HYPERKALEMIA:

POTASSIUM: normal serum K = 3.5 to 5 mmol/L
- Absorbed by intestine; largely stored intracellularly (98%)
- Secreted in urine by principal cells in connecting segment and cortical collecting duct
  - K+ renal secretion stimulated by
    - High serum K+
    - High aldosterone
    - High delivery of Na+ and water to distal potassium secretory sites
- Increased extracellular K+ levels → less electronegative RMP → partially depolarized membrane at rest

CAUSES:

Increased intake	• Diet • Constipation
Increased release from cell	• Hemolyzed blood drawn specimen = false +ve • Hyperglycemia in DM – context of insulin resistance/insufficiency • Tumor lysis syndrome • Metabolic acidosis (excess H+ → buffering system → increase in extracellular K+ to maintain electroneutrality)

Decreased renal excretion	• **CKD**
	• Reduced aldosterone secretion (ACEI/ARBs, NSAIDS, calcineurin inhibitors, heparin)
	• K-sparing diuretics
	  ○ Aldosterone antagonist (spironolactone, eplerenone)
	  ○ Blocker of Na+ channel in luminal membrane of principal cells of collecting duct (amiloride, triamterene)
	• Volume depletion
	• AKI

CLINICAL PRESENTATION: if K > 7 mmol/L in CKD pts (can be lower if acute rise in K+)
- Muscle weakness or paralysis
- ECG abnormalities
  - <u>> 6 mmol/L:</u> tall T wave
  - <u>> 7.5 mmol/L:</u> long PR interval; wide QRS duration; tall T wave
  - <u>> 9 mmol/L:</u> absent P wave; sinusoidal wave
- Cardiac conduction abnormalities / cardiac arrhythmia
  - AV block, bradycardia, ventricular arrhythmia, systole

TREATMENT: if pt is symptomatic or if K > 6.5 mmol/L → ER, where:
- IV calcium to antagonize membrane action (protect cardiac tissue)
- IV infusion insulin/glucose to drive extracellular potassium into cell
- Stop meds increasing K+ (RAAS inhibitors, NSAIDs)
- Remove excess K+ → K+ binders, diuretics (loop or thiazide), dialysis

POTASSIUM BINDERS: binds potassium in intestine

	Sodium polystyrene sulfonate	Calcium polystyrene sulfonate
Dose	15 – 30 mg po 3 times per week to daily	
Formulations	Suspension (contains sorbitol)	
	Powder (needs to be mixed with water)	
ADRs	Edema, anorexia, bad taste, constipation, diarrhea, intestinal necrosis (rare)	
Salt	15 g = 1.5 g of sodium	
Decreases drug absorption	Recommended to take drugs 2h before or 6h after these resins	

METABOLIC ACIDOSIS:

PATHOPHYSIOLOGY:
- Acid-base balance is maintained by elimination of CO_2 (by lungs) & elimination of non-volatile acid (by kidney) → affects plasma bicarbonate concentration
  - Normal serum bicarbonate level: 24 – 30 mmol/L
  - About 1 mEq/kg/day of acid eliminated by kidney (urinary excretion of H+ or ammonium)
- Metabolic acidosis developed if:
  - ↑ production of non-volatile acids
  - ↑ loss of bicarbonate
  - ↓ renal excretion of acid
- In CKD patients:
  - Ammonium excretion starts falling at eGFR 40-50 mL/min
    - Remaining nephrons eliminate 3-4x normal ammonium
  - Diminished excretion of titrable acid (primarily phosphoric acid) → phosphate diet restriction
    - Retained acid is buffered by bicarbonate in ECF, by tissue buffers and bone

COMPLIACTIONS:
- Bone resorption and osteopenia
- ↑ muscle protein catabolism and ↓ albumin synthesis
- ↑ secondary hyperparathyroidism
- ↓ respiratory reserve & exhaustion of body buffer systems resulting in ↑ severity of acute intercurrent illnesses
- ↓ NaK-ATPase activity in RBC, myocardial cells → impair heart contractility & produce CHF
- Endocrine disorders
  - Resistance to GH and insulin
  - ↑ TGs
- Systemic inflammation
- Hypotension and malaise
- ↑ mortality risk
- ↑ CKD progression

TREATMENT:
- Decrease dietary acid load = less protein and more fruits/vegetables
- Sodium bicarbonate 325 – 650 mg po BID/TID
  - USE: maintain serum bicarbonate within normal range
  - EVIDENCE: ↓ CKD progression, ↑ bone health, ↑ nutritional status
  - ADRs: GI intolerances, edema, metabolic alkalosis; increases sodium load
- Calcium citrate, calcium carbonate, calcium acetate also help to increase serum bicarbonate BUT not as efficient as sodium bicarbonate
- Dialysis corrects metabolic acidosis through HD dialysate solution, or PD solution containing sodium bicarbonate

HYPERURICEMIA:

PATHOPHYSIOLOGY:

- Uric acid is end product of purine metabolism (poorly soluble)
  - Kidney responsible for elimination of 2/3 of uric acid daily production
- HYPERURICEMIA = uric acid > 430 mmol/L males or > 360 mmol/L females
  - 90% cases due to CKD
  - Increased uric acid level induces oxidative stress and epithelial dysfunction → increases systemic & glomerular BP
- METABOLIC SYNDROME = insulin resistance linked to decreased uric acid secretion in renal tubule
- RENAL HYPERTENSION: leads to uric acid retention
  - DIURETICS: increase uric acid level

EPIDEMIOLOGY:

- Decreased eGFR = increased prevalence of hyperuricemia
  - CKD Stage 1-3 = 40-60%
  - CKD Stage 4-5 = 70%
- Increased incidence in natives and blacks
- Associated with increased risk of new onset of HTN and CVD

COMPLICATIONS:

- Uric acid deposit in joints → gout
- Uric acid deposit in kidney → kidney stones or nephrolithiasis

TREATMENT:

ACUTE ATTACK:

- DO NOT USE NSAIDs (indomethacin) – even just PRN
- Colchicine 0.3 – 0.6 mg po BID – TID PRN
  - Adjust dose based on eGFR
  - ADRs: NVD, fatigue, abdominal cramps
- Prednisone 25 – 50 mg po daily x 5-7 days (no taper needed)
  - ADRs: diabetes, HTN, fluid retention, insomnia, mood swing, GI discomfort

PROPHYLAXIS: xanthine oxidase inhibitors

- Allopurinol 100 – 400 mg po daily
  - EVIDENCE (few): decrease in eGFR progression and reduced BP in CKD pts with hyperuricemia
  - Adjust dose based on eGFR due to accumulation of oxypurinol (metabolite) which may increase risk of Stevens-Johnson syndrome, BM suppression, hepatotoxicity
  - Causes mobilization of uric acid from tissue deposit → increase risk of gout attacks when initiating
    - Use colchicine/prednisone for 5-7 days
  - ADRs: diarrhea, nausea, SJS syndrome, BM suppression, hepatotoxicity
- Febuxostat 40 – 80 mg po daily
  - For patients intolerant to allopurinol
  - ADRs: hepatotoxicity, nausea, rash (lower than allopurinol)