EMERGENCY MEDICINE

2nd Edition

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Foreword
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Contents

4

Metabolic, Renal and Endocrine

Acute Kidney Injury

In acute renal failure or acute kidney injury (AKI), an obstructive cause must be excluded 1st.

1. Acute kidney injury is an abrupt decline in renal function diagnosed by rapidly rising blood urea, or rise in serum creatinin 26 micro mols/L from the base line or within 48 hrs or urine output <0.5 mL/kg/hr for 6 hrs.
2. Oliguria is <400 mL/day or <30 mL/hr and anuria is <100 mL/day.

With the fall in BP (due to hypovolemia, vasodilatation or low cardiac output) there is gradual dilatation of preglomerular arteoles (mediated by angiotensin and NO) and vasoconstriction of postglomerular arterioles (by angiotensin II) maintaining the constant glomerular capillary hydrostatic pressure. There is interstitial inflammation independent of etiology.

NEPHROTOXIC DRUGS

Iodinated radio contrast agents—Nephropathy can be reduced by use of isotonic fluid Hartmann solution loading.

Nonsteroidal anti-inflammatory drugs (NSAIDs) or angiotensin-converting enzyme (ACE) interfere with auto regulation of renal blood flow and glomerular filtration rate (GFR) and can provoke acute pre renal failure particularly in patients >60 yrs with atherosclerotic cardiovascular disease with pre-existing chronic kidney disease (CKD) (serum creatinine >180).

Renal hypo perfusion is due to Na depletion, diuretic use, hypotension, heart failure, Nephrotic syndrome and Cirrhosis.

- Aminoglycosides
- Methotrexate
- AII angiotensin receptor blocker (ARB)
- Myoglobinuria in rhabdomyolysis
- Light chains in urine
- Recreational drugs.

Causes of AKI

- Pre-renal (70%) due to decreased renal perfusion. Hypovolemic—gastrointestinal hemorrhage, urinary or skin losses, low cardiac output, hypotension, sepsis, NSAID, ACE inhibitors, cardiac failure or decompensate liver cirrhosis.
- Renal 25%
  Causes: Ischemic 50%, Sepsis 35%, interstitial nephritis 10% (Eosinophil's in urine microscopy suggest interstitial nephritis), acute glomerulonephritis 5%.

  At risk are age >75 yrs, chronic kidney disease (CKD) eGFR <40 mL/minute, pre-existing renal impairment, hypertension, cardiac disease, peripheral vascular disease, diabetes and jaundice.

  Two components are involved in acute reduction of GFR

  1. *Vascular component*: Normally kidney receives 25% of the cardiac output but most of the blood supply is directed to renal cortex. Cortical pO_2 is 6.6–13.3 and because of counter current exchange there is progressive fall in pO_2 from cortex to medulla with pO_2 1.3–2.9 in proximal tubule and ascending limb despite their high metabolic activity (Na/K ATPase). In AKI renal blood flow is decreased by 30–50% and there is selective reduction in blood supply to outer medulla. There is also increased vasoconstriction of afferent arteriole caused by endothelin, angiotensin II, adenosine, thromboxane and sympathetic nerve activity.

     Impairment of endothelium attenuates the vasodilatation due to NO and prostaglandin. In sepsis there is release of tumor necrosis factor (TNF) alpha and endothelin causing renal vasoconstriction and leakage of fluid from the capillaries thereby further diminishing plasma volume.

2. *Tubular*: In hypoxia, integrin which mediates cell to cell adhesion, move from basolateral location to apical cell membrane leading to tubular cell desquamation and promote tubular cast formation and distal tubular obstruction. Damaged cells die not only from necrosis but also from apoptosis. Proximal tubular cells can undergo repair, regeneration and proliferation after injury in the outer cortex.

Glomerulonephritis (GN), disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura; hemolytic uremic syndrome, infections (Legionella, malaria, leptospirosis) and accelerated phase of hypertension are other causes of AKI.

- *Postrenal 5% (obstruction intrinsic or extrinsic)*: Urethral obstruction with palpable bladder, tumors, bladder neck obstruction by prostrate hypertrophy or carcinoma, neurogenic tumors, ureteric obstruction by stones, clot, sloughed papillae, tumors, lymphadenopathy, retroperitoneal fibrosis. Post obstructive diuresis (>4 L), hyperkalemia and renal tubular acidosis can occur after the release of obstruction. If hyperkalemia persists after reversal of renal failure then look for the presence of renal tubular acidosis (mild metabolic acidosis pH <7.35, bicarbonate <20 m moles/L, urine pH >5.3) treated by sodium citrate or sodium bicarbonate or potassium citrate.

