

MedLadder

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NEET SS Pediatrics

Complete Super-Speciality Review

12 Chapters • 24 Illustrations • 300 MCQs with Explanations

High-Yield • Exam-Oriented

Neonatology • Cardiology • Neurology • Pulmonology • Gastroenterology • Nephrology
Endocrinology • Hematology-Oncology • Infectious Diseases • Critical Care • Genetics • Developmental
Pediatrics

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Disclaimer: This book is for educational purposes only and is intended as a revision aid for the NEET SS examination. It does not replace standard textbooks or clinical judgment. Drug doses and guidelines change — always verify against current references. Consult standard texts (e.g., Nelson Textbook of Pediatrics) for definitive information.

Neonatology

Chapter 1: Neonatology

Neonatology carries disproportionate weightage in NEET SS Pediatrics — roughly one in every five questions in recent papers draws on the first month of life. DM Neonatology is among the most competitive super-speciality branches, and the exam tests it at a level well beyond MD Pediatrics: exact drug doses, trial-defined criteria (hypothermia eligibility, ROP treatment thresholds), and staging systems asked verbatim. This chapter distills the high-yield core — resuscitation, RDS, BPD, NEC, HIE, sepsis, inborn errors, apnea, ROP, and jaundice — to the facts that score.

Neonatal Resuscitation (NRP 8th Edition)

- **Initial steps** (first 60 seconds, the "Golden Minute"): provide warmth (radiant warmer, dry, remove wet linen), position head in sniffing position, clear airway only if obstructed or PPV required (routine suctioning of vigorous infants is NOT done), dry thoroughly, stimulate. Assess simultaneously: tone, breathing, heart rate.
- **PPV indications**: apnea/gasping, HR <100 bpm, or persistent central cyanosis despite free-flow O₂. Start PPV within 60 seconds of birth ("Golden Minute") if any present.
- **Oxygen**: begin PPV with 21% O₂ in term infants, 21–30% in preterm; titrate to target preductal SpO₂ (60–65% at 1 min, 80–85% at 5 min, 85–95% at 10 min). Avoid 100% O₂ in preterm (ROP/BPD risk) and in term infants unless HR remains <60 despite effective ventilation.
- **Corrective steps for ineffective PPV (MR SOPA)**: Mask adjustment, Reposition airway, Suction mouth then nose, Open mouth, Pressure increase, Alternative airway (LMA/ETT).
- **Chest compressions**: indicated if HR <60 bpm after at least 30 seconds of effective PPV. Technique: two-thumb encircling hands preferred; depth one-third AP diameter; rate 90 compressions + 30 breaths per minute (3:1 ratio, 120 events/min); 100% O₂ during compressions. Reassess every 60 seconds; stop compressions when HR ≥60.
- **Epinephrine**: indicated if HR <60 after 60 seconds of coordinated compressions + effective ventilation. Dose: **0.1–0.3 mL/kg of 1:10,000 (0.1 mg/mL) IV/IO** = 0.01–0.03 mg/kg; may repeat every 3–5 minutes. Endotracheal dose (while obtaining IV access): **0.5–1 mL/kg of 1:10,000** (0.05–0.1 mg/kg). Flush with 0.5–1 mL saline after IV dose.
- **Volume expansion**: 10 mL/kg isotonic crystalloid (normal saline) or O-negative blood over 5–10 min if blood loss suspected or poor perfusion despite resuscitation.
- **When to stop**: if no heart rate after 20 minutes of complete, effective resuscitation, redirection of care may be discussed (NRP: consider stopping at 20 min; individualize by etiology, gestational age, parental wishes). A persistent HR <60 at 10–20 min despite full measures predicts death or severe disability.

- **Post-resuscitation care:** avoid hyperthermia, monitor glucose, obtain blood gas, evaluate for HIE and therapeutic hypothermia eligibility.
- **Delayed cord clamping:** ≥30–60 seconds for vigorous term and preterm infants not requiring resuscitation; improves iron stores, reduces IVH and NEC in preterm.

Respiratory Distress Syndrome (Hyaline Membrane Disease)

- **Pathophysiology:** primary surfactant deficiency from immature type II pneumocytes → increased alveolar surface tension → atelectasis, decreased compliance, V/Q mismatch, hypoxemia, hypercarbia, acidosis; protein-rich exudate forms hyaline membranes. Incidence inversely proportional to gestational age (~60% at <28 weeks, <5% at term).
- **Risk factors:** prematurity (strongest), maternal diabetes, cesarean delivery without labor, perinatal asphyxia, multiple gestation, male sex, hydrops. **Protective:** prolonged ROM, maternal hypertension/preeclampsia, antenatal steroids, intrauterine growth restriction (stress accelerates lung maturity).
- **Clinical features:** onset within minutes–hours of birth; tachypnea, nasal flaring, expiratory grunting (glottic closure to maintain FRC), intercostal/subcostal retractions, cyanosis. Silverman-Anderson score grades severity.
- **Chest X-ray:** diffuse fine granular/ground-glass opacities with air bronchograms; severe disease shows "white-out" lung with loss of cardiac borders. Lung ultrasound: coalescent B-lines, absent A-lines.
- **Fetal lung maturity tests (rarely asked, know names):** lecithin/sphingomyelin (L/S) ratio ≥2.0 (≥2.5 in diabetic mothers), phosphatidylglycerol present, lamellar body count, TDx-FLM.
- **Antenatal corticosteroids: betamethasone 12 mg IM q24h × 2 doses OR dexamethasone 6 mg IM q12h × 4 doses** to mothers at 24–34 weeks (ACOG extends to 34 0/7–36 6/7 weeks for late preterm at risk within 7 days) at risk of preterm delivery within 7 days. Single course reduces RDS, IVH, NEC, and neonatal mortality; repeat courses not routinely recommended (BETADOSE/MACs data: growth concerns).
- **CPAP:** first-line for spontaneously breathing preterm infants with RDS; start 5–6 cm H₂O (PEEP maintains FRC, splints airway, reduces apnea). Early CPAP reduces need for intubation and BPD versus routine intubation (SUPPORT/COIN trials).
- **Surfactant replacement:** natural (animal-derived) preparations superior to synthetic protein-free ones.
- **Poractant alfa (Curosurf, porcine):** 200 mg/kg (2.5 mL/kg) first dose; repeat 100 mg/kg (1.25 mL/kg) q12h if still intubated; maximum 3 doses total.
- **Beractant (Survanta, bovine):** 100 mg/kg (4 mL/kg); repeat q6h up to 4 doses.
- **Calfactant (Infasurf, bovine):** 105 mg/kg (3 mL/kg); repeat q12h up to 3 doses.
- Give via ETT in 2–4 aliquots with position changes; transient bradycardia/desaturation common — pause and reoxygenate.
- **Prophylactic** (delivery room, <26–28 weeks) vs **rescue/early selective** (once RDS established, within 2 hours) — early rescue preferred; INSURE (INtubate-SURfactant-Extubate to CPAP) and LISA/MIST (less-invasive surfactant administration via thin catheter) minimize ventilation time.

- **Ventilation strategy:** low tidal volumes (4–6 mL/kg), permissive hypercapnia ($p\text{CO}_2$ 45–55 mmHg if pH >7.20), adequate PEEP, target SpO_2 90–95% in preterm (SUPPORT/BOOST-II: 85–89% increased mortality/NEC; >95% increased ROP).
- **Complications:** air leak (pneumothorax — sudden desaturation, asymmetric chest, shift; transillumination positive; treat with needle thoracentesis then chest tube), pulmonary hemorrhage, IVH, PDA, BPD.

Bronchopulmonary Dysplasia

- **NIH (2001) definition:** supplemental O_2 requirement for **≥28 days** after birth. Severity graded at **36 weeks postmenstrual age** (infants <32 weeks GA) or **56 days postnatal age/discharge** (≥32 weeks GA):
- **Mild:** breathing room air at assessment point.
- **Moderate:** need for <30% O_2 .
- **Severe:** need for ≥30% O_2 and/or positive pressure (PPV or nasal CPAP).
- **Pathophysiology ("new BPD"):** arrested alveolarization and dysmorphic vascular growth in extremely preterm infants, not the fibrosis of classic Northway BPD; driven by volutrauma, oxygen toxicity, inflammation (chorioamnionitis, sepsis), PDA, fluid overload, and nutritional deficits.
- **Prevention strategies** (exam favorite):
- Antenatal corticosteroids; early CPAP avoiding intubation; surfactant; gentle ventilation (volume-targeted, low tidal volume).
- **Vitamin A 5000 IU IM 3×/week for 4 weeks** (reduces BPD in ELBW infants).
- **Caffeine citrate** (CAP trial: reduces BPD, improves neurodevelopment).
- Avoid hyperoxia (target SpO_2 90–95%); judicious fluids; early PDA treatment; adequate nutrition.
- Postnatal systemic steroids (dexamethasone) reduce BPD but increase cerebral palsy risk — reserve for ventilator-dependent infants after first week (DART protocol: low-dose taper); inhaled steroids not effective.
- **Management:** diuretics (furosemide/chlorothiazide) for pulmonary edema, bronchodilators, supplemental O_2 to keep SpO_2 90–95%, treat intercurrent infection/GERD, RSV prophylaxis (palivizumab), aggressive nutrition, monitor for pulmonary hypertension (echocardiography) and cor pulmonale.
- **Prognosis:** most outgrow by 2 years via new alveolar growth; at risk for reactive airway disease, exercise intolerance, and neurodevelopmental impairment.

