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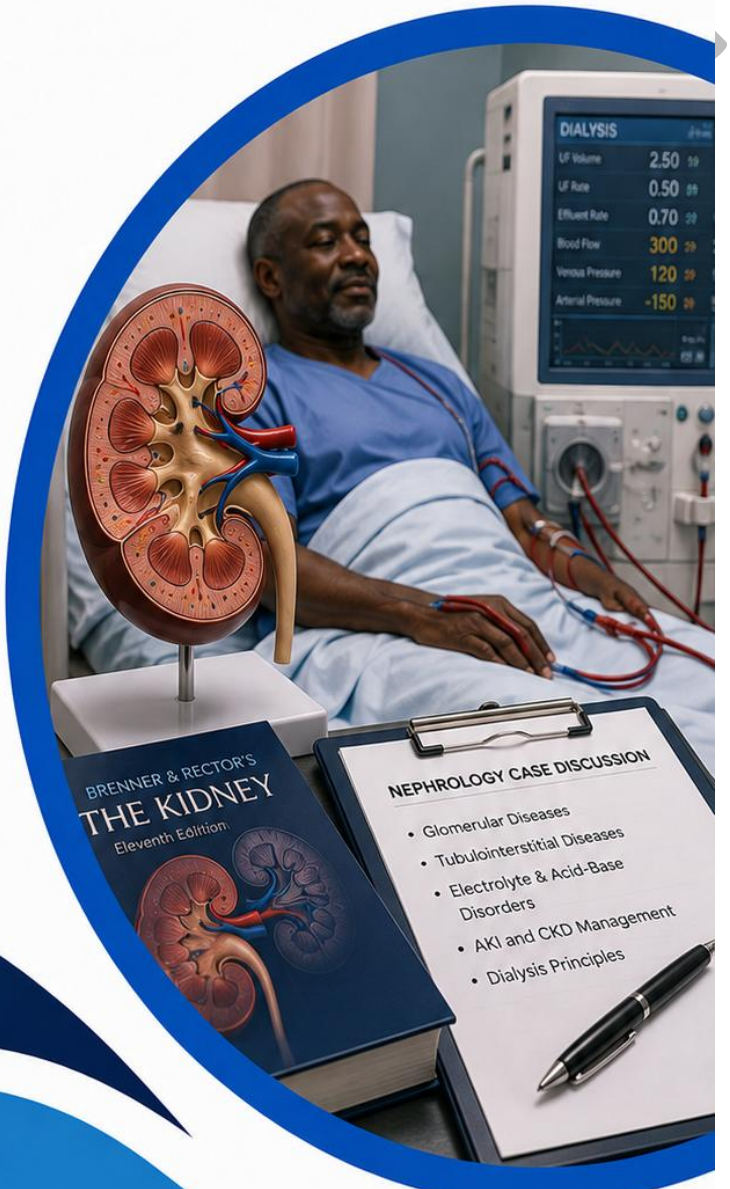
MED 616

NEPHROLOGY II



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Course code: MED 616

Course title: Nephrology II

Course credit load: 2 Units

Series 1: Glomerulonephritis and Nephrotic Syndrome

- **Part 1.1: Approach to Glomerular Disease**
    - Sub Part 1.1.1: Structure and function of the glomerulus
    - Sub Part 1.1.2: Classification of glomerular disease
    - Sub Part 1.1.3: Investigation of glomerular disease
- **Part 1.2: Nephritic Syndrome and Glomerulonephritis**
    - Sub Part 1.2.1: Pathophysiology and presentation of nephritic syndrome
    - Sub Part 1.2.2: IgA nephropathy and post-infectious glomerulonephritis
    - Sub Part 1.2.3: Rapidly progressive glomerulonephritis
- **Part 1.3: Nephrotic Syndrome**
    - Sub Part 1.3.1: Pathophysiology and presentation of nephrotic syndrome
    - Sub Part 1.3.2: Minimal change disease and focal segmental glomerulosclerosis
    - Sub Part 1.3.3: Membranous nephropathy
- **Part 1.4: Complications and Management of Glomerular Disease**
    - Sub Part 1.4.1: Complications of nephrotic syndrome
    - Sub Part 1.4.2: General management principles of glomerular disease
    - Sub Part 1.4.3: Immunosuppressive therapy in glomerular disease

Introduction

This opening Series of **Nephrology II** works through disease affecting the glomerulus, the kidney's fundamental filtration unit, building from normal structure and function through to the two major clinical syndromes glomerular disease characteristically produces, **nephritic syndrome**, dominated by inflammation and blood in the urine, and **nephrotic syndrome**, dominated by significant protein loss, before closing with the complications and management principles shared across this whole disease category.

The aim of this Series is to equip you with an understanding of glomerular structure and function and the classification and investigation of glomerular disease, the pathophysiology and presentation of nephritic syndrome including IgA nephropathy, post-infectious glomerulonephritis, and rapidly progressive glomerulonephritis, the pathophysiology and presentation of nephrotic syndrome including minimal change disease, focal segmental glomerulosclerosis, and membranous nephropathy, and the complications and management of glomerular disease.

This Series opens with the **approach to glomerular disease**, moves through **nephritic syndrome and glomerulonephritis** and **nephrotic syndrome**, and closes with **complications and management of glomerular disease**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 1.1:** describe glomerular structure and function and classify glomerular disease
- **SLO 1.2:** discuss the investigation of glomerular disease
- **SLO 1.3:** describe the pathophysiology and presentation of nephritic syndrome, including IgA nephropathy and post-infectious glomerulonephritis
- **SLO 1.4:** describe rapidly progressive glomerulonephritis
- **SLO 1.5:** describe the pathophysiology and presentation of nephrotic syndrome
- **SLO 1.6:** describe minimal change disease, focal segmental glomerulosclerosis, and membranous nephropathy
- **SLO 1.7:** describe the complications of nephrotic syndrome
- **SLO 1.8:** discuss the general management and immunosuppressive therapy of glomerular disease

1.1 Approach to Glomerular Disease

1.1.1 structure and function of the glomerulus

A specialised filtration unit, structurally and functionally distinctive

The **glomerulus**, the kidney's fundamental filtration unit, comprises a specialised capillary tuft surrounded by Bowman's capsule, with the **glomerular filtration barrier**, consisting of the fenestrated endothelium, glomerular basement membrane, and podocyte foot processes, normally permitting filtration of water and small solutes while genuinely restricting passage of larger

molecules, particularly plasma proteins, given their considerable molecular size and negative charge.

Disease affecting any specific component of this genuinely three-layered filtration barrier disrupts normal glomerular function, producing either inflammation-driven blood and inflammatory cell leakage into the urine, or, where the barrier's genuine size and charge selectivity is specifically compromised, significant protein leakage into the urine, and understanding which specific component is affected in a given condition directly explains the specific clinical syndrome that condition characteristically produces.

Fill in the blank: The glomerular filtration barrier normally restricts passage of larger molecules given their considerable molecular size and negative _____.

1.1.2 classification of glomerular disease

Two genuinely major clinical syndromes, and a wide range of specific causes

Glomerular disease is broadly classified into **nephritic syndrome**, characterised by haematuria, mild to moderate proteinuria, hypertension, and reduced kidney function, reflecting genuine glomerular inflammation, and **nephrotic syndrome**, characterised by significant proteinuria, hypoalbuminaemia, and oedema, reflecting genuine, significant compromise of the barrier's normal size and charge selectivity, discussed further across the following two Parts of this Series.

Within each of these two broad syndromes, a genuinely wide range of specific histological diagnoses exist, each with a genuinely distinct underlying pathophysiology, natural history, and treatment approach, and, genuinely importantly, some specific conditions can present with overlapping or mixed nephritic-nephrotic features, meaning this classification framework, while genuinely useful, should be applied as a guide rather than a rigid, absolute division.

Fill in the blank: Nephrotic syndrome reflects genuine, significant compromise of the filtration barrier's normal size and charge _____.

1.1.3 investigation of glomerular disease

Urinalysis as the essential starting point, biopsy for definitive diagnosis

Urinalysis, including microscopy for red cell casts, already a genuinely specific finding for glomerular inflammation, and quantification of proteinuria, forms the essential initial investigation for suspected glomerular disease, alongside serum creatinine assessing overall kidney function, and specific serological testing, including complement levels and autoantibody panels, where a genuinely specific underlying cause is suspected based on the clinical presentation.

Renal biopsy, direct histological examination of kidney tissue, remains the genuinely definitive investigation for confirming the specific underlying glomerular diagnosis in the great majority of cases, given how directly the specific histological pattern identified shapes both prognosis and the most appropriate treatment approach, discussed further across the remaining Parts of this Series.

Fill in the blank: Renal biopsy remains the genuinely definitive investigation for confirming the specific underlying glomerular _____.

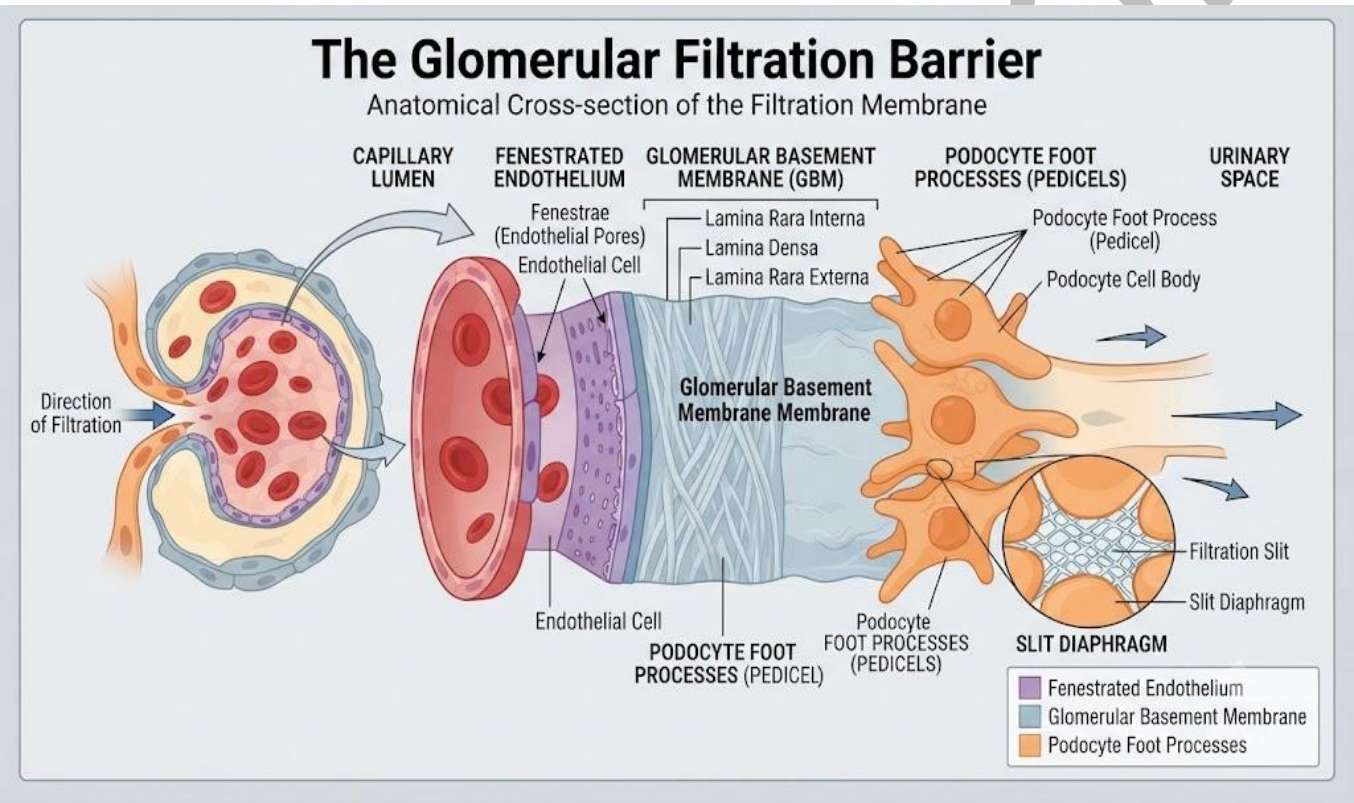

Figure 1.1: A labelled diagram of the glomerular filtration barrier.

Pilot questions 1.1

1. Describe the components of the glomerular filtration barrier. (Linked to SLO 1.1)
2. Distinguish nephritic from nephrotic syndrome. (Linked to SLO 1.1)
3. Explain why some conditions present with mixed nephritic-nephrotic features. (Linked to SLO 1.1)
4. Describe the role of urinalysis in investigating glomerular disease. (Linked to SLO 1.2)
5. Explain why renal biopsy remains the definitive investigation for glomerular disease. (Linked to SLO 1.2)

1.2 Nephritic Syndrome and Glomerulonephritis

1.2.1 pathophysiology and presentation of nephritic syndrome

Glomerular inflammation producing a genuinely characteristic pattern

Nephritic syndrome results from genuine inflammation within the glomerulus, most commonly immune complex-mediated, disrupting normal glomerular architecture sufficiently to allow red cells and inflammatory cells to leak into the urine while genuinely, comparatively preserving the barrier's size and charge selectivity, producing the characteristic combination of **haematuria**, often described as tea-coloured or smoky urine, and mild to moderate proteinuria.

Hypertension and **reduced kidney function**, reflecting the genuine reduction in glomerular filtration rate this inflammatory process produces, complete the characteristic nephritic syndrome presentation, and recognising this specific combination of findings directly prompts consideration of the specific underlying causes discussed in the remaining two sub-Parts of this Part, each producing this genuinely shared clinical syndrome through a distinct underlying mechanism.

Fill in the blank: Nephritic syndrome most commonly results from _____ complex-mediated glomerular inflammation.

1.2.2 iga nephropathy and post-infectious glomerulonephritis

Two genuinely common causes, with genuinely distinct timing patterns

IgA nephropathy, the most common cause of glomerulonephritis worldwide, results from mesangial deposition of immunoglobulin A, characteristically presenting with visible haematuria occurring genuinely synchronously with, or within a day or two of, an upper respiratory tract infection, a genuinely distinctive timing pattern directly distinguishing it from post-infectious glomerulonephritis discussed next.

Post-infectious glomerulonephritis, most classically following streptococcal infection, presents with nephritic syndrome developing genuinely one to three weeks after the preceding infection, reflecting the time genuinely required for immune complex formation and deposition, a specific delayed timing pattern directly contrasting with the synchronous presentation already discussed for IgA nephropathy.

Fill in the blank: Post-infectious glomerulonephritis presents with nephritic syndrome developing genuinely one to three weeks after the preceding _____.

1.2.3 rapidly progressive glomerulonephritis

A genuine renal emergency demanding urgent recognition

Rapidly progressive glomerulonephritis, a genuine nephrological emergency characterised by rapid, significant decline in kidney function over days to weeks, results from genuinely severe glomerular inflammation, histologically characterised by crescent formation, and can arise from several distinct underlying immune mechanisms, including anti-glomerular basement membrane disease and specific vasculitic conditions.

Prompt recognition and urgent renal biopsy, already discussed as the definitive investigation in the previous Part, genuinely matter given the narrow treatment window during which aggressive immunosuppressive therapy, discussed further later in this Series, can genuinely prevent irreversible kidney failure, mirroring the same genuine treatment urgency already emphasised for other time-critical conditions throughout this programme.

Fill in the blank: Rapidly progressive glomerulonephritis is histologically characterised by _____ formation.

Table 1.1: Comparing causes of nephritic syndrome

Cause	Timing relative to infection	Genuine urgency
IgA nephropathy	Synchronous with infection	Not typically an emergency
Post-infectious glomerulonephritis	One to three weeks after infection	Not typically an emergency
Rapidly progressive glomerulonephritis	Variable, can be genuinely rapid	Genuine renal emergency

Pilot questions 1.2

1. Describe the pathophysiology of nephritic syndrome. (Linked to SLO 1.3)
2. Describe the characteristic presentation of nephritic syndrome. (Linked to SLO 1.3)
3. Distinguish IgA nephropathy from post-infectious glomerulonephritis by timing. (Linked to SLO 1.3)
4. Describe rapidly progressive glomerulonephritis. (Linked to SLO 1.4)
5. Explain why prompt recognition of rapidly progressive glomerulonephritis genuinely matters. (Linked to SLO 1.4)

1.3 Nephrotic Syndrome

1.3.1 pathophysiology and presentation of nephrotic syndrome

Compromised barrier selectivity, producing a genuinely characteristic triad

Nephrotic syndrome results from genuine damage predominantly affecting the podocyte component of the glomerular filtration barrier already discussed, compromising the barrier's normal size and charge selectivity and allowing significant protein loss into the urine, producing the characteristic triad of **significant proteinuria**, **hypoalbuminaemia**, resulting from this ongoing protein loss, and **oedema**, resulting from the reduced plasma oncotic pressure this hypoalbuminaemia produces.

The oedema characteristic of nephrotic syndrome typically presents initially as periorbital swelling, particularly noticeable on waking, before progressing to more generalised, dependent oedema affecting the legs, and this genuinely distinctive presentation, alongside the significant proteinuria and hypoalbuminaemia already discussed, directly distinguishes nephrotic from nephritic syndrome despite both sharing the common underlying glomerular origin already established in Part 1.1.

Fill in the blank: Nephrotic syndrome results from genuine damage predominantly affecting the _____ component of the glomerular filtration barrier.

1.3.2 minimal change disease and focal segmental glomerulosclerosis

Two genuinely related conditions with a genuinely important age distinction

Minimal change disease, the most common cause of nephrotic syndrome in children, is genuinely characterised by an essentially normal glomerular appearance on light microscopy despite the significant proteinuria present, with the underlying podocyte abnormality only visible on electron microscopy, and genuinely, characteristically responds well to corticosteroid therapy, discussed further later in this Series.

Focal segmental glomerulosclerosis, more commonly affecting adults, shows genuine scarring affecting only a portion of glomeruli and only part of each affected glomerulus, hence its specific descriptive name, and, in genuine contrast to minimal change disease's typically favourable treatment response, focal segmental glomerulosclerosis frequently proves genuinely more treatment-resistant, carrying a correspondingly less favourable overall prognosis.

Fill in the blank: Focal segmental glomerulosclerosis shows genuine scarring affecting only a portion of glomeruli and only part of each affected _____.

1.3.3 membranous nephropathy

The most common cause of nephrotic syndrome in adults overall

Membranous nephropathy, the most common cause of nephrotic syndrome in adults overall, results from genuine immune complex deposition along the glomerular basement membrane itself, producing characteristic diffuse basement membrane thickening on histological examination, and can occur as **primary disease**, genuinely autoimmune in origin, or **secondary disease**, associated with an underlying malignancy, infection, or autoimmune condition.

Identifying whether a specific case of membranous nephropathy is genuinely primary or secondary carries direct clinical significance, since secondary cases require active investigation and treatment of the specific underlying trigger alongside kidney-directed treatment, and this genuine distinction, mirroring the primary-versus-secondary framework already established for other conditions discussed in earlier courses of this programme, closes this Part's coverage of nephrotic syndrome.