Most Common Causes of AKI

- Acute tubular necrosis, pyelonephritis, myeloma, acute interstitial nephritis (AIN), Atheroembolic and rhabdomyolysis.
- Rhabdomyolysis is usually caused by major trauma, narcotic overdose, vascular embolism and drugs and treated by maintaining polyuria urine >300 mL/hr, urine pH >6.5 (alkalinization) and correction of compartment syndrome.
- *Less common causes*: Vasculitis, acute GN, lupus nephritis and good pasture's syndrome. If purpuric rash then consider systemic vasculitis, Henoch-Schönlein purpura, cryoglobulinemia, drug reaction (acute tubular interstitial nephritis) and cholesterol emboli.

Investigations

- Full blood count (FBC), U and E, CK and urinary myoglobin (if urine shows blood on dipstick and no RBC on microscopy) to exclude rhabdomyolysis. Serum creatinine depends not only on urinary clearance of creatinine but also on rate of production and volume of distribution.
- Chest X-ray, and renal ultrasound, ECG, blood and urine culture, autoimmune/vasculitic screen (ANCA, ANA, immunoglobulin, cryoglobulins, and anti-GBM) if clinically indicated.

Sterile Pyuria

- Partially treated UTI, renal calculus disease, analgesic nephropathy, interstitial nephritis, renal TB and rarely proliferative glomerulonephritis.
- Sediment without cast—Under perfusion or obstructive uropathy.
- Proteinuria, and hematuria with RBC cast—glomerulonephritis or vasculitis.
- Granular and epithelial cell casts with minimal proteinuria—ATN.
- Pyuria with white cells and granular casts—Tubular or interstitial disease.
- Pyuria alone—infection.

Management

- Stabilize the patient while trying to improve renal functions. Volume depletion is corrected and BP is restored. Use Hartmann solution rather than normal saline as IV infusion as chloride in excess causes renal vasoconstriction.
- Seek underlying reversible causes of AKI (history is most helpful in identifying the cause). Is it acute or chronic? Seek previous renal functions results and renal size on ultrasound (small kidneys indicate chronic disease). Exclude impaction and pelvic malignancy by rectal examination. Search for and aggressively treat infections.
- Immediate concerns are hypoxia, hypovolemia, hyperkalemia, metabolic acidosis and pericarditis.
- *Immediate treatment*: Correct hypoxia by high flow O_2 keeping SpO_2 >92%. IV access.

- Treat hyperkalemia >5.5 mmols/L (>6.5 mmols life threatening) with IV calcium gluconate 10 mL 10% IV over 2–3 minutes. ECG changes (tall T waves, broad QRS, prolonged QT interval, prolonged PR interval, flat P-wave) improve in 1–3 min, if persistent then repeat IV calcium gluconate.
- An infusion of glucose and insulin (15 U in 250 mL 10% glucose) over 15–30 minutes. This will lower K by 0.5–1.5 mmols for 4–6 hrs.
- Salbutamol nebulizer 5–10 mg will lower K 0.5–1.5 mmol or inhaler (reduces K 0.6–1.0 mmol/L with in 3 min of 1200 microgram via MDI and spacer).
- Correct hypovolemia (JVP clearly visible, no posture drop in BP). In oliguric patient give 400 mL Hartmann solution +previous days urinary output
- Catheterize and measure hourly urine volumes. Provide early nutritional support with dietary Na up to 2 gm/day and with low K.
- Dipstick urine: If proteinuria, hematuria, nitrite and leukocyte indicate infection.
- Stop ACE, NSAID, diuretics except in pulmonary edema and other nephrotoxins. Do not use furosemide and dopamine as renal protection. Magnesium containing antacids should be avoided.

Acidosis is common and if bicarbonate <15 and pH <7.2 then 500 mL 1.26% sodium bicarbonate can be given IV although potential for volume overload should be recognized.

Hyperphosphatemia should be treated with calcium carbonate. Fluid overload, pulmonary edema in AKI consider O_2, GTN infusion, CPAP and renal referral.

Indications for Urgent Dialysis or Hemofiltration

If oliguria persists or biochemistry worsens urea >30 mmols/L or creatinin >300 micro mol/L (hemodialysis or hemofiltration) is urgently required.

