Parathyroid gland & Calcium Metabolism

Def: Calcium disorders are medical emergencies and common ward problems.

Distribution

Compartment	% Total Body Ca	Form
Bone	99%	Hydroxyapatite crystals
Extracellular fluid	1%	Ionized (50%), Protein-bound (40%), Complexed (10%)
Intracellular	<0.1%	Tightly regulated (~100 nM)

Critical Functions of Ionized Calcium (Ca^{2+})

- **Neuromuscular:** Membrane excitability, neurotransmitter release
- **Cardiac**: Myocardial contractility, conduction system stability
- **Coagulation:** Factor IV in clotting cascade
- **Cell signaling**: Second messenger for hormones
- **Bone mineralization**: Structural integrity

Calcium homeostasis: the triad

Three hormones maintain serum Ca^{2+} within narrow range (8.5–10.5 mg/dL):

Hormone	Stimulus for Secretion	Primary Target	Net Effect on Serum Ca^{2+}
PTH	↓ Ionized Ca^{2+} (via CaSR)	Bone, Kidney, Gut (indirect)	↑↑↑
Vitamin D ($1,25(OH)_2D$)	↑ PTH, ↓ PO_4	Gut, Bone, Kidney	↑↑
Calcitonin	↑ Ionized Ca^{2+}	Bone (osteoclasts)	↓ (minor role in humans)

Parathyroid Hormone (PTH): The Rapid Responder

Secretion

✓ Secretion trigger: ↓ Ionized Ca^{2+} detected by Calcium-Sensing Receptor (CaSR) on chief cells.

- ✓ CaSR = G-protein coupled receptor; gain-of-function → hypocalcemia; loss-of-function → hypercalcemia
- ✓ Half-life: 2–4 minutes (rapid response system)

PTH Actions (Within Minutes-Hours)

Target Organ	Mechanism	Effect
Bone	↑ RANKL → osteoclast activation	Ca^{2+} & PO_4 release from bone
Kidney	↑ Ca^{2+} reabsorption (DCT)	↓ Urinary Ca^{2+} excretion
	↓ PO_4 reabsorption (PCT)	↑ Urinary PO_4 excretion
	↑ 1α-hydroxylase activity	↑ $1,25(OH)_2D$ production → ↑ gut Ca^{2+} absorption

Vitamin D Actions

- Intestine: ↑ TRPV6 channels → ↑ Ca^{2+} absorption (duodenum)
- Bone: Permissive for mineralization; ↑ osteoclast activity (with PTH)
- Kidney: ↑ Ca^{2+} & PO_4 reabsorption
- Immune modulation: Anti-inflammatory effects

Note: CKD Alert: Loss of renal 1α-hydroxylase → ↓ calcitriol → secondary hyperparathyroidism.

Clinical Disorders: Hyperparathyroidism

1. Primary Hyperparathyroidism (PHPT)

-Epidemiology: Most common cause of hypercalcemia in outpatients; ♀:♂ = 3:1; peak 50–60 yrs

-Etiology:

- Solitary adenoma (85%)
- Hyperplasia (15%)
- Carcinoma (<1%)

-Biochemical signature: ↑ Ca^{2+} + ↑ or inappropriately normal PTH

-Classic symptoms (stones, bones, groans, moans):

- Renal: Nephrolithiasis (calcium oxalate), nephrocalcinosis

- Skeletal: Osteitis fibrosa cystica (rare now), osteoporosis
- GI: Nausea, constipation, pancreatitis
- Neuropsychic: Fatigue, depression, cognitive fog
- Asymptomatic PHPT: Now >80% of cases (detected on routine labs)

2. Secondary Hyperparathyroidism

- Cause: Compensatory ↑ PTH due to chronic hypocalcemia

- CKD (↓ renal 1α-hydroxylase → ↓ calcitriol → ↓ gut Ca^{2+} absorption)
- Vitamin D deficiency
- Malabsorption

- Biochemical signature: ↓ Ca^{2+} + ↑ PTH (appropriate response)

3. Tertiary Hyperparathyroidism

- ✓ Autonomous PTH secretion after long-standing secondary HPT (e.g., post-renal transplant)
- ✓ Biochemical signature: ↑ Ca^{2+} + ↑ PTH (like PHPT but history of CKD)

Clinical Disorders: Hypothyroidism

-Causes:

- Postsurgical (75%): Thyroidectomy/parathyroidectomy (most common cause).
- Autoimmune: Isolated or part of polyglandular syndromes
- Genetic: DiGeorge syndrome.
- Infiltrative: Hemochromatosis, Wilson disease

Clinical Presentation:

- Acute hypocalcemia (<7 mg/dL):

- ✓ Neuromuscular: Paresthesia's, carpopedal spasm, Chvostek's sign (facial nerve tap → twitch), Trousseau's sign (BP cuff → hand spasm)
- ✓ Cardiac: Prolonged QT interval → ventricular arrhythmias
- ✓ Seizures, laryngospasm (life-threatening)

- Chronic hypocalcemia:

- ✓ Basal ganglia calcification → parkinsonism
- ✓ Cataracts

- ✓ Dental enamel hypoplasia
- ✓ Dry skin, brittle nails

Diagnosis:

- ↓ Ionized Ca^{2+} + ↓ PTH (inappropriately low/undetectable)
- ↑ Phosphate (loss of PTH phosphaturic effect)

Management:

- Acute: IV calcium gluconate (10–20 mL of 10% solution over 10–20 min)
- Chronic:
  - ✓ First-line: Calcium carbonate/citrate + active vitamin D (calcitriol 0.25–1.0 µg/day)

Diagnostic Approach to Calcium Disorders

Step 1: Confirm abnormal calcium

- ✓ Repeat ionized calcium (or albumin-corrected total Ca)
- ✓ Check magnesium (hypomagnesemia → functional hypoparathyroidism)

Step 2: Measure PTH

Ca^{2+}	PTH	Diagnosis
↑	↑ or inappropriately normal	Primary HPT
↑	↓	Malignancy (PTHrP), granulomatous disease
↓	↑	Secondary HPT (CKD, Vit D def)
↓	↓ or inappropriately normal	Hypoparathyroidism

Step 3: Additional tests

- ✓ PHPT workup: 24-hr urine Ca, creatinine clearance.
- ✓ Hypocalcemia workup: Mg^{2+}, PO_4, 25(OH)D, renal function

Adrenal Gland

The adrenal glands (suprarenal glands) are paired endocrine organs situated atop the kidneys. Each gland functions as two distinct endocrine organs in one, comprising an outer cortex [Zona Glomerulosa (outer); Zona Fasciculata (middle); Zona Reticularis (inner)] and an inner medulla.

Functions by Zone

A. Zona Glomerulosa: Salt & Pressure

- Product: Aldosterone (mineralocorticoid)
- Stimuli: ↑K^+, Angiotensin II, ↓Na^+/volume (NOT ACTH!)
- Mechanism: Mineralocorticoid receptors → ENaC channels → Na^+ reabsorption, K^+ excretion

B. Zona Fasciculata: Stress & Metabolism

- Product: Cortisol (glucocorticoid)
- Regulation: Hypothalamic-pituitary-adrenal (HPA) axis
  - ✓ Stress → CRH → ACTH → Cortisol → negative feedback
- Actions:
  - ✓ Metabolic: Gluconeogenesis, lipolysis, proteolysis (↑blood sugar)
  - ✓ Anti-inflammatory: Inhibits phospholipase A_2, ↓COX-2, ↓cytokines (IL-1, IL-6, TNF-α)
  - ✓ Immunosuppressive: Lymphocyte apoptosis, thymic involution
  - ✓ Permissive: Potentiates catecholamines on vessels

C. Zona Reticularis: Secondary Sexual Characteristics

- Product: DHEA, androstenedione (weak androgens)
- Role: Adrenarche (pubic/axillary hair in puberty), estrogen precursor in postmenopausal women
- Clinical: Excess → hirsutism, virilization

D. Medulla: Fight or Flight

- Cells: Chromaffin (modified postganglionic sympathetic neurons)
- Innervation: Preganglionic sympathetic fibers (unusual—usually postganglionic innervate effectors)
- Products: 80% Epinephrine, 20% Norepinephrine, trace dopamine

- Regulation: Direct neural stimulation (NOT hormonal)

Major Clinical Disorders: The "Big Four"

1. Cushing's Syndrome (Hypercortisolism)

Causes:

- ✓ Corticosteroid drugs (most common)
- ✓ Cushing's disease (pituitary ACTH adenoma)
- ✓ Cortical adenoma/carcinoma
- ✓ Carcinoid/ectopic ACTH (e.g., small cell lung cancer)

Classic Features:

- ✓ Central obesity, moon facies, buffalo hump
- ✓ Proximal muscle weakness (difficulty rising from chair)
- ✓ Purple striae (>1 cm wide), easy bruising
- ✓ Hypertension, glucose intolerance
- ✓ Women: Hirsutism, oligomenorrhea

Diagnosis:

1. Screen: Late-night salivary cortisol OR 1 mg overnight dexamethasone suppression test

2. Confirm: Failure to suppress cortisol <1.8 μg/dL → Cushing's confirmed

3. Localize: Measure ACTH

- ✓ ACTH <10 pg/mL → adrenal source
- ✓ ACTH >20 pg/mL → pituitary vs ectopic (high-dose dexamethasone test, imaging)

2. Addison Disease (Primary Adrenal Insufficiency)

Def: is the failure of the adrenal cortex to produce adequate cortisol and aldosterone, usually due to autoimmune destruction of the gland.

Causes:

- Autoimmune (80% in developed countries) – often with other autoimmune diseases (thyroiditis, T1DM)
- TB (worldwide leading cause)
- Hemorrhage (Waterhouse-Friderichsen syndrome in meningococcemia)

Clinical Presentation:

Acute (Addisonian Crisis)	Chronic
Hypotension (refractory to fluids)	Fatigue, weight loss
Nausea/vomiting, abdominal pain	Hyperpigmentation (↑ ACTH/MSH)
Hyponatremia, hyperkalemia	Salt craving
Hypoglycemia	Postural dizziness

Diagnosis:

- Gold standard: ACTH stimulation (cosyntropin) test

  ✓ Give 250 μg cosyntropin IV → measure cortisol at 30/60 min
  ✓ Peak <18 μg/dL = adrenal insufficiency

- Confirmatory: ↑ ACTH (>100 pg/mL) in primary AI

Treatment:

✓ Glucocorticoid: Hydrocortisone 15–25 mg/day (2/3 AM, 1/3 PM)
✓ Mineralocorticoid: Fludrocortisone 0.1 mg/day (primary AI only)
✓ Stress dosing: Double/triple dose for fever/surgery; IM hydrocortisone 100 mg for crisis

3. Primary Hyperaldosteronism (Conn's Syndrome)

Def: is a disorder of autonomous excess aldosterone secretion from the adrenal zona glomerulosa, independent of the renin-angiotensin system (RAS). Most common curable cause of secondary hypertension (5–10% of hypertensives)

Etiology:

- Aldosterone-producing adenoma.
- Bilateral adrenal hyperplasia.

Clinical Clues:

✓ Resistant hypertension (≥3 drugs)
✓ Hypokalemia (only in 30–50% – absence does NOT rule it out)
✓ Metabolic alkalosis
✓ Absence of edema (unlike heart failure/renal disease)

Diagnosis:

1. Screening (in resistant hypertension or hypokalemia).
2. Confirmatory testing (saline suppression test, oral salt loading).
3. Subtype differentiation:
   - ✓ CT/MRI adrenals
   - ✓ Adrenal venous sampling (AVS) - gold standard for lateralization if surgery planned

Treatment:

- ✓ Unilateral adenoma → laparoscopic adrenalectomy
- ✓ Bilateral hyperplasia → spironolactone (mineralocorticoid receptor antagonist)

4. PHEOCHROMOCYTOMA

Def: is a catecholamine-secreting tumor arising from chromaffin cells of the adrenal medulla (or extra-adrenal paraganglia). It produces the classic triad of episodic hypertension, headache, and sweating.

Classic Triad (present in <25% of patients):

1. Episodic headache
2. Diaphoresis (profuse sweating)
3. Palpitations/tachycardia

Clinical Presentation:

- ✓ Paroxysmal or sustained hypertension
- ✓ Pallor (not flushing!)
- ✓ Anxiety/panic attacks
- ✓ Weight loss despite normal appetite

Diagnosis:

- ✓ 1st line: Plasma-free metanephrines OR 24-hr urine fractionated metanephrines
- ✓ Imaging: CT/MRI abdomen → functional imaging if metastatic disease suspected.