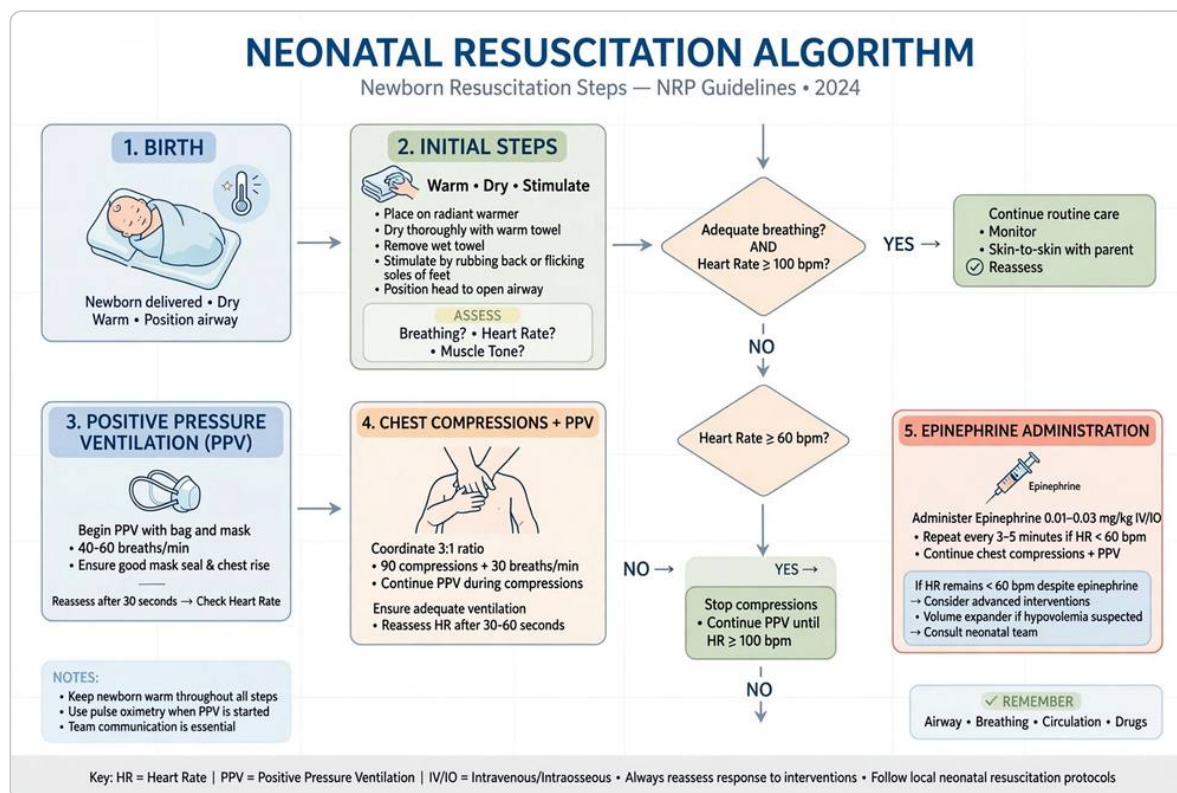


Figure 1.1 — Neonatal resuscitation algorithm (NRP)

Necrotizing Enterocolitis

- **Epidemiology:** most common surgical emergency in NICU; primarily preterm (<32 weeks, <1500 g); 90% of cases in preterm infants; formula feeding increases risk; breast milk protective.
- **Pathogenesis:** immature intestinal barrier + abnormal bacterial colonization + enteral feeding substrate + ischemia/hypoxia → mucosal injury, bacterial translocation, pneumatosis intestinalis, full-thickness necrosis, perforation.
- **Bell staging (modified):**
 - **Stage I (suspected):** IA — temperature instability, apnea, bradycardia, lethargy; mild abdominal distension, gastric residuals, guaiac-positive stools. IB — same + grossly bloody stools. X-ray: normal or mild ileus.
 - **Stage II (definite):** IIA (mildly ill) — absent bowel sounds ± abdominal tenderness; **pneumatosis intestinalis** on X-ray. IIB (moderately ill) — IIA + metabolic acidosis, thrombocytopenia; definite ascites, no perforation; portal venous gas may be present.
 - **Stage III (advanced):** IIIA (severely ill, intact bowel) — hypotension, bradycardia, apnea, DIC, neutropenia; generalized peritonitis, marked ascites. IIIB (perforated) — IIIA + **pneumoperitoneum**.
- **Diagnosis:** abdominal X-ray is key — pneumatosis intestinalis (pathognomonic), portal venous gas, fixed dilated loop, pneumoperitoneum (football sign, Rigler sign). Labs: thrombocytopenia, neutropenia, metabolic acidosis, hyponatremia.
- **Medical management** (Stages I–IIIA without perforation):
 - Stop all enteral feeds (NPO), orogastric decompression.

- IV fluids, correct electrolytes/acidosis, inotropes if hypotensive.
- Broad-spectrum antibiotics 7–14 days: **ampicillin + gentamicin + metronidazole (or clindamycin)**; add vancomycin if MRSA prevalent; antifungal if prolonged course.
- Serial abdominal examinations and X-rays (every 6–12h), parenteral nutrition.
- Monitor platelets, blood gases, abdominal girth.
- **Surgical indications: pneumoperitoneum** (absolute), clinical deterioration despite maximal medical therapy, abdominal wall erythema/edema, palpable mass with obstruction, fixed dilated loop on serial X-rays, positive diagnostic paracentesis (brown fluid, bacteria on Gram stain), portal venous gas with deterioration. Procedures: peritoneal drain (unstable ELBW as bridge) or laparotomy with resection ± stoma.
- **Prevention:** exclusive human milk, standardized feeding protocols with slow advancement, probiotics (controversial but evidence of benefit), antenatal steroids, avoid prolonged empiric antibiotics and H2 blockers.
- **Complications:** short bowel syndrome, strictures (colon most common, presents weeks later with obstruction), cholestasis, sepsis, neurodevelopmental impairment.

Hypoxic-Ischemic Encephalopathy

- **Sarnat staging:**
- **Stage I (mild):** hyperalert, jittery; normal muscle tone; hyperreflexia; no seizures; resolves <24 hours; normal outcome.
- **Stage II (moderate):** lethargic/obtunded; hypotonia; decreased deep tendon reflexes, weak Moro; miosis; **seizures common**; lasts 2–14 days; ~25–45% risk of abnormal outcome.
- **Stage III (severe):** stupor/coma; flaccid; absent reflexes and Moro; dilated/fixed pupils; prolonged/refractory seizures or status; persists days–weeks; >75% death or severe disability.
- **Therapeutic hypothermia** (only proven neuroprotective therapy; NNT ~7–9):
- **Inclusion:** gestational age ≥ 36 weeks, age ≤ 6 hours, evidence of perinatal asphyxia — **cord/early arterial pH ≤ 7.0 or base deficit ≥ 16 mmol/L**, OR (if no gas) 10-min Apgar ≤ 5 , continued resuscitation at 10 min — PLUS **moderate-to-severe encephalopathy** (altered consciousness with abnormal tone/reflexes) or clinical seizures.
- **Exclusions:** major congenital anomalies, severe IUGR (<1800 g in trials), moribund, severe coagulopathy with active bleeding, need for ECMO anticipated.
- **Protocol:** cool to **33–34°C (whole-body 33.5°C) for 72 hours**, then slow rewarm (0.5°C/hour); sedation, monitor for bradycardia, coagulopathy, subcutaneous fat necrosis.
- **aEEG (amplitude-integrated EEG):** bedside neuromonitoring; abnormal background (burst suppression, low voltage, flat trace) and absent sleep-wake cycling predict poor outcome; electrographic seizures detected even without clinical correlate — treat with phenobarbital (20 mg/kg load).
- **Workup:** cord/arterial blood gas, neuroimaging — cranial ultrasound (rules out hemorrhage) then **MRI brain at day 4–10** (diffusion-weighted): basal ganglia/thalamus injury (acute profound asphyxia) vs watershed injury (prolonged partial asphyxia); MR spectroscopy lactate peak.

- **Supportive care:** maintain normoglycemia, normocapnia, normal blood pressure; treat seizures; avoid hyperthermia; monitor multi-organ injury (myocardial ischemia, ATN, hepatic dysfunction, DIC).

Neonatal Sepsis

- **Definitions:** early-onset sepsis (EOS, <72 hours) — vertical transmission from maternal genital tract; late-onset sepsis (LOS, >72 hours–28 days) — nosocomial or community acquired.
- **EOS organisms:** **Group B Streptococcus** (most common in term), ***E. coli*** (most common in preterm/VLBW, especially with prolonged ROM), *Listeria monocytogenes*, *Klebsiella*. Risk factors: maternal GBS colonization, PROM >18h, maternal fever/chorioamnionitis, prematurity, previous GBS-septic infant.
- **LOS organisms:** **coagulase-negative Staphylococci** (most common, line-related), *S. aureus* (including MRSA), *Klebsiella/E. coli*, *Pseudomonas*, ***Candida*** (prolonged antibiotics, central lines, ELBW).
- **Clinical features:** nonspecific — temperature instability, apnea, bradycardia, respiratory distress, poor feeding, lethargy, hypotonia, hypoglycemia/hyperglycemia, jaundice, mottling, shock.
- **Workup:**
 - **Blood culture** — gold standard; obtain BEFORE antibiotics; 1 mL minimum in neonates; two-site cultures for suspected line infection.
 - CBC with differential: I/T (immature-to-total neutrophil) ratio ≥ 0.2 suggests sepsis; neutropenia more predictive than neutrophilia; thrombocytopenia in LOS/gram-negative.
 - **CRP:** rises 6–12h after insult; better for monitoring response (serial) than single early value; two normal CRPs 24h apart have high negative predictive value.
 - **Procalcitonin:** rises earlier (2–4h), more specific than CRP in first 48h; physiologic surge in first 24h of life limits interpretation.
 - **Lumbar puncture indications:** clinical signs of meningitis (seizures, bulging fontanelle), positive blood culture, LOS evaluation (always do LP in LOS workup unless unstable), unsatisfactory response to therapy. In EOS, LP if symptomatic or blood culture positive; routine LP in well-appearing EOS evaluation is debated — do it if meningitis suspected or culture positive. CSF interpretation: term WBC >20–30/mm³ abnormal; protein higher than older children; Gram stain.
 - Urine culture: low yield in first 72h (EOS); include in LOS workup (suprapubic or catheterized).
- **Empiric antibiotics:**
 - **EOS: ampicillin + gentamicin.** Ampicillin 50 mg/kg/dose IV q12h (<7 days); gentamicin 4 mg/kg/dose IV q24h (term). Add **cefotaxime** (50 mg/kg/dose q12h) if meningitis suspected (better CSF penetration than gentamicin; avoid ceftriaxone — displaces bilirubin, calcium precipitation).
 - **LOS: vancomycin + gentamicin** (covers CoNS/MRSA + gram-negatives); add cefotaxime if meningitis; add amphotericin B/fluconazole if fungal suspected.
- Narrow once cultures return (48–72h); stop if cultures negative and infant well (EOS rule-out 36–48h).
- **Prevention:** maternal GBS screening at 35–37 weeks with intrapartum penicillin prophylaxis (penicillin G 5 MU then 2.5–3 MU q4h), hand hygiene, line bundles, human milk.

