection of isotope, hence increasing the flow of urine at the renal pelvis (F+20 renogram). This diuresis can help determine whether the original trace pattern has been caused by obstruction, in which case the curve will continue to be flattened (type 2 obstruction), or by stasis, in which case the curve will fall (type 3a obstruction). A partial response to furosemide may be due to renal impairment of partial obstruction (type 3b obstruction). Type 4 obstruction is indicated by the 'double peak' phase, or Homsy's sign. In this case the system may follow a normal pattern of washout until about 15 minutes after injection. At this time the curve will fall, hence indicating obstruction at maximal flow across the pelviureteric junction. This indicates decompensation, where the pelviureteric junction cannot tolerate the increased urine load at maximal diuresis (1.13).
The Whitaker test

Despite the use of diuretics, either in the form of F+20 or F-15 renography, some test results will still be inconclusive as to the presence of obstruction. The Whitaker test is another, more invasive, method of investigating equivocal cases of suspected obstruction. It may also be used in patients with poor renal function when a dynamic renogram is not appropriate. A fine bore nephrostomy is inserted into the renal pelvis and a catheter inserted into the bladder. Both the nephrostomy and bladder catheter are connected to pressure transducers. Contrast medium is injected into the renal pelvis at a rate similar to that of maximal diuresis. The bladder pressure is recorded with a gradual increase in pressure of the renal pelvis. An increase in pressure indicates ureteric obstruction.

Captopril test

The Captopril test is used to investigate cases of renovascular hypertension caused by possible renal artery stenosis. Patients with renal artery stenosis have high serum levels of angiotensin II. Captopril reduces angiotensin II formation and therefore relaxes efferent arterioles. The GFR subsequently falls.

Before the test angiotensin-converting inhibitors should be stopped. The test is performed following a baseline dynamic renogram. Captopril is given and a repeat renogram taken 30 minutes later. The test is positive if there is a drop in GFR or delayed transit times.

Acute renal failure

Acute renal failure is sudden onset of renal impairment that takes place over a short duration of time, such as days or weeks. It is characterized by an increase in the serum creatinine, which is reversible.

Classification

Acute renal failure may be classified by its aetiology as pre-renal, renal or post-renal:

Pre-renal renal failure

The commonest cause of pre-renal renal failure is hypotension. The kidneys are able to maintain a constant GFR over a wide range of perfusion pressures, a mechanism known as autoregulation. The commonest cause of hypotension is shock, whether secondary to hypovolaemia, sepsis or cardiogenic. Vascular causes such as renal artery stenosis or renal vein thrombosis may also be considered. If the cause of hypotension is prolonged or severe, the decrease in blood flow and hence GFR will lead to acute tubular necrosis.

Renal causes

Renal causes of acute renal failure may be due to systemic disease or secondary to specific insults (Table 1.3).

<table>
<thead>
<tr>
<th>Table 1.3 Renal causes of acute renal failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic disease</strong></td>
</tr>
<tr>
<td>SLE</td>
</tr>
<tr>
<td>HSP</td>
</tr>
<tr>
<td>Sarcoid</td>
</tr>
<tr>
<td><strong>Surgical / trauma</strong></td>
</tr>
<tr>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Aortic aneurysm repair</td>
</tr>
<tr>
<td>Burns</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td><strong>Glomerular causes</strong></td>
</tr>
<tr>
<td>Vasculitis (e.g. Wegener’s granulomatosis)</td>
</tr>
<tr>
<td>Infective (e.g. endocarditis)</td>
</tr>
<tr>
<td>Primary glomerulonephritis (e.g. IgA nephropathy)</td>
</tr>
<tr>
<td><strong>Interstitial causes</strong></td>
</tr>
<tr>
<td>Drug related (e.g. aminoglycosides, NSAIDS, diuretics, anti-epileptics)</td>
</tr>
<tr>
<td>Systemic disease (e.g. SLE)</td>
</tr>
</tbody>
</table>

HSP = Henoch–Schönlein purpura; IgA = immunoglobulin A; NSAID = non-steroidal anti-inflammatory drug; SLE = systemic lupus erythematosus

Post-renal renal failure

Post-renal renal failure is otherwise known as obstructive uropathy. It may occur as a result of malignant obstruction, either by local spread of prostatic or bladder malignancy, or by secondary infiltration of the retroperitoneum causing malignant retroperitoneal fibrosis. Tumours that commonly
metastasize to the retroperitoneum include adenocarcinoma of the breast and colorectal tumours. Stone disease only rarely causes obstructive uropathy, either by causing ureteric obstruction to patients with a solitary renal unit, or in the case of large bilateral staghorn calculi obstructing both kidneys. More distal causes include benign prostatic hyperplasia or urethral stricture causing chronic high pressure retention of urine leading to bilateral hydrourereters and hydronephrosis.