Treatment

Preoperative Preparation (Crucial)

Goal: Block catecholamine effects to prevent intraoperative cardiovascular collapse

1. α-blockade first (10-14 days pre-op):
    - Target: Orthostatic hypotension, nasal stuffiness, mild tachycardia (HR 90-100 bpm)
2. β-blockade second (only after full α-blockade):
    - Never give beta-blocker alone (unopposed α-stimulation → hypertensive crisis)
3. Volume expansion:
    - High salt diet + IV fluids pre-op (catecholamine-induced vasoconstriction causes chronic volume depletion)

Diabetes Mellitus – Complications, Management & Perioperative Preparation

Diabetes Mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It represents a spectrum of diseases rather than a single condition, with significant global health implications.

Classification and Types

1. Type 1 Diabetes Mellitus (T1DM)

- Autoimmune destruction of pancreatic β-cells leading to absolute insulin deficiency
- Accounts for approximately 5–10% of all diabetes cases
- Often diagnosed in childhood/adolescence, but can occur at any age (including Latent Autoimmune Diabetes in Adults/LADA)

2. Type 2 Diabetes Mellitus (T2DM)

- Insulin resistance combined with progressive β-cell dysfunction
- Represents 90–95% of diabetes cases globally
- Strongly associated with obesity, sedentary lifestyle, and genetic predisposition
- Often develops gradually; may remain undiagnosed for years

3. Gestational Diabetes Mellitus (GDM)

- Diabetes first recognized during pregnancy (typically 24–28 weeks)
- Affects approximately 1 in 7 live births globally (varying by region)
- Increases risk of subsequent type 2 diabetes for both mother and child

4. Other Specific Types

- Monogenic diabetes: Including neonatal diabetes (first 6 months of life) and Maturity-Onset Diabetes of the Young.
- Exocrine pancreatic diseases: Pancreatitis, pancreatectomy, cystic fibrosis
- Drug-induced: Glucocorticoids, atypical antipsychotics, immunosuppressants
- Endocrinopathies: Cushing's syndrome, acromegaly, hyperthyroidism

Classic Symptoms

- Polyuria
- Polydipsia
- Polyphagia
- Unexplained weight loss
- Fatigue and blurred vision
- Slow-healing infections

Complication of Diabetes

Acute and Chronic Complications

I. Acute:

- Diabetic Ketoacidosis (DKA): More common in T1DM; medical emergency characterized by hyperglycemia, ketosis, and metabolic acidosis
- Hyperosmolar Hyperglycemic State (HHS): More common in T2D; severe hyperglycemia with dehydration

II. Chronic Microvascular:

- Diabetic retinopathy (leading cause of blindness)
- Diabetic nephropathy (leading cause of end-stage renal disease)
- Diabetic neuropathy (peripheral and autonomic)

III. Chronic Macrovascular:

- Atherosclerotic cardiovascular disease (2–4× increased risk)
- Cerebrovascular disease
- Peripheral artery disease

Diagnostic Criteria:

Diabetes is diagnosed by demonstrating hyperglycemia through any of the following ADA criteria (confirmed by repeat testing unless unequivocal) :

Test	Diagnostic Threshold
Hemoglobin A1C	≥6.5%
Fasting Plasma Glucose (FPG)	≥126 mg/dL after ≥8 hours fasting
2-hour Plasma Glucose	≥200 mg/dL

Random Plasma Glucose	≥200 mg/dL with classic hyperglycemia symptoms

Management Approaches:

Lifestyle Interventions

- Medical nutrition therapy and carbohydrate awareness
- Regular physical activity (150+ minutes/week moderate intensity)
- Weight management (5–10% reduction significantly improves glycemic control)

Pharmacological Treatment

Type 1 Diabetes:

- ✓ Intensive insulin therapy (multiple daily injections or continuous subcutaneous insulin infusion/pumps).
- ✓ Continuous Glucose Monitoring (CGM) increasingly standard of care.

Type 2 Diabetes:

- ✓ First-line: Metformin (unless contraindicated)
- ✓ Second-line/add-on: GLP-1 receptor agonists, SGLT2 inhibitors, DPP-4 inhibitors, sulfonylureas, thiazolidinediones, or basal insulin
- ✓ Cardiorenal protection: GLP-1 RAs and SGLT2 inhibitors prioritized for patients with ASCVD, heart failure, or CKD regardless of A1C

PERIOPERATIVE MANAGEMENT: THE SURGICAL PATIENT

Perioperative diabetes management aims to prevent hyperglycemia-related complications (infection, poor wound healing, dehydration) while avoiding hypoglycemia during the surgical period.

Preoperative Assessment

Risk Stratification

- Hemoglobin A1C: Target <7-8% for elective surgery; delay elective procedures if >8-9% or optimize first
- Complication screening: cardiovascular disease, renal dysfunction, neuropathy (increases fall risk), gastroparesis (aspiration risk)

- Medication review: Current antihyperglycemic agents, insulin regimens, timing of last doses
- Surgery classification: Minor (<2 hours, eating same day) vs. Major (>2 hours, NPO status)

Preoperative Fasting Guidelines

- Clear liquids: Allowed up to 2 hours before surgery (contains sugar for hypoglycemia prevention)
- Solids: Stop 6-8 hours preoperatively
- Morning surgery: Hold breakfast and diabetes medications
- Afternoon surgery: Light breakfast permitted (finished 4 hours prior) with half-dose short-acting insulin if needed

Perioperative Glycemic Targets

Timing	Blood Glucose Target	Rationale
Preoperative	80-180 mg/dL	Prevent acute complications
Intraoperative	100-180 mg/dL	Avoid hypoglycemia under anesthesia
Postoperative (ICU)	140-180 mg/dL	Reduced mortality vs. tighter control
Postoperative (general)	100-180 mg/dL	Balance safety and healing

Avoid aggressive targets <80 mg/dL or >250 mg/dL due to infection risk and ketoacidosis potential

Preoperative Preparation of Patients with Obstructive Jaundice

Obstructive Jaundice (also called surgical jaundice) is a type of jaundice caused by physical blockage of the bile ducts, preventing bile from draining from the liver into the intestine.

Definition & Pathophysiology

Definition: Elevated serum bilirubin due to obstruction of bile flow at any level of the biliary tree—from the small intrahepatic canaliculi to the ampulla of Vater.

Key Mechanism:

- Bile cannot flow normally → conjugated bilirubin accumulates in liver → regurgitates into blood → conjugated (direct) hyperbilirubinemia
- Bile acids retained → pruritus, malabsorption, hepatocellular damage

Common Causes

- Extrahepatic Obstruction (Surgical Causes): Pancreatic head cancer, distal cholangiocarcinoma
- Intrahepatic Obstruction (Medical Causes)
  - ✓ Primary sclerosing cholangitis (PSC)
  - ✓ Primary biliary cholangitis (PBC)
  - ✓ Drug-induced cholestasis (anabolic steroids, chlorpromazine, erythromycin)
  - ✓ Sepsis-associated cholestasis
  - ✓ Infiltrative diseases (lymphoma, sarcoidosis, amyloidosis)
  - ✓ Viral hepatitis (severe cases)
  - ✓ Benign recurrent intrahepatic cholestasis

Clinical Features

Symptoms

1. Jaundice: Progressive, often painless; dark urine (bilirubinuria)
2. Pruritus: Often severe, due to bile salt deposition in skin.
3. Acholic (pale/clay-colored) stools: Absence of bile pigments in intestine.
4. Malabsorption: Steatorrhea, vitamin K deficiency (coagulopathy), weight loss
5. Pain: May be absent (painless jaundice = "surgical jaundice" hallmark); present in stones, cholangitis.

6. Fever/Chills.

Signs

- Jaundice (scleral icterus → generalized)
- Hepatomegaly (smooth, firm)
- Palpable gallbladder (Courvoisier's sign) = distended, palpable, nontender gallbladder suggests malignant obstruction of distal CBD; implies long-standing gradual obstruction rather than stone disease (which causes fibrosis)
- Pruritic skin excoriations
- Bruising/bleeding tendency (vitamin K deficiency)

Obstructive jaundice is not just a liver problem—it triggers systemic derangements that dramatically increase surgical risk:

Complication	Risk Increase vs. Non-Jaundiced Patients
Postoperative infection	3–5x higher
Acute kidney injury	4–6x higher
Wound dehiscence	3x higher
Mortality (major surgery)	20–40% vs. 2–5%

Key principle: Surgery on an unprepared jaundiced patient = operating on a metabolically poisoned patient. Preparation is not optional—it's mandatory.

Pathophysiology: Why Jaundice Makes Patients Vulnerable

Bile duct obstruction → toxic bile acids accumulate → systemic "cholestatic syndrome":

System	Mechanism	Clinical Consequence
Coagulation	↓ Bile → ↓ fat-soluble vitamin K absorption → ↓ Factors II, VII, IX, X	Spontaneous bleeding, uncontrolled surgical hemorrhage
Renal	Endotoxemia + bile acids → renal vasoconstriction → "Hepatorenal syndrome"	Pre-renal AKI, oliguria

Cardiovascular	Bile acids → myocardial depression + vasodilation	Refractory hypotension during anesthesia
Immune	Impaired Kupffer cell function → endotoxemia	Bacterial translocation → sepsis, wound infection
Wound healing	↓ Collagen synthesis + impaired neutrophil function	Dehiscence, fistula formation

Critical insight: Bilirubin >10 mg/dL correlates with exponentially increasing mortality—preoperative optimization saves lives.

Stepwise Preoperative Preparation (The 5-Day Protocol)

Day 1: Diagnose & Stabilize

A. Confirm obstruction & identify cause

Imaging Modality	Role
Ultrasound (first-line)	Dilated bile ducts (>6 mm) + identify stones/mass
MRCP	Non-invasive duct mapping (preferred for benign disease)
CT abdomen	Assess resectability in suspected malignancy
ERCP/EUS	Therapeutic + diagnostic (tissue sampling)

B. Rule out Cholangitis (Emergency)

- Charcot's triad: Fever + jaundice + RUQ pain (only 50–70% present)
- Reynolds' pentad: + Hypotension + Altered mental status → septic shock
- Action: If suspected → immediate antibiotics (piperacillin-tazobactam) + urgent biliary drainage (ERCP preferred)

C. Initial labs

- CBC, CMP (bilirubin, ALT/AST, ALP, GGT), INR/PTT, albumin
- Blood cultures if febrile
- Type & screen (anticipate transfusion need)

Day 2: Correct Coagulopathy

Why: Vitamin K-dependent clotting factors have short half-lives (Factor VII = 6 hrs)

Intervention	Protocol	When to Recheck
Vitamin K	10 mg IV slowly (over 30 min)	INR at 6–12 hrs post-IV dose
FFP **(Fresh Frozen Plasma)**	10–15 mL/kg if: • INR >1.5 + active bleeding • Emergency surgery	INR 30 min post-infusion
Prothrombin Complex Concentrate (PCC)	25–50 units/kg if rapid reversal needed (e.g., intracranial bleed)	INR 15 min post-infusion

Day 3: Optimize Nutrition & Renal Function

A. Nutritional support

- Problem: Malabsorption of fats + fat-soluble vitamins (A, D, E, K) → cachexia

- Action:

- ✓ Start medium-chain triglyceride (MCT) diet (absorbed without bile)
- ✓ IV multivitamins + vitamin K supplementation
- ✓ Albumin <3.0 g/dL → consider albumin infusion pre-op (controversial but used in major centers)

B. Renal protection

- ✓ Hydration: 1.5–2 L/day IV fluids (avoid nephrotoxins)
- ✓ Monitor: Strict I/O, daily weights, creatinine
- ✓ Mannitol: 12.5–25 g IV intraoperatively if high AKI risk (controversial)

Day 4: Preoperative Biliary Drainage?