- Oliguria <200 mL in 12 hrs or anuria <50 mL in 12 hrs or pulmonary edema.
- Hyperkalemia persistent >6.5 mmol/L with pulmonary edema resistance to treatment.
- Severe acidosis pH <7.2.
- Uremic encephalopathy, pericarditis and neuropathy/myopathy.

- Persistent plasma Na >155 mmol/L or <120 mmol/L.
- Pulmonary edema not responding to diuretics or CPAP.
- Drug overdose with dialyzable toxin.

There is no evidence that early or late dialysis influences the final outcome.

Continuous filtration is no better than intermittent dialysis though continuous therapy is preferred in cerebral edema and liver failure and intermittent in patients with increased bleeding risk. However, if dialysis is used it needs to be daily. If filtration is used it should be 35 mL/kg/hr or greater.

Hepato renal syndrome is mostly due to hypovolemia or cardiomyopathy caused by aggressive paracentesis, sepsis, diuretics or lactulose diarrhea. It is treated with IV albumin and terlipressin.

Adult Polycystic Kidney Disease

Adult polycystic kidney disease (ADPKD) is an autosomal dominant mutation on this short arm of chromosome 16. These are mutations of proteins (polycystin-1 and polycystin-2).

Incidence 1/2500 may be associated with polycystic liver disease with nodular enlargement of liver (LFT usually normal), berry aneurysm of cerebral arteries (10%), Mitral valve prolapse 25% (a systemic manifestation of collagen defect).

Patients with ADPKD 1/3 develop hypertension, 1/3 develops renal failure and 1/3 remains asymptomatic.

Presents as bilateral masses in the flanks which are bimanually ballotable. One can get above them and percussion may be resonant (colon lying over it). Usual presentations are hematuria after trauma, renal colic, renal failure, UTI or hypertension.

Hepatic, pancreatic, ovarian cysts and berry aneurysm are common. Liver cysts develop in 80% of patients and are more common in women.

Diagnosed by at least 2 cyst unilateral or bilateral <30 yrs, 2 cysts in each kidney 30–59 yrs, and 4 cyst in each kidney in >60 yrs.

Treatment

- ACE or ARB.
- Avoiding high impact sports (to avoid abdominal trauma, e.g. Rugby, Boxing).
- Low salt diet (6 g/day), protein 1 g/kg and sufficient intake of fluids (noncaffeinated beverages) to produce 2–3 L urine/day,
- Ideal weight and regular exercise (walking or swimming) are helpful.
- Patient is advised to inform the diagnosis to 1-degree relatives so that they can be screened.
- For screening individual should be >18 yrs old and expected to have children.
- Anticoagulants and low dose aspirin should be avoided.
- For UTI use IV fluroquinolone.
- Renal stones are X2 more common. There are usually uric acid stones.
- Exogenous estrogens and repeated pregnancies lead to cysts in the liver. Therefore, use minimal dose of estrogens.

Nephrotic Syndrome

- Normal urinary protein <150 mg/day.
- Micro albuminuria: 30–300 mg/day—early sign of diabetic nephropathy.

Nephrotic syndrome presents as proteinuria >3.0 g/day, low albumin and edema (pedal, sacral, facial or periorbital). Dyslipidemia, prothrombotic tendency (due to loss of proanticoagulant protein) and mild immune suppression due to loss of immunoglobulin is also a feature. They need renal biopsy to be treated effectively.

If proteinuria >2 gm/day + microscopic hematuria + renal impairment → need renal biopsy.

Causes

- Glomerulonephritis (GN), diabetes mellitus, myeloma, vasculitis (SLE, Wegener's granuloma), amyloidosis.
- *Minimal change GN*: Usually primary, selective proteinuria, effacement of podocytes on electron

microscopy, good response to steroids and occasionally associated with Hodgkin's disease.

- *Membranous GN*: Primary or secondary (Hodgkin's disease, lymphoma, carcinoma, diabetes, SLE, gold and penicillamine, amyloidosis, malaria, HBV, HIV and syphilis).
  - Associated with nonselective proteinuria, immune deposits in the basement membrane and may response to steroids/immunosuppressant. 30% improve, 30% static and 40% worsen.
  - *Poor prognostic factors*: Male gender, hypertension, heavy proteinuria, renal failure and interstitial inflammation.