**Chronic renal failure**

Chronic renal failure is a progressive deterioration in renal function over a long time-scale, which may be over a period of many years. Ultimately the chronic renal failure may progress to end-stage renal failure, where death is inevitable if renal replacement therapy is not implemented. There are a number of clinical manifestations. The patient can be asymptomatic until the GFR is below 20. Features such as nocturia and metabolic acidosis may be present. More specific features can be related to metabolic, excretory and endocrine sequelae.

Anaemia is common and the causes are multifactorial. A failing kidney is unable to produce sufficient erythropoietin, resulting in anaemia. Bone marrow function is depressed, resulting in decreased erythropoiesis and the life span of erythrocytes may diminish. Intake and absorption of iron is reduced because of the chronic disease state. Neuropathy may ensue, resulting in sensory, motor and autonomic neuropathies. Endocrine function is abnormal due to hyperparathyroidism. Hyperparathyroidism can also contribute to renal osteodystrophy, a metabolic bone disease, which produces a range of pathologies including osteomalacia, osteoporosis and osteosclerosis. An important cause of death in patients with chronic renal failure is from ischaemic heart disease. Hypertension is present in the majority of patients secondary to sodium retention, and atherosclerosis is accelerated. In late stages, a metabolic acidosis may ensue, leading to uraemia and convulsions (Table 1.4).

Ultimately, a patient with end-stage renal failure will require renal replacement therapy, whether in the form of dialysis or renal transplant.

**Dialysis**

Dialysis entails the exchange of solutes from the blood to a dialysis solution through a semipermeable membrane. This may be in the form of peritoneal dialysis or haemodialysis.

<table>
<thead>
<tr>
<th>Table 1.4 Common causes of chronic renal failure</th>
</tr>
</thead>
</table>
| **Congenital** | Polycystic kidney disease  
Alports’ syndrome |
| **Acquired** | Vascular  
Renal artery stenosis  
Hypertension  
Diabetes  
Glomerular disease (e.g. IgA nephropathy)  
Interstitial disease (e.g. sarcoid)  
Systemic inflammatory disease (e.g. SLE) |
| **Idiopathic** |

IgA = immunoglobulin A; SLE = systemic lupus erythematosus

Peritoneal dialysis uses the peritoneum as a semipermeable membrane and thus enables solute exchange between peritoneal capillaries and the dialysis solution. A Tenckhoff catheter is inserted into the peritoneum through which a dialysis solution is instilled. Chemical equilibrium is achieved after time and the fluid is removed from the abdomen. Continuous ambulatory peritoneal dialysis describes the commonest regimen by which 2 litres of solution are exchanged four times a day.

**Haemodialysis**

In haemodialysis, blood is taken from the body and passed through a dialysis machine that contains a semipermeable membrane. Blood is then returned to the body. The patient usually dialses three to four times a week. In order to perform haemodialysis, appropriate vascular access is required. In the short term wide bore central venous catheters can be used but in the long term a more permanent solution is needed. An arteriovenous fistula or prosthetic graft may provide a more permanent needling site (1.14).

Steal syndrome is a complication of an arteriovenous fistula. Blood is ‘stolen’ from the palmar arch and this can ultimately lead to necrosis of the digits (1.15).

**Renal transplantation**

The ideal management of end-stage renal failure is renal transplantation. This enables patients to lead a near normal
life. The costs associated with transplantation are considerably less than lifelong dialysis. Transplants may originate from cadaveric or living (related or unrelated) donors (Table 1.5). Patients must undergo lifelong immunosuppression.

### Table 1.5 Renal transplantation: 5-year survival of graft and patients

<table>
<thead>
<tr>
<th></th>
<th>Cadaveric transplant</th>
<th>Living donor transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft survival</td>
<td>66.7%</td>
<td>80.2%</td>
</tr>
<tr>
<td>Patient survival</td>
<td>81.1%</td>
<td>90.2%</td>
</tr>
</tbody>
</table>

Source: US Scientific Registry of Transplant recipients

Further reading