When drainage is INDICATED:

Scenario	Drainage Method	Rationale
Cholangitis	ERCP with stent/naso-biliary drain	Source control for sepsis
Bilirubin >20 mg/dL	ERCP or PTBD	↓ Mortality in major hepatectomy/Whipple
Neoadjuvant therapy planned	ERCP stent	Enable chemotherapy/radiation

Severe malnutrition (albumin <2.8)	PTBD	Improve synthetic function pre-op

When drainage is NOT routinely recommended:

- ✓ Benign strictures (risk of stent-induced cholangitis)
- ✓ Simple choledocholithiasis → proceed directly to ERCP + stone extraction ± cholecystectomy
- ✓ Palliative surgery for unresectable cancer (drainage adds morbidity without survival benefit)

Day 5: Final Preoperative Checklist

Parameter	Target Goal	Action if Not Met
Total bilirubin	<10 mg/dL (ideally <8)	Delay surgery if >15 without drainage
INR	<1.5	Repeat Vit K ± FFP
Albumin	>3.0 g/dL	Continue nutritional support
Renal function	Stable creatinine	Hydration ± nephrology consult
Infection	Afebrile x48h, WBC normalizing	Continue antibiotics until source controlled

Intraoperative Considerations

Risk	Prevention Strategy
Bleeding	Have FFP/cryo/platelets available; avoid hypothermia
Hypotension	Preload with 1–2 L crystalloid; have vasopressors ready
Renal injury	Maintain MAP >65 mmHg; avoid nephrotoxins; consider mannitol
Wound infection	Double antibiotic prophylaxis (e.g., cefazolin + metronidazole)

Management of Portal Hypertension in Cirrhosis

- Cirrhosis is the end-stage result of chronic liver disease characterized by diffuse hepatic fibrosis with the formation of regenerative nodules, leading to architectural distortion and impaired liver function.

- Portal hypertension (PHTN) is the cornerstone complication of liver cirrhosis, arising when scar tissue obstructs blood flow through the liver, increasing resistance in the portal venous system. Once portal pressure rises (>5 mmHg above normal). This elevated pressure drives the major life-threatening sequelae of cirrhosis: gastroesophageal varices with risk of hemorrhage, ascites, spontaneous bacterial peritonitis, and hepatic encephalopathy

Complications of Cirrhosis

Complication	Mechanism
Ascites	Portal hypertension, hypoalbuminemia, sodium retention
Variceal hemorrhage	Portal hypertension → collateral vessel formation
Hepatic encephalopathy	Ammonia and neurotoxin accumulation, impaired detoxification
Spontaneous bacterial peritonitis (SBP)	Bacterial translocation in ascitic fluid
Hepatorenal syndrome	Renal vasoconstriction due to splanchnic vasodilation
Hepatocellular carcinoma	Chronic inflammation and regeneration → malignant transformation
Coagulopathy	Decreased synthesis of clotting factors, thrombocytopenia

Core concept: Portal pressure gradient (HVPG) >10 mmHg = "clinically significant PHTN" → complications begin. Goal of therapy: Reduce HVPG by ≥20% or to <12 mmHg.

Pathophysiology basis

Portal hypertension in cirrhosis is not merely a mechanical obstruction. It involves three key components:

1. Increased intrahepatic resistance due to fibrosis and regenerative nodules,
2. Splanchnic vasodilation driven by nitric oxide and other vasodilators, and
3. A hyperdynamic circulatory state with increased cardiac output.

This triad perpetuates a vicious cycle of worsening portal pressure and progressive liver dysfunction. Therapeutic strategies aim to interrupt this cycle at multiple points.

Screening and Primary Prophylaxis

All patients diagnosed with cirrhosis should undergo screening upper endoscopy to detect esophageal or gastric varices. The presence and size of varices guide prophylactic therapy:

- Patients without varices require repeat endoscopy every two to three years.
- Those with small varices need annual surveillance; prophylaxis may be considered if additional risk factors exist, such as red wale signs on endoscopy or decompensated liver disease.
- Patients with medium or large varices should receive primary prophylaxis to prevent the first variceal bleed.

Note:

- ✓ The cornerstone is non-selective beta-blockers propranolol or nadolol which reduce portal pressure by decreasing cardiac output and inducing splanchnic vasoconstriction.
- ✓ An alternative is endoscopic variceal band ligation, particularly in patients who cannot tolerate beta-blockers or have contraindications. Combination therapy is not recommended for primary prophylaxis.

Acute Variceal Hemorrhage: A Clinical Emergency

Variceal bleeding presents as hematemesis, melena, or hemodynamic instability and carries high short-term mortality. Management must be rapid, coordinated, and multidisciplinary.

Initial resuscitation follows standard trauma protocols:

- ✓ In acute variceal bleeding, prioritize airway protection (especially with encephalopathy), give fluids cautiously, and transfuse blood restrictively to a hemoglobin target of 7–8 g/dL. Over-transfusion raises portal pressure and increases rebleeding risk.
- ✓ Pharmacologic therapy should begin immediately, even before endoscopy. Vasoactive agents terlipressin where available, or octreotide/somatostatin induce splanchnic vasoconstriction, reducing portal inflow and controlling

bleeding in up to half of patients. These infusions should continue for three to five days to prevent early rebleeding.

- ✓ Antibiotic prophylaxis with a third-generation cephalosporin such as ceftriaxone is mandatory for all patients with acute variceal bleeding, regardless of fever or leukocytosis.
- ✓ Upper endoscopy should be performed within twelve hours of admission by an experienced endoscopist. Band ligation is preferred for esophageal varices; sclerotherapy or cyanoacrylate injection may be used for gastric varices.
- ✓ If bleeding persists despite pharmacologic and endoscopic measures, temporary balloon tamponade with a Sengstaken-Blakemore tube may bridge to definitive therapy.
- ✓ Rescue therapies include early TIPS placement ideally within 72 hours in patients with Child-Pugh class B or C cirrhosis who fail initial management. Balloon-occluded retrograde transvenous obliteration may be considered for isolated gastric varices.

Secondary Prophylaxis

Survivors of a variceal bleed face a seventy percent risk of rebleeding within one year. Dual therapy is the standard of care:

- ✓ combine non-selective beta-blockers with repeated endoscopic band ligation sessions every one to two weeks until variceal eradication is achieved. Lifelong beta-blocker therapy should continue thereafter.
- ✓ For patients who rebleed despite optimal medical and endoscopic therapy, TIPS should be strongly considered, particularly if liver function is reasonably preserved. Covered stents reduce shunt dysfunction and hepatic encephalopathy risk compared to bare stents.

Ascites and Related Complications

Ascites develops when portal hypertension, hypoalbuminemia, and renal sodium retention converge.

Initial management includes:

1. Sodium restriction and diuretic therapy typically spironolactone alone or combined with a loop diuretic.
2. Patients with large-volume ascites benefit from therapeutic paracentesis with intravenous albumin to prevent post-paracentesis circulatory dysfunction.

3. Refractory ascites defined as inadequate response to high-dose diuretics or early recurrence after paracentesis warrants consideration of TIPS in selected patients without severe encephalopathy or advanced liver failure. Otherwise, repeated large-volume paracentesis with albumin remains the mainstay.
4. All patients with ascites should undergo diagnostic paracentesis at initial presentation and during any clinical deterioration to exclude spontaneous bacterial peritonitis.
5. Long-term antibiotic prophylaxis is indicated after a first episode of SBP, in patients with low ascitic fluid protein, or in those with impaired renal or liver function.

Hepatic Encephalopathy

Portosystemic shunting allows gut-derived toxins, particularly ammonia, to bypass hepatic clearance and reach the brain. Precipitating factors gastrointestinal bleeding, infection, constipation, or electrolyte disturbances must be identified and corrected.

management includes:

1. First-line therapy is lactulose, a non-absorbable disaccharide that acidifies the colonic lumen, trapping ammonia as ammonium and promoting its excretion.
2. The dose is titrated to produce two to three soft bowel movements daily.
3. Rifaximin, a non-absorbable antibiotic, reduces ammonia-producing gut bacteria and is added for recurrent episodes despite lactulose.

Role of Trans jugular Intrahepatic Portosystemic Shunt (TIPS)

TIPS creates an intrahepatic portosystemic shunt that effectively lowers portal pressure.

It is indicated for:

- ✓ Refractory or recurrent variceal bleeding despite optimal medical and endoscopic therapy.
- ✓ Refractory ascites in patients with preserved hepatic function and no history of overt encephalopathy.

Note: TIPS is contraindicated in patients with severe liver failure, uncontrolled encephalopathy, or right heart failure. Covered stents are preferred to reduce shunt stenosis and dysfunction.

Liver Transplantation

Liver transplantation remains the only definitive cure for portal hypertension in cirrhosis.

- Early referral to a transplant center is essential once decompensation occurs marked by variceal bleeding, ascites, or encephalopathy.
- Transplant evaluation should not be delayed until end-stage disease; timely listing improves outcomes significantly.

General Principles and Monitoring

1. Avoid all nephrotoxic agents, especially NSAIDs, which precipitate acute kidney injury and hepatorenal syndrome.
2. Vaccinate against hepatitis A and B, influenza, and pneumococcus.
3. Screen for hepatocellular carcinoma every six months with ultrasound.
4. Encourage alcohol abstinence and provide nutritional support protein restriction is rarely needed and may worsen sarcopenia.
5. Monitor renal function, electrolytes, and mental status closely during diuretic therapy or acute illness.

Conclusion

- The management of portal hypertension in cirrhosis is dynamic and multifaceted. Success hinges on early detection of varices, aggressive prevention of the first bleed, rapid response to acute hemorrhage, and vigilant long-term surveillance.
- Pharmacotherapy, endoscopy, interventional radiology, and transplantation form an integrated continuum of care.
- With systematic application of these principles, morbidity and mortality can be substantially reduced even in advanced cirrhosis.

Management of Hematemesis & Melena – A Practical Approach

Def. Hematemesis (vomiting blood) and melena (black, tarry stools) are classic signs of upper gastrointestinal bleeding a common and potentially life-threatening emergency. The source is usually proximal to the ligament of Treitz: esophagus, stomach, or duodenum.

Definitions & Clinical Significance

Term	Definition	Likely Source
Hematemesis	Vomiting of bright red blood or "coffee grounds" (oxidized blood)	Upper GI tract (proximal to ligament of Treitz)
Melena	Black, tarry, malodorous stools	Upper GI bleed OR small bowel bleed (≥50–100 mL blood)
Hematochezia	Bright red/maroon rectal bleeding	Usually lower GI, BUT rapid massive UGIB can present this way

Common Causes:

Cause	% of UGIB	Key Clinical Clues
Peptic ulcer disease	40–50%	Epigastric pain, NSAID/aspirin use, H. pylori
Esophageal varices	10–20%	Stigmata of liver disease (jaundice, ascites, spider angiomata)
Gastritis/erosions	15–20%	Alcohol, stress (ICU patients), NSAIDs
Mallory-Weiss tear	5–10%	History of retching/vomiting before bleeding
Malignancy (gastric/esophageal CA)	5%	Weight loss, dysphagia, age >55

Management

Effective management hinges on rapid assessment, aggressive resuscitation, timely diagnosis, and cause-specific treatment.

Step 1: Recognize the Emergency and Assess Severity

Not all GI bleeding is equal. Your first task is to distinguish stable from unstable patients:

- Unstable (high-risk) features:

- Hemodynamic instability: tachycardia, hypotension, orthostatic changes.
- Altered mental status or syncope.
- Massive hematemesis ("coffee-ground" suggests older, slower bleed; fresh red blood suggests active, rapid bleed).
- Comorbidities: cirrhosis, chronic kidney disease, advanced age, anticoagulant use.

- Stable features:

- Normal vital signs at rest and standing.
- Small amount of blood, no ongoing bleeding.
- No comorbidities increasing mortality risk.

Key point: Hematemesis with hemodynamic instability is a true emergency. Do not delay resuscitation for history or exams.

Step 2: Resuscitation – The ABCs Come First

Airway:

- Patients with massive hematemesis, altered consciousness (GCS <8), or hepatic encephalopathy are at high risk of aspiration.
- Consider early endotracheal intubation to protect the airway—especially before endoscopy.

Breathing:

- Administer supplemental oxygen.
- Monitor for hypoxia, especially if aspiration occurs.

Circulation:

- Secure two large-bore IV lines (16–18 gauge).
- Give isotonic crystalloids (normal saline or lactated Ringer's) rapidly in unstable patients.

- Transfuse packed red blood cells to a restrictive target hemoglobin of 7–8 g/dL in most patients.
  - ✓ Exception: Patients with coronary artery disease may tolerate a slightly higher target (8–9 g/dL).
  - ✓ Why restrictive? Over-transfusion increases portal pressure (in cirrhosis) and may worsen bleeding.
- Correct coagulopathy if present:
  - ✓ Fresh frozen plasma or prothrombin complex concentrate for elevated INR.
  - ✓ Platelets if count <50,000/μL (especially before endoscopy).
  - ✓ Vitamin K for warfarin reversal.
- Reverse anticoagulants urgently:
  - Andexanet alfa for factor Xa inhibitors.
  - Protamine for heparin.

Step 3: Early Risk Stratification

Use validated scores to guide urgency and disposition:

- Glasgow-Blatchford Score (GBS): Calculated from labs and vitals before endoscopy.

- Score 0: Very low risk—may be managed as outpatient.
- Score ≥2: Requires hospitalization.
- Score ≥12: High risk for intervention or death.

