Diagnosis of kidney and urinary tract diseases

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Nephrological syndromes

• Normal kidney function: numerous cellular processes to maintain body homeostasis. Disturbances in any of these functions lead to constellation of kidney abnormalities. The clinical manifestation will often be initially identified as a complex of symptoms, abnormal physical findings, and laboratory changes.

• Consequence of systemic illness or occurs as a primary renal disease

• It consists of several elements:
  – Disturbances in urinary volume
  – Abnormalities of urine sediment
  – Abnormal excretion of proteins
  – Reduction of glomerular filtration rate.
    • A reduced GFR leads to retention of nitrogenous waste products (azotaemia) such as creatinine and urea
  – Presence of hypertension and/or oedema
  – Electrolyte abnormalities
  – In some syndromes, fever/pain
Urine volume

• **Urine volume**
  - Normal amount of urine: 1000-2000 ml/day
  - **Anuria:** the complete absence of urine formation (<50 ml/day)
    • Total urinary tract obstruction
    • Total renal artery or vein occlusion
    • Shock
    • ATN and cortical necrosis can occasionally causes
  - **Oliguria:** 24-h urine output less than 500 ml/day
    • Any cause of acute renal failure
    • Congestive heart failure
    • Decreased fluid consumption, increased extrarenal fluid loss
  - **Polyuria:** 24-h urine output >3000 ml
    • Excretion of nonabsorbable solutes (such as glucose)
    • Excretion of water (defect of ADH production or renal responsiveness)
Evaluation of polyuria

Polyuria $\rightarrow$ Urine osmolality $\downarrow$

$<250$ mosmol/L $\rightarrow$ Primary polydypsia

$>300$ mosmol/L $\rightarrow$ Diabetes insipidus

Nonabsorbable solute diuresis

Glucose, mannitol, radiocontrast, high protein feeding, resolving ATN, diuretics

Vasopressine insensitivity (failure of renal tubules to respond to vasopressin)

Hypercalcemia, hypokalemia, multiple myeloma, analgesic nephropathy, drugs, etc.

Psychogenic

Hypothalamic disease

Normal solute (primarily as urea and electrolytes) excretion: 600-800 mosmol/day
Evaluation of polyuria

• **Diabetes mellitus** – glucose depresses reabsorption of NaCl and water in the proximal tubule. More water than Na is lost, causing hypernatremia and hypertonicity of the plasma.

• **Resolving ATN** – tubule damage results in direct impairment of Na reabsorption and indirectly reduces the responsiveness of the tubule to aldosterone – significant natriuresis and polyuria.

• **Deliberate polydipsia** – extracellular fluid volume is normal or expanded and plasma vasopressin concentration is reduced.

• **Diabetes insipidus** – selective destruction of the vasopressin secreting neurons.
Proteinuria

- Normal individuals excrete <150 mg/d of total protein and <30 mg/d of albumin
- Detection of proteinuria by dipstick examination
- The dipstick measurement detects mostly albumin
- More exact determination of proteinuria should employ a 24-hour urine collection or a spot morning protein/creatinine ratio (mg/g)
  - Microalbuminuria: 30-300 mg/d or 30-350 mg/g
  - Proteinuria: 300-3500 mg/d or 300-3500 mg/g
  - Nephrotic syndrome: >3500 mg/d or >3500 mg/g
- The pattern of proteinuria on urine protein electrophoresis (UPEP) can be classified as „glomerular”, „tubular” or „abnormal” depending on the origin of the urine proteins.
  - Glomerular selective: mostly albumin (minimal change)
  - Glomerular nonselective: all plasma proteins (FSGS)
  - Tubular (tubular injury)
  - Abnormal proteins (plasma cell dyscrasias)
Types of proteinuria

- **Physiological Proteinuria**
  - <0.15 g/day
- **Selective Proteinuria**
  - 0.1 - 0.2 g/day
  - 0.5 - 1.5 g/day
- **Non-Selective Proteinuria**
  - >1.5 g/day
  - Fusion of glomerular epithelial cell foot processes.
  - Disruption of the basement membrane (immun complex diseases).
- **Tubular Proteinuria**
  - (Tamm-Horsfall protein)
  - Molecular weight (kDa): 10

Proteinuria types and their molecular weight ranges:
- Globulins: 820 kDa
- Albumin: 120 kDa
- 69 kDa
- 53 kDa
Urine sediment analysis

- Prerenal acute renal failure
  - "inactive urine sediment" - **hyaline casts** from normal constituents of urine – Tamm-Horsfall protein, which is secreted by epithelial cells of the loop of Henle

- Postrenal acute renal failure
  - "inactive urine sediment" – although hematuria and pyuria are common

- Acute tubular necrosis
  - **Pigmented** "muddy brown" casts and casts containing **epithelial cells**, which suggest an ischemic or nephrotoxic etiology (together with mild tubular proteinuria)