Inborn Errors of Metabolism Presenting in the Neonate

- **Red flags:** parental consanguinity, previous sibling death/SIDS, poor feeding, vomiting, lethargy progressing to coma, seizures, hyperammonemia, metabolic acidosis with increased anion gap, hypoglycemia, unusual odor, hepatomegaly, cataracts.
- **Hyperammonemia differential** (ammonia >100 $\mu\text{mol/L}$ in neonate is abnormal; normal <50):
- **Urea cycle defects:** OTC deficiency (most common UCD, X-linked — males severely affected, females variable), CPS1, ASS, ASL deficiencies. Hallmarks: hyperammonemia with **respiratory alkalosis** (ammonia stimulates medullary respiratory center), normal glucose, no ketosis, low BUN.
- **Organic acidemias** (propionic, methylmalonic, isovaleric acidemia): hyperammonemia + **high anion gap metabolic acidosis** + ketosis + neutropenia/thrombocytopenia; isovaleric acidemia smells of "sweaty feet."
- **MSUD:** hyperammonemia is mild/late; dominant feature is branched-chain amino acid elevation.
- Transient hyperammonemia of the newborn (THAN): preterm infant, severe hyperammonemia without UCD — treat as UCD emergently.
- **Maple syrup urine disease (MSUD):** deficiency of **branched-chain α -ketoacid dehydrogenase** → accumulation of **leucine, isoleucine, valine**; **maple syrup/burnt sugar odor** of urine and cerumen; presents day 4–7 with poor feeding, lethargy, seizures, opisthotonos; **leucine is the neurotoxic** amino acid. Diagnosis: plasma amino acids, urine organic acids (alloisoleucine pathognomonic). Acute treatment: stop protein, IV dextrose + insulin (anabolism), dialysis for severe; chronic: BCAA-restricted diet, thiamine-responsive variant exists.
- **Galactosemia (classic, GALT deficiency):** autosomal recessive; presents after milk feeds with vomiting, jaundice, hepatomegaly, hypoglycemia, cataracts (**oil-drop cataracts**), and **E. coli sepsis** susceptibility. Diagnosis: reducing substances in urine (positive Clinitest, negative glucose oxidase), GALT enzyme assay, Beutler spot test. Treatment: **immediate lactose/galactose-free diet (soy formula)** — life-saving; cataracts may reverse if treated early. Long-term: ovarian failure, developmental delay despite diet.
- **Emergency management of suspected IEM:** stop all protein feeds, IV 10% dextrose (8–10 mg/kg/min glucose), correct acidosis, **ammonia scavengers** (sodium benzoate + sodium phenylacetate), consider **hemodialysis** (most effective ammonia removal), treat hyperammonemia >400 $\mu\text{mol/L}$ or encephalopathy aggressively. Draw critical samples BEFORE treatment: blood gas, glucose, ammonia, lactate, plasma amino acids, urine organic acids, acylcarnitine profile.
- **Newborn screening:** tandem MS/MS on dried blood spot at 24–48h screens MSUD, organic acidemias, fatty acid oxidation defects, PKU, galactosemia, hypothyroidism.

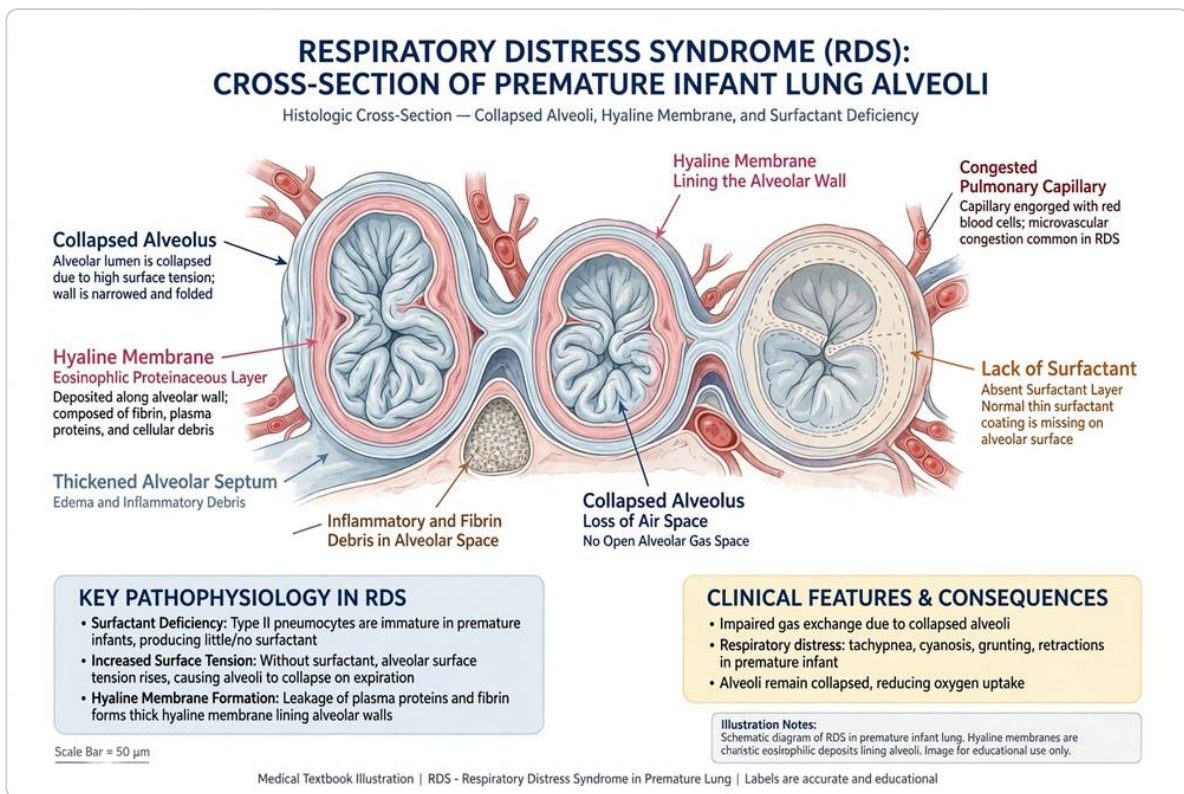


Figure 1.2 — RDS: surfactant deficiency and hyaline membranes

Apnea of Prematurity

- **Definition:** cessation of breathing ≥ 20 seconds, or shorter if accompanied by bradycardia (<100) or desaturation; common in infants <34 weeks (nearly universal <28 weeks) due to immature respiratory control.
- **Types:** central (no respiratory effort), obstructive (effort without airflow), mixed (most common).
- **Rule out secondary causes:** sepsis, hypoglycemia, anemia, PDA, GERD, intracranial pathology, NEC, electrolyte disturbances — new/worsening apnea is sepsis until proven otherwise.
- **Caffeine citrate** (drug of choice; CAP trial):
- **Loading dose 20 mg/kg IV/PO** (caffeine citrate; = 10 mg/kg caffeine base), **maintenance 5 mg/kg/day once daily** (may increase to 10 mg/kg/day).
- Therapeutic range 8–20 mcg/mL; wide safety margin, routine levels unnecessary.
- Benefits: reduces BPD, PDA ligation, improves neurodevelopmental outcome at 18–21 months.
- Continue until 34–36 weeks PMA and apnea-free for 5–7 days.
- **Alternatives:** aminophylline/theophylline (narrower therapeutic index, more GI side effects); doxapram (last resort, hypertension/GI effects).
- **Non-pharmacologic:** tactile stimulation, CPAP for obstructive/mixed apnea, prone positioning, avoid hypothermia, transfusion for anemia of prematurity.

Retinopathy of Prematurity

- **Pathophysiology:** two phases — Phase 1 (hyperoxia): supplemental O₂ suppresses VEGF → vaso-obliteration of developing retinal vessels; Phase 2 (hypoxia, ~32–34 weeks PMA): avascular retina becomes hypoxic → VEGF surge → pathologic neovascularization, fibrosis, retinal detachment.
- **Screening (AAP/AAO):** birth weight ≤1500 g OR gestational age ≤30 weeks; selected infants 1500–2000 g with unstable clinical course (prolonged ventilation, sepsis). First exam at **31 weeks PMA or 4 weeks chronological age, whichever is LATER**; follow-up per findings until vascularization complete.
- **ICROP classification:**
 - **Zones:** Zone I (posterior, circle centered on optic disc with radius twice disc–macula distance — worst prognosis), Zone II (mid-periphery), Zone III (anterior crescent — best prognosis).
 - **Stages:** 1 — demarcation line; 2 — ridge; 3 — extraretinal fibrovascular proliferation; 4 — partial retinal detachment (4A extrafoveal, 4B foveal); 5 — total retinal detachment.
 - **Plus disease:** dilation and tortuosity of posterior pole vessels (≥2 quadrants) — marker of activity/severity; pre-plus is intermediate.
 - **Aggressive posterior ROP (AP-ROP):** fulminant posterior disease, rapid progression.
 - **Type 1 ROP (treatment-requiring, ETROP):** Zone I, any stage with plus disease; Zone I, stage 3 without plus; Zone II, stage 2 or 3 with plus. Type 2: observe closely.
 - **Treatment:** **laser photocoagulation** of avascular retina (ablates VEGF source) — standard; **intravitreal anti-VEGF (bevacizumab)** preferred for Zone I/AP-ROP (BEAT-ROP trial) but higher recurrence risk, needs prolonged follow-up; surgery (scleral buckle/vitrectomy) for stage 4–5.
 - **Prevention:** judicious oxygen (SpO₂ 90–95%), avoid fluctuations, adequate nutrition/IGF-1, minimize transfusions.

Neonatal Jaundice

- **Physiologic jaundice:** appears day 2–3, peaks day 3–5 (<12–15 mg/dL term), resolves by 1 week (term) / 2 weeks (preterm); unconjugated; due to increased RBC turnover, immature UGT1A1 conjugation, increased enterohepatic circulation.
- **Breastfeeding jaundice** (early, inadequate intake, exaggerated enterohepatic circulation) vs **breast milk jaundice** (late, day 5–7, β-glucuronidase/pregnanediol in milk deconjugating bilirubin; persists weeks; benign — continue breastfeeding).
- **Pathologic jaundice criteria** (any one): onset <24 hours of age; rise >5 mg/dL/day or >0.2 mg/dL/hour; total bilirubin >95th percentile for age in hours (Bhutani nomogram); **direct (conjugated) bilirubin >2 mg/dL** or >20% of total; jaundice persisting >1 week (term) or >2 weeks (preterm); pale stools/dark urine, hepatosplenomegaly.
- **Differential of early/pathologic jaundice:** hemolytic — ABO/Rh incompatibility (positive DCT/Coombs), G6PD deficiency, hereditary spherocytosis, cephalohematoma/bruising; infective — sepsis, TORCH; metabolic — hypothyroidism, galactosemia; conjugated — biliary atresia (pale stools by 2 weeks = urgent Kasai before 60 days), choledochal cyst, neonatal hepatitis.

