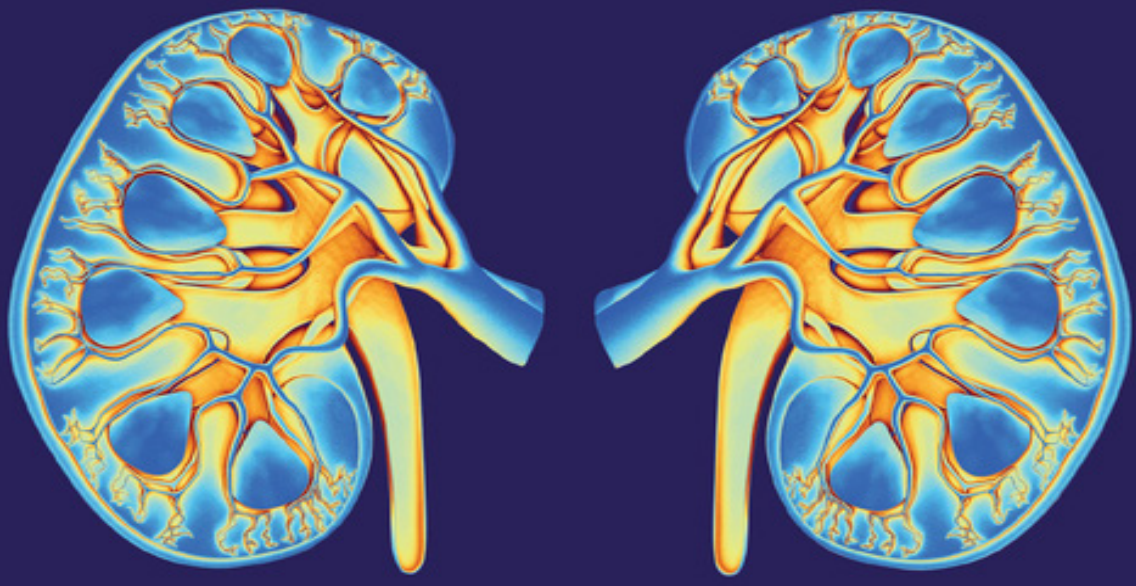
SIXTH EDITION

RENAL NURSING

CARE AND MANAGEMENT OF PEOPLE WITH KIDNEY DISEASE



EDITED BY
NICOLA THOMAS AND **HELEN NOBLE**

WILEY Blackwell

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Foreword

Chronic kidney disease is a global health burden and has become a major public health issue, as it is common, harmful, often treatable and preventable. Although progress has been made in identifying chronic kidney disease earlier and delaying the need for dialysis and transplantation, the number of people affected by kidney disease continues to grow each year. Over 2 million people worldwide currently receive treatment with dialysis or a kidney transplant to stay alive, yet this number may only represent 10% of people who actually need the treatment to live.

Acute kidney injury (AKI) accounts for 8–16% of hospital admissions, with >1% of health service expenditure being attributed to AKI in the UK. The International Society of Nephrology has an ambitious aim to prevent all avoidable deaths from AKI worldwide by 2025. Nurses play a key role in the early recognition and treatment of AKI, and nurses working in kidney care are no exception. They have a crucial role in adding quality to care.

People with chronic kidney disease have a wide range of physical and emotional needs. These include encouragement to achieve behavioural change goals they have set themselves, support with decision-making, education about their condition, traditional basic care needs individually delivered with compassion, and an understanding of the complexity of kidney disease along with other co-morbidities. The skills and competencies required to address these needs are the foundation of high-quality care delivered by both registered and non-registered nurses. Caring for people with kidney disease is a 'hands-on' job requiring an understanding of psychology – the person, the carers and the families, and your own; knowledge of the biology and pathophysiology of the kidney; expertise in the nursing of the acutely unwell, and the management of complex long-term conditions; as well as emotional resilience. Kidney care nurses recognise the people they care for have a common disease, but each individual's experience is unique, requiring support and encouragement appropriate to their age, cultural background, and degree of health literacy. As such, nurses specialising in kidney care are pivotal to the multi-professional team. Not only do they bring their understanding of kidney disease and experience of managing others in a similar situation, they also are the advocate for holistic care and act as a catalyst for shared decision-making.

To achieve such high standard of care, the appropriate education and training is needed to develop this vast knowledge base and practical skills. Nurses access specialist knowledge in a variety of formats, either e-learning, textbooks such as this, or even social media. Since the dissolution of national renal courses, there is a lack of educational standardisation, which the Association of Renal Nurses UK (ANN UK) has begun to address with the launch of an online renal course designed for registered nurses with at least 6 months' experience in kidney care. This is the first step towards developing a national educational framework for kidney care nurses. As part of this educational framework, the 6th edition of *Renal Nursing* will provide you with the information you need to understand the fundamentals of kidney care. Use this textbook in conjunction with gaining practical hands-on experience in dialysis units, inpatient wards, outpatient settings, and home therapies and you will have the knowledge and skills to make a vast difference to many people with kidney disease.

Karen Jenkins President of the Association of Nephrology Nurses, UK

Preface

We have very much enjoyed editing the sixth edition of this successful book for nurses and allied healthcare professionals working in nephrology, dialysis, and transplantation, along with expert colleagues. The past 5 years have again seen tremendous changes in kidney care in the UK, particularly improvements in patient experience, such as developments in peer support programmes and renal arts. Chapter 3 of this textbook is always warmly received, as it provides a patient and carer perspective on care and encourages us to think in the 'patient's shoes'.

This book is generally for those who are new to kidney care. Nurses who are studying on preregistration courses and practitioners who are commencing a post-registration course in renal nursing will find it particularly helpful. It also serves as an excellent foundation for nurses wishing to refresh their knowledge about an area of kidney care in which they are currently not practising, or for other members of the multi-professional team. This new edition is again written in a style that promotes kidney care for what it is: a dynamic, varied, and rewarding specialty.

Each chapter has been written by an expert in their field. Kidney nurses in the twenty-first century face a constant challenge to keep abreast of developments in care and management. What does not change is the constant physical and psychosocial challenges that patients and their families have to face. This must always be in our minds. During our long careers in renal nursing, we have heard the repeated request from patients that we emphasise what *can* be done rather than what cannot. The word *restriction* should not be part of a kidney nurse's vocabulary: Why not fluid or dietary *allowance*? As in the fifth edition, we have endeavoured to use language in this book which puts patients at the centre of care.

We are delighted that the Association of Nephrology Nurses, UK (ANN-UK), launched in 2018, is going from strength to strength and aims to reintroduce a framework for renal nursing education in the UK. We hope that this latest edition complements that vision and will continue to encourage kidney nurses to care for their patients with compassion, sensitivity, and understanding.

Professor Nicola Thomas
(London) and Professor Helen Noble (Belfast)
March 2024

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The History of Kidney Dialysis and Transplantation

CHAPTER 1

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LEARNING OUTCOMES

- to understand the evolution of haemodialysis (HD), peritoneal dialysis (PD), and transplantation.
- to appreciate the challenges that healthcare professionals working in kidney care have had to overcome.
- to evaluate the changing focus of kidney care in the twenty-first century.
- to identify the opportunities for nurses working in kidney care in the future.

INTRODUCTION

The introduction of dialysis as a life-saving treatment for end-stage kidney disease (ESKD) was not the result of any large-scale research programme; rather, it emerged from the activities of a few pioneering individuals who were able to use ideas, materials, and methods from a range of developing technologies.

Haemodialysis (HD), as a routine treatment for ESKD, was initiated in the 1960s, followed by continuous ambulatory peritoneal dialysis (CAPD) in the late 1970s. The recognition of the need for immunosuppression in transplantation in the 1960s enabled it to become the preferred treatment for many patients.

HAEMODIALYSIS

THE BEGINNING

It was the Romans who first used a form of dialysis therapy by giving hot baths to patients to remove urea. The action of the hot water made the patient sweat profusely and this, together with the toxins diffusing through the skin into the bath water, would temporarily relieve symptoms. However, the Romans did not understand why the treatment worked. The effect was to leave the patient fatigued but, as the only hope, this treatment was still used on occasion into the 1950s.

The first time that the term *dialysis* was used was in 1854, by Thomas Graham, a Scottish chemist (Graham 1854). He used *dialysis* to describe the transport of solutes through an ox bladder, and this was the catalyst for other researchers working in a similar field to focus on the membrane.

Membranes were made from a variety of substances, including parchment and collodion (Eggerth 1921). Collodion is a syrupy liquid that dries to form a porous film and allows the passage of small-molecular-weight substances, whilst being impermeable to substances with a molecular weight greater than 5 kDa. In 1889, B.W. Richardson referred to the use of collodion membranes in the dialysis of blood. So, by this method, living animals were dialysed in experimental conditions (Richardson 1889), but the limiting factor that prevented the treatment being used in humans at this time was the lack of suitable materials.

PRE-1920

It was not until 1913 that the first article on the technique of HD, named the *artificial kidney*, was reported. Experimental dialysis was performed on animals by using variances in the composition of dialysis fluid (Abel et al. 1914). Substances could be added to the solution to avoid their net

Renal Nursing: Care and Management of People with Kidney Disease, Sixth Edition. Edited by Nicola Thomas and Helen Noble.

removal. The main aim of the experiments was the removal of salicylates. The removal of fluid and toxins accumulated due to kidney disease was not, at this time, considered.

In 1914, Hess and McGuigan were experimenting with dialysis in a pharmacology laboratory in Chicago. As a result, they were able to transfer sugar from tissue to blood and from the blood across a collodion membrane. The design of the dialyser minimised the length of blood tubing from the patient, and a high blood flow was achieved by connection to the carotid artery in an effort to minimise the necessity to use an anticoagulant. A single U-shaped collodion tube was inserted into a glass cylinder with a rubber stopper at one end. The blood flow both to and from the dialyser was at one end, with a port for adjusting the pressure inside the tube. These experiments were only performed on animals. The only anticoagulant available was in the form of an extract obtained from crushed leech heads, called hirudin. This was far from satisfactory, even though leeches were plentiful and readily available from the corner shop for around $25 per thousand.