Fill in the blank: Membranous nephropathy produces characteristic diffuse basement membrane _____ on histological examination.

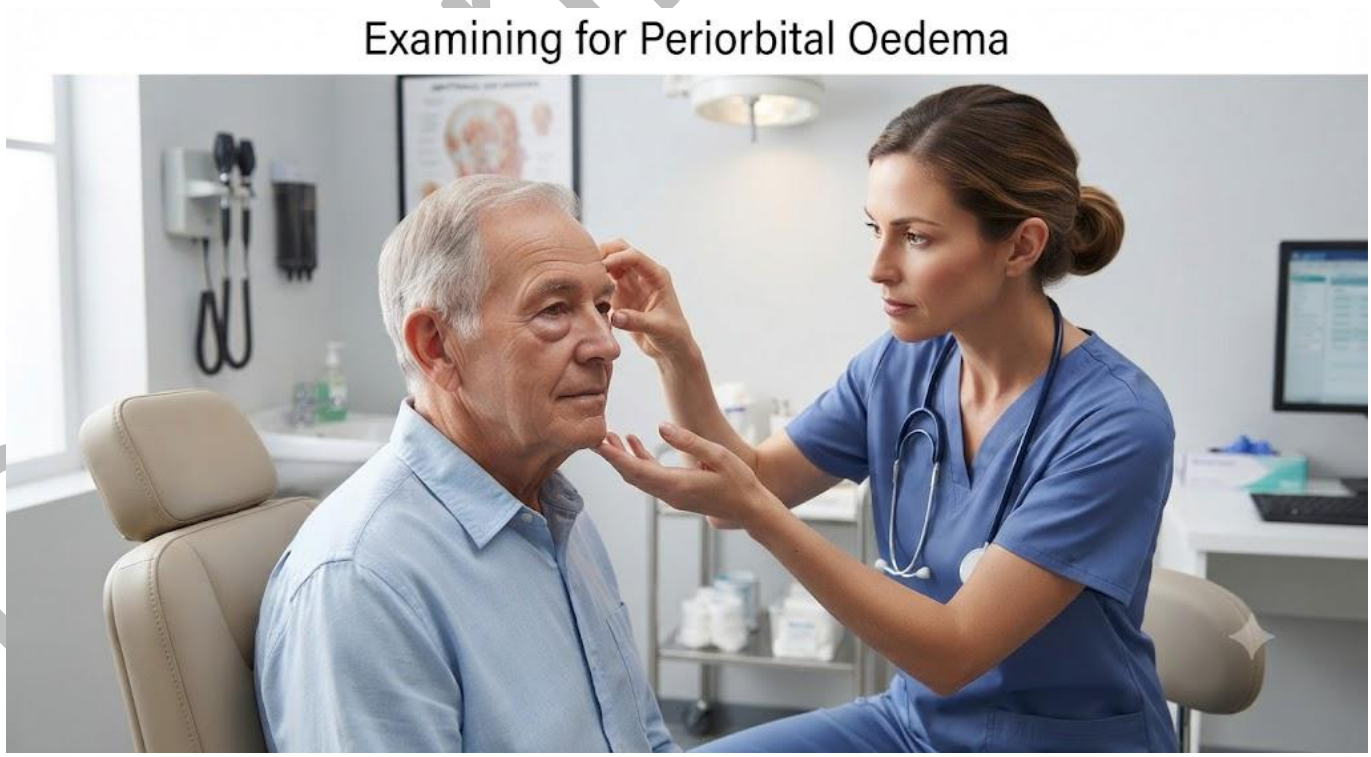

Figure 1.2: A clinician examining a patient for periorbital oedema.

Pilot questions 1.3

1. Describe the pathophysiology of nephrotic syndrome. (Linked to SLO 1.5)
2. Describe the characteristic triad of nephrotic syndrome. (Linked to SLO 1.5)
3. Describe minimal change disease. (Linked to SLO 1.6)
4. Distinguish focal segmental glomerulosclerosis from minimal change disease. (Linked to SLO 1.6)
5. Distinguish primary from secondary membranous nephropathy. (Linked to SLO 1.6)

1.4 Complications and Management of Glomerular Disease

1.4.1 complications of nephrotic syndrome

Consequences of significant, ongoing protein loss

Thromboembolism, already discussed in an earlier course of this programme, carries genuinely elevated risk in nephrotic syndrome, reflecting loss of natural anticoagulant proteins alongside the significant proteinuria itself, and **infection risk**, reflecting loss of immunoglobulins through the same compromised filtration barrier, together represent two of the genuinely most clinically significant complications this condition can produce.

Hyperlipidaemia, resulting from increased hepatic lipoprotein synthesis genuinely triggered by the low plasma oncotic pressure already discussed, and **acute kidney injury**, discussed further in the following Series of this course, complete the genuinely characteristic complication profile of nephrotic syndrome, and active, structured screening for each of these specific complications forms an essential part of comprehensive nephrotic syndrome management.

Fill in the blank: Thromboembolism risk in nephrotic syndrome reflects loss of natural _____ proteins alongside significant proteinuria.

1.4.2 general management principles of glomerular disease

Supportive measures alongside disease-specific treatment

Blood pressure control, particularly using agents that also genuinely reduce proteinuria, and **dietary sodium restriction**, supporting oedema management already discussed for nephrotic syndrome, form genuinely important supportive management measures applicable across the wide range of glomerular diseases this Series has covered, regardless of the specific underlying histological diagnosis.

Diuretic therapy, managing significant, symptomatic oedema, and prophylactic anticoagulation in selected, genuinely high-risk nephrotic patients given the thromboembolic risk already discussed, further complete this supportive management framework, and this genuinely comprehensive supportive approach, applied alongside the disease-specific treatment discussed in the following sub-Part, forms the complete management strategy for glomerular disease.

Fill in the blank: Diuretic therapy manages significant, symptomatic oedema alongside dietary sodium _____.

1.4.3 immunosuppressive therapy in glomerular disease

Targeting the underlying immune process directly

Corticosteroid therapy, already introduced as genuinely effective for minimal change disease earlier in this Series, forms the mainstay of immunosuppressive treatment for several glomerular diseases, with **additional immunosuppressive agents** genuinely added for patients with disease inadequately controlled on corticosteroids alone, or for conditions genuinely known to respond poorly to corticosteroid therapy alone, such as focal segmental glomerulosclerosis already discussed.

Treatment intensity, genuinely individualised according to the specific histological diagnosis, disease severity, and the patient's overall risk-benefit profile, closes this Series's coverage of glomerular disease, and this genuinely individualised, structured approach to immunosuppressive treatment selection reflects the same comprehensive clinical decision-making principle emphasised consistently throughout this whole course.

Fill in the blank: Additional immunosuppressive agents are genuinely added for patients with disease inadequately controlled on corticosteroids _____.

Table 1.2: Comparing causes of nephrotic syndrome and their genuinely typical treatment response

Cause	Typical patient population	Genuine treatment response
Minimal change disease	Most common in children	Typically responds well to corticosteroids
Focal segmental glomerulosclerosis	More common in adults	Frequently more treatment-resistant
Membranous nephropathy	Most common cause in adults overall	Variable, depends on primary or secondary cause

Pilot questions 1.4

1. List complications of nephrotic syndrome. (Linked to SLO 1.7)
2. Explain why nephrotic syndrome carries elevated thromboembolism and infection risk. (Linked to SLO 1.7)
3. Describe general supportive management measures for glomerular disease. (Linked to SLO 1.8)
4. Describe the role of corticosteroids in glomerular disease management. (Linked to SLO 1.8)
5. Explain why treatment intensity is genuinely individualised in glomerular disease. (Linked to SLO 1.8)

Series Summary

This opening Series worked through glomerular disease, from normal structure through to the two major clinical syndromes it can produce. Part 1.1 covered glomerular structure, classification, and investigation, while Part 1.2 turned to nephritic syndrome and glomerulonephritis. Part 1.3 covered nephrotic syndrome, and Part 1.4 closed with complications and management of glomerular disease.

You should now be able to classify, investigate, and manage glomerular disease across all four Parts of this Series, meeting the outcomes set for this Series. Series 2 turns next to acute kidney injury and acute drug poisoning and overdose.

Glossary of Terms

- **Focal segmental glomerulosclerosis:** scarring affecting a portion of glomeruli and part of each affected glomerulus.
- **Glomerular filtration barrier:** the fenestrated endothelium, basement membrane, and podocytes controlling filtration.
- **Haematuria:** blood in the urine, a characteristic feature of nephritic syndrome.
- **Hypoalbuminaemia:** low plasma albumin from significant urinary protein loss.
- **IgA nephropathy:** the most common cause of glomerulonephritis worldwide, from mesangial IgA deposition.
- **Membranous nephropathy:** the most common cause of nephrotic syndrome in adults overall.

- **Minimal change disease:** the most common cause of nephrotic syndrome in children.
- **Nephritic syndrome:** haematuria, proteinuria, hypertension, and reduced kidney function from glomerular inflammation.
- **Nephrotic syndrome:** significant proteinuria, hypoalbuminaemia, and oedema from compromised barrier selectivity.
- **Podocyte:** a specialised glomerular cell forming part of the filtration barrier.
- **Post-infectious glomerulonephritis:** nephritic syndrome developing one to three weeks after a preceding infection.
- **Rapidly progressive glomerulonephritis:** a genuine renal emergency with rapid decline in kidney function.

Concept Check Questions [Series 1]

Objective questions

1. The glomerular filtration barrier normally restricts passage of larger molecules given their considerable molecular size and negative _____. (Linked to SLO 1.1)
2. Post-infectious glomerulonephritis presents with nephritic syndrome developing genuinely one to three weeks after the preceding _____. (Linked to SLO 1.3)
3. Rapidly progressive glomerulonephritis is histologically characterised by _____ formation. (Linked to SLO 1.4)
4. Nephrotic syndrome results from genuine damage predominantly affecting the _____ component of the glomerular filtration barrier. (Linked to SLO 1.5)
5. Membranous nephropathy produces characteristic diffuse basement membrane _____ on histological examination. (Linked to SLO 1.6)

Short-answer questions

6. Distinguish nephritic from nephrotic syndrome. (Linked to SLO 1.1)
7. Distinguish IgA nephropathy from post-infectious glomerulonephritis by timing. (Linked to SLO 1.3)
8. Describe the characteristic triad of nephrotic syndrome. (Linked to SLO 1.5)
9. Distinguish primary from secondary membranous nephropathy. (Linked to SLO 1.6)
10. List complications of nephrotic syndrome. (Linked to SLO 1.7)

Long-answer questions

11. Discuss glomerular structure and function and the classification and investigation of glomerular disease. (Linked to SLO 1.1, 1.2)

12. Describe the pathophysiology and presentation of nephritic syndrome, including IgA nephropathy, post-infectious glomerulonephritis, and rapidly progressive glomerulonephritis. (Linked to SLO 1.3, 1.4)
13. Discuss the pathophysiology and presentation of nephrotic syndrome, including minimal change disease, focal segmental glomerulosclerosis, and membranous nephropathy. (Linked to SLO 1.5, 1.6)
14. Describe the complications of nephrotic syndrome. (Linked to SLO 1.7)
15. Discuss the general management and immunosuppressive therapy of glomerular disease. (Linked to SLO 1.8)

Answers to Concept Check Questions [Series 1]

Objective questions

1. Charge.
2. Infection.
3. Crescent.
4. Podocyte.
5. Thickening.

Short-answer questions

6. Nephritic syndrome shows haematuria and mild proteinuria; nephrotic syndrome shows significant proteinuria and oedema.
7. IgA nephropathy presents synchronously with infection, while post-infectious GN presents one to three weeks later.
8. The triad is significant proteinuria, hypoalbuminaemia, and oedema.
9. Primary disease is genuinely autoimmune, while secondary disease is associated with malignancy, infection, or another autoimmune condition.
10. Complications include thromboembolism, infection risk, hyperlipidaemia, and acute kidney injury.

Long-answer questions

11. **Basic response:** The glomerular filtration barrier comprises endothelium, basement membrane, and podocytes; disease is classified as nephritic or nephrotic syndrome; investigation uses urinalysis and, definitively, renal biopsy.

    Value-added response: A value-added response notes that some conditions present with overlapping nephritic-nephrotic features.

12. **Basic response:** Nephritic syndrome results from immune complex-mediated inflammation, presenting with haematuria and hypertension; IgA nephropathy presents synchronously with infection; post-infectious GN presents delayed; rapidly progressive GN is a genuine emergency with crescent formation.

    Value-added response: A value-added response notes that prompt biopsy and treatment can prevent irreversible kidney failure in rapidly progressive disease.

13. **Basic response:** Nephrotic syndrome results from podocyte damage, presenting with proteinuria, hypoalbuminaemia, and oedema; minimal change disease responds well to steroids in children; focal segmental glomerulosclerosis is more treatment-resistant; membranous nephropathy is the most common adult cause.

    Value-added response: A value-added response notes that identifying primary versus secondary membranous nephropathy directly shapes management.

14. **Basic response:** Complications include thromboembolism from loss of anticoagulant proteins, infection from immunoglobulin loss, hyperlipidaemia, and acute kidney injury.

    Value-added response: A value-added response notes that active, structured screening for these complications forms an essential part of management.

15. **Basic response:** General management includes blood pressure control, sodium restriction, and diuretics; immunosuppressive therapy centres on corticosteroids, with additional agents for inadequately controlled or resistant disease.

    Value-added response: A value-added response notes that treatment intensity is genuinely individualised according to histological diagnosis and severity.

Answers to Pilot Questions [Series 1]

Part 1.1

1. The barrier comprises fenestrated endothelium, basement membrane, and podocyte foot processes.
2. Nephritic syndrome shows haematuria and mild proteinuria; nephrotic syndrome shows significant proteinuria and oedema.

3. Some conditions affect the barrier in a way that produces overlapping features of both syndromes.
4. Urinalysis identifies red cell casts and quantifies proteinuria, guiding further investigation.
5. Biopsy provides the specific histological diagnosis directly shaping prognosis and treatment.

Part 1.2

1. Nephritic syndrome results from immune complex-mediated glomerular inflammation.
2. Presentation includes haematuria, mild proteinuria, hypertension, and reduced kidney function.
3. IgA nephropathy presents synchronously with infection, while post-infectious GN presents one to three weeks later.
4. It is a genuine renal emergency with rapid kidney function decline and crescent formation on biopsy.
5. Prompt treatment within a narrow window can prevent irreversible kidney failure.

Part 1.3

1. Nephrotic syndrome results from podocyte damage compromising barrier size and charge selectivity.
2. The triad is significant proteinuria, hypoalbuminaemia, and oedema.
3. Minimal change disease shows normal light microscopy appearance despite significant proteinuria, responding well to steroids.
4. Focal segmental glomerulosclerosis shows genuine scarring and is frequently more treatment-resistant.
5. Primary disease is autoimmune, while secondary disease is associated with an underlying trigger requiring investigation.

Part 1.4

1. Complications include thromboembolism, infection risk, hyperlipidaemia, and acute kidney injury.
2. Loss of anticoagulant proteins and immunoglobulins through the compromised barrier drives these risks.
3. Measures include blood pressure control, sodium restriction, and diuretic therapy.
4. Corticosteroids form the mainstay of immunosuppressive treatment for several glomerular diseases.
5. Treatment reflects the specific histological diagnosis, severity, and patient-specific risk-benefit profile.

References and Attributions [Series 1]

- Kumar, P., & Clark, M. (2020). Kumar and Clark's Clinical Medicine (10th ed.). Elsevier.
- Feehally, J., Floege, J., Tonelli, M., & Johnson, R. J. (2018). Comprehensive Clinical Nephrology (6th ed.). Elsevier.
- Kidney Disease: Improving Global Outcomes (2021). Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney International.
- National Institute for Health and Care Excellence (2023). Chronic Kidney Disease: Assessment and Management (NG203). NICE.

Figures, Plates, Tables, and Boxes

- Figure 1.1: A labelled diagram of the glomerular filtration barrier. AI-generated using the prompt: "Create a clean, accurate labelled anatomical diagram titled The Glomerular Filtration Barrier, showing a cross-section with the fenestrated endothelium, glomerular basement membrane, and podocyte foot processes clearly labelled in sequence. Educational anatomical diagram style, no photographic content."
- Table 1.1: Comparing causes of nephritic syndrome. AI-generated using the prompt: "Create a clean reference table titled Comparing Causes of Nephritic Syndrome, listing cause, timing relative to infection, and genuine urgency. Simple clinical reference table style with outside border."
- Figure 1.2: A clinician examining a patient for periorbital oedema. AI-generated using the prompt: "Create a realistic clinical illustration titled Examining for Periorbital Oedema, showing a clinician gently observing a seated patient's face and eye area for swelling, clinical examination room setting. Clean clinical illustration style, no text."
- Table 1.2: Comparing causes of nephrotic syndrome and their genuinely typical treatment response. AI-generated using the prompt: "Create a clean reference table titled Comparing Causes of Nephrotic Syndrome and Treatment Response, listing cause, typical patient population, and genuine treatment response. Simple clinical reference table style with outside border."

Course code: MED 616

Course title: Nephrology II

Course credit load: 2 Units

Series 2: Acute Kidney Injury and Acute Drug Poisoning and Overdose

- **Part 2.1: Approach to Acute Kidney Injury**
  - Sub Part 2.1.1: Definition and classification of acute kidney injury
  - Sub Part 2.1.2: Pre-renal, renal, and post-renal causes
  - Sub Part 2.1.3: Clinical presentation and investigation of acute kidney injury
- **Part 2.2: Management and Complications of Acute Kidney Injury**
  - Sub Part 2.2.1: General management principles of acute kidney injury
  - Sub Part 2.2.2: Indications for renal replacement therapy in acute kidney injury
  - Sub Part 2.2.3: Complications and prognosis of acute kidney injury
- **Part 2.3: Principles of Acute Drug Poisoning and Overdose**
  - Sub Part 2.3.1: General approach to the poisoned patient
  - Sub Part 2.3.2: Decontamination and enhanced elimination
  - Sub Part 2.3.3: Common drugs and toxins causing acute poisoning
- **Part 2.4: Management of Specific Poisonings**
  - Sub Part 2.4.1: Paracetamol poisoning
  - Sub Part 2.4.2: Salicylate poisoning
  - Sub Part 2.4.3: Other specific antidotes and management

Introduction

This Series turns to two genuinely acute, time-critical nephrological presentations, **acute kidney injury**, a sudden decline in kidney function demanding structured, urgent evaluation, and **acute drug poisoning and overdose**, where the kidney frequently plays a genuinely central role both as a target organ of toxicity and as a route for eliminating certain ingested substances, making this pairing genuinely coherent despite covering two seemingly distinct clinical scenarios.

The aim of this Series is to equip you with the ability to define and classify acute kidney injury and describe its pre-renal, renal, and post-renal causes, presentation, investigation, and management, including indications for renal replacement therapy and its complications and prognosis, and to describe the general approach to the poisoned patient, decontamination and enhanced elimination, common causes of acute poisoning, and the specific management of paracetamol and salicylate poisoning and other specific antidotes.