- Rockall Score: Incorporates age, comorbidities, and endoscopic findings—useful for prognosis after endoscopy.

Step 4: Diagnostic Workup

History (when stable):

- ✓ Timing, amount, and character of bleeding.
- ✓ Past history: PUD, cirrhosis, NSAID/alcohol use, anticoagulants.
- ✓ Symptoms suggesting cause: epigastric pain (PUD), dysphagia (varices/tumor), weight loss (malignancy).

Physical exam:

- ✓ Vital signs (including orthostatics).

- ✓ Stigmata of chronic liver disease: jaundice, spider angiomata, palmar erythema, caput medusae.
- ✓ Abdominal exam: tenderness, hepatosplenomegaly, ascites.
- ✓ Digital rectal exam: Confirm melena vs. hematochezia (maroon stools may indicate rapid upper GI bleed or lower source).

Labs:

- ✓ CBC, INR/PTT, creatinine, BUN, liver function tests, type and screen/crossmatch.
- ✓ Elevated BUN:creatinine ratio (>30:1) suggests upper GI bleed (due to digestion of blood proteins).

Endoscopy:

- ✓ Upper endoscopy is diagnostic and therapeutic.
- ✓ Perform within 24 hours for all admitted patients.
- ✓ Perform within 12 hours for high-risk patients (hemodynamic instability, ongoing bleeding, cirrhosis).

Step 5: Empiric Pharmacotherapy – Start Before Endoscopy

While preparing for endoscopy, initiate two key drug classes:

1. Proton Pump Inhibitor (PPI):

- ✓ Reduces gastric acidity, stabilizes clots, decreases rebleeding risk.
- ✓ Start IV infusion early—even before endoscopy.
- ✓ Continue high-dose IV PPI for 72 hours after endoscopic therapy for high-risk stigmata (active spurting, visible vessel, adherent clot).

2. Antibiotics in cirrhosis:

- ✓ All patients with cirrhosis and GI bleed must receive prophylactic antibiotics (e.g., ceftriaxone) for 5–7 days.
- ✓ Reduces bacterial infections, rebleeding, and mortality by 30%.

3. Vasoactive agents in suspected variceal bleed:

- ✓ If cirrhosis is known or suspected, start octreotide, somatostatin immediately even before endoscopy.
- ✓ Continue for 3–5 days to prevent early rebleeding.

Step 6: Endoscopic Therapy – Cause Dictates Treatment

Endoscopy identifies the source and allows targeted intervention:

Non-variceal causes (≈80% of cases):

- Peptic ulcer disease (most common):
  - ✓ High-risk stigmata: active spurting, non-bleeding visible vessel, adherent clot.
  - ✓ Therapy: Combination of epinephrine injection + thermal coagulation (e.g., gold probe) or mechanical clips.
- Mallory-Weiss tear: Usually self-limited; rarely needs intervention.
- Gastritis/erosions: Supportive care; rarely rebleeds.

Variceal causes (in cirrhosis):

- ✓ Esophageal varices: Band ligation is first-line.
- ✓ Gastric varices: Cyanoacrylate ("glue") injection.
- ✓ After banding, start or optimize non-selective beta-blockers (e.g., propranolol) for secondary prophylaxis.

Step 7: Rescue Therapies for Uncontrolled Bleeding

If bleeding persists despite endoscopy:

- Balloon tamponade (Sengstaken-Blakemore tube): Temporary bridge (<24 hours) for massive variceal bleed while arranging definitive therapy.
- Interventional radiology: Angiography with embolization for non-variceal arterial bleeding.
- TIPS (Transjugular Intrahepatic Portosystemic Shunt): For refractory variceal bleeding in Child-Pugh B/C cirrhosis.
- Surgery: Rarely needed today; reserved for failures of all other modalities (e.g., gastrectomy for ulcer).

Step 8: Secondary Prevention and Disposition

After bleeding is controlled:

- Non-variceal:

- ✓ Continue oral PPI for 4–8 weeks (longer if ulcer from NSAIDs or H. pylori).
- ✓ Test for and eradicate H. pylori if present.
- ✓ Discontinue NSAIDs; use alternatives for pain.

- Variceal:

- ✓ Lifelong non-selective beta-blocker.
- ✓ Repeat endoscopy in 1–3 months for banding until varices eradicated.
- ✓ Refer for liver transplant evaluation if cirrhosis is decompensated.

Management Of Hemopneumothorax & Flail Chest

Part 1: Hemopneumothorax

Def: Hemopneumothorax is the coexistence of blood and air in the pleural space, typically resulting from penetrating trauma (stab, gunshot) or significant blunt injury (rib fractures lacerating lung or intercostal vessels). It compromises lung expansion, impairs gas exchange, and may progress to life-threatening hemorrhage or tension physiology.

Initial Assessment & Resuscitation

1. **Primary survey (ABCDE):** Secure airway first especially if respiratory distress, hypoxia, or altered mental status is present. Administer high-flow oxygen.
2. **Recognize tension physiology:** Hypotension, tracheal deviation, absent breath sounds, and distended neck veins demand immediate needle decompression followed by chest tube insertion do not wait for imaging.
3. **Circulation:** Two large-bore IV lines, crystalloid boluses, and early blood product transfusion if hemorrhagic shock is present. Target permissive hypotension (SBP 80–90 mmHg) in penetrating trauma until surgical control is achieved.

Diagnostic Confirmation

1. **Chest X-ray** (erect or supine): Shows absent lung markings with a fluid level ("air-fluid level") in the pleural space. In supine trauma patients, look for a "deep sulcus sign" (abnormally lucent costophrenic angle).
2. **Extended FAST ultrasound**: Rapidly identifies pleural fluid (blood) and lung sliding (to exclude pneumothorax). Bedside and radiation-free—ideal in unstable patients.
3. **CT chest:** gold standard in stable patients to quantify blood volume, identify ongoing bleeding sources, and detect associated injuries (e.g., lung laceration, diaphragmatic rupture).

Definitive Management: Chest Tube Thoracostomy

- ✓ **Indication:** Any hemopneumothorax with respiratory compromise, >300 mL initial output, or ongoing bleeding.

- ✓ **Tube selection:** Large-bore chest tube (36–40 Fr in adults) to ensure adequate drainage of clotted blood. Smaller tubes (28–32 Fr) may suffice for limited collections.
- ✓ **Insertion site:** "Triangle of safety" (mid-axillary line, 4th–5th intercostal space, above the rib to avoid neurovascular bundle).
- ✓ **Connection:** To an underwater seal drainage system with suction (−20 cm H_2O) to evacuate air and re-expand the lung.

Monitoring & Decision for Surgery

After tube placement, monitor closely:

- ➢ Initial output ≥1500 mL or ongoing output >200 mL/hour for 2–4 consecutive hours suggest active hemorrhage requires urgent surgical consultation.
- ➢ Persistent air leak beyond 5–7 days may indicate bronchopleural fistula.
- ➢ Failure of lung re-expansion suggests trapped lung (from clot or fibrosis) or ongoing air leak.

Indications for Operative Intervention

- Thoracotomy or VATS is indicated for:

- Massive initial output (>1500 mL).
- Persistent bleeding (>200 mL/h).
- Shock unresponsive to fluids/blood.
- Clotted hemothorax (retained clot causing fibrothorax)—VATS evacuation within 48–72 hours prevents empyema and lung entrapment.

Complications to Anticipate

- Empyema: From retained blood acting as culture medium prevented by complete evacuation.
- Fibrothorax: Organized clot forms peel around lung requires decortication.
- Re-expansion pulmonary edema: After rapid evacuation of chronic collections drain slowly (<1000 mL initially).

Part 2: Flail Chest

Flail Chest: A life-threatening chest wall injury caused by fracture of three or more adjacent ribs in at least two places, creating a free-floating segment of the chest wall. This segment moves paradoxically inward during inspiration and outward during expiration opposite to normal chest wall motion, impairing ventilation and often associated with underlying pulmonary contusion.

Recognition & Associated Injuries

- Physical exam: Visible paradoxical motion, crepitus, tenderness over multiple ribs. Beware: paradox may be masked by splinting or obesity—clinical suspicion must remain high after significant blunt trauma.
- Chest X-ray/CT: Confirms multiple rib fractures. CT better defines fracture pattern and associated injuries:
  - ✓ Pulmonary contusion (most critical).
  - ✓ Pneumothorax/hemopneumothorax.
  - ✓ Sternal fracture, aortic injury (in high-energy deceleration).

Core Principles of Management

Management focuses on three pillars: pain control, pulmonary hygiene, and respiratory support. The flail segment itself rarely requires surgical fixation—treat the physiology, not the radiograph.

1. Aggressive Multimodal Analgesia (Critical!)

Pain → splinting → atelectasis → pneumonia → respiratory failure. Break this cycle early:

- Regional anesthesia is first-line:
  - ✓ Erector spinae plane (ESP) block or serratus anterior plane (SAP) block ultrasound-guided, opioid-sparing, preserves cough strength.
  - ✓ Epidural analgesia (if no contraindications like coagulopathy or spinal injury).
- Systemic agents: Acetaminophen, low-dose ketamine infusion, and cautious short-acting opioids (avoid oversedation).

2. Pulmonary Toilet & Early Mobilization

- Incentive spirometry hourly while awake.
- Chest physiotherapy and assisted coughing.

- Early ambulation as tolerated—prevents atelectasis and pneumonia.

3. Respiratory Support Strategy

- Non-invasive ventilation (NIV): CPAP or BiPAP may support oxygenation and reduce work of breathing in alert patients without severe contusion. Avoid if:
  - Altered mental status.
  - Hemodynamic instability.
  - Severe pulmonary contusion with worsening hypoxia.
- Endotracheal intubation & mechanical ventilation:
  - Indicated for hypoxia (PaO_2 <60 mmHg on FiO_2 >0.5), hypercapnia, or inability to protect airway.
  - Ventilator strategy: Lung-protective ventilation (tidal volume 6 mL/kg ideal body weight, plateau pressure <30 cm H_2O) to avoid exacerbating pulmonary contusion.
  - Avoid routine positive pressure to "splint" the flail segment—this does not improve outcomes and may worsen contusion.

4. Surgical Rib Fixation (Emerging Role)

Indications remain selective but growing evidence supports fixation in:

- Flail chest with respiratory failure despite optimal medical management.
- Severe deformity impairing weaning from ventilation.
- Multiple displaced fractures in young, active patients to accelerate recovery.
- Associated need for thoracotomy (e.g., for hemopneumothorax evacuation)—fix ribs during same procedure.

Management Of Respiratory Failure & ARDS

I. Respiratory Failure:

Definition: Inability of the respiratory system to maintain adequate gas exchange

- Type 1 (Hypoxemic): PaO_2 <60 mmHg with normal/low $PaCO_2$
  - ✓ Pathophysiology: V/Q mismatch, shunt, diffusion impairment
  - ✓ Causes: Pneumonia, pulmonary edema, ARDS, PE, fibrosis
- Type 2 (Hypercapnic): $PaCO_2$ >50 mmHg ± hypoxemia
  - ✓ Pathophysiology: Alveolar hypoventilation
  - ✓ Causes: COPD exacerbation, neuromuscular disease, opioid overdose, chest wall deformities

Initial Management Principles:

1. Secure airway if GCS <8 or inability to protect airway

2. Correct hypoxemia:

   - ✓ Start with supplemental O_2 (titrate to SpO_2 88–92% in COPD; 94–98% otherwise)
   - ✓ Escalate to HFNC → NIV → intubation based on response

3. Treat underlying cause (e.g., antibiotics for pneumonia, bronchodilators for asthma/COPD)

4. Monitor: ABG q1–2h initially, continuous SpO_2, respiratory rate, work of breathing

Critical pearl: In COPD with chronic CO_2 retention, avoid aggressive O_2 therapy—start with 24–28% O_2 via Venturi mask and titrate carefully to prevent worsening hypercapnia.

II. Acute respiratory distress syndrome (ARDS):

Def: is defined by four essential criteria that must all be present:

1. First, the onset must be acute—within one week of a known clinical insult such as pneumonia, sepsis, aspiration, or trauma.
2. Second, chest imaging must show bilateral opacities on X-ray or CT that cannot be fully explained by pleural effusions, lobar collapse, or lung nodules alone.

3. Third, the respiratory failure must not be fully explained by cardiac failure or fluid overload; this often requires an echocardiogram to rule out hydrostatic pulmonary edema.
4. Fourth, hypoxemia must be present while the patient is on at least 5 cmH_2O of PEEP, and severity is stratified by the PaO_2/FiO_2 ratio: mild ARDS (200 to 300), moderate ARDS (100 to 200), and severe ARDS (100 or less).