THE 1920s

The first dialysis performed on a human was carried out by German physician Georg Haas in Giessen in the latter half of the 1920s. He performed six dialysis sessions in six patients. Handmade collodion membranes were used, and clotting was prevented by using hirudin and, later, a crude form of heparin. Haas used multiple dialysers concurrently to increase the surface area of blood exposed to the dialysis fluid. The six dialysers were arranged in parallel and he found that the arterial pressure of the blood was insufficient to propel the blood through the entire extracorporeal circuit. He therefore introduced a pump into the circuit. Haas received little support from his hospital and his colleagues, so by the late 1920s he gave up and the work was stopped. Haas died in 1971 at the age of 85 years, and he was honoured as the pioneer of dialysis.

Despite these treatments, carried out from the 1920s to the 1940s, those individuals with uraemia suffering from poor appetite and vomiting could be offered nothing more than bed rest and a bland salt-free diet composed mainly of vegetables, carbohydrate, and fat to reduce protein metabolism. Dialysis was not considered a realistic option, and the conservative therapy was only offered as a palliative measure.

In 1923, Heinrich Necheles became the founder of the contemporary dialyser. He experimented with the sandwiching of membranes, thus giving an increased surface area without the necessity for multiple dialysers. The membrane used was the peritoneum of a sheep. As this membrane was prone to expansion, support sheets were placed between the layers of membrane, thus allowing a large surface area of membrane to come into contact with the dialysis fluid. Other features introduced by Necheles were a heater, the priming of the pathway for the blood, and a filter to prevent clots returning to the patient.

THE 1930s

The 1930s saw great advances in synthetic polymer chemistry, resulting in the availability of cellulose acetate, which could be used as a membrane for HD. It was in 1937 that the first synthetic membrane was used by the American scientist William Thalhimer. The material, cellophane (a form of cellulose acetate), was used extensively in the sausage industry, and had the potential that was not recognised for some years. In the mid-1930s came the purification of heparin (Thalhimer et al. 1938), which could be used as an anticoagulant. Together, these two advances gave rise to the next stage of development, which took place in 1943.

THE 1940s AND 1950s

Willem Kolff, a physician working in Groningen in Nazi-occupied Holland, had his attention drawn to the work of a colleague who was concentrating plasma by using cellulose acetate as a membrane and immersing it in a weak solution of sugar. Kolff noticed that toxins in the blood were altered by this method (Kolff 1950). He built a rotating drum dialyser, which provided sufficient surface area for his first attempt at human dialysis (Kolff and Berk 1944). His machine consisted of 30 m of cellophane tube that was wound round a large cylinder. The cylinder was placed in a tank containing a weak solution of salts (the dialysate). The patient's blood was passed through the cellophane tube, the walls acting as a semipermeable membrane. Blood flow was achieved by the addition of a circuit containing a burette, which, when filled with blood, could be raised high enough to allow the blood to flow into the dialyser. The burette was then lowered, allowing the blood to drain back, and raised again to allow the blood to return to the patient. The slats in the construction of the cylinder were made of wood due to the shortage at this time of materials such as aluminium. Six hours were required for the treatment, and the efficiency of dialysis was reasonable (170 ml min^{-1} urea). Fluid could only be removed by increasing the osmotic pressure of the dialysate fluid by the addition of sugar, as an increase in pressure on the membrane would result in rupture (Kolff 1965).

The whole procedure was very time consuming and labour intensive, as the process required attention at all times to raise and lower the burette and observe the

membrane for rupture, which happened frequently. Repairs to the membrane were carried out by inserting a glass tube at the point of rupture.

Kolff's first clinical experience was gained with a 29-year-old woman with chronic nephritis. Her blood urea was kept stable for 26 days, but after 12 sessions of dialysis, her blood urea began to increase and she subsequently died.

After the war, in 1945, Kolff's technique was widely used, particularly in Sweden and the United States. The treatment was initially for acute kidney injury, when kidney function could be expected to return to normal following a short period of dialysis treatment. It was widely used in the Korean war in 1952 to treat trauma-induced acute kidney injury. This team, led by Paul Teschan, was trained to use the rotating drum dialyser and saved many lives by lowering the high potassium levels of those injured (Teschan 1955).

Some of the earliest research carried out on fluid removal from the blood using negative pressure was conducted by M.R. Malinow and W. Korzon at Michael Reese Hospital in Chicago in 1946 (Malinow and Korzon 1947). The device used was the earliest version of a dialyser with multiple blood paths and negative pressure capacity. It had parallel sections of cellulose acetate tubing and, by adding layers of tubing, the surface area of the device could be increased. The diffusion properties of this device were not considered, as it was intended only for removal of water from the blood. The device required a low priming volume and the circuit included a blood pump.

In the 1940s, interest in dialysis as a treatment for ESKD had spread throughout Europe and across to Canada as the need for dialysis was becoming widely recognized. After obtaining drawings of the Kolff dialyser, Russell Palmer and a colleague from Vancouver, in Canada, built a replica and dialysed their first patients in September 1947 (Palmer and Rutherford 1949).

Kolff was invited to take his artificial kidney to New York, where he trained physicians in the operation of the life-saving device. There was resistance from hospital staff at Mount Sinai Hospital, who only permitted the treatment to be administered in the surgical suite after normal surgical schedules were completed for the day. The first successful dialysis in Mount Sinai Hospital was in January 1948, in a female admitted to hospital having inserted mercury tablets into her vagina to induce an abortion (Fishman et al. 1948). Eight hours after the first dialysis using the Kolff machine, the patient passed urine and the dialysis was deemed a success. People with drug overdose were then regularly treated by use of the rotating drum dialyser until 1950.

To expand the use, the rotating drum needed to be modified to make it easier to use. Kolff enlisted the help of Dr. Carl Walter, who worked at the Peter Brent Brigham Hospital. Together with Edward Olson, an associate engineer from Fenwal, they set about designing and building a new version of the Kolff drum. Stainless steel was used for the drum, and refinements included a hose for filling the pan with 100 l of dialysate fluid, which was heated, and a hood to cover the drum. A tensioning device was used on the cellophane membrane as it had a tendency to stretch during use. The split connection for the patient's tubing was introduced, and this allowed the patient's tubing to remain stationary whilst the drum rotated. This was made leakproof, and a Lucite hood was added to overcome heat loss from the extracorporeal blood (Figure 1.1). These improvements paved the way for wider acceptance of the use of dialysis treatment (Merrill et al. 1950).

FIGURE 1.1 Artificial kidney machine (Kolff–Brigham), France, 1955. *Source:* With kind permission from Science and Society Picture Library.

When the Kolff–Brigham kidney was used, the heparin dose ranged from 6000 to 9000 units, and was infused prior to the start of the treatment. The dialyser was primed with blood, and the blood flow to the dialyser was limited to 200 ml at a time to prevent hypotension. To assist blood flow, a pump was inserted in the venous circuit rather than the arterial side, to minimise the probability of pressure buildup in the membrane, which would cause a rupture.

This version of the Kolff–Brigham dialysis machine was used from 1948; in all, over 40 machines were built and exported all over the world.

THE 1950s

The Allis-Chalmers Corporation was one of the first companies to produce dialysis machines commercially. They were prompted into manufacture when an employee

developed ESKD. There was no Kolff machine available and so the firm turned its attention to producing their version of the Kolff rotating drum. The resulting machine was commercially available for $5600 and Allis-Chalmers produced 14 of these machines and sold them all over the United States into the early 1950s.

In October 1956, the Kolff system became commercially available, so the unavailability of equipment could no longer be used as an excuse for non-treatment of patients. Centres purchased the complete delivery system for around $1200 and the disposables necessary for the treatment were around $60. The system was still mainly used for reversible acute kidney injury caused by drug overdose.

DEVELOPMENT OF THE DIALYSER FROM 1950s ONWARDS

Jack Leonards and Leonard Skeggs produced a plate dialyser, which would permit a reduction in the priming volume and allow negative pressure to be used to remove fluid from the patient's system (Skeggs et al. 1949). A modification to this design included a manifold system, which allowed variation of the surface area without altering the blood distribution. Larger dialysers followed, which necessitated the introduction of a blood pump.

In the late 1950s, Fredrik Kiil of Norway developed a parallel plate dialyser, with a large surface area (1 m^2), requiring a lower priming volume. A new cellulose membrane, Cuprophan, was used, and this allowed the passage of larger molecules than other materials that were available at that time. The Kiil dialyser could be used without a pump. Kiil dialysed the patients using their own arterial pressure. This dialyser was widely used because the disposables were relatively inexpensive when compared with other dialysers available at that time.

A crude version of the capillary-flow dialyser, the parallel dialyser, was developed, using a new blood pump with a more advanced version of the Alwall kidney (MacNeill 1949). However, it was John Guarino who incorporated the important feature of a closed system, a visible blood pathway.

To reduce the size of the dialyser without reducing the surface area, William Y. Inouye and Joseph Engelberg produced a plastic mesh sleeve to protect the membrane. This reduced the risk of the dialysis fluid coming into contact with the blood. This was a closed system, so the effluent could be measured to determine the fluid loss of the patient. It is the true predecessor of the positive- and negative-pressure dialysers used today.

The first commercially available dialyser was manufactured by Baxter and based on the Kolff rotating drum. It provided a urea clearance of approximately and was based on the coil design. The priming volume was 1200–1800 ml, and this was drained into a container at the end of treatment, refrigerated, and used for priming for the next treatment. It was commercially available in 1956 for $59.00.

The forerunner of today's dialyser was produced by Richard Stewart in 1960. The criteria for design of this hollow-fibre dialyser were low priming volume and minimal resistance to flow. The improved design contained 11 000 fibres, which provided a surface area of 1 m^2.