This Series opens with the **approach to acute kidney injury**, moves through its **management and complications** and the **principles of acute drug poisoning and overdose**, and closes with the **management of specific poisonings**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 2.1:** define and classify acute kidney injury and describe its pre-renal, renal, and post-renal causes
- **SLO 2.2:** describe the clinical presentation and investigation of acute kidney injury
- **SLO 2.3:** discuss the general management of acute kidney injury
- **SLO 2.4:** discuss indications for renal replacement therapy and the complications and prognosis of acute kidney injury
- **SLO 2.5:** describe the general approach to the poisoned patient, including decontamination and enhanced elimination
- **SLO 2.6:** describe common drugs and toxins causing acute poisoning
- **SLO 2.7:** describe the presentation and management of paracetamol and salicylate poisoning
- **SLO 2.8:** discuss other specific antidotes and management of poisoning

2.1 Approach to Acute Kidney Injury

2.1.1 definition and classification of acute kidney injury

A structured, standardised approach to a genuinely common presentation

Acute kidney injury, an abrupt decline in kidney function occurring over hours to days, is defined and staged using standardised criteria combining the specific magnitude of serum creatinine rise and the degree of reduced urine output, and this genuinely structured, standardised classification framework allows consistent recognition and severity grading across genuinely different clinical settings and practitioner experience levels.

Acute kidney injury is genuinely common in hospitalised patients, particularly those who are critically unwell, and its presence carries genuine, significant prognostic implications independent of the specific underlying cause, meaning active, structured screening for acute kidney injury, using the standardised criteria already discussed, forms a genuinely essential component of routine care for any acutely unwell hospitalised patient.

Fill in the blank: Acute kidney injury is defined and staged using standardised criteria combining serum creatinine rise and reduced urine _____.

2.1.2 pre-renal, renal, and post-renal causes

A genuinely structured anatomical framework for the differential diagnosis

Pre-renal acute kidney injury, the most common category overall, results from reduced renal perfusion, most commonly from hypovolaemia, hypotension, or reduced cardiac output already discussed in relation to heart failure in an earlier course of this programme, without genuine intrinsic kidney damage, and is genuinely, characteristically reversible with prompt correction of the underlying perfusion problem.

Intrinsic renal acute kidney injury, resulting from genuine direct kidney damage, including acute tubular necrosis, the most common intrinsic cause, and the glomerular diseases already discussed in Series 1 of this course, and **post-renal acute kidney injury**, resulting from urinary tract obstruction, discussed further in relation to nephrolithiasis in a later Series of this course, complete this genuinely structured, anatomically organised differential diagnosis framework.

Fill in the blank: Acute tubular necrosis is the most common cause of intrinsic _____ acute kidney injury.

2.1.3 clinical presentation and investigation of acute kidney injury

Often genuinely asymptomatic, identified through biochemical screening

Acute kidney injury is frequently genuinely asymptomatic in its earlier stages, identified through routine biochemical screening rather than specific symptomatic presentation, and, when symptoms do develop, they genuinely reflect either the underlying precipitating cause itself or the specific complications of acute kidney injury discussed further in the following Part, rather than a specific, characteristic symptom pattern unique to acute kidney injury alone.

Investigation combines serial serum creatinine and urine output monitoring, already discussed as the basis for the standardised classification framework, with a structured, systematic search for the underlying cause, including urinalysis, renal tract ultrasound to actively exclude post-renal obstruction already discussed in the previous sub-Part, and, where genuinely indicated, specific serological testing for suspected intrinsic renal causes.

Fill in the blank: Renal tract ultrasound is used to actively exclude post-renal _____ as a cause of acute kidney injury.

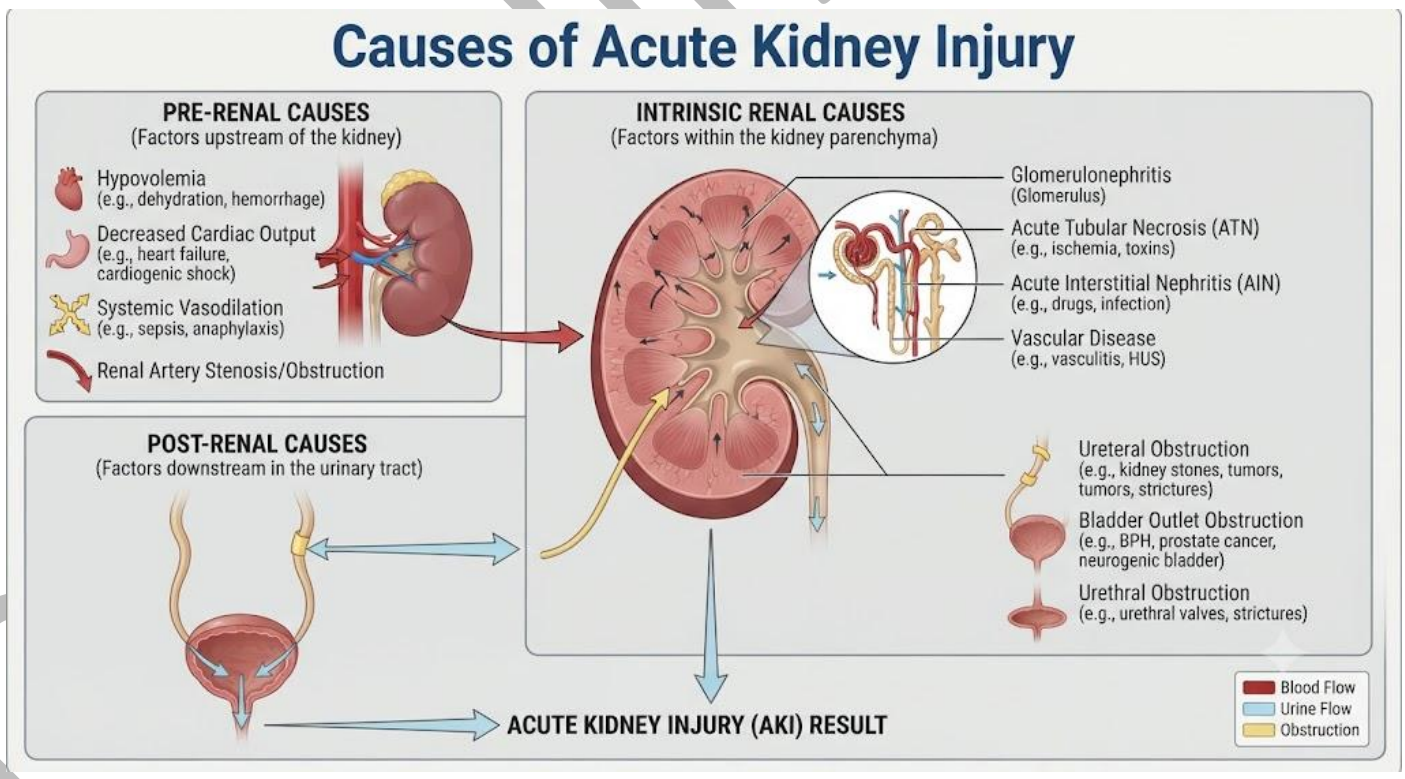

Figure 2.1: A labelled diagram comparing pre-renal, intrinsic renal, and post-renal causes of acute kidney injury.

Pilot questions 2.1

- Describe how acute kidney injury is defined and staged. (Linked to SLO 2.1)
- Describe pre-renal acute kidney injury. (Linked to SLO 2.1)
- Distinguish intrinsic renal from post-renal acute kidney injury. (Linked to SLO 2.1)
- Explain why acute kidney injury is frequently asymptomatic in its earlier stages. (Linked to SLO 2.2)
- Describe the investigation approach for suspected acute kidney injury. (Linked to SLO 2.2)

2.2 Management and Complications of Acute Kidney Injury

2.2.1 general management principles of acute kidney injury

Correcting the underlying cause and avoiding further harm

Management of acute kidney injury prioritises correcting the underlying cause identified through the structured investigation already discussed, including appropriate fluid resuscitation for pre-renal causes, and **avoiding further nephrotoxic insult**, including reviewing and, where genuinely possible, discontinuing nephrotoxic medication, mirroring the same medication review principle already discussed in relation to polypharmacy in an earlier course of this programme.

Careful fluid balance monitoring, avoiding both inadequate volume replacement risking ongoing pre-renal injury and excessive fluid administration risking genuine volume overload given the kidney's reduced capacity to excrete excess fluid, and monitoring for and correcting specific electrolyte disturbances, discussed further in the following sub-Part, complete this genuinely structured, comprehensive supportive management approach.

Fill in the blank: Management includes avoiding further nephrotoxic insult by reviewing and discontinuing nephrotoxic _____.

2.2.2 indications for renal replacement therapy in acute kidney injury

A structured threshold for escalating to dialysis support

Renal replacement therapy, already discussed in principle elsewhere in this programme, is indicated in acute kidney injury for genuinely specific circumstances, including refractory hyperkalaemia, refractory metabolic acidosis, genuine fluid overload unresponsive to diuretic

therapy, and uraemic complications, each representing a genuine failure of conservative management to adequately address the specific consequence of severe acute kidney injury.

This structured, criteria-based approach to renal replacement therapy initiation, rather than an arbitrary decision based on creatinine level alone, genuinely ensures this invasive intervention is reserved for patients who genuinely require it, and active, regular reassessment for these specific indications forms an essential, ongoing component of managing any patient with significant, established acute kidney injury.

Fill in the blank: Renal replacement therapy is indicated for refractory hyperkalaemia, refractory metabolic acidosis, and genuine fluid _____.

2.2.3 complications and prognosis of acute kidney injury

Genuine short-term risks, and meaningful long-term implications

Hyperkalaemia, already discussed as an indication for renal replacement therapy, carries genuine, immediate risk of life-threatening cardiac arrhythmia, and **fluid overload**, producing pulmonary oedema already discussed in an earlier course of this programme, represent two of the genuinely most immediately dangerous complications of acute kidney injury requiring active, structured monitoring and prompt treatment where identified.

Prognosis genuinely varies considerably depending on the underlying cause and severity, with the great majority of patients with pre-renal acute kidney injury genuinely recovering full kidney function following prompt correction, though a meaningful proportion of patients with more severe or intrinsic renal acute kidney injury genuinely progress towards chronic kidney disease, discussed in the following Series of this course, underlining why appropriate long-term follow-up genuinely matters following any significant episode of acute kidney injury.

Fill in the blank: A meaningful proportion of patients with severe acute kidney injury genuinely progress towards chronic kidney _____.

Table 2.1: Indications for renal replacement therapy in acute kidney injury

Indication	Genuine clinical significance	Urgency
Refractory hyperkalaemia	Risk of life-threatening cardiac arrhythmia	Urgent
Refractory fluid overload	Risk of pulmonary oedema and respiratory compromise	Urgent

Uraemic complications	Reflects genuinely significant, established kidney failure	Urgent

Pilot questions 2.2

1. Describe the general management priorities for acute kidney injury. (Linked to SLO 2.3)
2. List indications for renal replacement therapy in acute kidney injury. (Linked to SLO 2.4)
3. Describe hyperkalaemia as a complication of acute kidney injury. (Linked to SLO 2.4)
4. Describe the typical prognosis for pre-renal versus intrinsic renal acute kidney injury. (Linked to SLO 2.4)
5. Explain why long-term follow-up matters following significant acute kidney injury. (Linked to SLO 2.4)

2.3 Principles of Acute Drug Poisoning and Overdose

2.3.1 general approach to the poisoned patient

Structured resuscitation, then identifying what was taken

Assessment of the poisoned patient follows the same structured airway, breathing, circulation approach already emphasised throughout this course, alongside a genuinely careful, structured history establishing what substance was taken, the specific quantity, and the timing of ingestion, information genuinely essential for accurately anticipating the expected clinical course and guiding the specific management approach discussed further across this Part.

Collateral history, from family, friends, or emergency responders, and physical evidence, including tablet packaging genuinely found at the scene, can provide genuinely valuable additional information where the patient themselves is unable to provide a reliable history, whether from reduced consciousness or, in some cases, genuine reluctance to disclose the full circumstances of the ingestion.

Fill in the blank: A careful, structured history establishes the substance taken, specific quantity, and _____ of ingestion.

2.3.2 decontamination and enhanced elimination

Reducing absorption, and, in selected cases, accelerating clearance

Activated charcoal, adsorbing many ingested substances within the gastrointestinal tract to reduce their systemic absorption, is genuinely most effective when administered within a relatively narrow window following ingestion, and its effectiveness genuinely varies depending on the specific substance ingested, since certain substances, including alcohols and some metals, are genuinely not effectively adsorbed by activated charcoal.

Enhanced elimination techniques, including urinary alkalinisation for certain specific poisonings discussed further later in this Series, and haemodialysis for selected, genuinely severe poisonings with a dialysable substance, offer further treatment options in appropriately selected cases, and the specific decision to pursue enhanced elimination genuinely depends on the specific substance involved and the severity of the clinical presentation.

Fill in the blank: Activated charcoal is genuinely most effective when administered within a relatively narrow window following _____.

2.3.3 common drugs and toxins causing acute poisoning

A genuinely wide range of substances, each with its own characteristic pattern

Paracetamol and **salicylates**, discussed in genuine detail across the following Part of this Series given their genuine frequency and specific management requirements, alongside opioids, already discussed in an earlier course of this programme in relation to overdose management, and benzodiazepines, together represent some of the genuinely most commonly encountered substances in acute poisoning presentations.

Toxidromes, recognisable clusters of clinical signs and symptoms characteristic of a specific class of poisoning, provide genuinely valuable diagnostic clues even where the specific substance ingested remains uncertain, allowing a structured, syndrome-based approach to initial assessment and management before the specific causative substance has been definitively confirmed.

Fill in the blank: Toxidromes are recognisable clusters of clinical signs and symptoms characteristic of a specific class of _____.

Figure 2.2: A clinician assessing a poisoned patient's airway and level of consciousness.

Pilot questions 2.3

1. Describe the structured approach to assessing the poisoned patient. (Linked to SLO 2.5)
2. Describe the role of collateral history and physical evidence. (Linked to SLO 2.5)
3. Describe activated charcoal and its limitations. (Linked to SLO 2.5)
4. Describe enhanced elimination techniques. (Linked to SLO 2.5)
5. Describe toxidromes and their diagnostic value. (Linked to SLO 2.6)

2.4 Management of Specific Poisonings

2.4.1 paracetamol poisoning

A genuinely deceptive early presentation, with genuinely serious delayed risk

Paracetamol poisoning, genuinely, particularly dangerous given the frequently minimal or entirely absent initial symptoms despite potentially severe underlying toxicity, produces delayed hepatotoxicity, already discussed as a cause of acute liver failure in an earlier course of this

programme, through accumulation of a genuinely toxic metabolite once the normal detoxification pathway becomes overwhelmed following significant ingestion.

N-acetylcysteine, the specific antidote for paracetamol poisoning, replenishes the specific protective substance genuinely depleted by significant paracetamol overdose, and its administration, guided by a specific treatment nomogram plotting paracetamol level against time since ingestion, is genuinely most effective when given early, mirroring the same timing principle already discussed for antiviral therapy in an earlier course of this programme.

Fill in the blank: N-acetylcysteine replenishes the specific protective substance genuinely depleted by significant paracetamol _____.

2.4.2 salicylate poisoning

A genuinely complex, mixed acid-base disturbance

Salicylate poisoning, resulting from aspirin overdose, produces a genuinely characteristic, complex mixed acid-base disturbance, an initial respiratory alkalosis from direct respiratory centre stimulation, followed by a genuinely superimposed metabolic acidosis as the toxicity progresses, alongside tinnitus, vomiting, and, in severe cases, confusion and coma reflecting genuine central nervous system toxicity.

Urinary alkalinisation, already introduced as an enhanced elimination technique earlier in this Series, is genuinely particularly effective for salicylate poisoning specifically, since alkalinising the urine genuinely traps the ionised form of salicylate within the renal tubule, promoting its elimination, and, for genuinely severe poisoning, haemodialysis offers a further, more aggressive treatment option.

Fill in the blank: Urinary alkalinisation genuinely traps the ionised form of salicylate within the renal _____, promoting elimination.

2.4.3 other specific antidotes and management

A genuinely wide range of substance-specific reversal agents

Naloxone, already discussed in principle for opioid overdose in an earlier course of this programme, and **flumazenil**, reversing benzodiazepine toxicity, illustrate the genuinely wide range of specific antidotes available for particular poisoning categories, though flumazenil genuinely requires careful, cautious use given the genuine risk of precipitating seizures in patients with certain underlying conditions or combined substance ingestion.

Supportive care, addressing the specific complications a given poisoning produces regardless of whether a specific antidote exists, closes this Series's coverage of acute poisoning and, indeed, this whole course's coverage of nephrology and toxicology, reflecting the same genuinely comprehensive, individualised clinical management philosophy that has run consistently throughout this entire programme of study.

Fill in the blank: Flumazenil genuinely requires careful, cautious use given the genuine risk of precipitating _____ in certain patients.

Table 2.2: Comparing paracetamol and salicylate poisoning

Feature	Paracetamol poisoning	Salicylate poisoning
Early symptoms	Often minimal or absent	Tinnitus, vomiting, hyperventilation
Key organ risk	Liver, hepatotoxicity	Complex acid-base disturbance, CNS toxicity
Specific treatment	N-acetylcysteine	Urinary alkalinisation, dialysis if severe

Pilot questions 2.4

1. Explain why paracetamol poisoning is genuinely particularly dangerous. (Linked to SLO 2.7)
2. Describe N-acetylcysteine and its use. (Linked to SLO 2.7)
3. Describe the acid-base disturbance characteristic of salicylate poisoning. (Linked to SLO 2.7)
4. Describe urinary alkalinisation for salicylate poisoning. (Linked to SLO 2.7)
5. Describe naloxone and flumazenil as specific antidotes. (Linked to SLO 2.8)

Series Summary

This Series covered acute kidney injury and acute drug poisoning and overdose. Part 2.1 covered the definition, classification, causes, presentation, and investigation of acute kidney injury, while Part 2.2 turned to its management, renal replacement therapy indications, complications, and

prognosis. Part 2.3 covered the principles of acute drug poisoning and overdose, and Part 2.4 closed with the management of specific poisonings.

You should now be able to recognise, investigate, and manage acute kidney injury and acute drug poisoning across all four Parts of this Series, meeting the outcomes set for this Series. Series 3 turns next to chronic kidney disease and dialysis.

Glossary of Terms

1. **Activated charcoal:** a substance adsorbing ingested toxins within the gastrointestinal tract.
2. **Acute kidney injury:** an abrupt decline in kidney function occurring over hours to days.
3. **Acute tubular necrosis:** the most common cause of intrinsic renal acute kidney injury.
4. **Enhanced elimination:** techniques accelerating clearance of an ingested toxic substance.
5. **Flumazenil:** the specific antidote reversing benzodiazepine toxicity.
6. **N-acetylcysteine:** the specific antidote for paracetamol poisoning.
7. **Naloxone:** the specific antidote reversing opioid toxicity.
8. **Post-renal acute kidney injury:** acute kidney injury resulting from urinary tract obstruction.
9. **Pre-renal acute kidney injury:** acute kidney injury from reduced renal perfusion without intrinsic damage.
10. **Renal replacement therapy:** dialysis support used for specific severe complications of acute kidney injury.
11. **Toxidrome:** a recognisable cluster of signs and symptoms characteristic of a poisoning class.
12. **Urinary alkalinisation:** an enhanced elimination technique particularly effective for salicylate poisoning.