Remember: ARDS represents non-cardiogenic pulmonary edema caused by increased alveolar-capillary permeability following direct or indirect lung injury.

II. Pathophysiology:

Lung Injury Insult (e.g., sepsis)

↓

↑ Alveolar-capillary permeability

↓

Protein-rich fluid floods alveoli ("stiff lungs")

↓

Inflammation → hyaline membranes → fibrosis

Result:

- ✓ Shunt physiology (blood passes non-ventilated alveoli) → refractory hypoxemia
- ✓ Decreased compliance ("stiff lungs") → high pressures needed for ventilation
- ✓ Ventilator-induced lung injury (VILI) if managed improperly → worse outcomes

III. Core Management: The 5 Pillars

1: Lung-Protective Ventilation (Most important intervention)

Parameter	Target	Why It Matters
Tidal volume	4–8 mL/kg predicted body weight (start 6 mL/kg)	↓ Volutrauma → 9% absolute mortality reduction (ARDSNet trial)
Plateau pressure	<30 cmH_2O	Prevents alveolar overdistension
Driving pressure	<14 cmH_2O (Pplat – PEEP)	Strong predictor of survival

PEEP	≥5 cmH_2O; ↑ for moderate-severe ARDS	Prevents cyclic alveolar collapse (atelectrauma)
FiO_2	Titrate to SpO_2 88–95%	Minimizes oxygen toxicity

Pillar 2: Prone Positioning

1. Indication: Moderate-severe ARDS (PaO_2/FiO_2 <150)
2. Protocol: ≥16 hours/day for ≥4 days
3. Evidence: ↓ Mortality by 16%/.
4. Mechanism: More homogeneous ventilation, ↓ VILI, improved secretion drainage
5. Contraindications: Unstable spine, raised ICP, pregnancy, recent sternotomy

Pillar 3: Conservative Fluid Strategy

- After initial resuscitation, aim for neutral/negative fluid balance
- Evidence: Fluids and Catheters Treatment Trial → ↓ ventilator days & ICU stay without ↑ mortality
- How:
  - ✓ Avoid routine fluid boluses once hemodynamically stable
  - ✓ Use diuretics/CRRT to remove excess fluid
  - ✓ Target Central Venous Pressure ≤4 mmHg if possible

Pillar 4: Adjunctive Therapies (Selected Cases)

Therapy	When to Consider	Evidence
Neuromuscular blockade	Early severe ARDS (first 48h)	↓ Mortality modestly (ACURASYS); limit to ≤48h to avoid ICU weakness
Corticosteroids	Early moderate-severe ARDS (<14d)	Methylprednisolone 1–2 mg/kg/day may ↓ duration; avoid late (>14d)
Inhaled vasodilators (iNO, epoprostenol)	Refractory hypoxemia	Transient ↑ oxygenation only—no mortality benefit; rescue therapy

Venovenous Extracorporeal Membrane Oxygenation	Refractory hypoxemia despite optimal care	Consider if predicted mortality >80% (e.g., PaO_2/FiO_2 <80 on FiO_2 1.0)

Pillar 5: Treat the Underlying Cause

1. Sepsis: Early antibiotics, source control
2. Pneumonia: Appropriate antimicrobials
3. Aspiration: Nothing by Mouth, elevate Head of Bed (HOB), Consider Proton Pump Inhibitor
4. Trauma/Pancreatitis: Supportive care + specific management

Avoid: Routine β-agonists (harmful), surfactant (no benefit in adults), high-dose steroids upfront

Complications to Anticipate

Complication	Prevention
Ventilator-associated pneumonia (VAP)	HOB elevation, oral care, sedation holidays
ICU-acquired weakness	Minimize sedation, early mobilization
Barotrauma (pneumothorax)	Strict plateau pressure limits
AKI	Conservative fluids, avoid nephrotoxins
Stress ulcers	Standard pharmacologic prophylaxis

Management of Coagulopathy & Disseminated Intravascular Coagulation (DIC)

Def. Coagulopathy represents any defect in the coagulation system whether inherited or acquired that impairs hemostasis. This broad category includes:

- Factor deficiencies (congenital or acquired)
- Platelet disorders (quantitative or qualitative)
- Vascular abnormalities
- Combined defects (liver disease, vitamin K deficiency)

Def. DIC is a specific acquired syndrome characterized by widespread activation of coagulation within the vasculature, leading to:

- Intravascular fibrin deposition (microthrombi)
- Consumption of platelets and coagulation factors
- Secondary activation of fibrinolysis
- Organ dysfunction from ischemia and bleeding from hemostatic depletion

Critical Concept: DIC is not a primary disease but a complication of underlying pathology.

The DIC Paradox

The central teaching point of DIC is its dual nature:

- Thrombotic phase: Widespread microvascular clotting → organ ischemia
- Hemorrhagic phase: Consumption of factors/platelets + fibrinolysis → bleeding

Patients may present with either phenotype dominant, or both simultaneously depending on the tempo of disease and compensatory mechanisms.

Etiology

1. Infections: Gram-negative sepsis, severe COVID-19, meningococcemia
2. Obstetric: Placental abruption, amniotic fluid embolism, retained dead fetus
3. Malignancy: Acute promyelocytic leukemia (APL), adenocarcinomas
4. Trauma: Severe tissue injury, brain trauma, massive transfusion.
5. Toxic/Immunologic: Snake envenomation, ABO incompatibility, transfusion reactions.

Pathophysiological Mechanisms

I. Initiation Phase:

Tissue factor (TF) exposure or expression triggers the extrinsic pathway. This occurs through:

- Endothelial injury releasing TF
- Monocyte activation expressing TF in response to cytokines
- Direct activation by cancer procoagulants or endotoxin

II. Amplification Phase:

Thrombin generation accelerates through positive feedback loops, consuming:

- Fibrinogen → fibrin
- Prothrombin → thrombin
- Factors V, VIII
- Platelets

III. Compensatory/Fibrinolytic Phase:

Plasmin activation attempts to dissolve fibrin, generating fibrin degradation products (FDPs) that:

- Antagonize thrombin
- Interfere with fibrin polymerization
- Further impair platelet function

IV. Decompensated Phase:

When consumption exceeds synthesis and hepatic clearance of activated factors is overwhelmed, both bleeding and thrombosis manifest clinically.

Clinical Assessment

History and Physical Examination

I. Bleeding Manifestations:

- Cutaneous: Petechiae, purpura, hematomas, oozing from venipuncture sites
- Mucosal: Epistaxis, gingival bleeding, menorrhagia
- GI/GU: Hematemesis, melena, hematuria
- CNS: Headache, altered consciousness (intracranial hemorrhage)

- Respiratory: Hemoptysis
- Iatrogenic: Prolonged bleeding post-procedure, surgical site oozing

II. Thrombotic Manifestations:

- Renal: Oliguria, rising creatinine (cortical necrosis)
- Neurological: Confusion, focal deficits, seizures
- Digital: Acral cyanosis, ischemic gangrene
- GI: Mesenteric ischemia, infarction
- Pulmonary: Dyspnea, hypoxemia (microvascular thrombosis)

Clinical Phenotypes of DIC

Phase	Characteristics	Common Settings
Acute DIC (suppressed fibrinolysis)	Predominant thrombosis, organ failure	Sepsis, trauma
Acute DIC (primary fibrinolysis)	Catastrophic hemorrhage	Obstetric catastrophes, prostate surgery
Chronic DIC	Subclinical or mild bleeding, thrombosis risk	Solid tumors, retained dead fetus
Localized DIC	Isolated thrombosis (e.g., Kasabach-Merritt in giant hemangiomas)	Vascular malformations

Diagnostic Approach

Initial Laboratory Evaluation

Screening Tests:

Test	Rationale	Expected Finding in DIC
Platelet count	Consumption	Thrombocytopenia (often <100,000/μL)
PT (Prothrombin Time)	Extrinsic/common pathway	Prolonged (>1.5× control)
aPTT (Activated Partial Thromboplastin Time)	Intrinsic/common pathway	Prolonged
Fibrinogen	Consumption + acute phase	Low or normal (acute phase may mask)
D-dimer/FDPs	Fibrinolysis	Markedly elevated
Peripheral smear	Microangiopathy	Schistocytes (fragmented RBCs)

Advanced Testing:

- Specific factor assays: Demonstrate multiple factor deficiencies (II, V, VIII)

- Antithrombin level: May guide therapy (low levels reduce heparin efficacy)
- Thromboelastography (TEG)/Rotational Thromboelastometry (ROTEM): Whole-body viscoelastic assessment showing:
  - ✓ Prolonged reaction time (coagulation factor deficiency)
  - ✓ Decreased maximum amplitude (platelet dysfunction/fibrinogen deficiency)
  - ✓ Increased lysis index (hyperfibrinolysis)

General Management Principles

Core Principles:

1. Maintain tissue perfusion: Correct hypothermia, acidosis, and hypocalcemia all impair coagulation enzyme function.
   - Hypothermia (<34°C impairs coagulation enzymes)
   - Acidosis (pH <7.2 reduces clotting factor activity by 50%)
   - Hypocalcemia (Ca^{2+} required for multiple coagulation steps; citrate in blood products chelates calcium)
2. Balanced component therapy: Avoid dilutional coagulopathy with excessive crystalloid/packed red cells
3. Goal-directed replacement: Use point-of-care testing or rapid labs to guide specific component therapy
4. Pharmacological adjuncts: Integrate antifibrinolytics and procoagulants appropriately

Blood Component Therapy

Component	Contents	Indications
Fresh Frozen Plasma (FFP)	All coagulation factors	PT/aPTT >1.5× normal, bleeding
Platelets	Platelets	Count <10-20,000/μL (prophylaxis) or <50,000/μL (active bleeding/procedure)
Cryoprecipitate	Fibrinogen, VIII, vWF, XIII	Fibrinogen <100-150 mg/dL
Fibrinogen concentrate	Fibrinogen only	Fibrinogen deficiency, preferred for volume control
Prothrombin Complex Concentrate (PCC)	II, VII, IX, X (± proteins C/S)	Warfarin reversal, specific factor replacement

Management of Sepsis & Multiple Organ Dysfunction Syndrome (MODS)

Def Sepsis: Life-threatening organ dysfunction caused by a dysregulated host response to infection.

Def Septic Shock: A subset of sepsis with particularly profound circulatory, cellular, and metabolic abnormalities, associated with a greater risk of mortality than sepsis alone. Specifically:

- Persistent hypotension requiring vasopressors to maintain MAP ≥65 mmHg
- Serum lactate >2 mmol/L despite adequate volume resuscitation

Pathophysiology: The "Perfect Storm"

Infection → Pathogen recognition (TLRs) → Cytokine storm (TNF-α, IL-6, IL-1)

↓

Endothelial injury → Capillary leak → Microthrombi → Mitochondrial dysfunction

↓

Tissue hypoperfusion → Cellular hypoxia → Organ dysfunction → MODS

Critical Concepts:

- Dysregulated immunity: Simultaneous hyperinflammation and immunosuppression ("immunoparalysis")
- Microcirculatory failure: Organ hypoperfusion persists even after macrocirculation (BP) is restored
- Mitochondrial dysfunction: Cells cannot utilize oxygen → "cytopathic hypoxia"

Def MODS: The presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention. OR Two or more organs failing at the same time because of sepsis or other critical illness.

How to Recognize Sepsis

Quick Screening: qSOFA

Use this at the bedside to identify patients at risk:

Sign	Finding
Quick mental status change	Confusion or decreased alertness
Systolic blood pressure	≤100 mmHg
Oxygen/breathing	Respiratory rate ≥22 breaths/min

If 2 or more are present → patient is high risk. Act fast!

Full Assessment: SOFA Score

SOFA = Sequential Organ Failure Assessment

Measures dysfunction in 6 organs:

1. Lungs (oxygenation)
2. Liver (bilirubin)
3. Kidneys (creatinine)
4. Brain (Glasgow Coma Scale)
5. Heart/Circulation (blood pressure, need for medications)
6. Blood (platelets)

Rise in SOFA score by 2 points = sepsis

The Golden Hour - First 60 Minutes

The 1-Hour Bundle (Do These Immediately)

Action	Why It Matters
1. Measure lactate	Shows if tissues aren't getting enough oxygen; >2 is abnormal
2. Get blood cultures	Find the bacteria before giving antibiotics; take 2 sets from different veins
3. Give antibiotics	Every hour delay increases risk of death; give broad-spectrum drugs
4. Give fluids	30 mL/kg (about 2 liters for average adult) if blood pressure is low or lactate ≥4
5. Start vasopressors	If still low blood pressure after fluids, use medications to raise it

Remember: Do NOT delay antibiotics to wait for cultures. Draw cultures, then immediately give antibiotics.