Future designs for the dialyser focused on refining the solute and water removal capabilities, as well as reducing the size and priming requirements of the device, thus allowing an even higher level of precise individual care.

EMERGENCE OF HOME HAEMODIALYSIS

It was the development of Scribner's shunt (see next section on vascular access) that led to the first dialysis unit being established for patients at the University of Washington Hospital. Belding Scribner also developed a central dialysate delivery system for multiple use and set this up in the chronic care centre, which had 12 beds. These beds were quickly taken and his plan for expansion was rejected. The only alternative was to send the patients home, so the patient and family were trained to perform the dialysis and care for the shunts. Home dialysis was strongly promoted by Scribner.

Stanley Shaldon reported in 1961 that a patient dialysing at the Royal Free Hospital in London was able to self-care by setting up his own machine, initiating, and terminating dialysis (Figure 1.2); so home HD in the UK was made possible. The shunt was formed in the leg for vascular access, to allow the patient to have both hands free for the procedures. Hence, Shaldon was able to report the results of his first patient to be placed on overnight home HD in November 1964. With careful patient selection, the venture was a success. Scribner started to train patients for home at this time, and his first patient was a teenager assisted by her mother. Home dialysis was selected for this patient so that she would not miss her high-school education. The average time on dialysis was 14 hours twice weekly. To allow freedom for the patient, overnight dialysis was widely practised. At first, emphasis was on selection of the suitable patient and family, even to the extent of a stable family relationship, before the patient could be considered for home training (Baillod et al. 1965).

From these beginnings, large home HD programmes developed in the United States and the United Kingdom, thus allowing expansion of the dialysis population without increasing hospital facilities. Many patients could now be

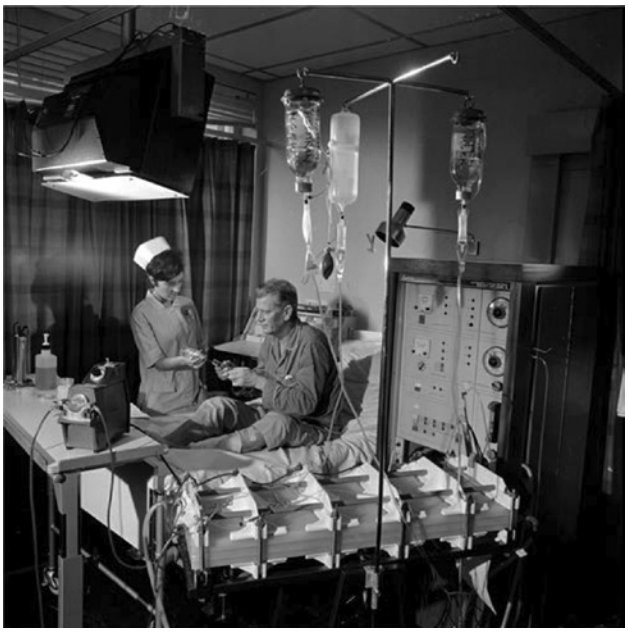

FIGURE 1.2 Patient and nurse with dialysis machine and Kiil dialyser, 1968. *Source:* With kind permission from Science and Society Picture Library.

considered for home treatment, often with surprisingly good results, as the dialysis could be moulded to the requirements of the individual, rather than the patients conforming to a set pattern. However, with the development in the late 1970s and early 1980s of CAPD as the first choice for home treatment, the use of home HD steadily dwindled. It is now, however, seeing renewed interest. The National Institute for Clinical Excellence (NICE) published guidance on home versus hospital HD (NICE 2002) and recommended all suitable patients should be offered the choice between home HD or HD in a hospital/satellite unit. Sadly this has not led top wide-scale uptake of home HD, with only 1,396 adult patients were receiving HHD for ESKD in the UK in 2021, which represents 2.0% of the whole population who require replacement therapy for ESKD (UK Renal Registry 2023).

VASCULAR ACCESS FOR HAEMODIALYSIS

It was Sir Christopher Wren, of architectural fame, who in 1657 successfully introduced drugs into the vascular system of a dog. In 1663, Sir Robert Boyle injected successfully into humans. Prison inmates were the subjects and the cannula used was fashioned from a quill. For HD to become a widely accepted form of treatment for ESKD, a way to provide long-term access to the patient's vascular system had to be found. Until this problem was solved, long-term treatment could not be considered. In order for good access to be established, a tube or cannula had to be inserted into an artery or vein, thus giving rise to good blood flow from the patient. The repeated access for each treatment quickly led to exhaustion of blood vessels for cannulation. The need for a system whereby a sufficiently large blood flow could be established for dialysis, without destroying a section of blood vessel every time dialysis was required, was imperative.

In the 1950s, Teschan, in the 11th Evacuation Hospital in Korea, was responsible for developing a method of heparin lock for continuous access to blood vessels. The cannulae were made from Tygon tubing and stopcocks, and the blood was prevented from clotting by irrigation with heparinised saline. It was not a loop design, as the arterial and venous segments were not joined together.

In 1960, in the United States, George Quinton, an engineer, and Belding Scribner, a physician, made use of two new synthetic polymers – Teflon and Silastic – and, using the tubing to form the connection between a vein and an artery, were able to reroute the blood outside the body (usually in the leg). This was known as the arteriovenous (AV) shunt. The tubing was disconnected at a union joint in the centre, and each tube then connected to the lines of the dialysis machine. At the end of treatment, the two ends were then reconnected, establishing a blood flow from the artery to the vein outside the body. In this way, repeat dialysis was made possible without further trauma to the vascular system.

This external shunt, whilst successful, had drawbacks. It was a potential source of infection, often thrombosed, and had a restrictive effect on the activity of the patient. In 1966, Michael Brescia and James Cimino developed the subcutaneous radial artery-to-cephalic vein AV fistula (Cimino and Brescia 1962), with Cimino's colleague, Kenneth Appel, performing the surgery.

The AV fistula required less anticoagulation, had reduced infection risk, and gave access to the bloodstream without danger of shunt disconnection. Subsequently, a number of synthetic materials have been introduced to create internal AV fistulae (grafts).

FURTHER DEVELOPMENTS

Monitoring and total control of the patient's therapy became more important as dialysis became widespread, and so equipment development has continued. Machines incorporated temperature monitoring, positive-pressure gauges, and flow meters. Negative-pressure monitoring followed, as did a wide range of dialysers with varying

surface areas, ultrafiltration capabilities, and clearance values. Automatic mixing and delivery of the dialysate and water supply to the machine greatly increased the margin of safety for the procedure and made the dialysis therapy much easier to manage. The use of microprocessors, allowing the nurse to programme a patient's requirements (such as blood flow, duration of dialysis, and fluid removal), has resulted in a prescription for an individual's needs. Average dialysis time was reduced to 4 hours, three times weekly.

The early 1970s saw the overall number of patients on kidney replacement therapy (KRT) increase due to the increased awareness brought about by the availability of treatment. Free-standing units for the sole use of kidney dialysis came into being, leading to dialysis becoming a full-time business. Committees for patient selection were disbanded, and dialysis facilities were demanded within easy reach of patients' homes. This expectation led to the emergence of small satellite units, managed and monitored by larger units, as a popular alternative to home HD treatment.

PERITONEAL DIALYSIS

Peritoneal dialysis (PD) as a form of therapy for ESKD was brought about as a result of the innovative efforts and the tenacity of many pioneers over the past two centuries. It was probably the early Egyptian morticians who first recognised the peritoneum and peritoneal cavity, with the peritoneal cavity described in 3000 BC in the Ebers papyrus as a cavity in which the viscera were somehow suspended. In Ancient Greek times, Galen, a physician, made detailed observations of the abdomen whilst treating the injuries of gladiators.

The earliest reference to what may be interpreted as PD was in the 1740s when Christopher Warrick reported to the Royal Society in London that a 50-year-old woman suffering from ascites was treated by infusing Bristol water and claret wine into the abdomen through a leather pipe (Warrick 1744). The patient reacted violently to the procedure, and it was stopped after three treatments. However, the patient was reported to have recovered and was able to walk 7 miles (13 km) a day without difficulty. A modification of this therapy was subsequently tried by Stephen Hale of Teddington in England. Two trocars were used – one on each side of the abdomen – allowing the fluid to flow in and out of the peritoneal cavity during an operation to remove ascites (Hale 1744).

Subsequent experiments on the peritoneum (Wegner 1877) determined the rate of absorption of various solutions, the capacity for fluid removal (Starling and Tubby 1894), and evidence that protein could pass through the peritoneum. It was also noted that the fluid in the peritoneal cavity contained the same amount of urea that is found in the blood, indicating that urea could be removed by PD (Rosenberg 1916). This was followed by Putnam in 1923, suggesting that the peritoneum might be used to correct physiological problems. He observed that under certain circumstances fluids in the peritoneal cavity can equilibrate with plasma and that the rate of diffusion was dependent on the size of the molecules. At this time it was also suggested that the clearance of solutes was proportional to their molecular size and solution pH, and that a high flow rate maximised the transfer of solutes, which also depended on peritoneal surface area and blood flow (Putman 1923).

George Ganter was looking for a method of dialysis that did not require the use of an anticoagulant (Ganter 1923). He prepared a dialysate solution containing normal values of electrolytes and added dextrose for fluid removal. Bottles were boiled for sterilisation and filled with the solution, which was then infused into the patient's abdomen through a hollow needle.

The first treatment was carried out on a woman who was suffering acute kidney injury following childbirth. Between 1 and 3 l of fluid were infused at a time, and the dwell time was 30 minutes to 3 hours. The blood chemistry was reduced to within acceptable limits. The patient was sent home but, unfortunately, she died, as it was not realised that it was necessary to continue the treatment in order to keep the patient alive.

Ganter recognised the importance of good access to the peritoneum, as it was noted that it was easier to instill the fluid than it was to attain a good return volume. He was also aware of the complication of infection, and indeed it was the most frequent complication that he encountered. Ganter identified four principles, which are still regarded as important today:

1. There must be adequate access to the peritoneum.
2. Sterile solutions are needed to reduce infection.
3. Glucose content of the dialysate must be altered to remove greater volumes of fluid.
4. Dwell times and fluid volume infused must be varied to determine the efficiency of the dialysis.