Concept Check Questions [Series 2]

Objective questions

- Acute kidney injury is defined and staged using standardised criteria combining serum creatinine rise and reduced urine _____. (Linked to SLO 2.1)
- Renal replacement therapy is indicated for refractory hyperkalaemia, refractory metabolic acidosis, and genuine fluid _____. (Linked to SLO 2.4)
- Activated charcoal is genuinely most effective when administered within a relatively narrow window following _____. (Linked to SLO 2.5)

- N-acetylcysteine replenishes the specific protective substance genuinely depleted by significant paracetamol _____. (Linked to SLO 2.7)
- Flumazenil genuinely requires careful, cautious use given the genuine risk of precipitating _____ in certain patients. (Linked to SLO 2.8)

Short-answer questions

1. Distinguish intrinsic renal from post-renal acute kidney injury. (Linked to SLO 2.1)
2. List indications for renal replacement therapy in acute kidney injury. (Linked to SLO 2.4)
3. Describe toxidromes and their diagnostic value. (Linked to SLO 2.6)
4. Describe the acid-base disturbance characteristic of salicylate poisoning. (Linked to SLO 2.7)
5. Describe naloxone and flumazenil as specific antidotes. (Linked to SLO 2.8)

Long-answer questions

6. Discuss the definition, classification, causes, presentation, and investigation of acute kidney injury. (Linked to SLO 2.1, 2.2)
7. Describe the management, renal replacement therapy indications, complications, and prognosis of acute kidney injury. (Linked to SLO 2.3, 2.4)
8. Discuss the general approach to the poisoned patient, including decontamination and enhanced elimination. (Linked to SLO 2.5, 2.6)
9. Describe the presentation and management of paracetamol and salicylate poisoning. (Linked to SLO 2.7)
10. Discuss other specific antidotes and management of poisoning. (Linked to SLO 2.8)

Answers to Concept Check Questions [Series 2]

Objective questions

11. Output.
12. Overload.
13. Ingestion.
14. Overdose.
15. Seizures.

Short-answer questions

16. Intrinsic renal causes involve direct kidney damage, while post-renal causes involve urinary tract obstruction.
17. Indications include refractory hyperkalaemia, refractory acidosis, fluid overload, and uraemic complications.
18. Toxidromes are recognisable symptom clusters providing diagnostic clues even before the substance is confirmed.
19. Initial respiratory alkalosis is followed by superimposed metabolic acidosis as toxicity progresses.
20. Naloxone reverses opioid toxicity, while flumazenil reverses benzodiazepine toxicity with careful, cautious use.

Long-answer questions

21. **Basic response:** Acute kidney injury is defined by standardised creatinine and urine output criteria, classified as pre-renal, intrinsic renal, or post-renal; presentation is often asymptomatic; investigation combines serial monitoring with a structured cause search.

    Value-added response: A value-added response notes that renal tract ultrasound actively excludes post-renal obstruction.

22. **Basic response:** Management corrects the underlying cause and avoids nephrotoxic insult; renal replacement therapy is indicated for refractory hyperkalaemia, acidosis, fluid overload, or uraemia; prognosis varies with cause and severity.

    Value-added response: A value-added response notes that a meaningful proportion of severe cases progress towards chronic kidney disease.

23. **Basic response:** Assessment follows structured resuscitation with a careful history; activated charcoal reduces absorption within a narrow window; enhanced elimination includes urinary alkalinisation and dialysis for selected poisonings.

    Value-added response: A value-added response notes that toxidromes provide diagnostic clues before the specific substance is confirmed.

24. **Basic response:** Paracetamol poisoning presents with minimal early symptoms despite serious hepatotoxicity risk, treated with N-acetylcysteine; salicylate poisoning produces mixed acid-base disturbance, treated with urinary alkalinisation or dialysis.

    Value-added response: A value-added response notes that N-acetylcysteine is most effective when given early, guided by a treatment nomogram.

25. **Basic response:** Naloxone reverses opioid toxicity and flumazenil reverses benzodiazepine toxicity, alongside comprehensive supportive care for poisonings without a specific antidote.

    Value-added response: A value-added response notes that flumazenil requires cautious use given seizure risk in certain patients.

Answers to Pilot Questions [Series 2]

Part 2.1

1. Acute kidney injury is staged using standardised creatinine rise and urine output criteria.
2. Pre-renal acute kidney injury results from reduced renal perfusion without intrinsic kidney damage.
3. Intrinsic renal disease involves direct kidney damage, while post-renal disease involves urinary tract obstruction.
4. It is often identified through routine biochemical screening rather than specific symptoms.
5. Investigation combines serial monitoring, urinalysis, renal tract ultrasound, and targeted serology.

Part 2.2

6. Priorities include correcting the underlying cause and avoiding further nephrotoxic insult.
7. Indications include refractory hyperkalaemia, refractory acidosis, fluid overload, and uraemic complications.
8. Hyperkalaemia carries genuine risk of life-threatening cardiac arrhythmia.
9. Pre-renal disease typically recovers fully with prompt correction, while intrinsic disease carries greater progression risk.
10. A meaningful proportion of severe cases progress towards chronic kidney disease, requiring follow-up.

Part 2.3

11. Assessment follows airway, breathing, circulation, alongside a careful history of substance, quantity, and timing.
12. Collateral history and physical evidence provide valuable information when the patient cannot provide a reliable history.

13. Activated charcoal adsorbs toxins to reduce absorption, though not effective for all substances such as alcohols.
14. Techniques include urinary alkalinisation and haemodialysis for selected severe, dialysable poisonings.
15. Toxidromes are recognisable symptom clusters providing diagnostic clues before the substance is confirmed.

Part 2.4

1. Paracetamol poisoning often shows minimal early symptoms despite potentially severe underlying hepatotoxicity.
2. N-acetylcysteine replenishes the depleted protective substance, guided by a treatment nomogram.
3. Initial respiratory alkalosis is followed by superimposed metabolic acidosis as toxicity progresses.
4. Urinary alkalinisation traps ionised salicylate within the renal tubule, promoting elimination.
5. Naloxone reverses opioid toxicity, while flumazenil reverses benzodiazepine toxicity with cautious use.

References and Attributions [Series 2]

1. Kumar, P., & Clark, M. (2020). Kumar and Clark's Clinical Medicine (10th ed.). Elsevier.
2. Feehally, J., Floege, J., Tonelli, M., & Johnson, R. J. (2018). Comprehensive Clinical Nephrology (6th ed.). Elsevier.
3. Kidney Disease: Improving Global Outcomes (2012). Clinical Practice Guideline for Acute Kidney Injury. Kidney International Supplements.
4. National Poisons Information Service (2023). TOXBASE Clinical Toxicology Database. NPIS.

Figures, Plates, Tables, and Boxes

1. Figure 2.1: A labelled diagram comparing pre-renal, intrinsic renal, and post-renal causes of acute kidney injury. AI-generated using the prompt: "Create a clean, accurate labelled

educational diagram titled Causes of Acute Kidney Injury, showing the kidney and urinary tract with three labelled sections indicating pre-renal causes upstream of the kidney, intrinsic renal causes within the kidney, and post-renal causes downstream in the urinary tract. Educational anatomical diagram style, no photographic content."

2. Table 2.1: Indications for renal replacement therapy in acute kidney injury. AI-generated using the prompt: "Create a clean reference table titled Indications for Renal Replacement Therapy in Acute Kidney Injury, listing indication, genuine clinical significance, and urgency. Simple clinical reference table style with outside border."
3. Figure 2.2: A clinician assessing a poisoned patient's airway and level of consciousness. AI-generated using the prompt: "Create a realistic clinical illustration titled Assessing the Poisoned Patient, showing a clinician checking a patient's airway and consciousness level in an emergency department bed, urgent but organised atmosphere. Clean clinical illustration style, no text."
4. Table 2.2: Comparing paracetamol and salicylate poisoning. AI-generated using the prompt: "Create a clean reference table titled Comparing Paracetamol and Salicylate Poisoning, listing feature, paracetamol poisoning, and salicylate poisoning. Simple clinical reference table style with outside border."

Course code: MED 616

Course title: Nephrology II

Course credit load: 2 Units

Series 3: Chronic Kidney Disease and Dialysis

- **Part 3.1: Approach to Chronic Kidney Disease**
  - Sub Part 3.1.1: Definition, staging, and causes of chronic kidney disease
  - Sub Part 3.1.2: Clinical presentation of chronic kidney disease
  - Sub Part 3.1.3: Investigation of chronic kidney disease
- **Part 3.2: Complications and Management of Chronic Kidney Disease**
  - Sub Part 3.2.1: Complications of chronic kidney disease
  - Sub Part 3.2.2: General management principles of chronic kidney disease
  - Sub Part 3.2.3: Slowing progression of chronic kidney disease
- **Part 3.3: Principles of Dialysis**
  - Sub Part 3.3.1: Indications and principles of dialysis
  - Sub Part 3.3.2: Haemodialysis
  - Sub Part 3.3.3: Peritoneal dialysis
- **Part 3.4: Acute and Chronic Dialysis in Practice**
  - Sub Part 3.4.1: Acute dialysis
  - Sub Part 3.4.2: Chronic dialysis and vascular and peritoneal access
  - Sub Part 3.4.3: Complications of dialysis

Introduction

This Series turns to **chronic kidney disease**, a genuinely progressive, longstanding decline in kidney function frequently reflecting the cumulative endpoint of many of the conditions already discussed across this course, before working through **dialysis**, the genuinely essential renal replacement therapy this condition can ultimately require, spanning both the acute dialysis

already introduced in Series 2 and the genuinely distinct considerations chronic, longer-term dialysis presents.

The aim of this Series is to equip you with the ability to define, stage, and describe the causes of chronic kidney disease, its presentation, investigation, complications, and management, including strategies to slow disease progression, and to describe the indications, principles, and modalities of dialysis, including acute dialysis, chronic dialysis and vascular and peritoneal access, and the complications of dialysis.

This Series opens with the **approach to chronic kidney disease**, moves through its **complications and management** and the **principles of dialysis**, and closes with **acute and chronic dialysis in practice**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 3.1:** define, stage, and describe the causes of chronic kidney disease
- **SLO 3.2:** describe the clinical presentation and investigation of chronic kidney disease
- **SLO 3.3:** describe the complications of chronic kidney disease
- **SLO 3.4:** discuss the general management and progression-slowing strategies for chronic kidney disease
- **SLO 3.5:** describe the indications, principles, and modalities of dialysis, including haemodialysis and peritoneal dialysis
- **SLO 3.6:** discuss acute dialysis
- **SLO 3.7:** describe chronic dialysis and vascular and peritoneal access
- **SLO 3.8:** discuss the complications of dialysis

3.1 Approach to Chronic Kidney Disease

3.1.1 definition, staging, and causes of chronic kidney disease

A genuinely progressive, longstanding decline defined by structured criteria

Chronic kidney disease, genuinely defined as abnormal kidney structure or function persisting for three months or longer, is staged according to estimated glomerular filtration rate and the specific degree of albuminuria present, with these two parameters together genuinely providing

considerably greater prognostic information than either measure considered in isolation, directly guiding the intensity of monitoring and management appropriate for a given patient.

Diabetes mellitus and **hypertension**, already discussed in genuine depth in earlier courses of this programme, together represent the most common causes of chronic kidney disease overall, alongside the glomerular diseases already discussed in Series 1 of this course, and genuine, active screening for chronic kidney disease in patients with these specific recognised risk factors, rather than waiting for symptomatic presentation, forms a genuinely essential preventive strategy this Series returns to throughout.

Fill in the blank: Chronic kidney disease is genuinely defined as abnormal kidney structure or function persisting for three months or _____.

3.1.2 clinical presentation of chronic kidney disease

Often genuinely silent until advanced, given considerable renal functional reserve

Chronic kidney disease is frequently genuinely asymptomatic through its earlier stages, reflecting the kidney's considerable functional reserve capacity already introduced conceptually in relation to physiological reserve in an earlier course of this programme, with symptoms typically only developing once kidney function has declined genuinely, significantly, mirroring the pattern already established for acute kidney injury in the previous Series of this course, though over a genuinely much more prolonged timescale.

When symptoms do develop, they genuinely reflect the accumulating complications discussed in the following Part of this Series, including fatigue from anaemia, pruritus, and, in advanced disease, symptoms of uraemia, and this genuinely delayed, insidious symptomatic presentation directly underlines why active, structured screening in at-risk populations already discussed in the previous sub-Part genuinely matters, rather than relying on symptomatic presentation alone.

Fill in the blank: Symptoms of chronic kidney disease typically only develop once kidney function has declined genuinely, _____.

3.1.3 investigation of chronic kidney disease

Confirming persistence, staging severity, and identifying the underlying cause

Serial estimated glomerular filtration rate measurements, confirming genuine persistence of reduced kidney function over the three-month timeframe already established in the formal definition, alongside **urine albumin-to-creatinine ratio**, quantifying the specific degree of

albuminuria already discussed as central to formal staging, together confirm the diagnosis and establish disease severity.

Renal tract imaging, typically ultrasound, assesses kidney size and structure, genuinely helpful in distinguishing acute from chronic kidney disease given the characteristic small, structurally abnormal kidneys longstanding chronic disease frequently produces, and further investigation directed at identifying the specific underlying cause, where genuinely not already established, completes this Part's coverage of chronic kidney disease investigation.

Fill in the blank: Renal tract ultrasound is genuinely helpful in distinguishing acute from chronic kidney disease given characteristic small, structurally _____ kidneys.

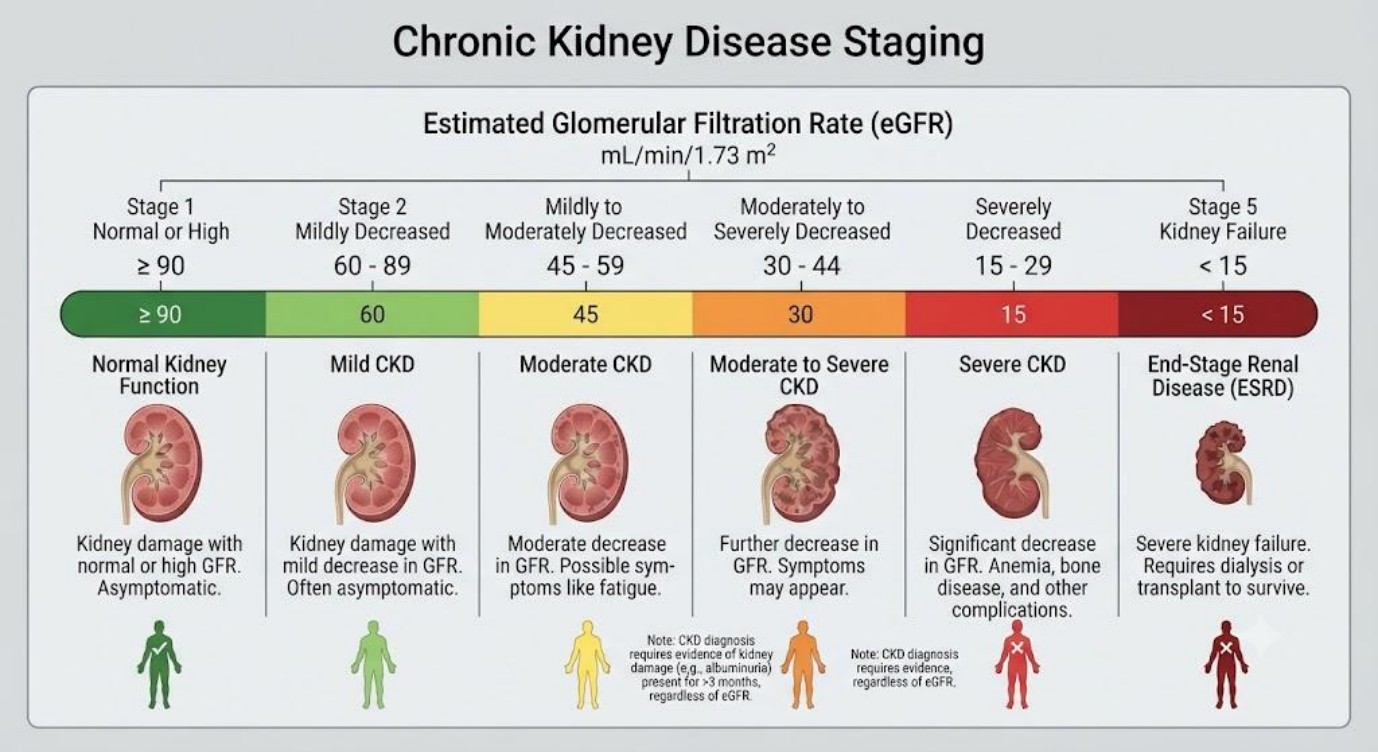

Figure 3.1: A labelled reference diagram of chronic kidney disease staging by estimated glomerular filtration rate.

Pilot questions 3.1

- Describe the formal definition of chronic kidney disease. (Linked to SLO 3.1)
- Describe how chronic kidney disease is staged. (Linked to SLO 3.1)
- List the most common causes of chronic kidney disease. (Linked to SLO 3.1)

- Explain why chronic kidney disease is frequently asymptomatic through its earlier stages. (Linked to SLO 3.2)
- Describe the investigation approach for chronic kidney disease. (Linked to SLO 3.2)

3.2 Complications and Management of Chronic Kidney Disease

3.2.1 complications of chronic kidney disease

A genuinely wide-ranging pattern reflecting multiple failing homeostatic functions

Anaemia, already discussed in relation to reduced erythropoietin production in an earlier course of this programme, and **mineral bone disease**, resulting from disrupted calcium, phosphate, and vitamin D homeostasis as kidney function progressively declines, represent two of the genuinely most characteristic complications of chronic kidney disease, alongside cardiovascular disease, given the genuinely, meaningfully elevated cardiovascular risk this condition independently carries.

Metabolic acidosis and **hyperkalaemia**, reflecting the kidney's genuinely reduced capacity to excrete acid and potassium as function declines, alongside fluid overload from reduced sodium and water excretory capacity, complete this genuinely wide-ranging complication profile, and active, structured screening and management of each specific complication forms an essential, ongoing component of comprehensive chronic kidney disease care throughout its natural history.

Fill in the blank: Mineral bone disease results from disrupted calcium, phosphate, and vitamin _____ homeostasis in chronic kidney disease.

3.2.2 general management principles of chronic kidney disease

Comprehensive, structured, multi-faceted long-term care

Blood pressure control, particularly using agents genuinely offering additional renal protective benefit already discussed in relation to proteinuria reduction in Series 1 of this course, and management of specific complications already discussed in the previous sub-Part, including erythropoiesis-stimulating agents for anaemia and phosphate binders for mineral bone disease, form genuinely essential components of comprehensive chronic kidney disease management.