- **Evaluation:** total + direct bilirubin, blood group/Rh of mother and baby, DCT, CBC/reticulocyte count, G6PD screen, review Bhutani hour-specific nomogram.
- **Phototherapy:** converts unconjugated bilirubin to water-soluble photoisomers excreted in bile/urine; blue-green light 460–490 nm; irradiance $\geq 30 \mu\text{W}/\text{cm}^2/\text{nm}$; maximize skin exposure, eye protection, monitor temperature/hydration. AAP 2022: phototherapy thresholds based on gestational age, age in hours, and neurotoxicity risk factors.
- **Exchange transfusion (double-volume):**
- **AAP thresholds (term, ≥ 35 weeks):** approximately $\geq 25 \text{ mg/dL}$ total bilirubin in well infants; **lower ($\sim 20 \text{ mg/dL}$)** with neurotoxicity risk factors — **isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, albumin $< 3.0 \text{ g/dL}$.**
- Indications regardless of level: signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high-pitched cry — **kernicterus spectrum**), or bilirubin rising despite intensive phototherapy.
- **Volume:** double-volume exchange = **160 mL/kg** (term; $\sim 2\times$ blood volume of 80 mL/kg); removes $\sim 85\%$ of circulating RBCs and $\sim 50\%$ of bilirubin; use reconstituted whole blood (O Rh-negative or type-specific, < 7 days old).
- Complications: hypocalcemia (citrate binding — give calcium gluconate if symptomatic/QTc prolonged), hyperkalemia, hypoglycemia, arrhythmia, NEC, infection, death ($\sim 0.3\text{--}0.5\%$).
- **IVIG:** 0.5–1 g/kg over 2 hours in isoimmune hemolytic disease when bilirubin rising despite intensive phototherapy or within 2–3 mg/dL of exchange level — reduces need for exchange transfusion.
- **Kernicterus prevention pearl:** never let a jaundiced infant $< 24\text{h}$ old go uninvestigated; ABO incompatibility (mother O, baby A/B) is the commonest hemolytic cause in term well infants.

Practice MCQs

Q1. A term infant is born limp and apneic with HR 80 bpm after drying and stimulation. The next best step is: A) Provide free-flow oxygen B) Begin chest compressions C) Administer epinephrine D) Initiate positive pressure ventilation **Answer: D** — Apnea/gasping or HR < 100 bpm after initial steps is an indication for PPV within the Golden Minute. Compressions are only for HR < 60 after 30 s of effective PPV; epinephrine follows failed compressions.

Q2. During neonatal resuscitation, chest compressions are started but HR remains 50 bpm after 60 seconds of coordinated compressions and effective ventilation. The correct epinephrine dose/route is: A) 0.1–0.3 mL/kg of 1:10,000 IV B) 1 mL/kg of 1:1000 IV C) 0.5 mL/kg of 1:1000 endotracheal D) 0.01 mL/kg of 1:10,000 IV **Answer: A** — IV/IO epinephrine is 0.1–0.3 mL/kg of 1:10,000 (0.01–0.03 mg/kg), repeated every 3–5 min. The endotracheal dose is 0.5–1 mL/kg of 1:10,000 while IV access is obtained.

Q3. A 28-week preterm infant develops grunting, nasal flaring, and retractions 30 minutes after birth. Chest X-ray shows diffuse ground-glass opacities with air bronchograms. The most likely diagnosis is: A) Transient tachypnea of newborn B) Neonatal pneumonia C) Meconium aspiration syndrome D) Respiratory distress syndrome **Answer: D** — Preterm infant with immediate-onset distress and ground-glass X-ray with air bronchograms is

classic RDS from surfactant deficiency. TTN occurs in term/late-preterm C-section babies with perihilar streaking.

Q4. A mother at 30 weeks gestation is in preterm labor. The evidence-based antenatal steroid regimen is: A) Betamethasone 12 mg IM every 24 hours × 2 doses B) Dexamethasone 12 mg IM single dose C) Hydrocortisone 100 mg IV every 8 hours D) Prednisolone 40 mg oral daily × 5 days **Answer: A** — Betamethasone 12 mg IM q24h × 2 doses (or dexamethasone 6 mg IM q12h × 4 doses) given to mothers at 24–34 weeks at risk of delivery within 7 days reduces RDS, IVH, NEC, and mortality.

Q5. A 26-week, 800 g infant with RDS remains intubated after the first surfactant dose. The preferred poractant alfa (Curosurf) repeat dosing is: A) 100 mg/kg every 6 hours up to 4 doses B) 200 mg/kg every 24 hours C) Single dose only; repeats are ineffective D) 100 mg/kg every 12 hours, maximum 3 doses total **Answer: D** — Poractant alfa: 200 mg/kg (2.5 mL/kg) first dose, then 100 mg/kg (1.25 mL/kg) every 12 hours if still intubated, maximum 3 doses total. (Beractant is 100 mg/kg q6h up to 4 doses.)

Q6. An infant born at 27 weeks gestation requires supplemental oxygen for 30 days. At 36 weeks postmenstrual age, he needs 25% oxygen via nasal cannula. The correct classification is: A) Mild BPD B) Severe BPD C) Chronic lung disease, not BPD D) Moderate BPD **Answer: D** — NIH definition: $O_2 \geq 28$ days establishes BPD; at 36 weeks PMA (<32-week infant), <30% O_2 = moderate BPD, $\geq 30\%$ O_2 or positive pressure = severe, room air = mild.

Q7. Which intervention has NOT been shown to reduce the incidence of bronchopulmonary dysplasia? A) Vitamin A 5000 IU IM three times weekly B) Caffeine citrate therapy C) Inhaled corticosteroids D) Early nasal CPAP avoiding intubation **Answer: C** — Inhaled corticosteroids do not reduce BPD. Vitamin A, caffeine (CAP trial), and early CPAP are proven preventive strategies; postnatal systemic dexamethasone reduces BPD but increases cerebral palsy risk.

Q8. A 10-day-old 1200 g preterm infant develops abdominal distension, bloody stools, and apnea. Abdominal X-ray shows pneumatosis intestinalis without free air. Bell staging and management are: A) Stage IIA — NPO, NG decompression, ampicillin + gentamicin + metronidazole B) Stage IA — observe and continue feeds C) Stage IIB — peritoneal drain only D) Stage IIIB — emergency laparotomy **Answer: A** — Pneumatosis intestinalis defines definite NEC (Stage IIA, mildly ill without systemic toxicity). Management is medical: NPO, decompression, broad-spectrum antibiotics covering anaerobes. Pneumoperitoneum (IIIB) mandates surgery.

Q9. The single absolute indication for surgical intervention in necrotizing enterocolitis is: A) Portal venous gas on X-ray B) Thrombocytopenia <50,000 C) Pneumoperitoneum D) Fixed dilated loop on serial films **Answer: C** — Pneumoperitoneum indicates perforation and is an absolute indication for surgery. Portal venous gas, fixed loops, and clinical deterioration are relative indications prompting surgical consultation.

Q10. A term infant with severe birth asphyxia is stuporous, flaccid with absent Moro reflex, and has prolonged seizures on day 1. This corresponds to Sarnat stage: A) Stage I B) Stage II C) Stage III D) Cannot be staged before 72 hours **Answer: C** — Stupor/coma, flaccidity, absent primitive reflexes, and refractory seizures define Sarnat Stage III (severe), which carries >75% risk of death or severe disability.

Q11. A 38-week infant born through meconium with cord pH 6.9 is lethargic, hypotonic with weak reflexes at 3 hours of age. The most appropriate next step is: A) Begin therapeutic hypothermia after confirming eligibility B) Start phenobarbital prophylaxis C) Immediate MRI brain D) Observe for 24 hours before deciding **Answer: A** —

This infant meets cooling criteria: ≥ 36 weeks, ≤ 6 hours old, cord pH ≤ 7.0 , and moderate (Sarnat II) encephalopathy. Therapeutic hypothermia ($33.5^{\circ}\text{C} \times 72\text{h}$) must begin within 6 hours; MRI is done at day 4–10.

Q12. Which of the following is an exclusion criterion for therapeutic hypothermia in HIE? A) Cord pH 6.95 B) Gestational age 37 weeks C) Major congenital anomaly D) 10-minute Apgar score of 4 **Answer: C** — Major congenital anomalies exclude infants from cooling trials/protocols. Cord pH ≤ 7.0 , term gestation, and low Apgar are inclusion features. Other exclusions: severe IUGR, moribund state, severe coagulopathy with active bleeding.

Q13. A 5-day-old term infant presents with poor feeding, lethargy, temperature instability, and respiratory distress. Mother had PROM for 24 hours. Blood culture is pending. The best empiric antibiotic regimen is: A) Vancomycin + ceftriaxone B) Meropenem + vancomycin C) Cefotaxime alone D) Ampicillin + gentamicin **Answer: D** — Early-onset sepsis ($<72\text{h}$... extended here as vertical transmission risk): ampicillin + gentamicin covers GBS, E. coli, and Listeria. Ceftriaxone is avoided in neonates (bilirubin displacement, calcium precipitation); add cefotaxime only if meningitis is suspected.

Q14. In the evaluation of suspected late-onset neonatal sepsis, which statement is correct? A) Lumbar puncture is unnecessary if blood culture is negative B) Coagulase-negative Staphylococcus is the most common organism C) Urine culture has no role after 72 hours D) CRP is most sensitive in the first 2 hours **Answer: B** — CoNS (line-related) is the commonest LOS pathogen. LP is mandatory in LOS workup; urine culture is included after 72h; CRP rises at 6–12h (procalcitonin rises earlier at 2–4h).

Q15. A 6-day-old neonate presents with vomiting, poor feeding, seizures, and a sweet/burnt-sugar odor to the urine. Labs show elevated branched-chain amino acids. The deficient enzyme is: A) Galactose-1-phosphate uridylyltransferase B) Branched-chain α -ketoacid dehydrogenase C) Ornithine transcarbamylase D) Phenylalanine hydroxylase **Answer: B** — Maple syrup odor + elevated leucine/isoleucine/valine = MSUD, caused by branched-chain α -ketoacid dehydrogenase deficiency. Leucine is the neurotoxic amino acid; alloisoleucine is pathognomonic.

Q16. A 4-day-old infant has hyperammonemia ($600\text{ }\mu\text{mol/L}$), respiratory alkalosis, normal glucose, and no ketosis. The most likely diagnosis is: A) Methylmalonic acidemia B) Maple syrup urine disease C) Urea cycle defect D) Galactosemia **Answer: C** — Hyperammonemia with respiratory alkalosis (ammonia stimulates the respiratory center), normal glucose, and absent ketosis is classic for a urea cycle defect (e.g., OTC deficiency). Organic acidemias cause high-anion-gap metabolic acidosis with ketosis instead.