Key Treatment Principles

1. Find and Control the Source

Antibiotics alone are not enough. You must:

Source	What to Do

Lung infection (pneumonia)	Antibiotics; drain pleural fluid if present
Abdominal infection	CT scan; surgical drainage if abscess; remove infected gallbladder/appendix
Urinary infection	Relieve blockage (catheter/stent); remove infected stones
Skin/soft tissue infection	Surgical cut-out of dead tissue (debridement)
Infected IV line	Remove the line immediately

2. Give the Right Antibiotics

- Start broad (cover many possible bacteria)
- Give within 1 hour of recognizing sepsis
- Narrow down later when culture results return (48-72 hours)
- Usually treat for 7 days (shorter if source controlled quickly)

3. Support Blood Pressure

First: Give fluids (balanced crystalloids like Lactated Ringer's or Plasma-Lyte)

If still low pressure: Start norepinephrine through central line

- Target blood pressure: MAP ≥65 mmHg (about systolic >90 mmHg)
- Add vasopressin if needing high doses of norepinephrine
- Consider steroids (hydrocortisone) if still unstable

Organ Specific Support in MODS

When organs fail, they need support while the infection is treated:

I. Lungs - ARDS (Acute Respiratory Distress Syndrome)

Problem: Acute kidney injury causes oliguria/anuria and accumulation of waste products, electrolyte imbalances, and metabolic acidosis due to failed filtration and loss of homeostasis.

Management:

- Mechanical ventilation with low tidal volumes (6 mL/kg ideal body weight)
- Higher PEEP to keep air sacs open
- Prone positioning (lying on stomach) for severe cases
- Conservative fluids (don't overload with IV fluids)

II. Kidneys - Acute Kidney Injury

Problem: Impaired renal excretory function leads to oliguria or anuria due to diminished glomerular filtration rate, resulting in the systemic accumulation of nitrogenous waste products (urea, creatinine), electrolyte imbalances, and metabolic acidosis from failure to eliminate solutes and maintain homeostasis.

Management:

- Avoid kidney-toxic drugs
- Dialysis if: severe acidosis, high potassium, fluid overload, or confusion from uremia

III. Brain - Sepsis-Associated Encephalopathy

Problem: Systemic inflammation triggers neuroinflammation, disrupting the blood-brain barrier and neuronal function to produce sepsis-associated encephalopathy—a reversible spectrum of altered mental status (confusion to coma) without structural brain injury.

Management:

- Treat the sepsis (this usually improves)
- Minimize sedating drugs
- Check for other causes (low glucose, bleeding, stroke)

IV. Blood - Coagulopathy/DIC

Problem: DIC is a consumptive coagulopathy where uncontrolled thrombin generation causes simultaneous microvascular thrombosis (organ ischemia) and hemorrhage (from depleted clotting factors)—the defining thrombotic-hemorrhagic paradox.

Management:

- Use prophylactic anticoagulation only in thrombotic-predominant coagulopathy without active bleeding.
- Transfuse platelets only for active hemorrhage or prior to invasive procedures—not for low counts alone in stable patients.

Important Do's and Don'ts

Do:

- ✓ Act fast (first hour is critical)

- ✓ Give antibiotics quickly
- ✓ Use balanced crystalloids (LR or Plasma-Lyte) not plain saline
- ✓ Control the infection source
- ✓ Use low tidal volume ventilation
- ✓ Mobilize patient early when stable
- ✓ Reassess antibiotics daily and narrow when possible

Don't:

- ✗ Delay antibiotics to finish workup
- ✗ Give too much fluid after initial resuscitation
- ✗ Use hydroxyethyl starch fluids (harmful to kidneys)
- ✗ Transfuse blood just because hemoglobin is low (transfuse if <7 g/dL or active bleeding)
- ✗ Give steroids to everyone (only for shock not responding to fluids and vasopressors)

Management of Electrical Injury

Key Concept: Electrical injury ≠ Thermal burn. The pathophysiology involves direct tissue necrosis, electrothermal heating, and membrane depolarization making management fundamentally different from flame burns.

Mechanisms of Injury

1. Direct Electrical Damage

- Cellular membrane disruption → Na^+/K^+ pump failure → cell death
- Thresholds to remember:
  - ≥1 mA: Perception
  - ≥10-20 mA: "Let-go" threshold (can't release grip)
  - ≥50 mA: Respiratory arrest possible
  - ≥100 mA: Ventricular fibrillation risk

2. Thermal Conversion (Joule heating)

- Heat = $I^2 \times R \times$ Time
- Internal burns often deeper than external appearance (iceberg phenomenon)

3. Mechanical Injury

- Tetanic contractions → fractures/dislocations
- Forceful falls from height (secondary trauma)

4. Electroporation

- Non-thermal cell membrane pore formation → delayed cell death

Clinical Classification

I. By Voltage (Most clinically relevant)

- Low voltage (<1000V): Household current (110-240V)
  - ✓ AC (Alternating Current): More dangerous due to tetany; causes VF
  - ✓ DC (Direct Current): Single muscle contraction; throws victim (often fewer deep injuries)

- High voltage (>1000V): Industrial/power lines
  - ✓ Arc injuries, massive tissue destruction, compartment syndrome risk

II. By Injury Pattern

1. True electrical contact (current passes through body)
2. Arc/Flash (superficial thermal burns, no current transmission)
3. Flame (clothing ignition—treat as thermal burn)

Emergency Department Assessment

Primary Survey (ABCDE with electrical twists)

A - Airway

- ✓ Rapid edema potential (fluid resuscitation needs differ from thermal burns)
- ✓ Early intubation threshold if oral commissure burn (pediatric biting hazard)

B - Breathing

- ✓ Electrical injury to respiratory center (medullary dysfunction)
- ✓ Paralysis of diaphragm/intercostals from tetany (AC current)

C - Circulation

- ✓ ECG immediately: Look for arrhythmias, ST changes, QT prolongation
- ✓ Rule of immediate concern: Any loss of consciousness, abnormal rhythm, or transthoracic pathway → continuous monitoring 24-48 hours
- ✓ Hypotension suggests: Massive tissue injury, internal bleeding from fractures, or myocardial stunning

D - Disability/Neuro

- ✓ Acute spinal cord injuries (fall mechanism)
- ✓ "Spinal shock" from direct current through spinal cord
- ✓ Transient paralysis (concussive myelopathy) - may resolve in hours-days

E - Exposure

- ✓ Look for entry and exit wounds (often multiple)
- ✓ Arcing may cause clothing to explode off—document thoroughly

Critical Physical Exam Findings

Finding	Significance
Rhabdomyolysis risk	Compartment syndrome, myoglobinuria → acute kidney injury
Painless compartment	Electrical injury destroys nerves first—absence of pain does NOT rule out compartment syndrome
Cataracts (delayed)	Occurs months later in ~5-20% of high-voltage injuries
Tympanic membrane rupture	Explosion effect from arc

Diagnostic Workup

1. Essential Labs

- CK (Creatine Kinase): Often >1000 U/L in significant injuries; trending predicts rhabdomyolysis
- Myoglobin: Serum and urine (tea-colored urine is late sign)
- Electrolytes: Hyperkalemia from cell lysis (cardiac arrest risk)
- ABG: Metabolic acidosis, carbon monoxide (if in enclosed space with arc)
- Troponins: May be elevated without true MI (myocardial stunning vs. necrosis)

2. Imaging

- EKG: Minimum 4-6 hours monitoring if:

  ✓ EKG abnormal, OR
  ✓ Loss of consciousness, OR
  ✓ Transthoracic pathway, OR
  ✓ High voltage exposure

- CT C-spine/Head: If fall mechanism or altered mental status

- X-rays: Tetanic fractures (shoulder dislocations, vertebral compression fractures common)

Management Strategies

A. Immediate Stabilization

1. Ensure scene safety (EMT principle): Don't become the second victim

2. Fluid Resuscitation (DIFFERS FROM STANDARD BURNS):

- ✓ Parkland Formula does NOT apply
- ✓ Goal: Urine output 75-100 mL/hr (vs. 30-50 in thermal burns) to flush myoglobin
- ✓ If myoglobinuria present: Mannitol ± alkalinization (pH > 6.5) to prevent cast formation

3. Cardiac Monitoring

- ✓ Asymptomatic + low voltage + normal ECG: 2-4 hours observation sufficient
- ✓ High voltage/ECG changes/Loss of consciousness: 24-hour monitoring (arrhythmia risk persists)

B. Surgical Considerations

- ✓ Escharotomy: If circumferential chest/limb burns compromise ventilation/perfusion
- ✓ Fasciotomy: Early and aggressive (compartment syndrome develops within hours)
- ✓ Clues: Rising CK, pain out of proportion (if sensation intact), tense compartments
- ✓ Debridement: Delayed (days later) to demarcate viable vs. non-viable tissue
- ✓ Amputation: Sometimes necessary for "mummified" limbs

C. Special Populations

- ✓ Pediatric oral commissure burns: Labial artery bleeding risk 2-3 weeks post-injury when eschar separates
- ✓ Pregnant patients: Fetal monitoring (uterus is low-resistance pathway)

Complications (The "Hidden" Sequelae)

1. Acute (0-7 days)

- Cardiac arrhythmias (late VF can occur up to 48 hours post-injury)
- Acute kidney injury (myoglobinuric)

- Cerebral edema (electroporation of blood-brain barrier)
- Disseminated intravascular coagulation (DIC) in massive injuries

2. Subacute (1-4 weeks)

- Sepsis from infected necrotic tissue
- Gastrointestinal perforation (delayed necrosis from current passing through abdomen)
- Cataract formation (high voltage)

3. Chronic (>1 month)

- Neurological: Peripheral neuropathy, spinal cord deficits, cognitive impairment ("electrical encephalopathy")
- Psychiatric: PTSD common (lightning/electrical injuries have high psychiatric morbidity)
- Orthopedic: Heterotopic ossification in injured muscles

Coma & Disturbances of Consciousness

I. Terminology

Term	Definition	Clinical Clue
Coma	Unarousable unresponsiveness; eyes remain closed; absent sleep-wake cycles	GCS ≤8; no purposeful response to pain; requires airway protection
Stupor	Arousable only with vigorous/painful stimulation; immediately returns to unresponsiveness when stimulation ceases	"Shake-and-shout" elicits brief eye opening/movement; no sustained interaction
Obtundation	Moderately reduced alertness with slowed cognition; requires repeated verbal stimulation to engage	Responds to voice but answers slowly/confused; drifts to sleep without stimulation
Lethargy	Mildly drowsy but easily arousable to normal alertness with minimal stimulation	Opens eyes spontaneously or to voice; maintains brief conversation before drifting
Delirium	Acute (<1 week) fluctuating disturbance in attention, awareness, and cognition ± altered arousal	Inattention on bedside testing (e.g., months backward); waxing/waning symptoms; often hyperactive or hypoactive
Vegetative State	Preserved sleep-wake cycles with spontaneous eye opening BUT no reproducible evidence of awareness of self/environment	Eyes open/closed cyclically; may have reflexive movements (grimacing, grasping) but no purposeful behavior
Minimally Conscious State (MCS)	Inconsistent but reproducible purposeful behaviors demonstrating partial awareness	Follows simple command intermittently; visual tracking; intelligible verbalization; or purposeful movement to command

Neuroanatomy Of Consciousness: The "Two-Hit" Model

Consciousness requires BOTH:

Component	Function	Lesion Effect
Arousal (Reticular Activating System - RAS)	Brainstem "on switch" → projects to thalamus → cortex	Bilateral thalamic or brainstem injury → coma

Awareness (Cerebral Cortex)	Content of consciousness (thoughts, perception)	Diffuse cortical injury → coma; focal → deficits without coma

The Coma Differential: "Vitamins" Mnemonic

A systematic approach to causes:

Category	Causes	Key Clues
Vascula	ICH, SAH, large ischemic stroke, venous sinus thrombosis	Sudden onset; headache; focal signs
Infection	Meningitis, encephalitis, brain abscess, sepsis	Fever (may be absent in elderly); nuchal rigidity
Trauma	Epidural/subdural hematoma, DAI, cerebral contusion	History of head injury (even minor in elderly on anticoagulants)
Anoxic	Cardiac arrest, near-drowning, CO poisoning	Witnessed arrest; cherry-red lips (CO)
Metabolic	Hypoglycemia, hepatic/uremic encephalopathy, hyponatremia	Abnormal glucose/electrolytes; stigmata of liver/kidney disease
Ictal	Non-convulsive status epilepticus (NCSE)	Subtle twitching; prior seizure history; EEG required
Neoplasm	Primary brain tumor, metastases, carcinomatous meningitis	Progressive decline; headache worse in AM
Substances	Opioids, benzos, alcohol, anticholinergics	Pinpoint pupils (opioids) vs. dilated (anticholinergics)