There are reports of 101 patients treated with PD in the 1920s (Abbott and Shea 1946; Odel et al. 1950). Of these, 63 had reversible causes, 32 irreversible, and in 2 the diagnosis was unknown. There was recovery in 32 of 63

cases of reversible renal failure. Deaths were due to uraemia, pulmonary oedema, and peritonitis.

Stephen Rosenak, working in Europe, developed a metal catheter for peritoneal access but was discouraged by the results because of the high incidence of peritonitis. In Holland, P.S.M. Kop, who was an associate of Kolff during the mid-1940s, created a system of PD by using materials for the components that could easily be sterilised: porcelain containers for the fluid, latex rubber for the tubing, and a glass catheter to infuse the fluid into the patient's abdomen. Kop treated 21 patients and had a successful outcome with 10.

Morton Maxwell, in Los Angeles in the latter part of the 1950s, had been involved with HD, and it was his opinion that HD was too complicated for regular use. Aware of the problems with infection, he designed a system for PD with as few connections as possible. Together with a local manufacturer, he formulated a peritoneal solution and customised a container and plastic tubing set and a single polyethylene catheter. The procedure was to instill 2 L of fluid into the peritoneum, leave it to dwell for 30 minutes, and return the fluid into the original bottles. This would be repeated until the blood chemistry was normal. This technique was carried out successfully on many patients and the highly regarded results were published in 1959. This became known as the Maxwell technique (Maxwell et al. 1959). This simple form of dialysis recognised that it was no longer necessary (as with HD), to have expensive equipment with highly specialised staff in a large hospital to initiate dialysis.

THE PERITONEAL DIALYSIS CATHETER

Up to the 1970s, PD was used primarily for patients who were not good candidates for HD, or who were seeking a gentler form of treatment. Continuous flow using two catheters (Maxwell and Merrill 1953) was still sometimes used, but the single-catheter technique was favoured because of lower infection rates.

The polyethylene catheter was chosen by Paul Doolan (Doolan et al. 1959) at the Naval Hospital in San Francisco when he developed a procedure for the treatment to use under battlefield conditions in the Korean War. Because of the flexibility of the catheter, it was considered for long--term treatment. A young physician called Richard Ruben decided to try this procedure, known as the Doolan technique (Ruben et al. unpublished work), on a female patient who improved dramatically, but deteriorated after a few days without treatment. The patient was therefore dialysed repeatedly at weekends and allowed home during the week, with the catheter remaining in place. This was the first reported long-term treatment using a permanent indwelling catheter.

PD catheters at this time were made from tubing available on the hospital ward and included gallbladder trocars, rubber catheters, whistle-tip catheters, and stainless-steel sump drains. However, as with polyethylene plastic tubes, the main challenge was kinking and blockage. Maxwell described a nylon catheter with perforations at the curved distal end, and this was the catheter that became commercially available. Advances in the manufacture of the silicone peritoneal catheter by Palmer (Palmer et al. 1964) and Gutch (Gutch 1964) included the introduction of perforations at the distal end, and later Tenckhoff included the design of a shorter catheter, a straight catheter, and a curled catheter. He also added the Dacron cuff, either single or double, to help to seal the openings through the peritoneum (Tenckhoff and Schechter 1968). He was also responsible for the introduction of the trocar that gave easy placement of the catheter. Dimitrios Oreopoulos, a Greek physician, was introduced to PD in Belfast, Northern Ireland, during his training and he noted the difficulties encountered with the catheters there. He had been shown a simple technique for inserting the catheter by Norman Dean from New York City, which allowed access to be used repeatedly.

PERITONEAL DIALYSIS AT HOME

In 1960, Scribner and Boen (Boen 1959) set up a PD programme that would allow patients to be treated at home. An automated unit was developed which could operate unattended overnight. The system used 40 L containers that were filled and sterilised at the University of Washington. The bottles were then delivered to the patient's home and returned after use. The machine was able to measure the fluid in and out of the patient by a solenoid device. An indwelling tube was permanently implanted into the patient's abdomen, through which a tube was inserted for each dialysis treatment. The system was open, and therefore was vulnerable to peritonitis. A new method was then used, whereby a new catheter was inserted into the abdomen for each treatment and removed after the treatment ended. This was still carried out in the home, when a physician would attend the patient at home for insertion of the catheter, leaving once the treatment had begun. The carer was trained to discontinue the treatment and remove the catheter. The wound was covered by a dressing, and the patient would be free of dialysis until the next week. This treatment was carried out by Tenckhoff et al. (1965) in a patient for 3 years, requiring 380 catheter punctures.

The large 40 L bottles of dialysate were difficult to handle, and delivery to the home and sterilisation were not easy. Tenckhoff, at the University of Washington, installed a water 'still' into the patient's home, to provide a sterile water supply. The water was mixed with sterile concentrate to provide the correct solution, but this method was not satisfactory as it remained cumbersome and dangerous due to the high pressure in the still. Various refinements were tried using this method, including a reverse osmosis unit, and this was widely used later for HD treatment.

Lasker, in 1961, realised the potential of this type of treatment and concentrated on the idea of a simple version by instilling 2 L of fluid by a gravity-fed system. This proved to be cheaper to maintain but was labour intensive. Later that year, he was approached by Ira Gottscho, a businessman who had lost a daughter through kidney disease, and together they designed the first peritoneal cycler machine. The refinements included the ability to measure the fluid in and out and the ability to warm the fluid before the fill cycle. Patients were sent home using the automated cycler treatment as early as 1970, even though there was a bias for HD at that time.

In 1969, Oreopoulos accepted a position at the Toronto Western Hospital and, together with Stanley Fenton, decided to use the Tenckhoff catheter for long-term treatment. Because of a lack of space and facilities at the hospital, it was necessary to send the patients home on intermittent PD. He reviewed the Lasker cycler machine and ordered a supply, and by 1974 was managing over 70 patients on this treatment at home. Similar programmes were managed in Georgetown University and also in the Austin Diagnostic Clinic in the USA.

BEGINNING OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

It was in 1975, following an unsuccessful attempt to haemodialyse a patient at the Austin Diagnostic Clinic, that an engineer, Robert Popovich, and Jack Moncrief became involved in working out the kinetics of 'long-dwell equilibrated dialysis' for this patient. It was determined that five exchanges each of 2 L day^{-1} would achieve the appropriate blood chemistry, and that the removal of 1–2 L of fluid from the patient was needed per day. Thus came the evolution of CAPD (Popovich et al. 1976).

The treatment was so successful that the Austin group was given a grant to allow it to continue dialysing patients with CAPD. Strangely, the group's first description and account of this clinical experience was rejected by the American Society for Artificial Internal Organs. At this time, the treatment was called 'a portable/wearable equilibrium dialysis technique'. The stated advantages compared to HD included:

- good steady-state biochemical control;
- more liberal diet and fluid intake;
- improvement in anaemia.

The main challenges were protein loss (Popovich et al. 1978) and infection. It was recognised that the source of infection was almost certainly related to the use of the bottles. Oreopoulos found that collapsible polyvinylchloride (PVC) containers for the solution were available in Canada. Once the fluid was instilled, the bag could then be rolled up and concealed under the clothing. The fluid could be returned into the bag during draining by gravity, without a disconnection taking place (Oreopoulos et al. 1978). New spike connections were produced for access to the bag of fluid, and a Luer connection for fitting to the catheter, together with tubing devised for HD, greatly reduced the chances of infection. The patients treated on an intermittent basis (by intermittent peritoneal dialysis or IPD) were rapidly converted to CAPD and evaluation of the new treatment was rapid, due to the large numbers being treated. Following approval by the US Food and Drug Administration, many centres were then able to develop CAPD programmes.

The first complete CAPD system was released to the market in 1979, giving a choice of three strengths of dextrose solution. Included in this system were an administration line and sterile items packed together to form a preparation kit, to be used at each bag change in an attempt to keep infection at bay. The regime proposed by Robert Popovich and Jack Moncrief entailed four exchanges over a 24-hour period, three dwell times of approximately 4 hours in the daytime, and 1 dwell overnight of 8 hours. This regime is the one often used today.

ADVANCES IN PERITONEAL DIALYSIS 1970s–2000s

The PD systems were continually being improved, with connectors moving from spike to Luer to eliminate as far as possible the accidental disconnection of the bag from the line. A titanium connector was found to be the superior form of adaptor for connection of the transfer set to the catheter, and probably led to a reduced infection rate (peritonitis). A disadvantage of this technique is the flow of fresh fluid down the transfer set along the area of disconnection, thus encouraging any bacteria from the disconnection to be instilled into the abdomen. The development

of the Y-system (flush before fill) in the mid-1980s in Italy resulted in a further decrease in peritonitis.

Automated PD in the form of continuous cyclic peritoneal dialysis (CCPD) was further developed by Diaz-Buxo in the early 1980s to enable patients who were unable to perform exchanges in the day to be treated with PD overnight.

Advances in CAPD included a dialysate that not only provides dialysis but that contains 1.1% amino acid, to be administered to patients who were malnourished. Those with diabetes were initially not considered for dialysis because of the complications of the disease. Carl Kjellstrand, at the University of Minnesota, suggested that insulin could be administered to those with diabetes by adding it to the PD fluid (Crossley and Kjellstrand 1971). However, this suggestion was not initially adopted because the 30-minute dwell did not give time for the drug to be absorbed into the patient. It became viable later, when long-dwell dialysis was initiated, and this gave the advantage of slow absorption, resulting in a steady state of blood sugar in the normal range, thus alleviating the need for painful injections (Flynn and Nanson 1979).

The realisation that patients are individuals, bringing their own problems associated with training, brought many exchange aid devices onto the market to assist the patient in the exchange procedure. These exchange devices were mainly used to assist such disabilities as blindness, arthritis (particularly of the hands), and patients prone to repeated episodes of peritonitis.