Cardiovascular risk reduction, given the genuinely elevated independent cardiovascular risk chronic kidney disease carries already discussed, and careful medication review avoiding further

nephrotoxic insult, mirroring the same principle already emphasised for acute kidney injury in the previous Series of this course, complete this genuinely comprehensive management framework applicable throughout the chronic kidney disease disease course.

Fill in the blank: Cardiovascular risk reduction genuinely matters given the elevated independent cardiovascular risk chronic kidney disease _____.

3.2.3 slowing progression of chronic kidney disease

Genuine strategies delaying, rather than reversing, disease progression

Blood pressure and proteinuria control, already discussed as central management measures in the previous sub-Part, genuinely, measurably slow chronic kidney disease progression, and **glycaemic control** in patients with diabetic kidney disease specifically, addressing this genuinely most common underlying cause already discussed earlier in this Series, offers a further, genuinely important progression-slowing intervention where relevant to the individual patient's underlying cause.

Newer therapeutic agents, offering genuine additional renal protective benefit beyond blood pressure and glycaemic control alone in appropriately selected patients, represent a genuinely evolving area of chronic kidney disease management, and this Part closes on the theme that, while chronic kidney disease progression genuinely cannot always be entirely prevented, meaningful delay is genuinely achievable through comprehensive, structured, multi-faceted management.

Fill in the blank: Blood pressure and proteinuria control genuinely, measurably slow chronic kidney disease _____.

Table 3.1: Comparing key complications of chronic kidney disease

Complication	Underlying mechanism	Key management approach
Anaemia	Reduced erythropoietin production	Erythropoiesis-stimulating agents
Mineral bone disease	Disrupted calcium, phosphate, vitamin D homeostasis	Phosphate binders, vitamin D analogues
Cardiovascular disease	Independently elevated risk from chronic kidney disease itself	Comprehensive cardiovascular risk reduction

Pilot questions 3.2

1. List complications of chronic kidney disease. (Linked to SLO 3.3)
2. Describe mineral bone disease in chronic kidney disease. (Linked to SLO 3.3)
3. Describe the general management approach to chronic kidney disease. (Linked to SLO 3.4)
4. Explain why blood pressure and proteinuria control genuinely slow disease progression. (Linked to SLO 3.4)
5. Describe the role of glycaemic control in slowing chronic kidney disease progression. (Linked to SLO 3.4)

3.3 Principles of Dialysis

3.3.1 indications and principles of dialysis

Replacing the kidney's essential filtration function

Dialysis, replacing the kidney's essential filtration function once native kidney function has declined sufficiently to no longer adequately sustain normal homeostasis, is indicated for genuinely established kidney failure, whether from advanced chronic kidney disease already discussed throughout this Series, or the acute indications already discussed in Series 2 of this course, and operates through the fundamental principle of removing accumulated waste products and excess fluid via a semi-permeable membrane.

Diffusion, movement of solutes across the semi-permeable membrane down their concentration gradient, and **ultrafiltration**, movement of fluid across the membrane driven by a pressure gradient, together form the two fundamental physical processes underlying both major dialysis modalities discussed in the following two sub-Parts of this Part, each modality applying these same fundamental principles through a genuinely distinct practical mechanism.

Fill in the blank: Diffusion is movement of solutes across the semi-permeable membrane down their concentration _____.

3.3.2 haemodialysis

Filtering blood through an external, artificial membrane

Haemodialysis, circulating the patient's blood through an external artificial dialysis membrane, requires genuine vascular access, discussed further in the following Part of this Series, and

typically involves sessions lasting several hours, performed several times weekly in the great majority of patients requiring long-term dialysis, a genuinely significant time commitment directly relevant to the patient's overall quality of life and daily routine.

The dialysis membrane and specific dialysate composition genuinely allow controlled removal of accumulated waste products and excess fluid while genuinely, carefully preserving essential substances, and this specific, controlled process directly reflects the same diffusion and ultrafiltration principles already established in the previous sub-Part, applied through this genuinely specific extracorporeal, external mechanism.

Fill in the blank: Haemodialysis requires genuine vascular _____ and typically involves sessions lasting several hours.

3.3.3 peritoneal dialysis

Using the body's own peritoneal membrane as the filtering surface

Peritoneal dialysis, using the patient's own peritoneal membrane as the genuine filtering surface rather than an external artificial membrane, involves instilling dialysate fluid into the peritoneal cavity through a permanently placed peritoneal catheter, allowing diffusion and ultrafiltration to occur across this natural membrane before the fluid, now containing removed waste products, is drained and replaced.

This modality offers genuine practical advantages for appropriately selected patients, including the ability to perform treatment at home without requiring the specific, external equipment haemodialysis demands, though it genuinely requires the patient or a carer to be capable of performing the specific technique reliably, and this genuine trade-off between the two modalities directly informs the individualised modality selection discussed further in the following Part of this Series.

Fill in the blank: Peritoneal dialysis instils dialysate fluid into the peritoneal cavity through a permanently placed peritoneal _____.

Figure 3.2: A patient undergoing a haemodialysis session.

Pilot questions 3.3

1. Describe the indications for dialysis. (Linked to SLO 3.5)
2. Describe diffusion and ultrafiltration. (Linked to SLO 3.5)
3. Describe haemodialysis. (Linked to SLO 3.5)
4. Describe peritoneal dialysis. (Linked to SLO 3.5)
5. Compare the practical advantages and requirements of haemodialysis and peritoneal dialysis. (Linked to SLO 3.5)

3.4 Acute and Chronic Dialysis in Practice

3.4.1 acute dialysis

A genuinely urgent, typically temporary intervention

Acute dialysis, already introduced in the context of specific indications for renal replacement therapy in Series 2 of this course, is typically delivered using haemodialysis given its genuinely more rapid ability to correct severe, acute biochemical derangement compared with peritoneal

dialysis, and, unlike the chronic dialysis discussed in the following sub-Part, is genuinely often temporary, continued only until the underlying acute kidney injury has resolved sufficiently.

Vascular access for acute dialysis typically uses a temporary central venous catheter, given the genuine urgency and short-term nature of the anticipated treatment course, in contrast to the more durable vascular access options discussed in the following sub-Part for patients genuinely requiring longer-term, chronic dialysis treatment, and this specific access choice directly reflects the anticipated treatment duration for each particular clinical scenario.

Fill in the blank: Acute dialysis typically uses haemodialysis given its genuinely more rapid ability to correct severe, acute biochemical _____.

3.4.2 chronic dialysis and vascular and peritoneal access

Durable access supporting genuinely long-term treatment

Arteriovenous fistula, a surgically created connection between an artery and vein allowing genuinely durable, long-term haemodialysis vascular access, is the genuinely preferred access option for patients requiring chronic haemodialysis, given its considerably lower infection and complication risk compared with a central venous catheter, though it genuinely requires a period of maturation following surgical creation before it becomes usable for dialysis.

Peritoneal dialysis catheter, already introduced in the previous Part, provides the durable access route genuinely required for chronic peritoneal dialysis, and, for patients where an arteriovenous fistula is genuinely not feasible or has not yet matured, an arteriovenous graft or a tunnelled central venous catheter offer alternative, though generally less preferred, chronic haemodialysis access options.

Fill in the blank: Arteriovenous fistula requires a period of _____ following surgical creation before it becomes usable for dialysis.

3.4.3 complications of dialysis

Genuine risks specific to each modality, requiring active monitoring

Haemodialysis-related complications include vascular access infection or thrombosis, intradialytic hypotension, a significant blood pressure fall during the treatment session itself, and, over the longer term, cardiovascular complications reflecting the genuinely significant cardiovascular burden chronic kidney disease and dialysis together carry, already discussed earlier in this Series.

Peritoneal dialysis-related complications include **peritonitis**, infection of the peritoneal cavity, a genuinely serious complication requiring prompt recognition and treatment, and catheter-related mechanical complications, and this Series closes on the same theme of modality-specific, structured complication awareness that has run consistently throughout this whole course's coverage of renal disease and its treatment.

Fill in the blank: Peritonitis is infection of the peritoneal cavity, a genuinely serious complication of peritoneal _____.

Table 3.2: Comparing haemodialysis and peritoneal dialysis

Feature	Haemodialysis	Peritoneal dialysis
Filtering surface	External artificial membrane	Patient's own peritoneal membrane
Typical location	Dialysis unit or, in selected cases, home	Home-based
Key complication	Vascular access infection or thrombosis	Peritonitis

Pilot questions 3.4

1. Describe acute dialysis and its typical vascular access. (Linked to SLO 3.6)
2. Describe the arteriovenous fistula and its advantages for chronic haemodialysis. (Linked to SLO 3.7)
3. Describe alternative chronic vascular access options. (Linked to SLO 3.7)
4. List complications of haemodialysis. (Linked to SLO 3.8)
5. Describe peritonitis as a complication of peritoneal dialysis. (Linked to SLO 3.8)

Series Summary

This Series covered chronic kidney disease and dialysis. Part 3.1 covered the definition, staging, causes, presentation, and investigation of chronic kidney disease, while Part 3.2 turned to its complications, management, and progression-slowing strategies. Part 3.3 covered the principles of dialysis, including haemodialysis and peritoneal dialysis, and Part 3.4 closed with acute and chronic dialysis in practice.

You should now be able to describe and manage chronic kidney disease and dialysis across all four Parts of this Series, meeting the outcomes set for this Series. Series 4 turns next to urinary tract infection, hypertension, and nephrolithiasis.

Glossary of Terms

1. **Arteriovenous fistula:** a surgically created artery-vein connection providing durable chronic haemodialysis access.
2. **Chronic kidney disease:** abnormal kidney structure or function persisting for three months or longer.
3. **Diffusion:** movement of solutes across a semi-permeable membrane down their concentration gradient.
4. **Estimated glomerular filtration rate:** a measure used to stage chronic kidney disease severity.
5. **Haemodialysis:** dialysis circulating blood through an external artificial dialysis membrane.
6. **Mineral bone disease:** disrupted calcium, phosphate, and vitamin D homeostasis in chronic kidney disease.
7. **Peritoneal dialysis:** dialysis using the patient's own peritoneal membrane as the filtering surface.
8. **Peritonitis:** infection of the peritoneal cavity, a complication of peritoneal dialysis.
9. **Renal tract ultrasound:** imaging used to distinguish acute from chronic kidney disease.
10. **Ultrafiltration:** movement of fluid across a membrane driven by a pressure gradient.
11. **Urine albumin-to-creatinine ratio:** a test quantifying the degree of albuminuria for chronic kidney disease staging.
12. **Vascular access:** the route allowing blood to be circulated through a haemodialysis membrane.

Concept Check Questions [Series 3]

Objective questions

- Chronic kidney disease is genuinely defined as abnormal kidney structure or function persisting for three months or _____. (Linked to SLO 3.1)
- Mineral bone disease results from disrupted calcium, phosphate, and vitamin _____ homeostasis in chronic kidney disease. (Linked to SLO 3.3)

- Diffusion is movement of solutes across the semi-permeable membrane down their concentration _____. (Linked to SLO 3.5)
- Arteriovenous fistula requires a period of _____ following surgical creation before it becomes usable for dialysis. (Linked to SLO 3.7)
- Peritonitis is infection of the peritoneal cavity, a genuinely serious complication of peritoneal _____. (Linked to SLO 3.8)

Short-answer questions

1. List the most common causes of chronic kidney disease. (Linked to SLO 3.1)
2. List complications of chronic kidney disease. (Linked to SLO 3.3)
3. Describe haemodialysis. (Linked to SLO 3.5)
4. Describe peritoneal dialysis. (Linked to SLO 3.5)
5. List complications of haemodialysis. (Linked to SLO 3.8)

Long-answer questions

6. Discuss the definition, staging, causes, presentation, and investigation of chronic kidney disease. (Linked to SLO 3.1, 3.2)
7. Describe the complications, management, and progression-slowing strategies for chronic kidney disease. (Linked to SLO 3.3, 3.4)
8. Discuss the indications, principles, and modalities of dialysis, including haemodialysis and peritoneal dialysis. (Linked to SLO 3.5)
9. Describe acute dialysis and chronic dialysis vascular and peritoneal access. (Linked to SLO 3.6, 3.7)
10. Discuss the complications of dialysis. (Linked to SLO 3.8)

Answers to Concept Check Questions [Series 3]

Objective questions

11. Longer.
12. D.
13. Gradient.
14. Maturation.
15. Dialysis.

Short-answer questions

16. The most common causes are diabetes mellitus and hypertension, alongside glomerular disease.
17. Complications include anaemia, mineral bone disease, cardiovascular disease, metabolic acidosis, and hyperkalaemia.
18. Haemodialysis circulates blood through an external artificial dialysis membrane.
19. Peritoneal dialysis uses the patient's own peritoneal membrane as the filtering surface.
20. Complications include vascular access infection or thrombosis, intradialytic hypotension, and cardiovascular disease.

Long-answer questions

21. **Basic response:** Chronic kidney disease is defined by persistent abnormal structure or function, staged by GFR and albuminuria; most common causes are diabetes and hypertension; presentation is often asymptomatic until advanced; investigation uses serial GFR, urine testing, and imaging.

    Value-added response: A value-added response notes that renal ultrasound helps distinguish acute from chronic disease given characteristic small kidneys.

22. **Basic response:** Complications include anaemia, mineral bone disease, cardiovascular disease, and metabolic derangement; management combines blood pressure control, complication-specific treatment, and cardiovascular risk reduction; progression is slowed through blood pressure, proteinuria, and glycaemic control.

    Value-added response: A value-added response notes that newer therapeutic agents offer additional renal protective benefit in selected patients.

23. **Basic response:** Dialysis is indicated for established kidney failure, operating through diffusion and ultrafiltration; haemodialysis uses an external membrane, while peritoneal dialysis uses the patient's own peritoneal membrane.

    Value-added response: A value-added response notes that peritoneal dialysis offers home-based treatment but requires reliable patient or carer technique.

24. **Basic response:** Acute dialysis typically uses haemodialysis via temporary central venous catheter access; chronic dialysis uses durable access such as an arteriovenous fistula or peritoneal dialysis catheter.

    Value-added response: A value-added response notes that arteriovenous fistula requires a maturation period before it becomes usable.

25. **Basic response:** Haemodialysis complications include vascular access infection, thrombosis, and intradialytic hypotension; peritoneal dialysis complications include peritonitis and catheter-related mechanical issues.

    Value-added response: A value-added response notes that peritonitis requires prompt recognition and treatment given its genuine severity.

Answers to Pilot Questions [Series 3]

Part 3.1

1. Chronic kidney disease is abnormal kidney structure or function persisting for three months or longer.
2. Staging uses estimated glomerular filtration rate and degree of albuminuria.
3. The most common causes are diabetes mellitus and hypertension.
4. The kidney's considerable functional reserve masks decline until function has significantly declined.
5. Investigation uses serial eGFR, urine albumin-to-creatinine ratio, and renal tract imaging.

Part 3.2

6. Complications include anaemia, mineral bone disease, cardiovascular disease, acidosis, and hyperkalaemia.
7. Mineral bone disease results from disrupted calcium, phosphate, and vitamin D homeostasis.
8. Management combines blood pressure control, complication-specific treatment, and cardiovascular risk reduction.
9. Reducing blood pressure and proteinuria genuinely reduces the ongoing glomerular stress driving progression.
10. Glycaemic control addresses diabetes, the most common underlying cause, slowing diabetic kidney disease progression.

Part 3.3

11. Dialysis is indicated for established kidney failure from advanced chronic disease or acute indications.
12. Diffusion moves solutes down a concentration gradient; ultrafiltration moves fluid via a pressure gradient.

13. Haemodialysis circulates blood through an external artificial dialysis membrane requiring vascular access.
14. Peritoneal dialysis uses the patient's own peritoneal membrane via a permanently placed catheter.
15. Haemodialysis requires external equipment and sessions; peritoneal dialysis allows home-based treatment requiring reliable technique.

Part 3.4

1. Acute dialysis typically uses haemodialysis via a temporary central venous catheter.
2. The fistula provides durable, lower-infection-risk access but requires a maturation period after creation.
3. Alternatives include arteriovenous graft or tunnelled central venous catheter.
4. Complications include vascular access infection, thrombosis, intradialytic hypotension, and cardiovascular disease.
5. Peritonitis is peritoneal cavity infection requiring prompt recognition and treatment.

References and Attributions [Series 3]

1. Kumar, P., & Clark, M. (2020). Kumar and Clark's Clinical Medicine (10th ed.). Elsevier.
2. Feehally, J., Floege, J., Tonelli, M., & Johnson, R. J. (2018). Comprehensive Clinical Nephrology (6th ed.). Elsevier.
3. Kidney Disease: Improving Global Outcomes (2024). Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International.
4. National Institute for Health and Care Excellence (2018). Renal Replacement Therapy and Conservative Management (NG107). NICE.

Figures, Plates, Tables, and Boxes

1. Figure 3.1: A labelled reference diagram of chronic kidney disease staging by estimated glomerular filtration rate. AI-generated using the prompt: "Create a clean, accurate labelled educational diagram titled Chronic Kidney Disease Staging, showing a horizontal scale of estimated glomerular filtration rate divided into labelled stages from

normal function through to kidney failure. Educational anatomical diagram style, no photographic content."

2. Table 3.1: Comparing key complications of chronic kidney disease. AI-generated using the prompt: "Create a clean reference table titled Comparing Key Complications of Chronic Kidney Disease, listing complication, underlying mechanism, and key management approach. Simple clinical reference table style with outside border."
3. Figure 3.2: A patient undergoing a haemodialysis session. AI-generated using the prompt: "Create a realistic clinical illustration titled Haemodialysis Session, showing a patient seated comfortably in a dialysis chair, connected via tubing to a dialysis machine, dialysis unit setting. Clean clinical illustration style, no text."
4. Table 3.2: Comparing haemodialysis and peritoneal dialysis. AI-generated using the prompt: "Create a clean reference table titled Comparing Haemodialysis and Peritoneal Dialysis, listing feature, haemodialysis, and peritoneal dialysis. Simple clinical reference table style with outside border."

Course code: MED 616

Course title: Nephrology II

Course credit load: 2 Units

Series 4: Urinary Tract Infection, Hypertension, and Nephrolithiasis

- **Part 4.1: Urinary Tract Infection**
  - Sub Part 4.1.1: Pathophysiology and classification of urinary tract infection
  - Sub Part 4.1.2: Clinical presentation of urinary tract infection
  - Sub Part 4.1.3: Investigation and management of urinary tract infection
- **Part 4.2: Complicated UTI and Recurrent Infection**
  - Sub Part 4.2.1: Pyelonephritis
  - Sub Part 4.2.2: Complicated UTI and catheter-associated infection
  - Sub Part 4.2.3: Recurrent urinary tract infection
- **Part 4.3: Hypertension**
  - Sub Part 4.3.1: Classification and pathophysiology of hypertension
  - Sub Part 4.3.2: Investigation of hypertension
  - Sub Part 4.3.3: Management of hypertension
- **Part 4.4: Nephrolithiasis**
  - Sub Part 4.4.1: Pathophysiology and types of renal stones
  - Sub Part 4.4.2: Clinical presentation of nephrolithiasis
  - Sub Part 4.4.3: Investigation and management of nephrolithiasis

Introduction

This Series turns to three genuinely common, everyday nephrological and urological presentations, **urinary tract infection**, spanning uncomplicated, complicated, and recurrent

disease, **hypertension**, already introduced in principle in earlier courses of this programme but revisited here with a genuinely specific nephrological focus, and **nephrolithiasis**, kidney stone disease, each demanding structured, systematic clinical assessment.