Clinical Approach: The 5-Minute Neuro Exam In Coma

Step 1: GLASGOW COMA SCALE (GCS) – Quantify Severity

Component	1 point	2 points	3 points	4 points	5/6 points

Eye (E)	None	To pain	To speech	Spontaneous	—
Verbal (V)	None	Incomprehensible	Inappropriate words	Confused	Oriented
Motor (M)	None	Extension (decerebrate)	Abnormal flexion (decorticate)	Withdrawal	Localizes pain → Obeys commands

GCS pitfalls:

- Intubated patients = max V score = 1 (not "T" for tube)
- Motor score most prognostic – localizing = better outcome than abnormal posturing

Step 2: BRAINSTEM REFLEXES – Localize the Lesion

Reflex	Pathway	Abnormal Finding	Localization
Pupillary light reflex	CN II → pretectal → CN III	Unilateral dilation → uncal herniation	Midbrain compression
Oculocephalic (Doll's eyes)	CN VIII → CN III/IV/VI	Absent movement → brainstem lesion	Pontine/midbrain injury
Oculovestibular (Cold caloric)	CN VIII → CN III/VI	No movement → brainstem failure	Pontine injury
Corneal reflex	CN V → CN VII	Absent blink → pons injury	Pontine lesion
Gag/cough reflex	CN IX/X	Absent → medullary failure	Medullary lesion

Herniation syndromes (progressive deterioration):

1. Uncal: CN III palsy (ipsilateral pupil dilation) → contralateral weakness
2. Central: Bilateral pinpoint pupils → decorticate → decerebrate → coma
3. Tonsillar: Cushing triad (HTN, bradycardia, irregular breathing) → respiratory arrest

Step 3: MOTOR POSTURING – Prognostic Clue

Posture	Description	Localization	Prognosis
Decorticate	Arms flexed, legs extended	Above red nucleus (thalamus/internal capsule)	Better

Decerebrate	Arms & legs extended, pronated	Below red nucleus (midbrain/upper pons)	Worse
Flaccid	No tone/movement	Medulla/spinal cord or diffuse injury	Poor

DIAGNOSTIC WORKUP: THE "COMA PROTOCOL"

Immediate Bedside Tests (First 5 Minutes)

- Blood glucose → if low: 25g D50W IV (or 1 mg glucagon IM if no IV)
- Oxygen saturation → give O_2 if <94%
- Naloxone 0.4–2 mg IV → if opioid overdose suspected (pinpoint pupils, respiratory depression)
- Flumazenil → avoid (lowers seizure threshold in TCA/benzo co-ingestion)

Essential Labs (First 30 Minutes)

Test	Why It Matters
Glucose, electrolytes (Na^+, Ca^{2+}), BUN/Cr	Hypoglycemia, hyponatremia, uremia
LFTs, ammonia	Hepatic encephalopathy
ABG	CO_2 retention (COPD), metabolic acidosis (DKA, toxins)
Toxicology screen	Limited utility (misses many drugs); treat clinically
TSH	Myxedema coma (rare but treatable)
Blood cultures	If fever ± nuchal rigidity

Imaging Decisions

Scenario	Imaging Choice	Rationale
Focal signs OR trauma OR sudden onset	Non-contrast Head CT STAT	Rules out hematoma, mass, herniation
Normal CT + no focal signs	MRI brain (after stabilization)	Detects encephalitis, anoxic injury, venous thrombosis
Suspected NCSE	EEG within 30 min	Gold standard for non-convulsive seizures

Prognosis: What to Tell Families

Factor	Favorable	Poor
Cause	Toxic/metabolic (reversible)	Anoxic brain injury, massive ICH
Pupils	Reactive	Bilaterally fixed/dilated
Motor	Localizing to pain	Decerebrate/decorticate/flaccid
Brainstem reflexes	Intact	Absent oculocephalic/corneal reflexes
Time to follow commands	<24h	>72h

Anoxic injury prognosis (after cardiac arrest):

- Poor predictors at 72h: Absent pupillary/corneal reflexes, myoclonus status, N20 absent on SSEP
- Never prognosticate before 72h (sedatives confound exam)

VENOMOUS BITES & STINGS

I. Framework: Understanding Venom Mechanisms

A. Venom Classification by Primary Toxicity

Toxin Type	Key Components	Clinical Effects	Prototype Envenomations
Neurotoxic	α-neurotoxins, β-neurotoxins, presynaptic phospholipases	Flaccid paralysis → ptosis, diplopia, dysphagia, respiratory failure	Elapids (cobras, kraits, mambas, coral snakes), some sea snakes
Hemotoxic	Metalloproteinases, thrombin-like enzymes, procoagulants/anticoagulants	Coagulopathy, thrombocytopenia, hemorrhage, DIC	Vipers (rattlesnakes, Russell's viper), some colubrids
Cytotoxic	Phospholipases A2, hyaluronidases	Local tissue necrosis, blistering, compartment syndrome	Vipers (saw-scaled viper), recluse spiders, some scorpions
Myotoxic	Myotoxins, phospholipases	Rhabdomyolysis → myoglobinuria, AKI, hyperkalemia	Sea snakes, rattlesnakes (some species), box jellyfish
Cardiotoxic	Cardiotoxins, Na^+/K^+ channel modulators	Arrhythmias, hypotension, direct myocardial depression	Some cobras, stonefish, box jellyfish

Snakebite Envenomation: Global Priority

A. Clinical Assessment: "The 4 D's" of Severity

Domain	Mild	Moderate-Severe	Life-Threatening
Local	Pain, minimal swelling	Rapidly progressive edema (>50% limb in 48h), blistering, necrosis	Compartment syndrome, limb-threatening ischemia
Hematologic	None	Thrombocytopenia (<100k), prolonged clotting times	Spontaneous bleeding (gums, GI, intracranial), DIC
Neurologic	None	Ptosis, diplopia, dysphagia	Respiratory paralysis, coma
Systemic	None	Nausea/vomiting, hypotension	Shock, AKI, ARDS

B. First Aid: Evidence-Based Vs. Harmful Myths

Recommended	Harmful / Ineffective
Pressure immobilization technique (PIT) for neurotoxic snakebites (elapids) – elastic bandage 40–70 mmHg pressure + splint limb	Tourniquets (↑ tissue necrosis, compartment syndrome)
Keep victim calm, immobilize limb, evacuate rapidly	Cutting/sucking wound (↑ infection, no venom removal)
Remove rings/jewelry before swelling progresses	Ice application (↑ tissue damage)
Note time of bite; if safe, photograph snake for ID	Electric shock, herbal remedies

PIT Technique: Apply broad pressure bandage starting distally → proximally (like sprain), covering entire limb. Bandage should be tight enough to blanch nail bed briefly but allow capillary refill. Only for elapids (Australia, Africa, Asia). Not for vipers (may worsen local necrosis).

C. Antivenom Administration

- Indication: Signs of envenomation (not just bite mark)
- Dosing: Species-specific; initial dose based on severity (e.g., 4–10 vials for severe viper bite)
- Administration: IV infusion diluted in NS over 1–2h; premedication NOT routinely recommended (delays treatment; steroids/antihistamines don't prevent anaphylaxis)
- Monitoring: Watch for acute reactions (anaphylaxis 5–20%) and serum sickness (5–23 days later)

Arthropod Envenomations

A. Hymenoptera (Bees, Wasps, Hornets, Fire Ants)

Reaction Type	Features	Management
Local	Pain, erythema <10 cm, resolves in 24h	Cold compress, analgesia
Large Local	Erythema >10 cm, peaks at 48h, lasts 5–10 days	Oral antihistamine ± short-course prednisone
Systemic (Anaphylaxis)	Urticaria, angioedema, respiratory/cardiovascular compromise	Epinephrine IM immediately → same algorithm as general anaphylaxis
Toxic Reaction	Multiple stings (>50 in adults) → direct venom toxicity (hemolysis, rhabdo, AKI)	Supportive care; dialysis if needed

Clinical Assessment: The "Venom" Approach

V – Vital signs & ABCDE stabilization

- Airway: Assess for angioedema (insect stings) or bulbar weakness (neurotoxic snakes)
- Breathing: Watch for respiratory muscle paralysis (elapids)
- Circulation: Hypotension from venom-induced shock or anaphylaxis

E – Exposure & history

- Critical questions:

- What bit/stung? (If unknown → describe morphology: snake color/pattern, spider markings)
- When did it occur? (Time guides antivenom urgency)
- Where on body? (Proximal bites → faster systemic absorption)
- Any first aid already applied? (Avoids repeating harmful interventions)

N – Neurological exam

- Ptosis, ophthalmoplegia, dysphagia → neurotoxic envenoming
- Altered mental status → cerebral hemorrhage (hemotoxic) or hypoxia

O – Observation of local effects

- Fang/tooth marks (snake: paired punctures; spider: 2 small puncta)
- Swelling progression (measure limb circumference hourly)
- Necrosis, blistering, compartment syndrome signs

M – Monitoring labs

Test	Frequency	Purpose
INR/PT, aPTT, fibrinogen	Baseline, 1h, 6h, 12h, then q12h until normal	Detect coagulopathy
CK	Baseline, 6h, 12h	Myotoxicity/rhabdomyolysis
Creatinine	Baseline, 24h	Acute kidney injury risk
FBC	Baseline, 6h	Thrombocytopenia

FIRST AID: WHAT TO DO (AND WHAT NOT TO DO)

☑ DO:

- Move patient away from danger zone

- Remove constricting items (rings, bracelets) before swelling develops [[9]]

- Immobilize limb with splint/sling (reduces lymphatic spread)

- Pressure immobilization bandage (PIB) for neurotoxic snakebites (Australia protocol):

  - Elastic bandage 15–20 cm wide

  - Wrap entire limb at 40–70 mmHg pressure (like sprain)

  - DO NOT use for cytotoxic/hemotoxic bites (may worsen necrosis)

- Rapid transport to facility with antivenom capability

❌ DO NOT (HARMFUL INTERVENTIONS):

- ❌ Tourniquets (↑ tissue necrosis risk)

- ❌ Incision/suction of wound (↑ infection, no venom removal benefit)

- ❌ Ice application to snakebites (↑ tissue damage)

- ❌ Electric shock therapy

- ❌ Alcohol/caffeine (↑ venom absorption)

Anaphylaxis & Transfusion Reactions

Anaphylaxis: The Acute Hypersensitivity Emergency

A. Definition & Pathophysiology

Definition: A sudden, severe, life-threatening systemic hypersensitivity reaction characterized by rapid onset of airway, breathing, and/or circulatory compromise.

Mechanisms:

- Immunologic (IgE-mediated): Most common (foods, drugs, venom). Antigen cross-links IgE on mast cells/basophils → degranulation → histamine, tryptase, leukotrienes
- Non-immunologic (direct mast cell activation): Opioids, radiocontrast, vancomycin ("Red Man Syndrome")
- Mixed: Exercise-induced, idiopathic

B. Clinical Presentation & Grading

Key Concept: Skin findings (urticaria, angioedema) occur in 80–90% but may be absent in severe reactions—never wait for rash to treat!

Grade	Features	Clinical Significance
Mild (Grade 1–2)	Skin/mucosal only (flushing, pruritus, urticaria)	May progress rapidly—monitor closely
Moderate (Grade 3)	PLUS respiratory (wheeze, stridor) OR GI (vomiting, diarrhea) OR cardiovascular (tachycardia, syncope)	Meets anaphylaxis criteria—requires epinephrine
Severe (Grade 4–5)	Hypotension/shock, airway obstruction, cardiac arrest	Immediate epinephrine + resuscitation

Diagnostic Criteria (NIAID/FAAN) – Anaphylaxis likely when ≥1 of:

1. Acute onset (mins–hrs) + involvement of skin/mucosa AND respiratory compromise OR reduced BP

2. Two or more systems involved after exposure to likely allergen

3. Reduced BP after known allergen exposure

C. Management: The Epinephrine-First Algorithm

Step 1: Immediate Actions

- Call for help/resuscitation team
- Stop allergen exposure
- Position: Supine (or recovery position if vomiting); avoid upright posture (can precipitate "empty ventricle syndrome" → sudden death).