PERITONEAL DIALYSIS: THE PRESENT

In some centres across the world, PD is often the first choice of treatment for ESKD, because of the lack of facilities for in-centre HD. However, the relative prevalence of PD in the United Kingdom has been declining since its peak in the early 1990s, possibly because of the availability of satellite HD and concerns over PD failure in the shorter-term. At the end of 2021 in the UK, 3903 adult patients were receiving PD for ESKD, compared to 3822 in 2020, which represented 5.6% of the KRT population (UK Renal Registry 2023).

TRANSPLANTATION

IN THE BEGINNING

Kidney transplantation as a therapeutic and practical option for KRT was first reported in published literature at the turn of the twentieth century. The first steps were small and so insignificant that they were overlooked or condemned.

The first known attempts at renal transplantation on humans were made without immunosuppression between 1906 and 1923 using pig, sheep, goat, and sub-human primate donors (Elkington 1964). These first efforts were conducted in France and Germany, but others followed. None of the transplants functioned for long, if indeed at all, and the recipients all died within a period of a few hours to 9 days later.

Of all the workers at this time, the contribution made by Alixis Carrel (1873–1944) remains the most famous. His early work in Lyons, France, and in Chicago involved the transplantation of an artery from one dog to another. This work later became invaluable in the transplantation of organs. In 1906, Carrel and Guthrie, working in the Hull Laboratory in Chicago, reported the successful transplantation of both kidneys in cats and later a double nephrectomy in dogs, reimplanting only one of the kidneys. He found that the secretion of urine remained normal, and the animal remained in good health, despite having only one kidney (Carrel 1983). Carrel was awarded the Nobel Prize in 1912 for his work on vascular and related surgery.

While at this stage there was no clear understanding of the problem, some principles were clearly learned. Vascular suture techniques were reviewed and the possibility of using pelvic implantation sites was investigated and practised. No further renal heterotransplantations (animal to human) were tried until 1963, when experiments using kidneys from chimpanzee (Reemtsma et al. 1964) and baboon were tried, with eventual death of the patients. This ended all trials using animal donation.

The first human-to-human kidney transplant was reported in 1936, by the Russian Voronoy, when he implanted a kidney from a cadaver donor of B-positive blood type into a recipient of O-positive blood type, a mismatch that would not be attempted today. The donor had died 6 hours before the operation and the recipient died 6 hours later without making any urine. The following 20 years saw further efforts in kidney transplantation, all without effective immunosuppression (Groth 1972). The extraperitoneal technique developed by French surgeons Dubost and Servelle became today's standard procedure.

THE FIRST SUCCESSES

The first examples of survival success of a renal transplant can probably be attributed to David Hume, who placed the transplanted kidney into the thigh of the patient, which functioned for 5 months. Then at the Peter Bent Brigham Hospital in Boston, Massachusetts, in December 1954, the first successful identical-twin transplant was performed by the surgeon Joseph E. Murray in collaboration with the

nephrologist John P. Merrill (Hume et al. 1955). The recipient survived for more than two decades. The idea of using identical twins had been proposed when it was noted by David C. Miller of the Public Health Service Hospital, in Boston, that skin grafts between identical twins were not rejected (Brown 1937). The application of this information resulted in rigorous matching, including skin grafting, prior to effective immunosuppression.

Over the period between 1951 and 1976 there were 29 kidney transplants performed between identical twins, and the survival rate for 20 years was 50%. Studies of two successfully transplanted patients, who were given kidneys from their non-identical twins, were also reported (Merrill et al. 1960). The first survived 20 years, dying of heart disease, and the second 26 years, dying of carcinoma of the bladder. Immunosuppression used in these cases was irradiation.

IMMUNOSUPPRESSION

It was Sir Peter Medawar who appreciated that rejection is an immunological phenomenon (Medawar 1944), and this led to research into weakening the immune system of the recipients to reduce the rejection. In animals, corticosteriods, total body irradiation, and cytotoxic drug therapy were used. Experiments in animals were still far from successful, as were similar techniques when used in humans. It was concluded that the required degree of immunosuppression would lead to destruction of the immune system and finally result in terminal infections.

A few patients were transplanted between 1960 and 1961 in Paris and Boston, using drug regimens involving 6-mercaptopurine or azathioprine, with or without irradiation. They all died within 18 months. Post-mortem examination of failed kidney grafts showed marked changes in the renal histology. At first it was thought unlikely that the changes were due to immunological rejection, but later it was convincingly shown that this was indeed the underlying process.

In the early days of kidney transplantation, the kidney was removed from either a living related donor or a cadaver donor and immediately transferred to the donor after first flushing the kidney with cold electrolyte solution such as Hartman's solution. In 1967, Belzer and his colleagues developed a technique for continuous perfusion of the kidney using oxygenated cryoprecipitated plasma, which allowed the kidney to be kept up to 72 hours before transplantation. This machine perfusion required constant supervision, and it was found that flushing the kidney with an electrolyte solution and storage at 0 °C in iced saline allowed the kidney to be preserved for 24 hours or more (Marshall et al. 1988). This was a major development in transplantation techniques.

During the 1950s, it was recognised that many of the survivors of the Hiroshima atomic bomb in 1945 suffered impairment to their immune system. It was concluded that radiation could therefore induce immunosuppression, and clinical total body irradiation was used to prolong the survival of renal transplants in Boston in 1958. This did improve the survival of some transplants; however, the overall outcomes were poor. There was clearly a need for a more effective form of immunosuppression than irradiation.

A breakthrough in immunosuppressive therapy occurred in 1962 at the University of Colorado, when it was discovered that the combination of azathioprine and prednisone allowed the prevention and in some cases reversal of rejection (Starzl et al. 1963). Transplantation could at last expand. A conference sponsored by the National Research Council and National Academy of Sciences in 1963 in Washington resulted in the first registry report, which enabled the tracing of all the early non-twin kidney recipients. In 1970, work commenced on the development of ciclosporin by Sandoz in Basel, Switzerland, following recognition of the potential (Borel et al. 1976). Clinical trials carried out in Cambridge, United Kingdom (Calne et al. 1979), showed that outcomes on renal transplantation were greatly improved, both with graft and with patient survival. Ciclosporin revolutionised immunosuppression protocols for patients who have been transplanted, even though this medication is itself nephrotoxic and its use needs close monitoring.

Tissue typing is a complex procedure. The use of united networks for organ sharing has increased the efforts of matching donor and recipient, and data available from these sources show a significant gain in survival of well-matched versus mismatched cadaver kidneys. Cross-matching remains as important today as it was at its conception. None of the immunosuppressive measures available today can prevent the immediate destruction of the transplanted organ by humoral antibodies in the hyperacute rejection phase. This was recognised as early as 1965 (Kissmeyer-Neilsen et al. 1966), and it may be that this phenomenon holds the key to the future of successful heterotransplantation.

THE PRESENT

Renal transplantation has been a dramatic success since the 1980s, with patient survival rates not less than 97% after 6 months' transplantation for both living related and cadaver transplants. At the end of 2021 in the UK, 39 189 adult patients were living with a kidney transplant for ESKD, which represented 56.4% of the KRT population.

THE FUTURE

There is no doubt that renal transplantation is the 'gold standard' for patients requiring KRT. giving, in general, a better quality of life than dialysis. However, donor organs remain in short supply, despite changes in UK law and in other countries (see Chapter 9). Encouragingly, there was a 15% increase in kidney transplants performed in the UK 2021 compared with 2020, with an increase in transplants from living donors by 36%, although transplant activity has not yet recovered to pre-pandemic levels (UK Renal Registry 2023).

CONCLUSION

Kidney replacement therapy has come a long way from the small beginnings of the hot baths in Rome. Refinements and improvements continue, but the challenge of providing acceptable person-centered therapies for all who need treatment for ESKD remains.

In summary, UK Renal Registry data (2023) report that in the United Kingdom at the end of 2021:

- 8,175 adult patients started KRT for ESKD in the UK in 2021, an increase of 7.3% from 2020.
- The incidence of kidney replacement therapy in adults was 154 pmp.
- The median age of patients receiving KRT was 63.7 years but varied with ethnicity (White 65.6 years; Asian 61.8 years; and Black 57.8 years).
- Diabetes remains the most common identifiable primary kidney disease and continues to account for an increasing proportion of patients starting KRT (31.3%).
- In 2021, 21% of patients started KRT on PD, compared to 21.8% in 2020. This is still a higher proportion than previous years.
- In 2021, only 5.8% of patients started KRT with a transplant, lower than previous years and likely due to ongoing COVID-related disruption.
- In summary, Figure 1.3 shows treatment modality of adult patients receiving KRT in 2020.

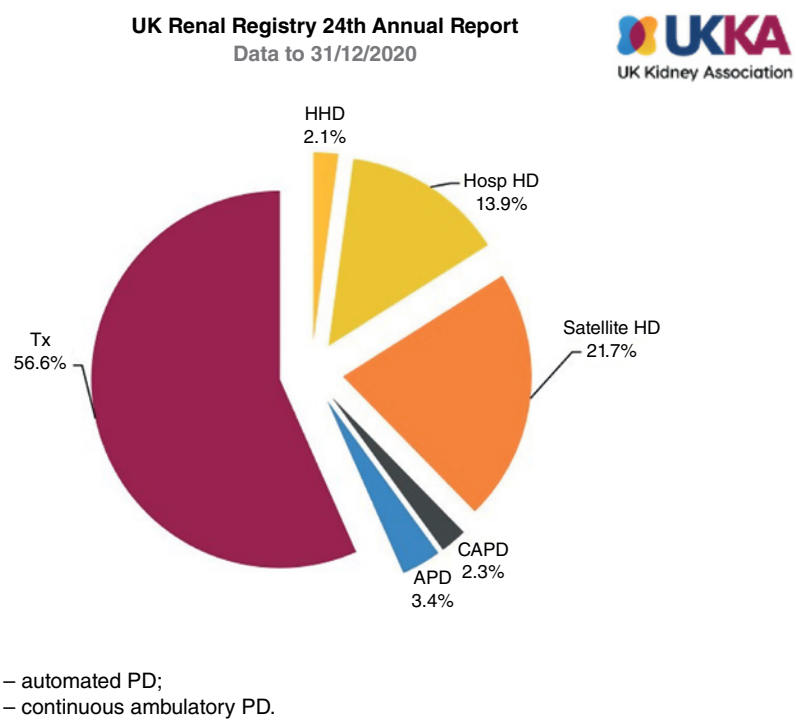

FIGURE 1.3 Treatment modality of adult patients receiving KRT in the UK (not including data from Scotland) on 31/12/2020.
Note: The data reported by the UK Renal Registry have been supplied by the UKRR of the UK Kidney Association. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the UKRR or the UK Kidney Association.