Chronic Renal Failure (Chronic Kidney Disease)

- Albumin creatinine ratio (ACR) (normal <3 mg/mmol), 3–30 mg/mmol microalbuminuria and >30 mg/mmol proteinuria.
- ACR 25 mg/mmol equivalent to urine dipstick one plus protein.
- Hematuria—dipstick and microscopy—Glomerular hematuria has red cell casts and positive on dipstick.
- Hyaline casts formed of Tamm-Horsfall protein in fever or exercise and not indicative of renal disease.
- In chronic renal failure there is inability of the body to excrete K, water and acid causing hyperkalemia, acidosis and hypervolemia and these require emergency treatment.
- Kidney makes erythropoietin and vitamin D, the lack of which causes anemia and metabolic bone disease.
- Chronic kidney disease (CKD) is a marker of cardiovascular risk.
- Uremic symptoms are anorexia, nausea, vomiting, cramps, restless legs, peripheral neuropathy, cognitive disturbances, hiccups, itch, pericarditis and sexual dysfunctions.
- *Stage 1*: CKD with normal GFR—GFR 90.
- *Stage 2*: CKD with mild impaired GFR—GFR 60–89.
- *Stage 3A*: CKD GFR—45–59 and ACR <30 mg/mmol low risk.

- *Stage 3B*: CKD GFR–30–44 and ACR >30 mg/mmol high risk.
- *Stage 4*: CKD severely impaired GFR—GFR 15–29 Preparation for dialysis.
- *Stage 5*: CKD End-stage renal failure—GFR <15 dialysis, transplantation or conservative care.
- Spot urine samples are taken for ACR.
- GFR is calculated from Cockcroft-Gaut formula =1.23 × (140-age) × weight in kg divided by plasma creatinine (micromol/L). For females— × 0.85.
- GFR—140-age × (weight/SCr × 72) and for women × 0.85.
- Normal GFR >90.

Referral to Renal Unit

Patients with CKD with GFR <30 mL/min, ACR (albumin: creatinine ratio) >70 mg/mmol or ACR 30 mg/mmol with hematuria or poorly controlled hypertension or suspected renal artery stenosis should be referred.

Causes

- Hypertension (25%)
- Diabetes (40%)
- Autosomal dominant polycystic kidney disease (ADPKD) (4%)
- NSAID Glomerulonephritis (15%).

RENOVASCULAR DISEASE

Renal artery stenosis (RAS) is due to atheroma (90%) and fibro muscular disease (young women presenting with severe hypertension).

It is mainly in elderly associated with other atheromatous diseases, peripheral vascular disease, congestive cardiac failure (CCF) and ischemic heart disease (IHD).

RENAL ARTERY STENOSIS PRESENTATION

- Systolic hypertension with low diastolic pressure and resistant to treatment.
- Deterioration of renal function (>30% increase in creatinine in 10 days) after ACE.
- Flash pulmonary edema with no significant myocardial ischemia.

- Audible vascular bruite in epigastrium, renal or iliofemoral.
- Presence of atrophic kidney (>1.5 cm disparity) and presence of urinary proteins.
- Diagnosed by MRA if GFR > 15 mL/min, CT angiography (risk of contrast nephropathy) or duplex ultrasound.
- Stenting mainly in young with fibromuscular renal artery stenosis.
- In atherosclerotic renovascular disease (ARVD) stenting mainly in patients presenting as acute renal failure or flash pulmonary edema.

Management

- Ultrasound of abdomen to exclude urinary tract obstruction and autosomal dominant polycystic kidney disease (ADPKD).
- Stop smoking, salt intake <2–4 gm/day, weight <25 BMI, waist < 102 cm in men and <88 cm in women, exercise, BP <130/80, BM <7 mmols, for statin and aspirin and Hb 10–12 g/100.
- Metformin can be used up to stage 1–3, gliclazide and repaglinide can be used in stage 4.
- All type 2 diabetes mellitus (T2DM) and T1DM after 5 yrs should have annual albumin creatinine ratio (ACR).
- Metformin reduced by 50% if eGFR <45 mL/min and stopped if eGFR 30 mL/min.
- All CKD patients should have BP 120-139/<90.
- All CKD patients with proteinuria ACR >70 mg should have BP 120-129/<80.
- If ACR >70 mg/mmol combination of ACE and ARB is recommended in hypertensive or nonhypertensive.
- All CKD patients with diabetes and ACR >3 mg/mmol should have ACE inhibitors and should have BP 120–129/<80.
- All patients with diabetes and microalbuminuria should have ACE inhibitors even if BP is normal.
- Angiotensin converting enzymes (ACE) inhibitors should be considered if ACR >30 mg/mmol, if hypertensive, and in ACR >70 mg/mmol if nonhypertensive.
- Target BP—130/85 with ACE. Check urea and electrolytes 10th day and in a month, if rise in creatinine >30% then stop ACE.