Q17. A 10-day-old breastfed infant presents with vomiting, jaundice, hepatomegaly, cataracts, and E. coli sepsis. Urine shows reducing substances but is negative on glucose oxidase testing. The definitive treatment is: A) Lactose-free (soy-based) formula B) High-protein diet C) Copper chelation D) Biotin supplementation **Answer: A** — Cataracts + E. coli sepsis + reducing substances (non-glucose) = classic galactosemia (GALT deficiency). Immediate removal of lactose/galactose with soy formula is life-saving; cataracts may reverse with early treatment.

Q18. A 29-week preterm infant has recurrent apneic episodes with bradycardia. Sepsis workup is negative. The drug of choice and loading dose are: A) Aminophylline 10 mg/kg B) Caffeine citrate 20 mg/kg C) Doxapram 5 mg/kg D) Phenobarbital 20 mg/kg **Answer: B** — Caffeine citrate 20 mg/kg loading (then 5 mg/kg/day maintenance) is first-line for apnea of prematurity; the CAP trial showed it also reduces BPD and improves neurodevelopment. Aminophylline has a narrower therapeutic index; doxapram is last-resort.

Q19. ROP screening is indicated in an infant with: A) Birth weight 1600 g, 33 weeks, stable course B) Term infant with prolonged oxygen C) Birth weight 1800 g, 34 weeks, stable course D) Birth weight 1400 g, 29 weeks gestation **Answer: D** — Screening criteria: birth weight ≤ 1500 g or GA ≤ 30 weeks (plus selected 1500–2000 g infants with unstable courses). First exam at 31 weeks PMA or 4 weeks chronological age, whichever is later.

Q20. A preterm infant's eye exam shows Zone I, Stage 3 ROP without plus disease. According to ETROP criteria, this is: A) Type 2 ROP — observe B) Type 1 ROP — treat with laser C) Pre-plus disease — re-examine in 1 week D) AP-ROP — requires vitrectomy **Answer: B** — Type 1 (treatment-requiring) ROP includes Zone I, stage 3 even without plus disease; also Zone I any stage with plus, and Zone II stage 2/3 with plus. Laser photocoagulation of the avascular retina is standard treatment.

Q21. Which finding defines pathologic (non-physiologic) neonatal jaundice? A) Onset on day 3 with peak 10 mg/dL B) Jaundice appearing within the first 24 hours of life C) Breast milk jaundice persisting 3 weeks in a thriving infant D) Bilirubin rise of 3 mg/dL/day **Answer: B** — Jaundice in the first 24 hours is always pathologic. Other criteria: rise >5 mg/dL/day, direct bilirubin >2 mg/dL, persistence >1 week (term)/2 weeks (preterm).

Q22. A term 3-day-old infant with ABO incompatibility has total bilirubin 26 mg/dL despite intensive phototherapy and is increasingly lethargic with hypertonia. The next best step is: A) Exchange transfusion B) Continue phototherapy and recheck in 12 hours C) Phenobarbital D) IVIG 2 g/kg **Answer: A** — Bilirubin ≥ 25 mg/dL in a term infant plus signs of acute bilirubin encephalopathy (lethargy, hypertonia) is an indication for double-volume exchange transfusion (160 mL/kg) regardless of exact level. IVIG (0.5–1 g/kg) is used when bilirubin is rising toward — but has not reached — exchange level.

Q23. During a double-volume exchange transfusion, the infant develops a prolonged QTc and carpopedal spasm. The most likely cause and treatment are: A) Hyperkalemia — calcium gluconate B) Citrate-induced hypocalcemia — IV calcium gluconate C) Hypoglycemia — IV dextrose bolus D) Hypothermia — rewarm blood **Answer: B** — Citrate in donor blood chelates calcium, causing hypocalcemia (prolonged QTc, tetany/seizures). Treat symptomatic hypocalcemia with IV calcium gluconate; monitor ionized calcium during the procedure.

Q24. A 27-week infant on CPAP develops sudden desaturation, hypotension, and asymmetric chest expansion with absent breath sounds on the right. Transillumination of the right chest is positive. The immediate management is: A) Increase CPAP pressure B) Needle thoracentesis of the right chest C) Surfactant administration D) Chest physiotherapy **Answer: B** — Sudden deterioration in a ventilated preterm with asymmetric chest and positive transillumination = tension pneumothorax. Immediate needle thoracentesis (2nd intercostal space, midclavicular line) followed by chest tube placement.

Q25. A mother is GBS-positive with inadequate intrapartum prophylaxis. Her term infant is well-appearing at 6 hours of age. The recommended management is: A) Discharge home with routine follow-up B) Lumbar puncture and cefotaxime C) Blood culture, CBC, and 48-hour observation with empiric ampicillin + gentamicin D) Oral amoxicillin for 7 days **Answer: C** — Inadequate IAP (<4 hours of penicillin before delivery) in a well-appearing term infant warrants limited evaluation (blood culture, CBC) plus empiric ampicillin + gentamicin with 36–48h observation; antibiotics are stopped if cultures are negative and the infant remains well. Routine LP is not required in a well-appearing infant.

Pediatric Cardiology

Chapter 2: Pediatric Cardiology

Pediatric Cardiology is the single highest-yield DM branch for NEET SS Pediatrics — Neonatology, Pediatric Cardiology, and Pediatric Critical Care aspirants all face heavy cardiology weightage. Expect 8–12 questions per paper, dominated by hemodynamics and cath-lab data (Qp:Qs, PVR, operability cutoffs), lesion-specific echo findings, surgical repair names with their physiology, and emergency algorithms (hypercyanotic spells, SVT, Kawasaki). This chapter is built around numbers, criteria, and decision points — exactly how NEET SS asks.

Acyanotic Lesions (Left-to-Right Shunts and Obstructive Lesions)

Ventricular Septal Defect (VSD)

- **Most common congenital heart defect** overall (isolated or with other lesions). Murmur: harsh holosystolic/pansystolic at left lower sternal border; thrill common with moderate-large defects.
- **Anatomic types:**
 - **Perimembranous (membranous)** — ~70–80% of VSDs; located in membranous septum beneath aortic valve; may develop **aortic cusp prolapse** with aortic regurgitation.
 - **Muscular** — mid-muscular, apical, or multiple ("Swiss-cheese" septum); highest rate of **spontaneous closure**.
 - **Outlet (supracristal/subarterial/doubly committed)** — beneath both semilunar valves; **never closes spontaneously**; strongly associated with **aortic valve prolapse and AR**; common in Asian populations.
 - **Inlet** — beneath AV valves; component of AV canal defects.
- **Natural history:** Small muscular VSDs frequently close spontaneously in the first 2 years of life. Large defects present at 4–8 weeks with CHF (tachypnea, poor feeding, failure to thrive) as pulmonary vascular resistance falls and left-to-right shunt increases.
- **Eisenmenger physiology:** Unrepaired large VSD → chronic high pulmonary blood flow → pulmonary vascular obstructive disease → PVR exceeds SVR → **shunt reversal (right-to-left)** → cyanosis, clubbing, erythrocytosis. **Closure is contraindicated** once Eisenmenger develops — closing the "pop-off" precipitates fatal RV failure.
- **Closure indications:** CHF refractory to medical therapy, failure to thrive, Qp:Qs $\geq$ 2:1 with LV volume overload, or any VSD with aortic cusp prolapse/AR. Surgical patch closure typically at 3–6 months for large symptomatic defects; device closure for selected muscular defects.

Atrial Septal Defect (ASD)

- **Types:** **Secundum** (fossa ovalis defect — most common, ~75%); **Primum** (lower septum, part of AV canal spectrum — strongly associated with **Down syndrome**); **Sinus venosus** (superior, near SVC entry — associated with **partial anomalous pulmonary venous return**, usually right upper pulmonary vein to SVC/RA junction); coronary sinus defect (rare).
- **Clinical:** Often asymptomatic in childhood; murmur is a **systolic ejection murmur at left upper sternal border** (increased pulmonary flow across normal pulmonary valve, NOT flow across the ASD itself) + **fixed widely split S2** (the hallmark — RV volume overload delays P2 equally in inspiration and expiration). Large defects → RV enlargement, atrial arrhythmias in adulthood.
- **Syndrome associations:** Secundum ASD — **Holt-Oram syndrome** (upper limb anomalies + ASD); primum ASD — Down syndrome.
- **Echo findings:** Direct visualization of defect, RV volume overload (dilated RA/RV), paradoxical septal motion; **bubble/contrast echo** shows right-to-left passage; **TEE** for device sizing and rim assessment.
- **Closure indications:** Qp:Qs $\geq 1.5:1$ with evidence of **RV volume overload** (the NEET SS cutoff — memorize it), paradoxical embolism, or documented orthodeoxia. **Device (Amplatzer) closure** for secundum ASD with adequate rims (≥ 5 mm, except aortic rim); **surgical closure** for primum, sinus venosus (with PAPVR baffling/Warden procedure), or large/deficient-rim secundum defects. Elective closure typically at 2–4 years; do NOT close if Eisenmenger physiology present.
- **Exam trap:** Primum ASD murmur and fixed split S2 are identical to secundum; the differentiator is the **left axis deviation on ECG** (primum) vs right axis deviation/incomplete RBBB (secundum).

Patent Ductus Arteriosus (PDA)

- **Presentation:** Continuous "**machinery**" murmur at left upper sternal border/infraclavicular area, **bounding pulses, wide pulse pressure**, hyperdynamic precordium. In preterm neonates: apnea, ventilator dependence, NEC risk from diastolic steal.
- **Medical closure (preterm neonates):** Cyclooxygenase inhibitors block prostaglandin-mediated ductal patency:
- **Indomethacin:** 0.2 mg/kg IV first dose, then 0.1 mg/kg at 12 and 24 hours (standard 3-dose course). Contraindicated in renal failure (rising creatinine/oliguria), active bleeding, platelets $< 50,000$ – $60,000$, NEC.
- **Ibuprofen:** 10 mg/kg first dose, then 5 mg/kg at 24 and 48 hours; fewer renal/mesenteric side effects than indomethacin.
- **Paracetamol (acetaminophen):** 15 mg/kg every 6 hours; acts via peroxidase inhibition — used when COX inhibitors are contraindicated or fail; increasingly first-line in many NICUs for its renal safety.
- All are ineffective once the ductus is fibrosed (term infants beyond ~2 weeks) — then **surgical ligation** (or device closure in larger infants/children).
- **Associations:** **Maternal rubella** (classic triad: PDA, cataracts, sensorineural deafness), prematurity, high altitude.