The aim of this Series is to equip you with an understanding of the pathophysiology, classification, presentation, investigation, and management of urinary tract infection, including pyelonephritis, complicated and catheter-associated infection, and recurrent infection, the classification, pathophysiology, investigation, and management of hypertension, and the pathophysiology, types, presentation, investigation, and management of nephrolithiasis.

This Series opens with **urinary tract infection**, moves through **complicated UTI and recurrent infection** and **hypertension**, and closes with **nephrolithiasis**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 4.1:** describe the pathophysiology, classification, and clinical presentation of urinary tract infection
- **SLO 4.2:** discuss the investigation and management of urinary tract infection
- **SLO 4.3:** describe pyelonephritis and complicated and catheter-associated urinary tract infection
- **SLO 4.4:** discuss recurrent urinary tract infection
- **SLO 4.5:** describe the classification, pathophysiology, and investigation of hypertension
- **SLO 4.6:** discuss the management of hypertension
- **SLO 4.7:** describe the pathophysiology, types, and clinical presentation of nephrolithiasis
- **SLO 4.8:** discuss the investigation and management of nephrolithiasis

4.1 Urinary Tract Infection

4.1.1 pathophysiology and classification of urinary tract infection

Ascending infection, most commonly from a genuinely predictable source

Urinary tract infection, most commonly resulting from ascending infection of bowel flora, particularly Escherichia coli, already discussed in principle in an earlier course of this programme, into the normally sterile urinary tract, is classified anatomically as **lower urinary**

tract infection, cystitis, confined to the bladder, or **upper urinary tract infection**, pyelonephritis, discussed further in the following Part of this Series, involving the kidney itself.

Urinary tract infection is genuinely, considerably more common in women given the anatomically shorter urethra facilitating ascending bacterial spread, and is further classified as **uncomplicated**, occurring in an otherwise healthy, non-pregnant woman with normal urinary tract anatomy, or **complicated**, discussed further in the following Part of this Series, occurring in the presence of a specific factor genuinely increasing infection risk or treatment complexity.

Fill in the blank: Urinary tract infection is genuinely, considerably more common in women given the anatomically shorter _____ facilitating ascending spread.

4.1.2 clinical presentation of urinary tract infection

Genuinely characteristic lower urinary tract symptoms

Lower urinary tract infection presents with dysuria, pain or burning on urination, urinary frequency, urgency, and, in some cases, suprapubic discomfort, a genuinely characteristic symptom cluster this Part aims to establish confident recognition of, and this specific symptom pattern, when genuinely present in an otherwise uncomplicated patient, frequently allows confident clinical diagnosis without necessarily requiring further investigation.

Atypical presentation, particularly in older patients, already discussed in relation to atypical infection presentation in an earlier course of this programme, can include confusion or non-specific functional decline rather than the classic symptoms already discussed, and actively considering urinary tract infection in this specific presentation pattern, rather than assuming an alternative cause, genuinely matters in this specific patient population.

Fill in the blank: Atypical presentation of UTI in older patients can include confusion or non-specific functional _____ rather than classic symptoms.

4.1.3 investigation and management of urinary tract infection

Often genuinely clinical diagnosis, with prompt, empirical treatment

Urine dipstick testing, detecting leucocyte esterase and nitrites, provides genuinely rapid supportive evidence for urinary tract infection, though genuinely, considerable diagnostic value rests on the clinical symptom pattern itself already discussed, and **urine culture**, confirming the specific causative organism and its antibiotic susceptibility, is genuinely reserved for atypical, complicated, or treatment-refractory presentations rather than every uncomplicated case.

Empirical antibiotic therapy, initiated based on the genuinely most likely causative organisms and local resistance patterns, forms the mainstay of uncomplicated urinary tract infection management, with a genuinely short treatment course typically adequate for uncomplicated lower urinary tract infection specifically, reflecting the generally more limited, superficial nature of this infection compared with the upper urinary tract infection discussed in the following Part of this Series.

Fill in the blank: Urine culture is genuinely reserved for atypical, complicated, or treatment-_____ presentations.

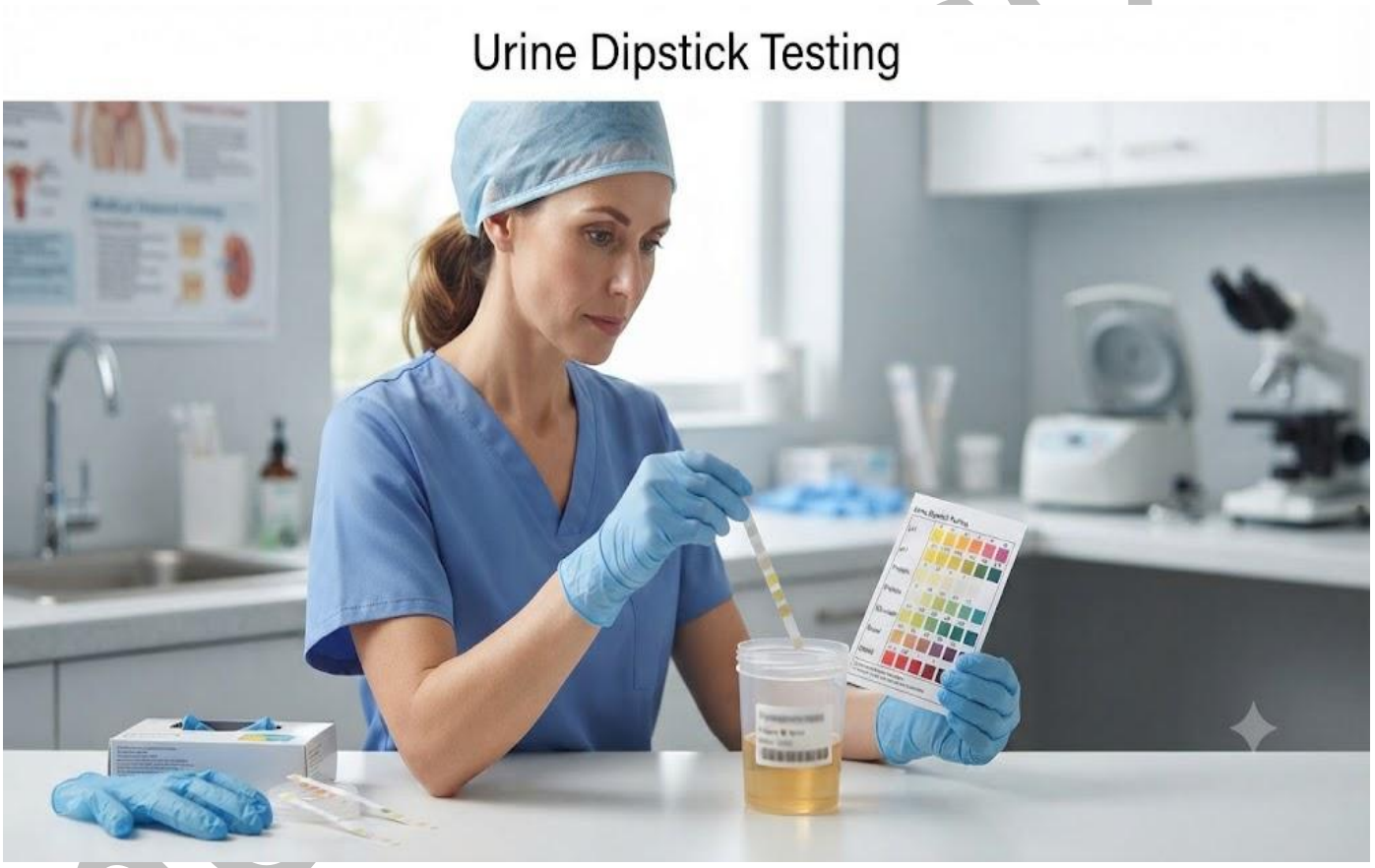

Figure 4.1: A clinician performing urine dipstick testing.

Pilot questions 4.1

- Describe the pathophysiology of urinary tract infection. (Linked to SLO 4.1)
- Distinguish lower from upper urinary tract infection. (Linked to SLO 4.1)
- Describe the classic symptom pattern of lower urinary tract infection. (Linked to SLO 4.1)

- Describe atypical urinary tract infection presentation in older patients. (Linked to SLO 4.1)
- Describe the investigation and management approach for uncomplicated urinary tract infection. (Linked to SLO 4.2)

4.2 Complicated UTI and Recurrent Infection

4.2.1 pyelonephritis

Ascending infection reaching the kidney itself

Pyelonephritis, infection of the kidney itself following ascending spread beyond the bladder already discussed in the previous Part, presents with fever, flank pain, and systemic symptoms, in addition to the lower urinary tract symptoms already discussed, and this genuinely more significant, systemic presentation directly reflects the deeper, more extensive tissue involvement pyelonephritis represents compared with simple cystitis.

Severity assessment genuinely matters given the range of clinical severity pyelonephritis can present with, from mild disease genuinely manageable with oral antibiotics on an outpatient basis, to genuinely severe disease presenting with sepsis, already discussed extensively in an earlier course of this programme, requiring hospital admission and intravenous antibiotic therapy, mirroring the same severity-directed management approach already established for sepsis generally.

Fill in the blank: Pyelonephritis presents with fever, flank pain, and systemic _____, in addition to lower urinary tract symptoms.

4.2.2 complicated uti and catheter-associated infection

Factors genuinely increasing infection risk and treatment complexity

Complicated urinary tract infection, occurring in the presence of structural or functional urinary tract abnormality, pregnancy, male sex, or significant immunocompromise already discussed in an earlier course of this programme, genuinely carries increased risk of treatment failure or complication, and recognising these specific risk factors directly informs both the investigation approach and treatment duration, typically longer than for uncomplicated infection already discussed.

Catheter-associated urinary tract infection, a genuinely common healthcare-associated infection, results from the indwelling catheter providing a direct route bypassing normal host defence mechanisms already discussed in principle in an earlier course of this programme, and management genuinely includes active consideration of catheter removal or replacement alongside appropriate antimicrobial therapy where genuine infection, rather than simple asymptomatic colonisation, is confirmed.

Fill in the blank: Catheter-associated urinary tract infection results from the indwelling catheter providing a direct route bypassing normal host _____ mechanisms.

4.2.3 recurrent urinary tract infection

A genuinely troublesome, sometimes challenging pattern requiring active investigation

Recurrent urinary tract infection, genuinely defined as a specific number of confirmed infections within a defined timeframe, warrants active investigation for an underlying predisposing factor, including structural urinary tract abnormality or, in postmenopausal women specifically, genuine oestrogen deficiency affecting normal urogenital tissue health, rather than simply treating each individual episode in genuine isolation.

Preventive strategies, including behavioural measures, and, in appropriately selected patients, prophylactic antibiotic therapy or, for postmenopausal women, topical oestrogen therapy addressing the underlying predisposing factor already discussed, form a genuinely comprehensive approach to recurrent urinary tract infection management, closing this Part's coverage on the theme of addressing underlying cause rather than symptomatic treatment alone.

Fill in the blank: Recurrent urinary tract infection warrants active investigation for an underlying predisposing _____.

Table 4.1: Comparing uncomplicated and complicated urinary tract infection

Feature	Uncomplicated UTI	Complicated UTI
Typical patient	Otherwise healthy, non-pregnant woman	Structural abnormality, pregnancy, male sex, immunocompromise
Genuine treatment failure risk	Low	Genuinely elevated
Typical treatment duration	Short course	Longer course

Pilot questions 4.2

1. Describe pyelonephritis and its typical presentation. (Linked to SLO 4.3)
2. Describe severity assessment in pyelonephritis. (Linked to SLO 4.3)
3. List factors genuinely defining a complicated urinary tract infection. (Linked to SLO 4.3)
4. Describe catheter-associated urinary tract infection. (Linked to SLO 4.3)
5. Describe the approach to investigating recurrent urinary tract infection. (Linked to SLO 4.4)

4.3 Hypertension

4.3.1 classification and pathophysiology of hypertension

Primary and secondary causes, with genuine nephrological relevance

Hypertension, already introduced in principle in earlier courses of this programme, is classified as **primary**, essential hypertension without a genuinely specific identifiable underlying cause, accounting for the great majority of cases, or **secondary**, resulting from a genuinely specific identifiable underlying cause, and this Series's specific nephrological focus emphasises the genuinely bidirectional relationship between hypertension and kidney disease already touched upon in Series 3 of this course.

Renal causes of secondary hypertension, including renal artery stenosis, reducing renal perfusion and triggering the renin-angiotensin-aldosterone system already discussed in an earlier course of this programme, and the chronic kidney disease and glomerular diseases already discussed extensively in earlier Series of this course, illustrate this genuinely bidirectional relationship, since hypertension both causes and results from kidney disease, a genuinely important, sometimes underappreciated clinical pattern.

Fill in the blank: Renal artery stenosis reduces renal perfusion and triggers the renin-angiotensin-aldosterone _____.

4.3.2 investigation of hypertension

Confirming the diagnosis, then actively screening for secondary causes and organ damage

Ambulatory or home blood pressure monitoring, providing genuinely more representative readings than a single clinic measurement, given the genuine possibility of white coat

hypertension, elevated readings specifically in the clinical setting, confirms the diagnosis before committing a patient to long-term antihypertensive treatment, mirroring the same principle of confirming genuine, sustained abnormality already established for other conditions throughout this course.

Screening for secondary causes, particularly in younger patients or those with genuinely resistant hypertension despite adequate treatment, alongside assessment for end-organ damage, including the renal, cardiac, and ophthalmological complications already discussed across this whole course, forms an essential, comprehensive component of hypertension investigation beyond simply confirming the diagnosis itself.

Fill in the blank: Screening for secondary causes is particularly important in younger patients or those with genuinely resistant hypertension despite adequate _____.

4.3.3 management of hypertension

Lifestyle measures alongside genuinely individualised pharmacological treatment

Lifestyle modification, including dietary sodium restriction, weight management, and regular physical activity, forms the genuinely essential foundation of hypertension management applicable to essentially every patient, and **pharmacological therapy**, when genuinely indicated, is individualised according to the patient's specific characteristics, including age, ethnicity, and coexisting conditions, particularly the renal considerations already discussed earlier in this Part given this Series's specific nephrological focus.

Blood pressure targets genuinely, sometimes require adjustment in patients with coexisting chronic kidney disease already discussed extensively in Series 3 of this course, given the genuine balance between adequate blood pressure control and avoiding excessive reduction risking renal hypoperfusion, and this genuinely individualised approach, closing this Part's coverage, directly reflects the specific nephrological perspective this Series brings to a condition already introduced more generally elsewhere in this programme.

Fill in the blank: Blood pressure targets genuinely, sometimes require adjustment in patients with coexisting chronic kidney _____.

Figure 4.2: A clinician measuring a patient's blood pressure.

Pilot questions 4.3

1. Distinguish primary from secondary hypertension. (Linked to SLO 4.5)
2. Describe renal causes of secondary hypertension. (Linked to SLO 4.5)
3. Explain why ambulatory or home blood pressure monitoring is genuinely valuable. (Linked to SLO 4.5)
4. Describe when screening for secondary causes of hypertension is particularly important. (Linked to SLO 4.5)
5. Describe the general management approach to hypertension. (Linked to SLO 4.6)

4.4 Nephrolithiasis

4.4.1 pathophysiology and types of renal stones

Crystallisation from genuinely supersaturated urine

Nephrolithiasis, kidney stone formation, results from genuine urinary supersaturation with stone-forming substances exceeding their solubility, allowing crystallisation and subsequent stone formation, and **calcium oxalate stones**, the most common stone type overall, alongside

less common types including uric acid stones, struvite stones associated with specific urinary tract infection, and cystine stones from a genuine inherited metabolic condition, illustrate the genuinely wide range of possible stone composition.

Risk factors for stone formation include inadequate fluid intake, dietary factors, and certain metabolic conditions genuinely predisposing to specific stone types already discussed, and identifying a patient's specific stone composition and relevant risk factors, discussed further in the investigation sub-Part of this Part, directly informs both acute management and genuinely important, longer-term preventive strategies.

Fill in the blank: Nephrolithiasis results from genuine urinary supersaturation with stone-forming substances exceeding their _____.

4.4.2 clinical presentation of nephrolithiasis

Genuinely severe, characteristic pain reflecting ureteric obstruction

Renal colic, genuinely severe, characteristically colicky flank pain radiating towards the groin, reflecting ureteric obstruction and spasm as a stone attempts to pass along the ureter, is the classic presenting symptom of nephrolithiasis, frequently accompanied by nausea, vomiting, and, where the stone genuinely causes mucosal irritation or injury, visible or microscopic haematuria.

Complications, including urinary tract obstruction, discussed in principle as a post-renal cause of acute kidney injury in Series 2 of this course, and, genuinely importantly, infection proximal to an obstructing stone, a genuine urological emergency given the risk of obstructed pyonephrosis, require active clinical consideration in any patient presenting with suspected renal colic, particularly where fever accompanies the presentation.

Fill in the blank: Infection proximal to an obstructing stone is a genuine urological emergency given the risk of obstructed _____.

4.4.3 investigation and management of nephrolithiasis

Confirming the diagnosis, then matching treatment to stone characteristics

Non-contrast computed tomography, the genuinely most sensitive imaging investigation for confirming suspected nephrolithiasis, identifies the specific stone location and size, directly informing the likelihood of spontaneous passage and the most appropriate specific treatment approach, and urinalysis alongside metabolic evaluation in appropriately selected, particularly recurrent, cases completes the genuinely comprehensive investigation approach.

Conservative management, adequate analgesia and hydration allowing spontaneous stone passage, is genuinely appropriate for smaller stones with a favourable expected passage likelihood, while **active intervention**, including extracorporeal shock wave lithotripsy or ureteroscopy, is reserved for larger stones or those genuinely unlikely to pass spontaneously, and this Series closes on the same theme of individualised, structured treatment selection consistently emphasised throughout this whole course.

Fill in the blank: Extracorporeal shock wave lithotripsy is reserved for larger stones or those genuinely unlikely to pass _____.

Table 4.2: Comparing common renal stone types

Stone type	Relative frequency	Genuinely notable association
Calcium oxalate	Most common overall	Dietary and metabolic risk factors
Struvite	Less common	Associated with specific urinary tract infection
Cystine	Rare	Genuine inherited metabolic condition

Pilot questions 4.4

1. Describe the pathophysiology of nephrolithiasis. (Linked to SLO 4.7)
2. List types of renal stones. (Linked to SLO 4.7)
3. Describe renal colic. (Linked to SLO 4.7)
4. Describe the key investigation for suspected nephrolithiasis. (Linked to SLO 4.8)
5. Distinguish conservative management from active intervention for nephrolithiasis. (Linked to SLO 4.8)

Series Summary

This Series covered urinary tract infection, hypertension, and nephrolithiasis. Part 4.1 covered the pathophysiology, presentation, investigation, and management of urinary tract infection, while Part 4.2 turned to pyelonephritis, complicated and catheter-associated infection, and recurrent infection. Part 4.3 covered hypertension, and Part 4.4 closed with nephrolithiasis.