REFERENCES

Abbott, W.E. and Shea, P. (1946). Treatment of temporary renal insufficiency (uraemia) by peritoneal lavage. *American Journal of the Medical Sciences* 211: 312.

Abel, J.J., Rowntree, L.G., and Turner, B.B. (1914). The removal of diffusable substances from the circulating blood of living animals by dialysis. *Journal of Pharmacology and Experimental Therapeutics* 5: 275–316.

Baillod, R.A., Comty, C., Ilahi, M. et al. (1965). *Proceedings of the European Dialysis and Transplant Association 2*, 99. Amsterdam: Excerpta Medica.

Boen, S.T. (1959). *Peritoneal Dialysis*, 26. Amsterdam: Van Gorcum.

Borel, J.F., Feurer, C., Gubler, H.U. et al. (1976). Biological effects of cyclosporin A. A new antilymphocytic agent. *Agents and Actions* 6: 468–475.

Brown, J.B. (1937). Homografting of the skin. With report of success in identical twins. *Surgery* 1: 558–563.

Byrne, C., Caskey, F., Castledine, C. et al. (2018). The twentieth annual report of the UK Renal Registry, Bristol. *Nephron* 139 (suppl1): 13–46.

Calne, R.Y., Rolles, K., White, D.J.G. et al. (1979). Cyclospor A initially as the only immunosuppressant in 34 recipients of cadaveric organs: 32 kidneys, 2 pancreases, and 2 livers. *Lancet* 1: 1033–1036.

Carrel, A. (1983). Results of the transplantation of blood vessels, organs and limbs. *JAMA* 250: 994–953.

Cimino, J.E. and Brescia, M.J. (1962). Simple venepuncture for haemodialysis. *New England Journal of Medicine* 267: 608–609.

Crossley, K. and Kjellstrand, C.M. (1971). Intraperitoneal insulin for control of blood sugar in diabetic patients during peritoneal dialysis. *British Medical Journal* 1: 269–290.

Doolan, P.D., Murphy, W.P. Jr., Wiggins, R.A., et al. (1959). An evaluation of intermittent peritoneal lavage. *American Journal of Medicine* 26: 831–844.

Eggerth, A.H. (1921). The preparation and standardization of collodion membranes. *Journal of Biological Chemistry* 48 (1): 203–221.

Elkington, J.R. (1964). Moral problems in the use of borrowed organs artificial and transplanted. *Annals of Internal Medicine* 60: 309–313.

Fishman, A.P., Kroop, I.G., Leiter, H.E. et al. (1948). Management of anuria in acute mercurial intoxication. *NY State Journal of Medicine* 48: 2393–2396.

Flynn, C.T., and Nanson, J.A. (1979). Intraperitoneal insulin with CAPD – an artificial pancreas. *Transactions of the American Society of Artificial Internal Organs* 25: 114–117.

Ganter, G. (1923). About the elimination of poisonous substances from the blood by dialysis. *Münchener Medizinische Wochenschrift (1950)* 70: 1478–1480.

Graham, T. (1854). The Bakerian lecture – on osmotic force. *Philosophical Transactions of the Royal Society of London* 144: 177–228.

Groth, C.G. (1972). Landmarks in clinical renal transplantation. *Surgery, Gynecology & Obstetrics* 134: 323–328.

Gutch, C.F. (1964). Peritoneal dialysis. *Transactions of the American Society of Artificial Internal Organs* 10: 406–407.

Hale, S. (1744). A method of conveying liquors into the abdomen during the operation of tapping. *Philosophical Transactions of the Royal Society* 43: 20–21.

Hess, C.L.V. and McGuigan, H. (1914). The condition of the sugar in the blood. *Journal of Pharmacology and Experimental Therapeutics* 6: 45–55.

Hume, D.M., Merrill, J.P., Miller, B.F., et al. (1955). Experience with renal homotransplantation in the human. Report of nine cases. *Journal of Clinical Investigation* 34: 327–382.

Kissmeyer-Neilsen, F., Olsen, S., Peterson, V.P., et al. (1966). Hyperacute rejection of kidney allografts, associated with pre-existing humoral antibodies against donor cells. *Lancet* 2: 662–665.

Kolff, W.J. (1950). Artificial kidney – treatment of acute and chronic uraemia. *Cleveland Clinic Quarterly* 17: 216–228.

Kolff, W.J. (1965). First clinical experience with the artificial kidney. *Annals of Internal Medicine* 62: 608–619.

Kolff, W.J. and Berk, H.T. (1944). The artificial kidney: a dialyser with a great area. *Acta Medica Scandinavica* 117: 121–134.

Legrain, M. and Merrill, J.P. (1953). Short term continuous transperitoneal dialysis. *New England Journal of Medicine* 248: 125–129.

MacNeill, A.E. (1949). Some possible uses of blood dialysers. Surgeons practice meeting, 23 September 1949, Bretton Woods, NH, *Proceedings of the New England Surgical Society*, p. 3.

Malinow, M.R. and Korzon, W. (1947). Experimental method for obtaining an ultrafiltrate of the blood. *Journal of Laboratory and Clinical Medicine* 31: 461–471.

Marshall, V.C., Jablonski, P., and Scott, D.F. (1988). Renal preservation. In: *Kidney Transplantation: Principles and Practice*, 3e (ed. P.J. Morris), 151–182. Philadelphia, PA: W.B. Saunders.

Maxwell, M.H., Rockney, R.E., and Kleeman, C.R. (1959). Peritoneal dialysis, techniques and application. *JAMA* 170: 917–924.

Medawar, P.B. (1944). The behaviour and fate of skin autografts and skin homografts in rabbits. *Journal of Anatomy* 78: 176–199.

Merrill, J.P., Murray, J.E., Harrison, J.H. et al. (1960). Successful homotransplantation of the kidney between non-identical twins. *New England Journal of Medicine* 262: 1251–1260.

Merrill, J.P., Thorn, G.W., Walter, C.W. et al. (1950). The use of an artificial kidney. 1. Technique. *Journal of Clinical Investigation* 29: 412–424.

National Institute for Clinical Excellence (2002). Guidance on Home compared with Hospital Haemodialysis for Patients with

End-Stage Renal Failure 2002, Technology Appraisal No. 48. https://www.nice.org.uk/guidance/ta48 (accessed 3 April 2024).

Odel, H.M., Ferris, D.O., and Power, H. (1950). Peritoneal lavage as an effective means of extrarenal excretion. *American Journal of Medicine* 9: 63–77.

Opelz, G. and Terasaki, P.I. (1974). Poor kidney transplant survival in recipients with frozen-blood transfusions or no transfusions. *Lancet* 2: 696–698.

Oreopoulos, D.G., Robson, M., Izatt, S. et al. (1978). A simple and safe technique for continuous ambulatory peritoneal dialysis. *Transactions of the American Society of Artificial Organs* 24: 484–489.

Palmer, R.A., Quinton, W.E., and Gray, J.F. (1964). Prolonged peritoneal dialysis for chronic renal failure. *Lancet* 1: 700–702.

Palmer, R.A. and Rutherford, P.S. (1949). Kidney substitutes in uraemia: the use of Kolff's dialyser in two cases. *Canadian Medical Association Journal* 60: 261–266.

Popovich, R.P., Moncrief, J.F., Decherd, J.F., et al. (1976). The definition of a novel portable/wearable equilibrium peritoneal dialysis technique. *Abstracts of the Transactions of the American Society of Artificial Organs* 5: 64.

Popovich, R.P., Moncrief, J.W., Nolph, K.D. et al. (1978). Continuous ambulatory peritoneal dialysis. *Annals of Internal Medicine* 88: 449–456.

Putman, T. (1923). The living peritoneum as a dialysing membrane. *American Journal of Physiology* 63: 548–555.

Reemtsma, K., McCracken, B.H., Schlegel, J.U. et al. (1964). Renal heterotransplantation in man. *Annals of Surgery* 160: 384–410.

Richardson, B.W. (1889). Practical studies in animal dialysis. *Asclepiad* 6: 331–332.

Rosenberg, M. (1916). Nitrogenous retention of substances in the blood and in other body fluids in the core of the kidneys. *Berlin Klinischen Wochenschrift* 53: 1314–1316.

Skeggs, L.T. Jr., Leonards, J.R., and Heisler, C.R. (1949). Artificial kidney: 11. Construction and operation of an improved continuous dialyser. *Proceedings of the Society for Experimental Biological Medicine* 72 (3): 539–543.

Starling, E.H. and Tubby, A.H. (1894). On the paths of absorption from the peritoneal cavity. *Journal of Physiology* 16: 140.

Starzl, T.E., Marchioro, T.L., and Waddell, W.R. (1963). The reversal of rejection in human renal homografts with subsequent development of homograft tolerance. *Surgical and Gynecological Obstetrics* 117: 385–395.

Tenckhoff, H., and Schechter, H. (1968). A bacteriologically safe peritoneal access device. *Transactions of the American Society of Artificial Internal Organs* 14: 181–186.