Step 2: Epinephrine (Adrenaline) – First-Line, Time-Sensitive

Population	Dose	Route	Site	Repeat
Adults & ≥30 kg	0.3–0.5 mg	IM	Anterolateral thigh (vastus lateralis)	q5 min if no response
Children <30 kg	0.01 mg/kg (max 0.3 mg)	IM	Anterolateral thigh	q5 min if no response

Step 3: Supportive Care

- Airway: High-flow O_2; prepare for intubation if stridor/worsening hypoxia

- Circulation: IV crystalloid bolus (adults 500–1000 mL; children 10–20 mL/kg).

- Adjuncts (after epinephrine):

  ✓ H1-antihistamine (e.g., diphenhydramine 25–50 mg IV)
  ✓ H2-antihistamine (e.g., famotidine 20 mg IV)
  ✓ Corticosteroids (e.g., methylprednisolone 125 mg IV) – may reduce biphasic reactions but no acute benefit.

Step 4: Monitoring & Disposition

- Observe minimum 4–6 hours post-reaction (risk of biphasic reaction: 1–20%)

- Discharge with epinephrine auto-injector prescription + allergist referral

- Patient education: trigger avoidance, action plan

Transfusion Reactions: Classification & Management

A. Framework: Acute vs. Delayed | Immunologic vs. Non-immunologic

Timing	Immunologic	Non-immunologic
Acute (<24h)	• Acute hemolytic • Febrile non-hemolytic (FNHTR • Allergic/anaphylactic • TRALI • Transfusion-associated graft-vs-host disease (TA-GVHD)	• TACO • Bacterial contamination • Hypotensive (e.g., ACE-I related)
Delayed (>24h)	• Delayed hemolytic • Post-transfusion purpura • Alloimmunization	• Iron overload • Transfusion-transmitted infection

B. Key Acute Reactions: Clinical Pearls

1. Acute Hemolytic Reaction (AHTR)

- **Cause:** ABO incompatibility (most severe) → complement activation → intravascular hemolysis
- **Triad:** Fever + flank pain + hemoglobinuria
- **Diagnosis:** ↑ free Hb, ↓ haptoglobin, positive direct antiglobulin test (DAT), hemoglobinuria
- **Management:** STOP transfusion → aggressive IV hydration → consider dialysis for AKI

2. Febrile Non-Hemolytic (FNHTR)

- **Cause:** Cytokines in stored blood OR recipient antibodies to donor leukocytes
- **Features:** Fever ± chills without hemolysis/hypotension
- **Prevention:** Leukoreduction of blood products

3. Allergic vs. Anaphylactic Transfusion Reactions

- Mild allergic: Urticaria only → slow transfusion + antihistamine
- Anaphylactic: Hypotension/bronchospasm → epinephrine immediately (same algorithm as above)
- Special cause: IgA deficiency with anti-IgA antibodies → use washed RBCs in future

4. TRALI (Transfusion-Related Acute Lung Injury)

- Pathophysiology: Donor anti-leukocyte antibodies → neutrophil activation in pulmonary capillaries → non-cardiogenic pulmonary edema
- Diagnostic criteria:
  - ✓ Acute hypoxemia (PaO_2/FiO_2 <300) within 6h of transfusion
  - ✓ Bilateral infiltrates on CXR
  - ✓ No circulatory overload (normal BNP, no elevated JVP)
  - ✓ No other ALI cause

5. TACO (Transfusion-Associated Circulatory Overload)

- **Cause:** Volume overload in susceptible patients (elderly, CKD, heart failure)
- **Features:** Hypertension, ↑ JVP, pulmonary edema, ↑ BNP
- **Prevention:** Slow transfusion rate (<2 mL/kg/hr), diuretics pre-transfusion in high-risk patients

C. Immediate Management of SUSPECTED Transfusion Reaction

STOP → ASSESS → REPORT → INVESTIGATE

1. STOP transfusion immediately; maintain IV access with normal saline (new tubing!)

2. ASSESS ABCs:

- ✓ Hypotension/shock → epinephrine if anaphylaxis; fluids if hypovolemic
- ✓ Respiratory distress → O_2; differentiate TRALI (PEEP often needed) vs TACO (diuretics)

3. REPORT to blood bank + complete transfusion reaction form

4. INVESTIGATE:

- ✓ Visual inspection: hemoglobinuria? (AHTR)
- ✓ Labs: CBC, haptoglobin, LDH, bilirubin, DAT, blood cultures
- ✓ CXR if respiratory symptoms
- ✓ Return untransfused blood bag + new blood sample to blood bank for clerical check + crossmatch verification

Principles of Drug Therapy & Management of Poisoning

Principles Of Rational Drug Therapy: The "5 Rights" Plus

Principle	Clinical Application	Pitfall to Avoid
Right drug	Match mechanism to pathophysiology (e.g., β-blocker for SVT, not digoxin)	"Therapeutic momentum" – continuing ineffective drugs
Right dose	Adjust for renal/hepatic function, age, weight	Fixed dosing in elderly → toxicity (e.g., digoxin)
Right route	IV for emergencies; oral for chronic therapy	Oral opioids in vomiting patient → aspiration
Right time	Antibiotics within 1h of sepsis recognition	Delaying naloxone in opioid overdose
Right patient	Check allergies, drug interactions, pregnancy status	Giving ACEi to pregnant woman → fetal toxicity
+ Right monitoring	Check levels (digoxin, phenytoin), INR, glucose	Giving warfarin without INR follow-up

Therapeutic index (TI) pearl:

- TI = Toxic dose / Therapeutic dose
- Narrow TI (digoxin, warfarin, lithium, theophylline) → requires level monitoring
- Wide TI (penicillin, acetaminophen therapeutic doses) → less monitoring needed

The Poisoned Patient: The "ABC-Tox" Approach

Step 1: ABCs + Immediate Life Threats (First 5 Minutes)

Threat	Recognition	Treatment
Airway	GCS <8, stridor, secretions	Intubate early (before edema worsens)
Breathing	Respiratory depression (opioids), pulmonary edema (salicylates)	Naloxone for opioids; CPAP for salicylates
Circulation	Hypotension (TCA, β-blocker), arrhythmia (digoxin)	Sodium bicarbonate for TCA; glucagon for β-blocker
Seizures	Benzodiazepines, isoniazid, theophylline	Lorazepam 2–4 mg IV; pyridoxine 5 g IV for INH
Hyperthermia	Serotonin syndrome, anticholinergic toxicity	External cooling; avoid antipyretics (ineffective)

Step 2: HISTORY – The "SAMPLE" Mnemonic for Toxicology

Letter	Question	Why It Matters
Substance	"What did you take?" (pill bottles, texts to friends)	Guides specific antidote use
Amount	"How many pills/tablets?"	Risk-stratifies (e.g., >10g acetaminophen = toxic)
Medications	Home meds (therapeutic misadventure common)	Lithium + NSAIDs → toxicity; SSRIs + tramadol → serotonin syndrome
Past history	Suicide attempts, substance use disorder	Predicts adherence to treatment
Last meal	Time of ingestion	Determines decontamination window
Events	Witnessed seizure, vomiting, altered mental status	Clues to toxidrome

Decontamination: When & When Not

A. Gastrointestinal Decontamination

Method	Indication	Contraindication	Evidence
Activated charcoal	Most ingestions within 1 hour; extended-release drugs up to 4h	Altered mental status (without airway protection), caustics, hydrocarbons	↓ Absorption 50–70% if given early
Gastric lavage	Rare: Life-threatening ingestion within 60 min (e.g., lithium, iron)	Caustics (perforation risk), hydrocarbons (aspiration)	Not routinely recommended (no mortality benefit)
Whole bowel irrigation	Sustained-release drugs, iron, packets (body stuffers)	Ileus, bowel obstruction	Polyethylene glycol (GoLYTELY) 2 L/h until rectal effluent clear

B. Dermal/Ocular Decontamination

- Skin: Remove clothing → irrigate with water × 15–20 min (hydrofluoric acid: use calcium gluconate gel)
- Eyes: Irrigate with NS/lactated Ringer's × 20 min minimum; check pH until neutral

Specific Antidotes: The Essential

Poison	Antidote	Mechanism
Opioids	Naloxone	Mu-receptor antagonist (0.04-0.4mg IV, repeat q2-3min)
Benzodiazepines	Flumazenil	GABA-A antagonist (CAUTION: Seizures in chronic users/TCA co-ingestion)
Acetaminophen	N-Acetylcysteine (NAC)	Replenishes glutathione (most effective within 8h)
Organophosphates	Atropine + Pralidoxime (2-PAM)	Atropine blocks muscarinic receptors; 2-PAM reactivates acetylcholinesterase
Beta-blockers	Glucagon	Bypasses beta-receptor via cAMP stimulation (+ high-dose insulin therapy)
Calcium Channel Blockers	Calcium gluconate/chloride + High-dose insulin + Lipid emulsion	Competitive antagonism at calcium channels
Digoxin	Digoxin-specific antibody (Fab)	Binds free digoxin (indicated for K^+ >5 mEq/L or life-threatening arrhythmias)
Cyanide	Hydroxocobalamin (preferred) or Nitrites + Thiosulfate	Binds cyanide to form cyanocobalamin (excreted in urine)
Methanol/Ethylene glycol	Fomepizole (or ethanol)	Inhibits alcohol dehydrogenase (prevents toxic metabolite formation) + Folate/Thiamine

Management of Poisoning

The Poisoned Patient: Initial Approach

"Treat the patient, not the poison"

Primary Survey (ABCDE):

- Airway: GCS <8 = definitive airway (intubation with RSI). Exception: Avoid succinylcholine in organophosphate poisoning (pseudocholinesterase inhibition)
- Breathing: Tachypnea suggests salicylates, metabolic acidosis, or stimulants; Bradypnea suggests opioids, sedatives

- Circulation: Hypotension (calcium channel blockers, beta-blockers, tricyclics); Hypertension (sympathomimetics, withdrawal)
- Disability: Pupil size (miosis vs. mydriasis), Temperature (hyperthermia in serotonin syndrome, NMS, salicylates)
- Exposure: Track marks, odors (bitter almonds = cyanide, garlic = arsenic/organophosphates)

Toxidromes: The "Five Finger Approach"

Recognizing patterns saves lives:

Toxidrome	Vital Signs	Pupils	Secretions	Mental Status	Common Causes
Anticholinergic	Tachycardia, hyperthermia, hypertension	Mydriasis (dilated)	Dry (dry as a bone)	Delirium, hallucinations	Diphenhydramine, atropine, TCAs, jimson weed
Cholinergic	Bradycardia, variable BP	Miosis (constricted)	Wet (SLUDGE: Salivation, Lacrimation, Urination, Defecation, GI upset, Emesis)	Confusion, weakness	Organophosphates, carbamates, nerve agents
Sympathomimetic	Tachycardia, hypertension, hyperthermia	Mydriasis	Dry	Agitation, paranoia	Cocaine, amphetamines, bath salts
Opioid	Bradycardia, hypotension, respiratory depression (<12/min)	Miosis (pinpoint)	Normal	CNS depression, coma	Heroin, morphine, fentanyl, methadone
Sedative-Hypnotic	Normal or depressed	Normal or small	Normal	Sedation, ataxia	Benzos, barbiturates, ethanol, Z-drugs

Decontamination Strategies

Gastric Decontamination (Evidence-Based):

- Activated Charcoal (AC):

- Indication: Within 1-2 hours of ingestion OR sustained-release preparations
- Dose: 1g/kg (max 50g)
- Contraindications: Unprotected airway, caustic ingestion, bowel obstruction, metals/lithium/alcohols (poor binding)

- Gastric Lavage:

- Rarely indicated. Only if <1 hour and life-threatening amount (colchicine, cyanide)
- Risk: Aspiration, esophageal perforation

- Whole Bowel Irrigation (WBI):

- Indications: Body packers (cocaine packets), iron tablets, sustained-release preparations
- Solution: Polyethylene glycol (GoLYTELY) 1-2 L/hr until rectal effluent clear

Enhanced Elimination:

- Urinary Alkalinization:

- Mechanism: Ion trapping (weak acids ionized in alkaline urine = trapped in tubules)
- Indications: Moderate-to-severe salicylate poisoning, phenobarbital overdose
- Target pH: 7.5-8.0 (monitor to prevent alkalosis)

- Hemodialysis (Indications):

- Low Vd + low protein binding + water soluble

- mnemonic: "I STUMBLE"

I (Isoniazid), S (Salicylates), T (Theophylline), U (Uremia), M (Methanol), B (Barbiturates), L (Lithium), E (Ethylene glycol)