Atrioventricular Septal Defect (AVSD / AV Canal)

- **Embryology:** Failure of endocardial cushion fusion → common AV valve, primum ASD continuous with inlet VSD.
- **Down syndrome:** ~40–50% of complete AVSD occurs in trisomy 21; conversely AVSD is the **most common cardiac lesion in Down syndrome** (complete form). Also seen in heterotaxy syndromes.
- **Rastelli classification** (based on chordal attachments of the superior bridging leaflet):
 - **Type A:** Chordae attach to the crest of the ventricular septum (most common).
 - **Type B:** Chordae attach to an anomalous papillary muscle on the RV side.
 - **Type C:** Superior leaflet is free-floating with no chordal attachments to the septum (associated with Tetralogy of Fallot).
- **Imaging:** "Goose-neck deformity" of the LV outflow on angiography (elongated, narrowed LVOT); ECG shows **left axis deviation** with left anterior hemiblock pattern.
- **Management:** Repair at **3–6 months** (earlier than VSD/ASD) because pulmonary vascular disease develops **rapidly** in AVSD, especially with Down syndrome. Two-patch or modified single-patch technique; postoperative **left AV valve regurgitation** and **complete heart block** are the feared complications.

Coarctation of the Aorta

- **Neonate:** Presents when the ductus arteriosus closes (24–72 hours) — **cardiogenic shock, metabolic acidosis, absent/delayed femoral pulses**. **Differential cyanosis** may occur if PDA persists with right-to-left shunting (pink upper body, blue lower body). **Prostaglandin E1 infusion** to reopen the ductus is the life-saving bridge.
- **Older child:** **Upper-extremity hypertension with lower-extremity hypotension, brachial-femoral pulse delay**, systolic murmur at left interscapular area. **Rib notching** (inferior rib erosion by dilated intercostal collaterals) appears after age 5–8 years — it takes years of collateral flow to erode bone, so its absence in an infant means nothing.
- **Associations:** **Bicuspid aortic valve** (~50% of coarctation patients), **Turner syndrome (45,XO)** — coarctation is the classic cardiac lesion of Turner.
- **Management:** Neonatal: PGE1 + surgical repair (end-to-end anastomosis, subclavian flap, or extended arch repair). Older child: **balloon angioplasty ± stenting** is preferred for native coarctation beyond infancy and for recoarctation. Lifelong follow-up for **residual hypertension and aneurysm** at repair site.

Aortic Stenosis

- Usually **bicuspid aortic valve** (most common cause of AS in children and young adults). Ejection systolic murmur at right upper sternal border radiating to carotids, with ejection click.
- **Critical AS in neonate:** Duct-dependent systemic circulation → PGE1 + urgent **balloon aortic valvuloplasty** (surgical valvotomy if balloon fails).
- **Intervention threshold:** Peak-to-peak catheter gradient ≥ 50 mmHg (or mean echo gradient ≥ 40 mmHg) with symptoms, LV dysfunction, or ST changes. Balloon valvuloplasty is first-line in children; **aortic valve**

replacement (Ross procedure — pulmonary autograft — preferred in growing children to avoid anticoagulation) for severe AR or failed valvuloplasty.

- **Exam danger:** Syncope, angina, or exertional symptoms in AS are **red flags for sudden death** — restrict strenuous exercise.

Pulmonary Stenosis

- Most common **isolated** obstructive lesion; classic association with **Noonan syndrome** (dysplastic pulmonary valve).
- Dome-shaped valve with post-stenotic dilatation of main pulmonary artery; ejection systolic murmur at left upper sternal border with ejection click that **decreases with inspiration** (unlike aortic click).
- **Balloon pulmonary valvuloplasty** is the treatment of choice when peak-to-peak gradient ≥ 40 mmHg (or lower with symptoms/RV dysfunction). Excellent long-term results; mild residual pulmonary regurgitation is expected and well tolerated.

Cyanotic Lesions

Tetralogy of Fallot (TOF)

- **Tetrad — memorize as "PROVe":** Pulmonary (RVOT) obstruction, **R**ight ventricular hypertrophy, **O**verriding aorta, **V**entricular septal defect (malalignment type). **Boot-shaped heart (coeur en sabot)** on chest X-ray from RVH with upturned apex and concave pulmonary bay; **right aortic arch** in ~25%.
- **Pathophysiology of cyanosis:** Severity of cyanosis depends on the degree of **RVOT obstruction**, not the VSD size. Obstruction is both fixed (infundibular hypoplasia) and **dynamic (infundibular spasm)**.
- **Hypercyanotic ("tet") spells:** Triggered by crying, feeding, fever, dehydration — anything that lowers SVR or provokes infundibular spasm. Spasm $\rightarrow$ sudden increase in right-to-left shunt across the VSD $\rightarrow$ profound cyanosis, hyperpnea, agitation $\rightarrow$ limpness, syncope, seizures, death. The murmur of PS **disappears during a spell** (no forward flow across RVOT) — a favorite exam clue.
- **Spell management (numbered algorithm):**
 - **Knee-chest position** (or squatting in older children) — increases SVR and venous return.
 - **High-flow oxygen** — pulmonary vasodilation, reduces hypoxic pulmonary vasoconstriction.
 - **IV fluid bolus** — increases preload and RV filling.
 - **Morphine 0.1 mg/kg SC/IV** — reduces hyperpnea and catecholamine-driven infundibular spasm.
 - **Propranolol** — IV 0.01–0.02 mg/kg or oral for prophylaxis; beta-blockade relieves infundibular spasm.
 - **Phenylephrine** (pure alpha-agonist) IV — raises SVR, forcing blood across the RVOT into the lungs.
 - **Sodium bicarbonate** if severe metabolic acidosis; **esmolol infusion** in ICU; emergent surgical intervention if refractory.
- **Definitive repair:** Complete intracardiac repair (VSD patch closure + RVOT resection/patch) at **3–6 months** electively. **Modified Blalock-Taussig shunt** (Gore-Tex graft from subclavian to pulmonary artery) as palliation for symptomatic neonates or unfavorable anatomy. Long-term post-repair issues: **pulmonary**

regurgitation (may need pulmonary valve replacement), residual VSD, RV dysfunction, ventricular arrhythmias/sudden death (QRS > 180 ms is a risk marker).

Transposition of the Great Arteries (TGA)

- **d-TGA:** Aorta arises from RV, pulmonary artery from LV — **two parallel circulations**; survival depends entirely on **mixing lesions** (ASD/PFO, VSD, PDA). Profound cyanosis from birth in an otherwise comfortable infant ("blue baby, no distress" — the circulation is parallel, so lungs are fine).
- **X-ray:** "**Egg-on-side**" appearance with **narrow mediastinum** (thymic involution + abnormal great vessel relationship).
- **Emergency stabilization:** **PGE1** to keep ductus open + **balloon atrial septostomy (Rashkind procedure)** — bedside in NICU, tears the atrial septum to improve mixing.
- **Definitive repair:** **Arterial switch operation (Jatene)** — transect and swap the great arteries with **coronary artery reimplantation**; performed in the **first 2 weeks of life** before LV "deconditions" (LV must still be able to handle systemic pressure). **Atrial switch (Mustard/Senning)** is historical — leaves the RV as systemic ventricle → late RV failure and arrhythmias; asked only as a complication question.
- **TGA with VSD + pulmonary stenosis** → **Rastelli procedure** (RV-to-PA conduit + VSD baffling of LV to aorta).

Truncus Arteriosus

- Single common arterial trunk arising from the heart, supplying systemic, pulmonary, and coronary circulations + a **VSD** (always present). **Collett & Edwards classification** (Type I–IV based on pulmonary artery origin pattern); truncal valve is often dysplastic/stenotic/regurgitant.
- Presents with **CHF + mild cyanosis** in the first weeks as PVR falls and pulmonary overcirculation develops. High risk of **early pulmonary vascular disease** — repair in the **neonatal period** (Rastelli-type repair: VSD closure + RV-to-PA homograft conduit). **22q11.2 deletion (DiGeorge)** association.

Total Anomalous Pulmonary Venous Return (TAPVR)

- All four pulmonary veins drain to the systemic venous circulation (RA or its tributaries) instead of the LA. An **ASD/PFO is obligatory for survival** (the only route for pulmonary venous blood to reach the left heart).
- **Types:** **Supracardiac** (most common — pulmonary veins → vertical vein → innominate → SVC; "**snowman**"/**figure-of-8** on X-ray), **Cardiac** (to coronary sinus or RA directly — least obstructed), **Infracardiac** (below diaphragm → portal system; **almost always obstructed**), **Mixed**.
- **Obstructed TAPVR:** Surgical emergency — severe cyanosis + **pulmonary edema ("white-out" lungs)** from birth, no cardiomegaly initially. Infracardiac type is the classic obstructed form. **Do NOT give prolonged PGE1** hoping for improvement — go to surgery.
- **Unobstructed TAPVR:** Mild cyanosis, RV volume overload, presentation similar to large ASD; repair electively but early (first months). Postoperative **pulmonary vein stenosis** is the dreaded complication.

Tricuspid Atresia

- Absent tricuspid valve → hypoplastic RV; survival requires **ASD** (right-to-left) and **VSD or PDA** (to supply pulmonary blood flow). Cyanosis severity depends on pulmonary blood flow.
- **ECG clue: Left axis deviation with LVH** in a cyanotic infant — essentially diagnostic pattern (most other cyanotic lesions show RAD/RVH).
- Management follows the **single-ventricle pathway**: PGE1 ± BT shunt neonatally → **bidirectional Glenn** at 4–6 months → **Fontan** at 2–4 years.

Hypoplastic Left Heart Syndrome (HLHS)

- Underdeveloped LV, mitral/aortic atresia or severe stenosis; systemic circulation is **duct-dependent** — collapse when ductus closes. Requires **PGE1 from birth**.
- **Staged palliation (Norwood pathway)**:
 - **Stage I — Norwood** (neonatal): atrial septectomy, neoaorta reconstruction (using pulmonary trunk), and pulmonary blood flow via **modified BT shunt** or **Sano shunt** (RV-to-PA conduit — better diastolic coronary perfusion, no diastolic steal).
 - **Stage II — Bidirectional Glenn** (4–6 months): SVC connected directly to pulmonary arteries (cavopulmonary anastomosis); IVC blood still returns to the heart.
 - **Stage III — Fontan** (2–4 years): IVC (via extracardiac conduit or lateral tunnel) connected to pulmonary arteries — complete separation, systemic venous return flows **passively** to lungs without a ventricular pump.
- Alternative: cardiac transplantation (limited donor availability). **Hybrid procedure** (bilateral PA bands + ductal stent) for high-risk neonates.