- Glomerulonephritis
  - **Red blood cell casts** (less often in acute tubulointerstitial nephritis)

- Interstitial nephritis
  - **White blood cell casts** and nonpigmented granular casts

- Chronic kidney disease
  - **Broad white blood cell casts** (as a sign of dilatation of tubules)
Urine sediment analysis

- Eosinophiluria (>5% of urine leukocytes)
  - Antibiotic-induced allergic interstitial nephritis

- Uric acid crystals (pleomorphic in shape)
  - Are common in concentrated urine of prerenal ARF, but can suggest acute urate nephropathy

- Oxalate (envelope-shaped) and hippurate (needle shaped) crystals
  - Ethylene-glycol ingestion
Reduction of glomerular filtration rate (GFR)

- Serum creatinine is the most widely used marker for GFR
  - Creatinine derives from muscle metabolism of creatine.
  - Creatinine is useful for estimating GFR because it is a small, freely filtered solute.
  - However, serum creatinine levels can increase acutely from dietary ingestion of cooked meat, and creatinine can be secreted in the proximal tubule through an organic cation pathway, leading the overestimation of the GFR.
  - The gradual loss of muscle from chronic illness, chronic use of glucocorticoids, or malnutrition can mask significant changes in GFR, with small changes in serum creatinine concentration.
Estimation of glomerular filtration rate using serum creatinine concentration, age, sex, race

• Equation from the Modification of Diet in Renal Disease study (MDRD):

\[
\text{GFR (mL/min per 1.73 m2)} = 186.3 \times P_c r \left( e^{-1.154} \right) \times \text{age} \left( e^{-0.203} \right) \times 0.742 \text{ (if female)} \times 1.21 \text{ (if black)}
\]
## Major syndromes in nephrology

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<tr>
<th>Syndrome</th>
<th>Important clues</th>
<th>Common findings</th>
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<tbody>
<tr>
<td>Acute renal failure</td>
<td>Oligo-anuria</td>
<td>Hypertension, hematuria, proteinuria, pyuria, casts, edema</td>
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<tr>
<td></td>
<td>Recent decline in GFR</td>
<td></td>
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<tr>
<td>Acute nephritis</td>
<td>Hematuria, RBC casts, azotemia, oliguria, edema, hypertension</td>
<td>Proteinuria, pyuria, circulatory congestion</td>
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<tr>
<td>Chronic renal failure</td>
<td>Azotemia for &gt;3 month, signs of uremia, symptoms and signs of renal osteodystrophy</td>
<td>Proteinuria, casts, polyuria, nocturia, edema, hypertension, electrolyte abnormalities</td>
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<tr>
<td>Nephrotic syndrome</td>
<td>proteinuria&gt;3,5 g per 24 h, hypalalbuminemia, edema, hyperlipidemia</td>
<td>Casts, lipiduria</td>
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<tr>
<td>Urinary tract obstruction</td>
<td>Azotemia, oliguria-anuria, urinary retention, slowing of urinary stream</td>
<td>Hematuria, pyuria, enuresis, dysuria</td>
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<tr>
<td>Urinary tract infection</td>
<td>bacteriuria&gt;10^5 colonies/ml, pyuria, leukocyte casts, bladder tenderness</td>
<td>Hematuria, mild azotemia, mild proteinuria, fever</td>
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Clinical features for major causes of acute renal failure (ARF)

- **Prerenal ARF** (poor fluid intake, NSAID/ACE inhibitor treatment, worsening heart failure)
  - Postural hypotension
  - Low jugular venous pressure
  - Dry mucus membranes
  - Decreased circulatory volume
  - High BUN/creat ratio
  - SG (specific gravity) >1018, $U_{Na} < 10$ mmol/l, or fractional excretion of sodium ($FE_{Na} < 1\%$)

\[
FE_{Na} = \frac{U_{Na} \times P_{cr} \times 100}{P_{Na} \times U_{cr}}
\]
Clinical features for major causes of acute renal failure (ARF)

- **Acute tubular necrosis** (ischaemia, exogenous or endogenous toxins)
  - Recent haemorrhage or severe hypotension
  - Nephrotoxic antibiotics, chemotherapy, exposure to radiocontrast
  - Rhabdomyolysis (seizures, postictal state, trauma, statin therapy)
  - Hemolysis – fever, other evidence of recent transfusion reaction
  - Ethylene-glycol ingestion-history of alcohol abuse, altered mental state

\[ SG < 1015, \ U_{Na} > 20 \text{ mmol/l}, \ FE_{Na} > 1\% , \] urine sediment
Clinical features for major causes of acute renal failure (ARF)

- Disease of small vessels and glomeruli (glomerulonephritis/vasculitis)
  - Postinfectious – new cardiac murmur
  - Autoimmune disease (SLE)- skin rash, arthralgia's
  - Hepatitis B or C
  - Anti-GBM-disease – sinusitis, lung haemorrhage, haemoptysis
  - ANCA-disease
  - Malignant hypertension- evidence of damage to other organs (heart failure, papilledema, headache)