Tenckhoff, H., Shilipetar, G., and Boen, S.T. (1965). One year experience with home peritoneal dialysis. *Transactions of the American Society of Artificial Internal Organs* 11: 11–14.

Teschan, P.E. (1955). Haemodialysis in military casualties. *Transactions of the American Society of Artificial Internal Organs* 2: 52–54.

Thalhimer, W., Solandt, D.Y., and Best, C.H. (1938). Experimental exchange transfusion using purified heparin. *Lancet* 11: 554–555.

Warrick, C. (1744). An improvement in the practice of tapping, whereby that operation instead for the relief of symptoms, became an absolute cure for ascites, exemplified in the case of Jane Roman. *Philosophical Transactions of the Royal Society* 43: 12–19.

Wegner, G. (1877). Surgical comments on peritoneal cavity with special emphasis on ovariotomy. *Archives of Klinischen Chirurgia* 20: 53–145.

UK Renal Registry (2023) UK Renal Registry 25th Annual Report – data to 31/12/2021, Bristol, UK. Available from https://ukkidney.org/audit-research/annual-report

CHAPTER 2

Applied Anatomy and Physiology, the Kidney Disease Process, and Kidney Investigations

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LEARNING OUTCOMES

- to understand the structure and main functions of the kidney, including the basic renal processes of filtration, reabsorption, and secretion.
- to identify the main conditions causing advanced kidney disease, and analyse the clinical features of these conditions.
- to explain the procedures commonly undertaken in the diagnosis of acute kidney injury (AKI) and chronic kidney disease (CKD).
- to gain knowledge and understanding of the investigations required in the diagnosis of renal impairment and provide a rationale for the use of these investigations and procedures.

INTRODUCTION

This chapter provides the reader with a detailed discussion of all aspects of renal physiology and its relationship to important pathophysiological processes in renal disease, and the investigations and procedures for diagnosing kidney conditions.

The first part of the chapter explores the normal renal anatomy and physiology as well as disease processes causing advanced kidney disease. The second part describes the investigations and procedures used in diagnosing acute kidney injury and chronic kidney disease. This is not intended as a complete reference to all kidney diseases; rather, it illustrates how altered renal physiology can affect the whole body, how other diseases can affect kidney function, and how some kidney conditions can be investigated.

STRUCTURE AND FUNCTIONS OF THE KIDNEY

The kidneys are paired organs lying in the retroperitoneum, on either side of the vertebral column. The upper pole of the kidney is at the spinal level of T12 and the lower pole at approximately L3. The right kidney is a little lower due to the presence of the liver on that side. Each kidney is approximately 11 cm long and weighs about 150 g (Figure 2.1).

On the concave surface of the kidney lies the hilum, from which the ureter and the main blood vessels and nerves access the kidney. The cut surface of the kidney reveals two distinct regions: a dark outer region called the cortex and a pale inner region called the medulla. The outer cortex is covered by a fibrous capsule and the whole kidney is surrounded by a pad of fat (Gerota's fascia) that offers some protection against injury. Broadly speaking, the cortex contains the filtering and reabsorptive components of the

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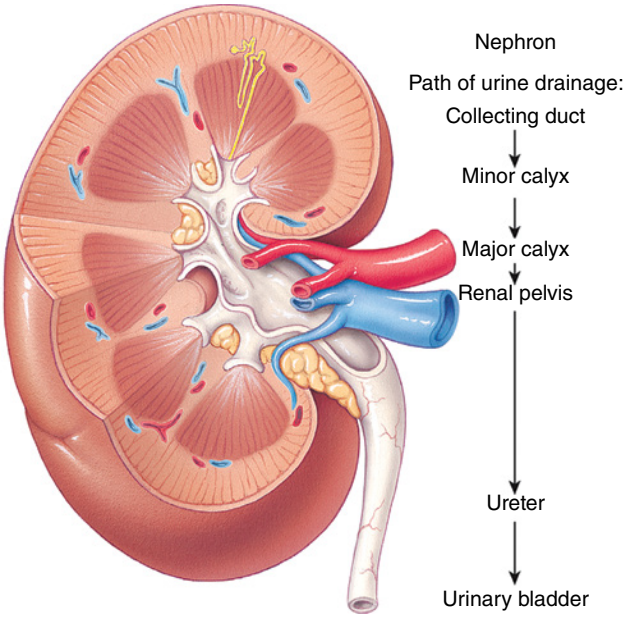

FIGURE 2.1 Structure of the kidney. *Source:* Tortora and Derrickson (2007). This material is reproduced with permission of John Wiley & Sons, Inc.

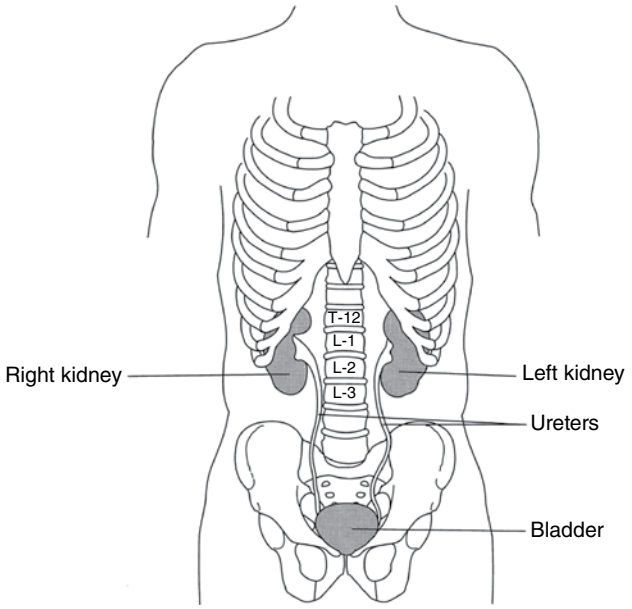

FIGURE 2.2 Relative position of the kidneys in the body.

nephrons, whilst the medulla contains the concentrating and diluting components of the nephrons and a system of collection ducts. These ducts funnel the urine into the pelvis at the heart of the medulla, from where it moves down the ureter into the bladder (Figure 2.2).

THE NEPHRON

The nephron is the functional unit of the kidney, and each kidney contains approximately 1 million nephrons (Figure 2.3). The structure of the nephron is related to its complex functions and contains five components, each performing a distinct process:

- the Bowman's capsule – forming a blind-ending capsule around a knot of capillaries called the glomerulus (site of filtration);
- the proximal convoluted tubule (site of bulk-phase reabsorption and some secretion);
- the loop of Henle (where concentration and dilution of urine mainly occurs);
- the distal convoluted tubule (the site of 'fine-tuning' reabsorption and more secretion);
- the collecting duct (also important for the concentration of urine and carrying urine into the renal pelvis).

These processes are interdependent and intimately related to each other by the shape of the nephron.

There are broadly two types of nephron found in the kidney (Figure 2.4). Approximately 85% of nephrons are cortical nephrons, which have short loops of Henle that are contained in the cortex of the kidney. The other 15% of nephrons are juxtamedullary nephrons and they have long loops of Henle, which extend deep into the medulla of the kidney. The long loops of Henle enable concentration of urine and conservation of water. The loops of Henle, together with the collecting ducts (which also pass through the medulla), give the pyramids of the medulla a striated appearance.

The main functions of the kidney are to rid the body of the end-product of metabolism and regulate the electrolytes found in the body fluids. A more detailed list of the functions of the kidney can be found in Box 2.1.

VERSATILITY OF URINE

Broadly speaking, there are three parameters that can vary to maintain the constancy of our bodily fluids: urinary volume, urinary concentration, and urinary content.

URINARY VOLUME

In a healthy person, the volume of urine produced per day can vary from as little as 300 ml, if no water is ingested or there is excessive water loss (as in diarrhoea), up to a maximum of 23l in cases of excessive fluid ingestion. In healthy people, urine output should not drop below