Ebstein Anomaly

- **Apical displacement of the septal and posterior tricuspid leaflets** ($\geq 8 \text{ mm/m}^2$ body surface area) → **atrialized portion of RV**, severe tricuspid regurgitation, RA enlargement.
- **ECG**: Giant P waves, **RBBB pattern**; **WPW (accessory pathway) in 10–25%** — the strongest lesion–arrhythmia association in congenital cardiology.
- **Maternal lithium** exposure association. Presentation ranges from neonatal cyanosis/CHF (severe) to incidental murmur in adults (mild). Surgical: **cone reconstruction** of tricuspid valve ± ASD closure; ablation of accessory pathway.

Hemodynamics & Cardiac Catheterization Data

Shunt Calculation (Fick Principle)

- $\text{Qp:Qs} = (\text{Systemic arterial O}_2 \text{ saturation} - \text{Mixed venous O}_2 \text{ saturation}) \div (\text{Pulmonary venous O}_2 \text{ saturation} - \text{Pulmonary arterial O}_2 \text{ saturation})$
- $\text{Qp:Qs} = (\text{SaO}_2 - \text{SvO}_2) / (\text{SpvO}_2 - \text{SpaO}_2)$

- A step-up in oxygen saturation between chambers localizes the shunt: RA step-up $\geq 7\%$ → ASD-level; RV step-up $\geq 5\%$ → VSD-level; PA step-up $\geq 5\%$ → PDA-level (aortic-to-PA shunt). Mixed venous saturation is best sampled from the **SVC** (above any shunt).
- **Oximetry run** is the cath-lab method for shunt detection and quantification; assumed pulmonary venous saturation ~95–98% if not directly measured.

Pulmonary Vascular Resistance and Operability

- **PVR (Wood units) = (Mean PAP – Mean LAP or PCWP) ÷ Pulmonary blood flow (Qp); indexed PVRi = PVR × BSA (Wood units·m²).**
- **Operability criteria (memorize these cutoffs — asked every year):**
- **PVRi < 6 WU·m²** (or PVR/SVR ratio < 0.3) → **operable** — close the defect.
- **PVRi 6–8 WU·m²** → **borderline/gray zone** — perform **acute vasoreactivity testing** (100% oxygen ± inhaled nitric oxide); a fall in PVR by $\geq 20\%$ with preserved cardiac output suggests reversibility.
- **PVRi > 8–10 WU·m²** (or PVR/SVR > 0.5) → **inoperable** — Eisenmenger physiology; closure will kill. Manage medically (see pulmonary hypertension section).
- **Vasoreactivity testing** is also used to select pulmonary hypertension patients for calcium-channel-blocker therapy (responders only).

Key Cath Numbers for NEET SS

- Normal mean PAP < 25 mmHg at rest (newer definition: > 20 mmHg = pulmonary hypertension); normal PVR < 3 WU (< 2 WU·m² indexed in children).
- **Aortic stenosis:** intervene at peak-to-peak gradient ≥ 50 mmHg. **Pulmonary stenosis:** balloon valvuloplasty at peak-to-peak gradient ≥ 40 mmHg. **Coarctation:** intervene at peak-to-peak gradient ≥ 20 mmHg with hypertension or LVH.
- Transseptal LA pressure (PCWP) estimates pulmonary venous/LA pressure; a high PCWP with high PAP suggests **pulmonary venous hypertension** (left-heart disease), not pulmonary arterial hypertension.

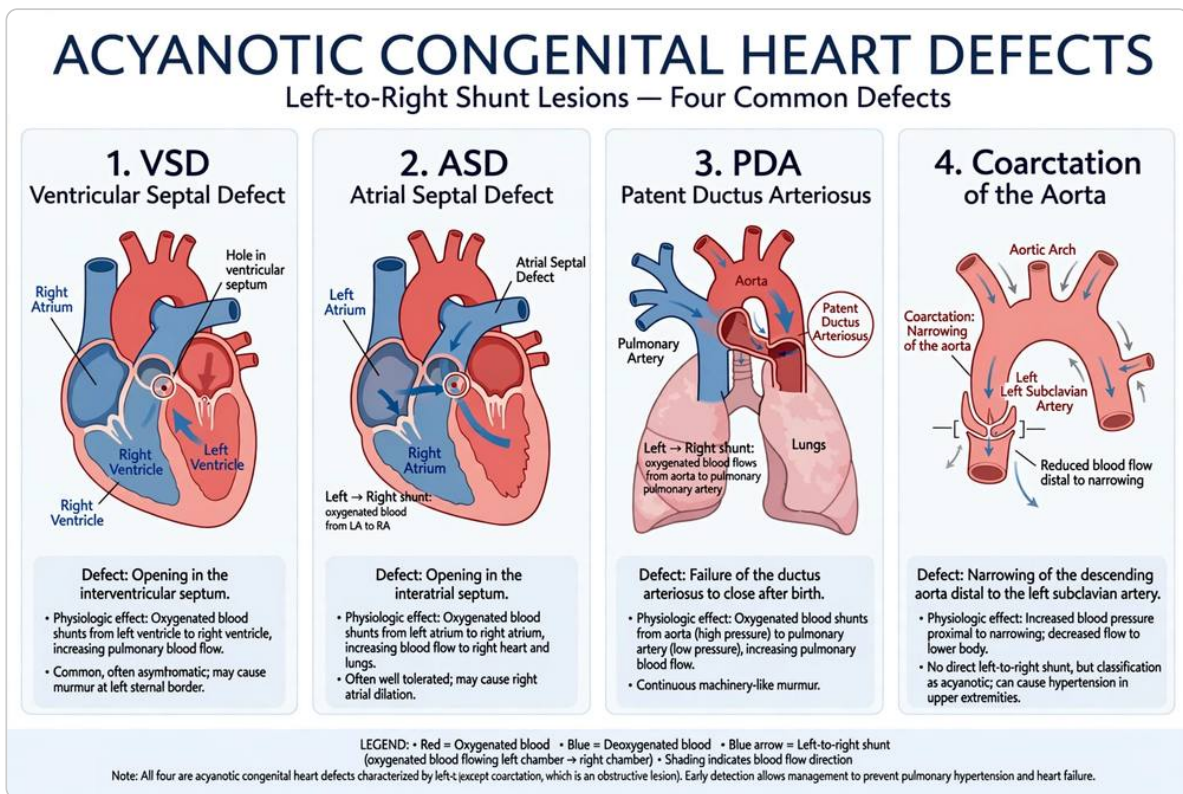


Figure 2.1 — Acyanotic congenital heart defects

Surgical Repairs: Shunts and Single-Ventricle Physiology

Systemic-to-Pulmonary Shunts

- **Modified Blalock-Taussig (BT) shunt:** Gore-Tex interposition graft between **subclavian artery and ipsilateral pulmonary artery** — the workhorse palliative shunt for TOF, tricuspid atresia, and pulmonary atresia. Complications: shunt thrombosis (heparin/aspirin prophylaxis), **pulmonary overcirculation/CHF** if too large, subclavian steal, distortion of PA.
- **Central shunt:** Direct Gore-Tex graft from ascending aorta to main pulmonary artery (for tiny neonates). **Waterston** (ascending aorta–RPA) and **Potts** (descending aorta–LPA) shunts are **historical** — abandoned due to uncontrollable pulmonary overcirculation and Eisenmenger risk; asked only as "which shunt is obsolete."

Arterial Switch (Jatene) vs Atrial Switch vs Rastelli

- **Arterial switch:** Anatomic correction for d-TGA; **coronary transfer is the critical step** — kinking causes ischemia/infarction. Long-term concerns: **neoaortic root dilatation/AR, coronary ostial stenosis, supraaortic pulmonary stenosis**.
- **Rastelli procedure:** For TGA + VSD + LVOT obstruction (or truncus): VSD patch baffles LV flow to the aorta + **RV-to-PA extracardiac conduit**. Conduit will need **replacement as the child grows** (no growth potential) — conduit stenosis/degeneration is the long-term issue.

Glenn and Fontan Physiology

- **Bidirectional Glenn (BDG):** SVC → pulmonary arteries (end-to-side). Pulmonary blood flow becomes **passive and non-pulsatile** from the upper body; IVC blood still mixes in the heart → mild residual cyanosis (sats 75–85%) is expected and normal.
- **Fontan completion:** IVC → pulmonary arteries via extracardiac conduit or lateral tunnel, usually **fenestrated** (small ASD-like pop-off to decompress high venous pressures at the cost of mild cyanosis). Post-Fontan saturations 90–95%.
- **Fontan physiology = chronically elevated systemic venous pressure with low cardiac output reserve.** There is no subpulmonary ventricle — pulmonary flow depends on the pressure gradient between systemic veins and the left atrium.
- **Fontan complications (high-yield list):**
 - **Protein-losing enteropathy (PLE)** — intestinal lymphangiectasia from venous/lymphatic congestion; hypoalbuminemia, edema, immunodeficiency; diagnosed by **elevated fecal alpha-1 antitrypsin**. Treat by lowering venous pressure (fenestration creation, pulmonary vasodilators, transplant evaluation).
 - **Plastic bronchitis** — branching airway casts from lymphatic leak into bronchi; life-threatening airway obstruction; treated with airway clearance, inhaled tPA/heparin, lymphatic interventions.
 - Atrial arrhythmias (intra-atrial reentry), thromboembolism (anticoagulation indicated), **Fontan-associated liver disease** (fibrosis/cirrhosis from chronic congestion — screen with elastography), cyanosis from venovenous collaterals.

Arrhythmias

Supraventricular Tachycardia (SVT)

- Most common symptomatic arrhythmia in children; usually **AV reentrant tachycardia** via accessory pathway (orthodromic) or AVNRT. Infants present with **CHF, poor feeding, pallor** (not palpitations — they can't report them); heart rate typically **220–300 bpm** in infants.
- **Acute management (numbered steps):**
 - Assess stability — hypotension, shock, or poor perfusion → **synchronized cardioversion (0.5–1 J/kg, double if needed)**.
 - Stable SVT → **vagal maneuvers: ice-cold cloth to the face** (diving reflex) in infants; **Valsalva/blowing through a straw** in older children. Carotid massage is avoided in small children.
 - **Adenosine: 0.1 mg/kg rapid IV push (max 6 mg)** with immediate saline flush; if no conversion, **0.2 mg/kg (max 12 mg)**. Give through the most proximal large-bore IV. Warn of transient flushing/chest discomfort/asystole.
 - Refractory → consider **esmolol, amiodarone**, or synchronized cardioversion; consult cardiology.
 - **Prevention:** Propranolol or digoxin for infants (avoid digoxin if WPW with antegrade conduction); **radiofrequency ablation** is definitive for children > 15 kg or > 4–5 years with recurrent SVT.