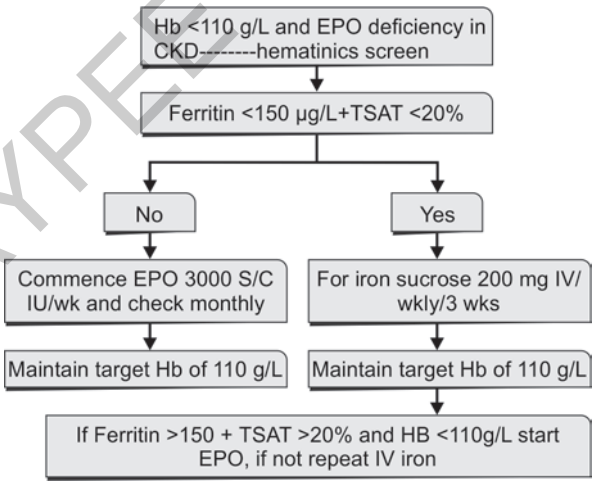
- Reducing BP <100–110 mm Hg may be detrimental.
- *Low protein diet*: Effect is slight and less important.
- Infection—Recurrent UTI (search for anatomical cause, i.e. obstruction or calculi).
- All for lipid lowering and smoking cessation.
- Alpha calcidol and phosphate binder (calcium carbonate) to prevent hyperparathyroidism and renal bone disease.
- NSAIDs should be avoided.

ANEMIA

Target Hb >110 g/L, usually develops in CRF when GFR <30–45 mL/min.

Causes

- Iron-deficiency (absolute or relative), EPO (erythropoietin) deficiency, reduced half-life of RBC, occult blood loss, uremic inhibitors and B_{12} or folate deficiency.
- Iron deficiency anemia—Absolute—ferritin <20 µg/L or <100 µg/L in chronic renal failure (CRF).
- Functional—transferrin saturation (TSAT) <20% and ferritin 100–200 µg/L



Monitoring on EPO

- FBC every 2 wks till target Hb then 1–3 monthly.
- Iron studies and TSAT 3 monthly.
- B_{12} and folate 6 monthly.

Side Effects of EPO

Hypertension 20–30%, hyperkalemia, myalgia and flu-like symptoms.

Mineral and Bone Disorder

- Increase in serum phosphate due to decreased excretion and decrease conversion to 1-25 (OH) D3 are the main reasons.
- 50% patients with GFR <60 have high PTH.
- Patients usually have high phosphate, low calcium and raised PTH.
- Monitor calcium, phosphate every 3/12 and PTH every 6/12.
- Prescribe phosphate binder if phosphate >1.5 mmol/L and active vitamin D analog one alpha.
- Pre renal failure—urine osmolality >500 mosm/L, urinary Na <20 and urine concentration normal while in ATN—Urine osmolality <350 mosm/L, urine Na >40 mmol/L and urine concentration dilute.
- cANCA—directed against proteinases and positive in Wegener's granulomatosis (WG) and microscopic polyarteritis (MPA).
- Chronic obstruction can impair the tubular function resulting in significant diuresis, so can be present even with good urine output. Erythrocyte sedimentation rate (ESR) may be raised due to CRF. Renal biopsy not indicated if kidneys are small.

Factors Causing Persistent Renal Damage

- Persistent activity of underlying cause.
- Hypertension, (BP >130/85 and BP> 125/75 in diabetics).
- Poor diabetic control.
- Proteinuria (consider ACE or ARBs).
- Dyslipidemia (for statins).
- Raised phosphate (consider phosphate binders and vitamin D one alpha).
- Restriction of K, phosphate and salt in diet.
- Anemia—Exclude the deficiency of Fe, B_{12} and folate and blood loss (EPO if Hb <11 g/dL except in ADPKD

EMERGENCY MEDICINE

Salient Features

- Designed to provide an up-to-date overview of the major presentations in acute medicine, and confidence in the management of acute and subacute emergencies
- It is intended to nestle alongside the stethoscope in every coat pocket it lives in, and be by the bedside at every medical emergency, it attends!

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