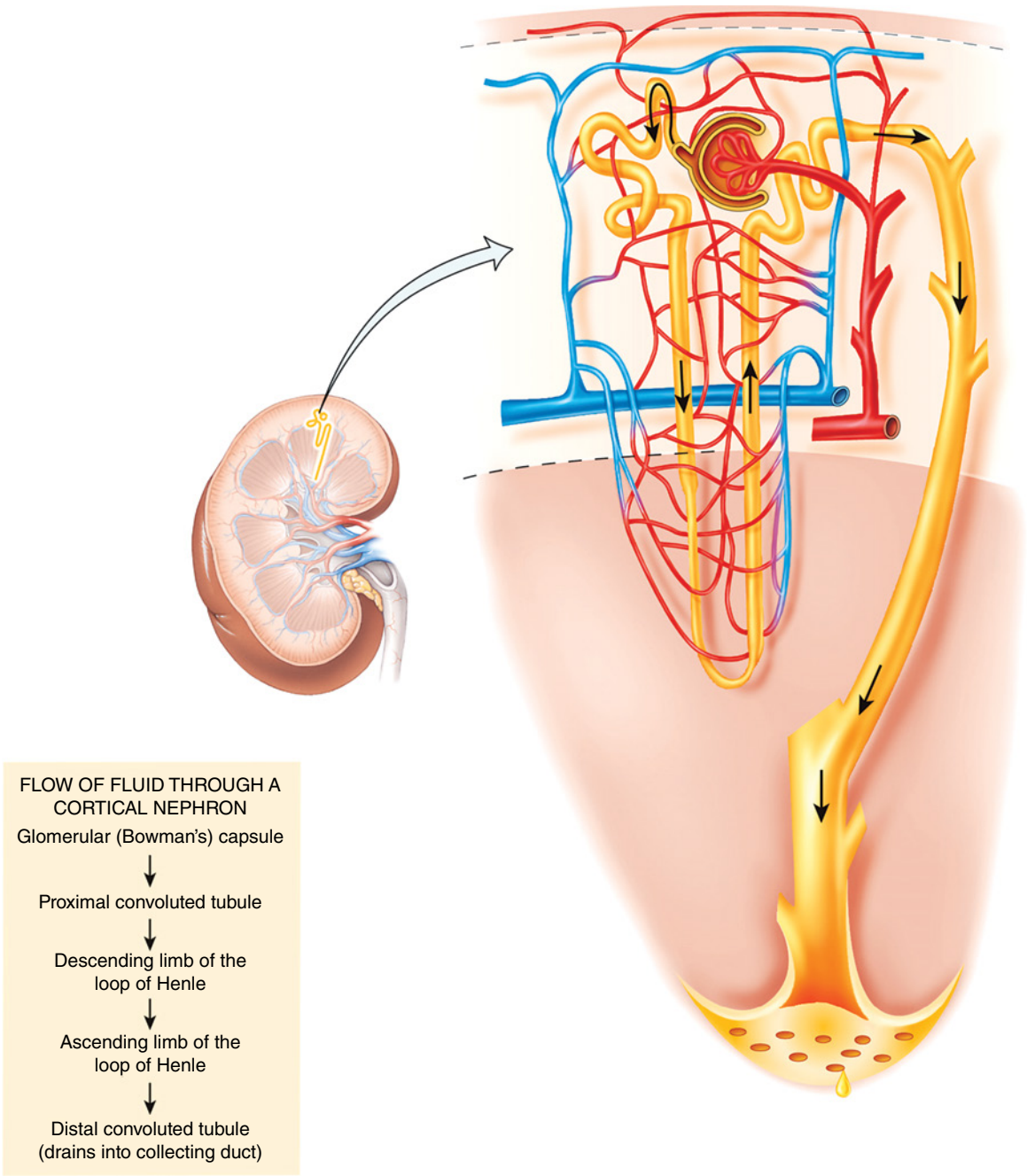

FIGURE 2.3 The parts of a nephron, collecting duct, and associated blood vessels. *Source:* Tortora and Derrickson (2007). This material is reproduced with permission of John Wiley & Sons, Inc.

300 ml per day because this is the absolute minimum water volume required to excrete the daily load of waste products. If the amount of waste products to be removed by the kidney rises, then the minimum urine volume must also rise. However, the average urine output per day is approximately 1500 ml. The kidneys' ability to vary the volume of daily urine output over such a wide range is essential if we are to maintain a constant body fluid volume in the face of adverse factors such as excessive heat, which causes sweating; colonic infections causing diarrhoea; or excessive thirst and water ingestion, as seen in the condition psychogenic polydipsia (Table 2.1).

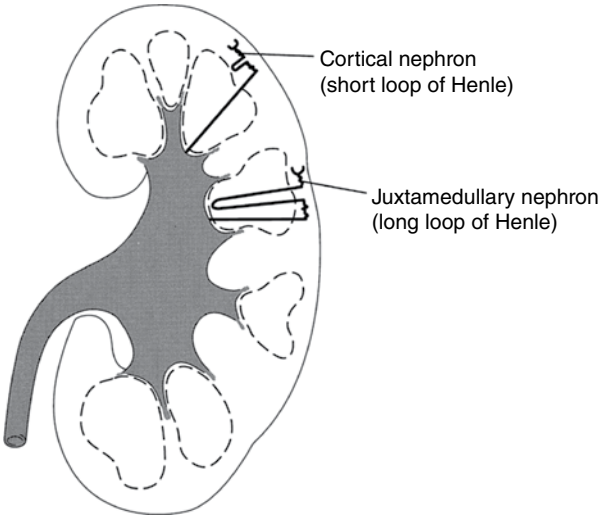

FIGURE 2.4 The position of the nephrons in the kidney.

Table 2.1 Normal fluid inputs and outputs.

Inputs (ml)		Outputs (ml)		
Water	1500	Urine[a]		1500
Food	500	Insensible loss	lungs	400
			skin[b]	400
Water of metabolism	400	Faeces[c]		100
Total		2400		2400

[a] Urinary volume is the only factor that can be regulated by the body to balance fluid inputs.
[b] This insensible loss of fluid through the skin is by simple evaporation (not sweat). Sweat is called 'sensible loss' and may reach up to 5 l per hour, for example, when a person is exercising excessively.
[c] Loss of fluid with the faeces can be as high as several litres per day in the presence of severe intestinal infections such as cholera.

BOX 2.1 THE FUNCTIONS OF THE KIDNEY

Excretory

- Excretion of metabolic waste products (e.g. urea and creatinine)

Regulatory

Regulation of:

- Body water volume
- Body fluid osmolality
- Electrolyte balance
- Acid–base balance
- Blood pressure

Metabolic

- Activation of vitamin D
- Production of renin
- Production of erythropoietin

URINARY CONCENTRATION

Though the volume of urine can vary over a wide range, the amount of solutes to be excreted by the kidney each day is much less variable. Thus, to excrete a fairly fixed volume of solutes each day in a variable volume of water, the kidney must have the ability to concentrate or dilute the urine. On a hot summer's day with little fluid intake, urine is dark in colour and of low volume, whereas if liberal amounts of beer have been consumed at a party, large volumes of watery urine are passed all evening.

The ability of the kidneys to excrete excess solutes in varying amounts of water by concentrating or diluting the urine is essential for maintaining a constant body osmolality (Box 2.2). The mechanism that controls the concentration or dilution of urine is often affected early on in renal disease, making it difficult to control both body fluid volume and osmolality in response to changes in fluid inputs and outputs. This can result in the individual tipping back and forth from states of dehydration to fluid overload.

URINARY CONTENT

The range of substances that can be constituents of urine is varied and includes:

- *Ions*. These include sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, and ammonium.
- *Metabolic waste*. Urea, creatinine, and uric acid are all waste.
- *Drug metabolites*. Most metabolites of pharmacological agents are eventually excreted from the body through the kidneys; many are detoxified in the liver first.
- *Other products of normal metabolism*. Metabolites of hormones can be detected in the urine by appropriate assays and may be a diagnostic aid.

Normal urine is clear in appearance, though it may vary in colour from pale to dark amber, depending on its concentration. Finally, normal urine has a pH that is

BOX 2.2 CONCEPTS OF OSMOSIS AND BODY OSMOLALITY

- Water can move between the different body fluid compartments across semipermeable membranes by the process of osmosis.
- The more concentrated a solution, the more water will be drawn into this solution.
- Any solute that can cause the movement of water across a semipermeable membrane is said to be 'osmotically active'.
- The osmotic activity of substances in solution is dependent on the number of dissolved particles in the solution and not on their size or charge.
- Sodium chloride (NaCl) dissociates in solution into Na^+ and Cl^- ions, so the number of osmotically active particles is almost double the number of NaCl molecules (but not exactly double because the dissociation is not complete; the solution consists of NaCl, Na^+, and Cl^- particles).
- Osmotically active particles in solution are measured by the unit called the osmole or milliosmole (mosm).
- Osmolality is measured in mosm per kg water and is a measure of the potential osmotic activity of dissolved solutes in solution.
- Normal body fluid osmolality is 285 mosm per kg water.
- The concentration (rather than the osmotic activity) of individual electrolytes is measured in mmol (millimoles) or μmol (micromoles) rather than mosmol

slightly acidic – around pH 6 – though urine can have a pH in the range 4.0–8.0 in cases of severe acidosis or alkalosis, respectively.

BASIC RENAL PROCESSES

GLOMERULAR FILTRATION

This is a process of filtration of plasma across the glomerular basement membrane from the glomerulus into the Bowman's capsule (Figure 2.5). The glomerular filtration surface is a unique structure composed of three layers:

1. The endothelial lining of the glomerular capillaries.
2. The basement membrane.
3. The epithelial cells of the Bowman's capsule, or podocytes. Filtration occurs between the slits formed by the finger-like processes of these cells (called pedicels), which surround glomerular capillaries.

These three layers are fused together and act as a barrier to the filtration of large-molecular-weight molecules, such as proteins.

Blood enters the glomerulus from branches of the renal artery, ending in the afferent arteriole. Blood then

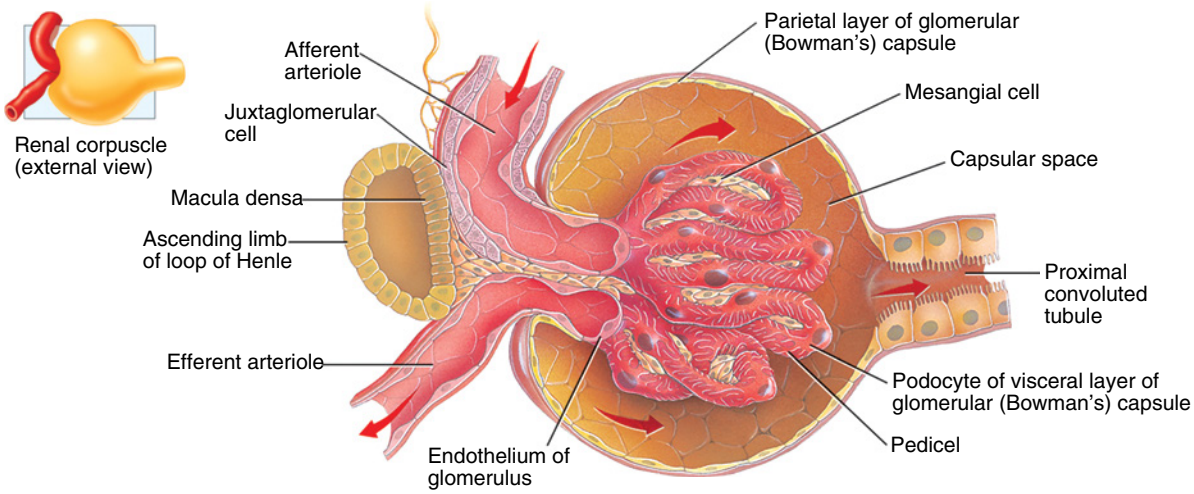

FIGURE 2.5 Structure of the glomerulus and Bowman's capsule. *Source:* Tortora and Nielsen (2009). This material is reproduced with permission of John Wiley & Sons, Inc.