You should now be able to describe and manage urinary tract infection, hypertension, and nephrolithiasis across all four Parts of this Series, meeting the outcomes set for this Series. Series 5 turns next to renal transplantation: indications, post-surgical management, and rejection.

Glossary of Terms

1. **Calcium oxalate stone:** the most common type of renal stone overall.
2. **Catheter-associated urinary tract infection:** infection resulting from an indwelling urinary catheter bypassing host defence.
3. **Complicated urinary tract infection:** infection with a factor genuinely increasing risk or treatment complexity.
4. **Nephrolithiasis:** kidney stone disease resulting from urinary supersaturation.
5. **Non-contrast computed tomography:** the most sensitive imaging investigation for suspected nephrolithiasis.
6. **Pyelonephritis:** infection of the kidney itself, presenting with fever and flank pain.
7. **Recurrent urinary tract infection:** a defined number of confirmed infections within a specific timeframe.
8. **Renal colic:** severe, colicky flank pain from ureteric obstruction by a stone.
9. **Secondary hypertension:** hypertension resulting from a genuinely specific identifiable underlying cause.
10. **Struvite stone:** a renal stone type associated with specific urinary tract infection.
11. **Uncomplicated urinary tract infection:** infection in an otherwise healthy, non-pregnant woman with normal anatomy.
12. **White coat hypertension:** elevated blood pressure readings specifically in the clinical setting.

Concept Check Questions [Series 4]

Objective questions

- Urinary tract infection is genuinely, considerably more common in women given the anatomically shorter _____ facilitating ascending spread. (Linked to SLO 4.1)
- Pyelonephritis presents with fever, flank pain, and systemic _____, in addition to lower urinary tract symptoms. (Linked to SLO 4.3)
- Renal artery stenosis reduces renal perfusion and triggers the renin-angiotensin-aldosterone _____. (Linked to SLO 4.5)

- Nephrolithiasis results from genuine urinary supersaturation with stone-forming substances exceeding their _____. (Linked to SLO 4.7)
- Extracorporeal shock wave lithotripsy is reserved for larger stones or those genuinely unlikely to pass _____. (Linked to SLO 4.8)

Short-answer questions

1. Describe atypical urinary tract infection presentation in older patients. (Linked to SLO 4.1)
2. List factors genuinely defining a complicated urinary tract infection. (Linked to SLO 4.3)
3. Distinguish primary from secondary hypertension. (Linked to SLO 4.5)
4. Describe renal colic. (Linked to SLO 4.7)
5. Distinguish conservative management from active intervention for nephrolithiasis. (Linked to SLO 4.8)

Long-answer questions

6. Discuss the pathophysiology, classification, presentation, investigation, and management of urinary tract infection. (Linked to SLO 4.1, 4.2)
7. Describe pyelonephritis, complicated and catheter-associated urinary tract infection, and recurrent urinary tract infection. (Linked to SLO 4.3, 4.4)
8. Discuss the classification, pathophysiology, investigation, and management of hypertension. (Linked to SLO 4.5, 4.6)
9. Describe the pathophysiology, types, and presentation of nephrolithiasis. (Linked to SLO 4.7)
10. Discuss the investigation and management of nephrolithiasis. (Linked to SLO 4.8)

Answers to Concept Check Questions [Series 4]

Objective questions

11. Urethra.
12. Symptoms.
13. System.
14. Solubility.
15. Spontaneously.

Short-answer questions

16. Older patients can present with confusion or non-specific functional decline rather than classic symptoms.
17. Factors include structural abnormality, pregnancy, male sex, and significant immunocompromise.
18. Primary hypertension has no specific identifiable cause, while secondary hypertension has a specific underlying cause.
19. Renal colic is severe, colicky flank pain radiating to the groin from ureteric obstruction by a stone.
20. Conservative management allows spontaneous passage of smaller stones, while active intervention treats larger, less likely to pass stones.

Long-answer questions

21. **Basic response:** UTI results from ascending bowel flora infection, classified as lower or upper and uncomplicated or complicated; presentation includes dysuria and frequency; investigation combines dipstick and culture; management uses empirical antibiotics.

    Value-added response: A value-added response notes that atypical presentation in older patients requires active consideration of UTI despite absent classic symptoms.

22. **Basic response:** Pyelonephritis presents with fever and flank pain, requiring severity-based management; complicated UTI carries elevated treatment failure risk; catheter-associated UTI requires catheter review; recurrent UTI warrants investigation for an underlying cause.

    Value-added response: A value-added response notes that postmenopausal women may benefit from topical oestrogen therapy for recurrent infection prevention.

23. **Basic response:** Hypertension is classified as primary or secondary, with genuine bidirectional relevance to kidney disease; investigation confirms diagnosis and screens for secondary causes and organ damage; management combines lifestyle and individualised pharmacological therapy.

    Value-added response: A value-added response notes that blood pressure targets may require adjustment in patients with coexisting chronic kidney disease.

24. **Basic response:** Nephrolithiasis results from urinary supersaturation, with calcium oxalate the most common stone type; presentation is characterised by renal colic, nausea, and haematuria.

Value-added response: A value-added response notes that infection proximal to an obstructing stone is a genuine urological emergency.

25. **Basic response:** Non-contrast CT is the most sensitive investigation; management ranges from conservative treatment for smaller stones to active intervention for larger stones.

    Value-added response: A value-added response notes that metabolic evaluation is appropriate in selected, particularly recurrent, cases.

Answers to Pilot Questions [Series 4]

Part 4.1

1. UTI most commonly results from ascending bowel flora infection, particularly Escherichia coli.
2. Lower UTI is confined to the bladder, while upper UTI involves the kidney itself.
3. Symptoms include dysuria, frequency, urgency, and suprapubic discomfort.
4. Older patients can present with confusion or functional decline rather than classic symptoms.
5. Investigation uses dipstick testing with culture reserved for atypical or complicated cases; management uses empirical antibiotics.

Part 4.2

6. Pyelonephritis presents with fever, flank pain, and systemic symptoms alongside lower urinary tract symptoms.
7. Severity ranges from mild disease manageable orally to severe disease requiring hospital admission for sepsis.
8. Factors include structural abnormality, pregnancy, male sex, and significant immunocompromise.
9. Catheter-associated UTI results from a catheter bypassing normal host defence, managed with catheter review.
10. Investigation seeks an underlying predisposing factor, such as structural abnormality or oestrogen deficiency.

Part 4.3

11. Primary hypertension has no specific identifiable cause; secondary hypertension has a specific underlying cause.
12. Renal causes include renal artery stenosis and chronic kidney disease or glomerular disease.
13. Ambulatory or home monitoring provides more representative readings, avoiding white coat hypertension.
14. Screening is particularly important in younger patients or those with resistant hypertension.
15. Management combines lifestyle modification with individualised pharmacological therapy.

Part 4.4

1. Nephrolithiasis results from urinary supersaturation with stone-forming substances exceeding solubility.
2. Types include calcium oxalate, uric acid, struvite, and cystine stones.
3. Renal colic is severe, colicky flank pain radiating to the groin from ureteric obstruction.
4. Non-contrast CT is the most sensitive investigation for suspected nephrolithiasis.
5. Conservative management allows spontaneous passage; active intervention treats larger or less passable stones.

References and Attributions [Series 4]

1. Kumar, P., & Clark, M. (2020). Kumar and Clark's Clinical Medicine (10th ed.). Elsevier.
2. Feehally, J., Floege, J., Tonelli, M., & Johnson, R. J. (2018). Comprehensive Clinical Nephrology (6th ed.). Elsevier.
3. National Institute for Health and Care Excellence (2023). Hypertension in Adults: Diagnosis and Management (NG136). NICE.
4. European Association of Urology (2023). Guidelines on Urolithiasis. European Association of Urology.

Figures, Plates, Tables, and Boxes

1. Figure 4.1: A clinician performing urine dipstick testing. AI-generated using the prompt: "Create a realistic clinical illustration titled Urine Dipstick Testing, showing a clinician dipping a test strip into a urine sample cup and comparing the colour change against a reference chart, clinical setting. Clean clinical illustration style, no text."
2. Table 4.1: Comparing uncomplicated and complicated urinary tract infection. AI-generated using the prompt: "Create a clean reference table titled Comparing Uncomplicated and Complicated Urinary Tract Infection, listing feature, uncomplicated UTI, and complicated UTI. Simple clinical reference table style with outside border."
3. Figure 4.2: A clinician measuring a patient's blood pressure. AI-generated using the prompt: "Create a realistic clinical illustration titled Measuring Blood Pressure, showing a clinician applying a blood pressure cuff to a seated patient's arm while checking a reading, clinical examination room setting. Clean clinical illustration style, no text."
4. Table 4.2: Comparing common renal stone types. AI-generated using the prompt: "Create a clean reference table titled Comparing Common Renal Stone Types, listing stone type, relative frequency, and genuinely notable association. Simple clinical reference table style with outside border."

Course code: MED 616

Course title: Nephrology II

Course credit load: 2 Units

Series 5: Renal Transplantation: Indications, Post-Surgical Management, and Rejection

- **Part 5.1: Indications and Assessment for Renal Transplantation**
  - Sub Part 5.1.1: Indications for renal transplantation
  - Sub Part 5.1.2: Recipient assessment and contraindications
  - Sub Part 5.1.3: Donor selection and transplant matching
- **Part 5.2: The Renal Transplant Procedure and Immediate Post-Surgical Management**
  - Sub Part 5.2.1: Principles of the transplant procedure
  - Sub Part 5.2.2: Immediate post-surgical management
  - Sub Part 5.2.3: Early post-surgical complications
- **Part 5.3: Immunosuppression and Rejection**
  - Sub Part 5.3.1: Principles of immunosuppressive therapy
  - Sub Part 5.3.2: Hyperacute and acute rejection
  - Sub Part 5.3.3: Chronic rejection
- **Part 5.4: Long-Term Management of the Transplant Recipient**
  - Sub Part 5.4.1: Management of rejection
  - Sub Part 5.4.2: Long-term complications of transplantation and immunosuppression
  - Sub Part 5.4.3: Long-term follow-up and outcomes

Introduction

This final Series closes the course with **renal transplantation**, the genuinely optimal treatment for appropriately selected patients with established kidney failure already discussed extensively across this course, working from the initial indications and assessment through the surgical procedure and immediate post-operative care to the genuinely lifelong considerations of immunosuppression, rejection, and long-term follow-up this treatment demands.

The aim of this Series is to equip you with an understanding of the indications for renal transplantation and recipient assessment, donor selection and transplant matching, the transplant procedure, immediate post-surgical management and early complications, the principles of immunosuppressive therapy, hyperacute, acute, and chronic rejection and their management, and the long-term complications, follow-up, and outcomes of renal transplantation.

This Series opens with **indications and assessment for renal transplantation**, moves through **the renal transplant procedure and immediate post-surgical management** and **immunosuppression and rejection**, and closes with **long-term management of the transplant recipient**.

Series Learning Outcomes

At the end of this Series, you should be able to:

- **SLO 5.1:** describe the indications for renal transplantation and recipient assessment
- **SLO 5.2:** discuss donor selection and transplant matching
- **SLO 5.3:** describe the transplant procedure, immediate post-surgical management, and early complications
- **SLO 5.4:** discuss the principles of immunosuppressive therapy
- **SLO 5.5:** describe hyperacute, acute, and chronic rejection
- **SLO 5.6:** discuss the management of rejection
- **SLO 5.7:** describe the long-term complications of transplantation and immunosuppression
- **SLO 5.8:** discuss long-term follow-up and outcomes of renal transplantation

5.1 Indications and Assessment for Renal Transplantation

5.1.1 indications for renal transplantation

Genuinely superior long-term outcomes compared with dialysis

Renal transplantation, indicated for appropriately selected patients with established kidney failure resulting from the chronic kidney disease already discussed extensively in Series 3 of this course, offers genuinely superior long-term outcomes, including both survival and quality of life, compared with the long-term dialysis already discussed in that same Series, making it the genuinely preferred treatment option for eligible patients wherever feasible.

Pre-emptive transplantation, performed before the patient genuinely requires dialysis at all, offers further, genuine additional benefit over transplantation delayed until after dialysis has already commenced, and this specific timing consideration, alongside broader eligibility assessment discussed in the following sub-Part, directly shapes the individualised transplant planning pathway for each appropriately identified candidate.

Fill in the blank: Renal transplantation offers genuinely superior long-term outcomes compared with long-term _____.

5.1.2 recipient assessment and contraindications

A genuinely comprehensive evaluation before proceeding to transplantation

Recipient assessment, genuinely comprehensive, evaluates overall surgical fitness, cardiovascular status given the elevated cardiovascular risk already discussed in relation to chronic kidney disease in Series 3, and active screening for malignancy or significant infection that could genuinely worsen following the immunosuppression transplantation requires, discussed further later in this Series, ensuring the patient is genuinely suitable to safely undergo both the surgical procedure and its lifelong subsequent management.

Absolute and relative contraindications, including active malignancy or significant, uncontrolled infection, genuinely limiting the safety of proceeding to transplantation and its required immunosuppression, and significant, irreversible cardiovascular disease genuinely limiting the patient's ability to safely tolerate the surgical procedure itself, require careful, structured consideration before a patient is genuinely accepted onto the transplant waiting list.

Fill in the blank: Recipient assessment includes active screening for malignancy or significant infection that could genuinely worsen following _____.

5.1.3 donor selection and transplant matching

Living and deceased donation, with genuine immunological matching

Living donor transplantation, from a genetically related or, increasingly, genuinely unrelated but suitable living donor, offers superior outcomes compared with deceased donor transplantation given the genuinely shorter waiting time and, typically, better organ quality, while **deceased donor transplantation**, from either a donor after brain death or, less commonly, donation after circulatory death, remains genuinely essential given the limited availability of suitable living donors relative to overall demand.

Immunological matching, including blood group compatibility and human leukocyte antigen matching already introduced in relation to autoimmune disease susceptibility in an earlier course of this programme, directly influences both the likelihood of successful transplantation and the genuine long-term risk of rejection, discussed in detail across the remainder of this Series, making careful, structured donor-recipient matching a genuinely essential component of the whole transplantation process.

Fill in the blank: Immunological matching includes blood group compatibility and human leukocyte _____ matching.

Figure 5.1: A clinician conducting a pre-transplant assessment consultation.

Pilot questions 5.1

- Describe the indications for renal transplantation. (Linked to SLO 5.1)
- Explain the benefit of pre-emptive transplantation. (Linked to SLO 5.1)
- Describe the components of recipient assessment. (Linked to SLO 5.1)
- Distinguish living from deceased donor transplantation. (Linked to SLO 5.2)
- Describe the role of immunological matching. (Linked to SLO 5.2)

5.2 The Renal Transplant Procedure and Immediate Post-Surgical Management

5.2.1 principles of the transplant procedure

A genuinely distinctive surgical approach, native kidneys typically retained

The **renal transplant procedure**, genuinely typically involving placement of the donor kidney within the iliac fossa rather than replacing either native kidney in its original anatomical location, connects the donor renal artery and vein to the recipient's iliac vessels and the donor ureter to the recipient's bladder, and native kidneys are genuinely, typically left in place unless a specific indication for their removal exists.

Cold ischaemia time, the duration the donor kidney spends without blood supply between retrieval and transplantation, genuinely, directly affects early graft function, with shorter cold ischaemia time generally associated with better outcomes, and this specific timing consideration directly explains why living donor transplantation, already discussed in the previous Part, typically achieves shorter cold ischaemia time and correspondingly favourable early outcomes compared with deceased donor transplantation.

Fill in the blank: Cold ischaemia time is the duration the donor kidney spends without blood supply between retrieval and _____.

5.2.2 immediate post-surgical management

Careful monitoring of the genuinely newly functioning graft

Immediate post-surgical monitoring, including careful fluid balance management given the genuine risk of both inadequate and excessive fluid administration already discussed in relation

to acute kidney injury in Series 2 of this course, and close monitoring of graft function through serial creatinine measurement and urine output, forms the genuinely essential foundation of immediate post-transplant care.

Immunosuppressive induction therapy, typically genuinely more intensive immunosuppression administered around the time of transplantation itself before transitioning to the maintenance immunosuppression discussed further later in this Series, reduces the genuine risk of early rejection during this specific, particularly vulnerable early post-transplant period when the recipient's immune system first genuinely encounters the donor organ.

Fill in the blank: Immunosuppressive induction therapy is genuinely more intensive immunosuppression administered around the time of transplantation _____.

5.2.3 early post-surgical complications

Genuine surgical and immediate functional risks

Delayed graft function, the transplanted kidney genuinely failing to function adequately immediately following transplantation, most commonly reflecting acute tubular necrosis already discussed in relation to intrinsic acute kidney injury in Series 2 of this course, genuinely requires temporary dialysis support until graft function recovers, and its likelihood correlates directly with the cold ischaemia time already discussed in the previous sub-Part.

Surgical complications, including vascular thrombosis, genuinely threatening the transplanted kidney's blood supply, and urine leak from the surgical ureteric connection, alongside wound infection, complete the genuinely characteristic early complication profile following renal transplantation, and prompt recognition and management of each specific complication genuinely matters given the direct threat these complications pose to early graft survival.

Fill in the blank: Delayed graft function most commonly reflects acute tubular _____, requiring temporary dialysis support.

Table 5.1: Comparing early post-surgical complications of renal transplantation

Complication	Underlying mechanism	Key management approach
Delayed graft function	Acute tubular necrosis	Temporary dialysis support
Vascular thrombosis	Blood supply compromise to graft	Urgent surgical intervention
Urine leak	Surgical ureteric connection breakdown	Surgical repair or drainage

Pilot questions 5.2

1. Describe the basic surgical approach to renal transplantation. (Linked to SLO 5.3)
2. Describe cold ischaemia time and its significance. (Linked to SLO 5.3)
3. Describe immediate post-surgical monitoring priorities. (Linked to SLO 5.3)
4. Describe delayed graft function. (Linked to SLO 5.3)
5. List surgical complications of renal transplantation. (Linked to SLO 5.3)

5.3 Immunosuppression and Rejection

5.3.1 principles of immunosuppressive therapy

Preventing the immune system from attacking the transplanted organ

Maintenance immunosuppressive therapy, genuinely, typically combining several agents with distinct mechanisms of action, including calcineurin inhibitors, antiproliferative agents, and corticosteroids, targets different components of the immune response to genuinely, comprehensively suppress the recipient's immune system's natural tendency to reject the genuinely foreign donor organ, continuing for the entire duration the transplant remains functional.