Haematuria with red cell casts, usually mild proteinuria
Pathophysiology of chronic kidney disease

• Two broad sets of mechanisms of damage:
  – Initiating mechanisms specific to the underlying aetiology (immune complexes, toxins)
  – A set of progressive mechanisms, involving hyperfiltration and hypertrophy of remaining viable nephrons, that are a common consequence following long-term reduction of renal mass
  – The short term adaptations of hypertrophy and hyperfiltration become maladaptive, as the increased intraglomerular pressure and flow predisposes to sclerosis and dropout of the remaining nephrons
Progression of chronic renal failure

Onset of proteinuria

Microalbuminuria

Hypertrophy of nephrons, hyperfiltration

Onset nephropathy

Urinary protein excretion

GFR mL/min

### Classification of chronic kidney disease (CKD)

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR mL/min per 1.73 m²</th>
<th>Clinical manifestations</th>
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<tbody>
<tr>
<td>0</td>
<td>&gt;90</td>
<td>Usually not associated with any symptoms. However, there may be symptoms from the underlying renal disease itself, such as edema, hypertension.</td>
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<tr>
<td>1</td>
<td>≥90</td>
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<td>2</td>
<td>60-89</td>
<td>Most evident complications include anaemia, easy fatigability, decreasing appetite, renal bone disease.</td>
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<td>3</td>
<td>30-59</td>
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<td>4</td>
<td>15-29</td>
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<tr>
<td>5</td>
<td>&lt;15</td>
<td><strong>Uremic syndrome</strong></td>
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Uremic syndrome

- Sodium and fluid retention – oedema
- Hypertension
- Hyperkalaemia
- Metabolic acidosis
- Phosphate retention and decreased calcitriol production – secondary hyperparathyroidism
- Cardiovascular abnormalities (heart failure, left ventricular hypertrophy)
- Pericardial effusion
- Anaemia
- Neuromuscular abnormalities – muscle cramps, fasciculation, restless leg syndrome
- Uremic foetor – urine like odour on the breath, derives from the breakdown of urea to ammonia in saliva
- Gastrointestinal abnormalities – anorexia, nausea, vomiting, mucosal ulceration at any level of the GI tract
- Dermatological abnormalities – pruritus, pallor, the patients may become more pigmented – deposition of urochroms.
Symptoms, signs and physical diagnostic of diseases of kidney and urinary tract

• Medical history
  – Previous respiratory tract infection
  – Dysuria
  – Kidney stone
  – Chronic infection, tuberculosis

• Signs
  – Oedema, acute hypertension, headache – symptoms of the acute nephritis
  – Chronic hypertension – chronic renal failure (glomerulonephritis)
  – Nausea, vomiting, diarrhoea, pruritus – uraemia
  – Abnormality of the urine amount and colour
  – Tenderness of kidney region
Clinical features for major causes of acute renal failure (ARF)

- **Diseases of the tubulointerstitium (allergic interstitial nephritis, acute pyelonephritis)**
  - Fever, flank pain and tenderness
  - Positive blood culture or eosinophilia (allergic nephritis)
  - White cell casts, proteinuria, positive urine culture

- **Diseases of large renal vessels (renal artery or vein thrombosis)**
  - Flank pain
  - Mild proteinuria, occasionally haematuria

- **Postrenal ARF**
  - History of renal stones or prostatic disease
  - Palpable bladder, flank or abdominal pain
  - Urine sediment is usually normal, haematuria due to the stones
Physical examination of the kidney-palpation-percussion

- The normal kidney is generally not palpable
  - A normal right kidney may be palpable, especially in thin patient
  - It may be slightly tender

- **Enlarged, palpable kidney:**
  - Polycystic kidney disease (bilateral enlargement)
  - Hydronephrosis
  - Tumour

- **Kidney tenderness (pressure or percussion in the costovertebral angle with fist)**
  - Kidney-stone
  - Kidney infection
Palpation of the right kidney

Left hand behind the patient, parallel to the 12th rib. Right hand in the right upper quadrant, lateral and parallel with the rectus muscle.

Lift the left hand, ask the patient to take a deep breath, press right hand fingers firmly and deeply just below the costal margin, and try to capture the kidney between your two hands. Ask the patient to breath out.
Kidney disease - hypertension

• The hypertension is obligatory:
  – Acute glomerulonephritis
  – Renal artery stenosis (sclerotic or fibromuscular hyperplasia

• Generally will cause hypertension:
  – Chronic glomerulopathy
  – Chronic pyelonephritis
  – Tubulointerstitial nephritis
  – Renal microangiopathies (Kimmelstiel-Wilson’s syndrome)
  – Nephropathies during pregnancy

• Kidney diseases generally without hypertension:
  – Focal nephritis
  – Kidney tumours
  – Amyloidosis
  – Nephrotic-syndrome