Balancing immunosuppression intensity genuinely requires weighing adequate rejection prevention against the meaningfully increased risk of infection and malignancy this same immunosuppression produces, discussed further in the following Series, and this genuine therapeutic balance, requiring ongoing, individualised adjustment throughout the transplant recipient's life, directly reflects the same risk-benefit clinical reasoning already emphasised consistently throughout this whole course.

Fill in the blank: Maintenance immunosuppressive therapy genuinely, typically combines calcineurin inhibitors, antiproliferative agents, and _____.

5.3.2 hyperacute and acute rejection

Two genuinely distinct timeframes, two genuinely distinct mechanisms

Hyperacute rejection, occurring within minutes to hours of transplantation, results from pre-existing recipient antibodies directed against the donor organ, and, given modern pre-transplant crossmatch testing genuinely designed to identify and exclude this specific incompatibility before transplantation proceeds, hyperacute rejection is now genuinely, considerably rare in appropriately screened, matched transplant pairs.

Acute rejection, occurring genuinely within the first several months following transplantation though it can occur later, results from either **T cell-mediated rejection**, direct cellular attack against the donor organ, or **antibody-mediated rejection**, and presents with declining graft function, often genuinely identified through routine monitoring before overt clinical symptoms develop, underlining why the structured follow-up monitoring discussed later in this Series genuinely matters.

Fill in the blank: Hyperacute rejection results from pre-existing recipient _____ directed against the donor organ.

5.3.3 chronic rejection

A genuinely gradual, progressive process over years

Chronic rejection, genuinely gradual, progressive decline in graft function occurring over months to years, reflects a genuinely complex combination of ongoing immune-mediated injury and non-immune factors, including the specific effects of long-term calcineurin inhibitor immunosuppression itself, and represents a genuinely major cause of eventual graft loss despite otherwise adequate immunosuppression.

Unlike the more acute rejection episodes already discussed, chronic rejection genuinely lacks a single, specific, highly effective treatment approach, and management focuses on genuinely optimising immunosuppression and addressing modifiable contributing factors where possible, though the genuinely progressive nature of this process means eventual graft loss, requiring return to dialysis or repeat transplantation, remains a genuine possibility despite comprehensive, structured management.

Fill in the blank: Chronic rejection is a genuinely major cause of eventual graft _____ despite otherwise adequate immunosuppression.

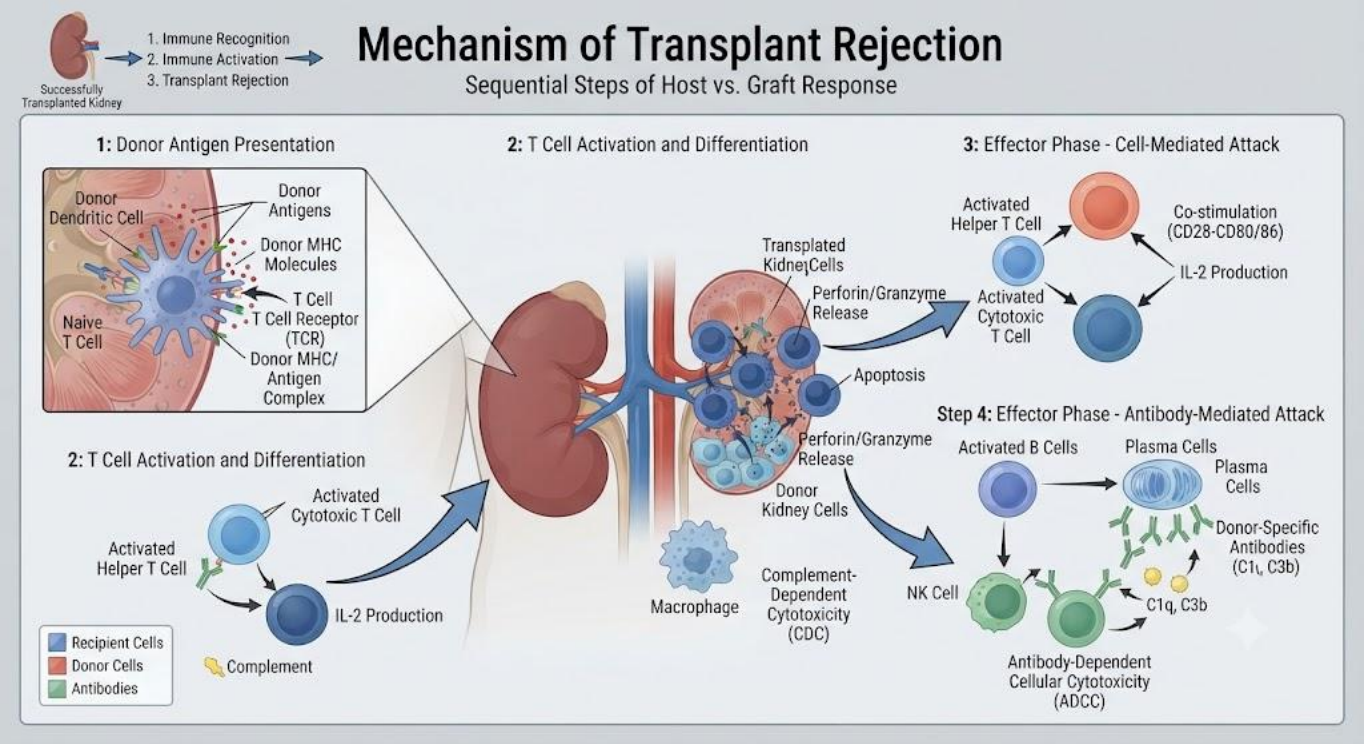

Figure 5.2: A labelled diagram of the immune mechanism underlying transplant rejection.

Pilot questions 5.3

1. Describe the classes of maintenance immunosuppressive therapy. (Linked to SLO 5.4)
2. Explain why balancing immunosuppression intensity genuinely matters. (Linked to SLO 5.4)
3. Describe hyperacute rejection and why it is now genuinely rare. (Linked to SLO 5.5)
4. Distinguish T cell-mediated from antibody-mediated acute rejection. (Linked to SLO 5.5)
5. Describe chronic rejection. (Linked to SLO 5.5)

5.4 Long-Term Management of the Transplant Recipient

5.4.1 management of rejection

Confirming rejection, then treating according to its specific type

Diagnosis of suspected rejection, using graft biopsy to genuinely confirm the diagnosis and distinguish the specific rejection type already discussed in the previous Part, directly guides the

most appropriate treatment approach, and **acute rejection**, whether T cell-mediated or antibody-mediated, is typically treated with intensified immunosuppression, often including high-dose corticosteroids as initial treatment, escalating to more specific, targeted therapy where genuinely required.

Chronic rejection, already discussed as lacking a single, specific highly effective treatment approach, is managed through the general optimisation strategies already introduced in the previous Part, and this genuine distinction in management approach between the more treatable acute rejection and the more genuinely challenging chronic rejection underlines why prompt recognition of declining graft function, discussed further in the following sub-Part, genuinely matters throughout the transplant recipient's lifelong follow-up.

Fill in the blank: Acute rejection is typically treated with intensified immunosuppression, often including high-dose _____ as initial treatment.

5.4.2 long-term complications of transplantation and immunosuppression

The genuine, ongoing cost of lifelong immune suppression

Infection risk, meaningfully elevated throughout the duration of immunosuppressive treatment, includes genuinely opportunistic infections already discussed in principle in an earlier course of this programme, and **malignancy risk**, particularly skin cancer and certain lymphoproliferative disorders, is genuinely, meaningfully elevated given the immune system's normal role in surveilling for and eliminating early malignant cells, a role genuinely, deliberately suppressed by transplant immunosuppression.

Cardiovascular disease, already discussed as elevated in chronic kidney disease in Series 3 of this course, genuinely remains elevated even following successful transplantation, reflecting both pre-existing risk and specific metabolic side effects certain immunosuppressive agents produce, and **calcineurin inhibitor nephrotoxicity**, genuine kidney damage from the immunosuppressive medication itself, illustrates the genuinely complex, ongoing balance transplant recipients and their clinicians must navigate throughout lifelong follow-up.

Fill in the blank: Calcineurin inhibitor nephrotoxicity is genuine kidney damage from the immunosuppressive _____ itself.

5.4.3 long-term follow-up and outcomes

Genuinely comprehensive, lifelong structured care

Structured, regular follow-up, monitoring graft function, immunosuppression levels, and actively screening for the specific long-term complications already discussed in the previous sub-Part, genuinely, directly improves long-term outcomes, and this genuinely lifelong follow-up commitment, extending well beyond the immediate post-transplant period already discussed earlier in this Series, forms an essential, ongoing component of comprehensive transplant care.

Overall outcomes following successful renal transplantation genuinely, considerably exceed those achievable with long-term dialysis alone, already established as the fundamental rationale for transplantation at the start of this Series, and this Series, and the entire course, closes on the same theme of coordinated, structured, individualised, lifelong clinical management that has run consistently throughout this whole programme of nephrological study.

Fill in the blank: Overall outcomes following successful renal transplantation genuinely, considerably exceed those achievable with long-term _____ alone.

Table 5.2: Comparing hyperacute, acute, and chronic rejection

Feature	Hyperacute rejection	Acute rejection
Timing	Minutes to hours	Weeks to months
Mechanism	Pre-existing recipient antibodies	T cell or antibody-mediated
Genuine current frequency	Now rare with modern crossmatching	More commonly encountered

Pilot questions 5.4

1. Describe how suspected rejection is diagnosed. (Linked to SLO 5.6)
2. Describe the treatment approach for acute rejection. (Linked to SLO 5.6)
3. List long-term complications of transplantation and immunosuppression. (Linked to SLO 5.7)
4. Describe calcineurin inhibitor nephrotoxicity. (Linked to SLO 5.7)
5. Describe the value of structured, regular long-term follow-up. (Linked to SLO 5.8)

Series Summary

This final Series closed the course with renal transplantation. Part 5.1 covered the indications for transplantation, recipient assessment, and donor selection, while Part 5.2 turned to the transplant procedure, immediate post-surgical management, and early complications. Part 5.3 covered immunosuppression and rejection, and Part 5.4 closed with the long-term management of the transplant recipient.

You should now be able to describe and manage the full pathway of renal transplantation, from indications through to long-term follow-up, across all four Parts of this Series, meeting the outcomes set for this Series. Across the full course, Series 1 covered glomerulonephritis and nephrotic syndrome, Series 2 covered acute kidney injury and acute drug poisoning and overdose, Series 3 covered chronic kidney disease and dialysis, Series 4 covered urinary tract infection, hypertension, and nephrolithiasis, and this Series has closed the course with renal transplantation, together forming a comprehensive foundation in Nephrology II.

Glossary of Terms

1. **Acute rejection:** rejection occurring within the first several months, T cell or antibody-mediated.
2. **Calcineurin inhibitor:** a class of immunosuppressive medication carrying genuine nephrotoxicity risk.
3. **Chronic rejection:** gradual, progressive graft function decline over months to years.
4. **Cold ischaemia time:** the duration the donor kidney spends without blood supply before transplantation.
5. **Delayed graft function:** the transplanted kidney genuinely failing to function adequately immediately post-transplant.
6. **Human leukocyte antigen:** a genetic marker used for immunological transplant matching.
7. **Hyperacute rejection:** rejection occurring within minutes to hours from pre-existing recipient antibodies.
8. **Immunosuppressive induction therapy:** intensive immunosuppression administered around the time of transplantation.
9. **Living donor transplantation:** transplantation from a living, related or unrelated, suitable donor.
10. **Maintenance immunosuppressive therapy:** combined ongoing immunosuppression preventing rejection long-term.
11. **Pre-emptive transplantation:** transplantation performed before the patient requires dialysis.

12. **T cell-mediated rejection:** acute rejection resulting from direct cellular immune attack on the graft.

Concept Check Questions [Series 5]

Objective questions

- Renal transplantation offers genuinely superior long-term outcomes compared with long-term _____. (Linked to SLO 5.1)
- Immunological matching includes blood group compatibility and human leukocyte _____ matching. (Linked to SLO 5.2)
- Delayed graft function most commonly reflects acute tubular _____, requiring temporary dialysis support. (Linked to SLO 5.3)
- Hyperacute rejection results from pre-existing recipient _____ directed against the donor organ. (Linked to SLO 5.5)
- Overall outcomes following successful renal transplantation genuinely, considerably exceed those achievable with long-term _____ alone. (Linked to SLO 5.8)

Short-answer questions

1. Explain the benefit of pre-emptive transplantation. (Linked to SLO 5.1)
2. Describe cold ischaemia time and its significance. (Linked to SLO 5.3)
3. Distinguish T cell-mediated from antibody-mediated acute rejection. (Linked to SLO 5.5)
4. Describe chronic rejection. (Linked to SLO 5.5)
5. List long-term complications of transplantation and immunosuppression. (Linked to SLO 5.7)

Long-answer questions

6. Discuss the indications for renal transplantation, recipient assessment, and donor selection and matching. (Linked to SLO 5.1, 5.2)
7. Describe the transplant procedure, immediate post-surgical management, and early complications. (Linked to SLO 5.3)
8. Discuss the principles of immunosuppressive therapy and hyperacute, acute, and chronic rejection. (Linked to SLO 5.4, 5.5)
9. Describe the management of rejection and the long-term complications of transplantation. (Linked to SLO 5.6, 5.7)
10. Discuss long-term follow-up and outcomes of renal transplantation. (Linked to SLO 5.8)

Answers to Concept Check Questions [Series 5]

Objective questions

11. Dialysis.
12. Antigen.
13. Necrosis.
14. Antibodies.
15. Dialysis.

Short-answer questions

16. Pre-emptive transplantation offers additional benefit over transplantation delayed until after dialysis begins.
17. Cold ischaemia time is the duration without blood supply, with shorter time associated with better outcomes.
18. T cell-mediated rejection is direct cellular attack, while antibody-mediated rejection involves antibodies against the graft.
19. Chronic rejection is gradual, progressive graft decline over months to years without a single specific treatment.
20. Complications include infection risk, malignancy risk, cardiovascular disease, and calcineurin inhibitor nephrotoxicity.

Long-answer questions

21. **Basic response:** Transplantation offers superior outcomes over dialysis for eligible patients; recipient assessment evaluates surgical fitness and screens for contraindications; donor selection compares living and deceased donation with immunological matching.

    Value-added response: A value-added response notes that pre-emptive transplantation offers further benefit over transplantation delayed until dialysis begins.

22. **Basic response:** The donor kidney is placed in the iliac fossa with native kidneys typically retained; immediate management monitors fluid balance and graft function with induction immunosuppression; early complications include delayed graft function and surgical complications.

    Value-added response: A value-added response notes that delayed graft function likelihood correlates directly with cold ischaemia time.

23. **Basic response:** Maintenance immunosuppression combines several agents targeting different immune components; hyperacute rejection is now rare given crossmatch testing;

acute rejection is T cell or antibody-mediated; chronic rejection is gradual and lacks specific treatment.

Value-added response: A value-added response notes the genuine therapeutic balance between adequate immunosuppression and its infection and malignancy risks.

24. **Basic response:** Acute rejection is treated with intensified immunosuppression; chronic rejection is managed through general optimisation; long-term complications include infection, malignancy, cardiovascular disease, and nephrotoxicity.

    Value-added response: A value-added response notes that graft biopsy confirms rejection type and directly guides treatment approach.

25. **Basic response:** Structured, regular follow-up monitors graft function and screens for complications; overall outcomes considerably exceed those achievable with dialysis alone.

    Value-added response: A value-added response notes that this lifelong follow-up commitment extends well beyond the immediate post-transplant period.

Answers to Pilot Questions [Series 5]

Part 5.1

1. Transplantation is indicated for appropriately selected patients with established kidney failure.
2. Pre-emptive transplantation offers additional benefit over transplantation delayed until dialysis begins.
3. Assessment evaluates surgical fitness, cardiovascular status, and screens for malignancy or infection.
4. Living donation offers shorter waiting time and better organ quality than deceased donation.
5. Immunological matching directly influences transplant success likelihood and long-term rejection risk.

Part 5.2

6. The donor kidney is placed in the iliac fossa, connected to the recipient's iliac vessels and bladder.
7. Cold ischaemia time is the duration without blood supply, with shorter time associated with better outcomes.
8. Priorities include fluid balance monitoring and close monitoring of graft function.
9. Delayed graft function is the transplanted kidney failing to function adequately immediately post-transplant.
10. Complications include vascular thrombosis, urine leak, and wound infection.

Part 5.3

11. Classes include calcineurin inhibitors, antiproliferative agents, and corticosteroids.
12. Balancing intensity weighs adequate rejection prevention against infection and malignancy risk.
13. Hyperacute rejection results from pre-existing antibodies, now rare given modern crossmatch testing.
14. T cell-mediated rejection is direct cellular attack, while antibody-mediated rejection involves antibodies.
15. Chronic rejection is gradual, progressive graft decline reflecting combined immune and non-immune factors.

Part 5.4

1. Suspected rejection is diagnosed using graft biopsy to confirm the diagnosis and specific type.
2. Acute rejection is typically treated with intensified immunosuppression, often high-dose corticosteroids.
3. Complications include infection risk, malignancy risk, cardiovascular disease, and nephrotoxicity.
4. Calcineurin inhibitor nephrotoxicity is genuine kidney damage from the immunosuppressive medication itself.
5. Structured follow-up monitors graft function and screens for complications, directly improving long-term outcomes.

References and Attributions [Series 5]

1. Kumar, P., & Clark, M. (2020). Kumar and Clark's Clinical Medicine (10th ed.). Elsevier.
2. Feehally, J., Floege, J., Tonelli, M., & Johnson, R. J. (2018). Comprehensive Clinical Nephrology (6th ed.). Elsevier.
3. Kidney Disease: Improving Global Outcomes (2020). Clinical Practice Guideline for the Care of Kidney Transplant Recipients. Transplantation.
4. British Transplantation Society (2021). Guidelines for Living Donor Kidney Transplantation. British Transplantation Society.

Figures, Plates, Tables, and Boxes

1. Figure 5.1: A clinician conducting a pre-transplant assessment consultation. AI-generated using the prompt: "Create a realistic clinical illustration titled Pre-Transplant Assessment Consultation, showing a clinician seated with a patient in a consultation room, reviewing paperwork together in an attentive discussion. Clean clinical illustration style, no text."
2. Table 5.1: Comparing early post-surgical complications of renal transplantation. AI-generated using the prompt: "Create a clean reference table titled Comparing Early Post-Surgical Complications of Renal Transplantation, listing complication, underlying mechanism, and key management approach. Simple clinical reference table style with outside border."
3. Figure 5.2: A labelled diagram of the immune mechanism underlying transplant rejection. AI-generated using the prompt: "Create a clean, accurate labelled educational diagram titled Mechanism of Transplant Rejection, showing recipient immune cells recognising donor antigens on a transplanted kidney and mounting an immune attack, with key steps labelled. Educational anatomical diagram style, no photographic content."
4. Table 5.2: Comparing hyperacute, acute, and chronic rejection. AI-generated using the prompt: "Create a clean reference table titled Comparing Hyperacute, Acute, and Chronic Rejection, listing feature, hyperacute rejection, and acute rejection. Simple clinical reference table style with outside border."