Wolff-Parkinson-White (WPW) Syndrome

- **ECG triad:** Short PR interval (< 120 ms) + delta wave (slurred upstroke of QRS) + wide QRS. Accessory (Bundle of Kent) pathway bypasses AV node.
- **Danger:** In **pre-excited atrial fibrillation**, AV nodal blockers (**adenosine, verapamil, digoxin, beta-blockers**) can accelerate conduction down the accessory pathway → **ventricular fibrillation and death**. Treat pre-excited AF with **procainamide or cardioversion**.
- **Associations:** **Ebstein anomaly** (10–25%), HCM. Definitive treatment: **catheter ablation** of the accessory pathway.

Long QT Syndrome (LQTS)

- **Genotypes:** **Type 1 (KCNQ1)** — triggered by **exercise, especially swimming**; **Type 2 (KCNH2)** — triggered by **auditory stimuli/emotional startle** (alarm clocks); **Type 3 (SCN5A)** — events at **rest/sleep**; poorest beta-blocker response.
- **Diagnosis:** QTc ≥ 470 ms (males) / ≥ 480 ms (females) on repeated ECGs, or Schwartz score; torsades de pointes is the lethal arrhythmia. Avoid QT-prolonging drugs (macrolides, ondansetron, antipsychotics — check crediblemeds).
- **Management:** **Beta-blockers (nadolol or propranolol)** first-line; **ICD** for survivors of cardiac arrest or recurrent syncope on therapy; left cardiac sympathetic denervation for refractory cases. All first-degree relatives need ECG screening.

Congenital Complete Heart Block

- **Maternal association:** **Anti-Ro/SSA and anti-La/SSB antibodies** (Sjögren syndrome, SLE — often the mother is asymptomatic). Antibodies cross the placenta at 16–24 weeks, causing fibrosis of the fetal AV node. Fetal echo surveillance is indicated in antibody-positive pregnancies.
- **ECG:** AV dissociation with slow ventricular escape rhythm; atrial rate normal.
- **Pacemaker indications (pediatric):** Symptomatic bradycardia/CHF, **ventricular dysfunction**, prolonged QTc, **wide-QRS escape rhythm**, complex ventricular ectopy, or **mean heart rate < 55 bpm** in infants (< 70 bpm if associated congenital heart disease). Asymptomatic isolated block with narrow-QRS escape and normal function can be observed with close follow-up.

Kawasaki Disease

Diagnostic Criteria (American Heart Association)

- **Fever ≥ 5 days PLUS ≥ 4 of 5** principal features:
- **Bilateral non-purulent conjunctival injection** (limbic sparing).
- **Oral mucosal changes** — strawberry tongue, cracked red lips, injected pharynx.
- **Polymorphous rash** (never vesicular/bullous).
- **Extremity changes** — acute: edema/erythema of hands and feet; subacute: **periungual desquamation**.

- **Cervical lymphadenopathy** ≥ 1.5 cm, usually unilateral, non-suppurative.
- **BCG scar reactivation** is a supportive clue in countries with neonatal BCG (erythema/induration at the BCG site).
- **Incomplete (atypical) Kawasaki:** Fever ≥ 5 days + only 2–3 criteria, with supportive **lab features** (elevated ESR/CRP, anemia, thrombocytosis after day 7, hypoalbuminemia, elevated ALT, sterile pyuria, leukocytosis) and/or **positive echo**. Incomplete KD is **more common in infants < 6 months**, who paradoxically carry the **highest coronary aneurysm risk** — maintain a low threshold for echo and treatment.

Echocardiographic Coronary Changes

- **Coronary artery dilation/aneurysm** defined by **z-score ≥ 2.5** (body-surface-area-adjusted); **giant aneurysm:** ≥ 8 mm internal diameter or **z-score ≥ 10** — highest risk of thrombosis, stenosis, and myocardial infarction.
- Ancillary echo findings: pericardial effusion, LV dysfunction, mitral regurgitation, coronary brightness/lack of tapering.
- **Echo timing:** At diagnosis, at **2 weeks**, and at **6–8 weeks**; more frequent surveillance if aneurysms are present.

Treatment

- **IVIG 2 g/kg as a single infusion** (over 10–12 hours), given **within the first 10 days of fever** (ideally by day 7) — the single most important step to prevent coronary aneurysms. IVIG resistance (persistent/recurrent fever ≥ 36 hours post-infusion): second IVIG dose, **corticosteroids** (methylprednisolone pulse), or **infliximab**.
- **Aspirin: High dose 80–100 mg/kg/day** (anti-inflammatory) during the acute febrile phase until afebrile 48–72 hours, then **low dose 3–5 mg/kg/day** (antiplatelet) for 6–8 weeks (longer if coronary abnormalities persist). Add **clopidogrel** for moderate aneurysms; **warfarin/heparin + aspirin** for giant aneurysms.
- **Follow-up:** Giant aneurysms need lifelong cardiology follow-up with stress testing/anticoagulation; small aneurysms often regress but the vessel wall remains abnormal.

MIS-C vs Kawasaki Disease

Feature	Kawasaki Disease	MIS-C
Age	< 5 years (peak 1–2 years)	Older children/adolescents (median 8–10 years)
GI symptoms	Mild	Prominent — abdominal pain, vomiting, diarrhea
Shock/myocardial dysfunction	Uncommon	Common — LV dysfunction, vasoplegic shock
Coronary aneurysms	Hallmark complication	Less frequent; dilation usually transient
COVID link	None	Recent SARS-CoV-2 infection/exposure , positive serology
Labs	Thrombocytosis (subacute)	Lymphopenia , very high ferritin/D-dimer/troponin/BNP, thrombocytopenia

Feature	Kawasaki Disease	MIS-C
Treatment	IVIG 2 g/kg + aspirin	IVIG + corticosteroids upfront; inotropes/anticoagulation as needed

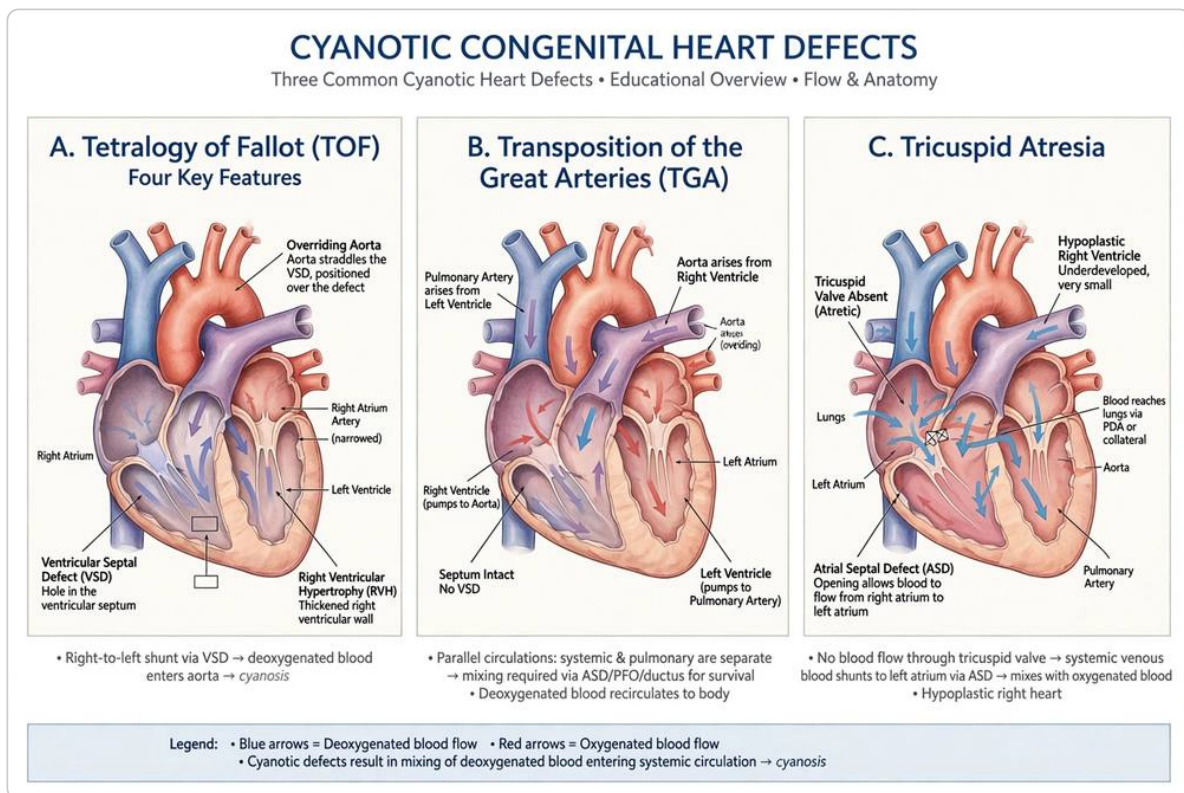


Figure 2.2 — Cyanotic congenital heart defects

Cardiomyopathies and Myocarditis

Hypertrophic Cardiomyopathy (HCM)

- **Genetics: Autosomal dominant** sarcomere-protein mutations — **MYH7 (beta-myosin heavy chain)** and **MYBPC3 (myosin-binding protein C)** are the two most common. Family screening with echo + genetic testing is mandatory.
- **Murmur dynamics (classic bedside physiology):** Harsh systolic murmur at left lower sternal border from dynamic LVOT obstruction. Murmur **increases** with maneuvers that **decrease preload/afterload** — **Valsalva, standing, nitrates, dehydration** (smaller LV cavity → more obstruction). Murmur **decreases** with maneuvers that **increase preload/afterload** — **squatting, handgrip, passive leg raise**. This is the exact opposite of most murmurs and is heavily tested.
- **Management: Beta-blockers** (or verapamil) first-line; **avoid nitrates, diuretics, and ACE inhibitors** in obstructive HCM (they worsen obstruction); **septal myectomy** for drug-refractory obstruction; **alcohol septal ablation** in selected adults. **ICD indications:** prior cardiac arrest, sustained VT, family history of sudden death, massive LVH (≥ 30 mm), unexplained syncope, NSVT on Holter. Restrict competitive strenuous sports.

Dilated Cardiomyopathy (DCM)

- **Most common cardiomyopathy in children.** LV dilation with **systolic dysfunction** (low ejection fraction). Causes: idiopathic, post-myocarditis, **Duchenne muscular dystrophy** (X-linked, cardiac involvement universal by late teens), anthracycline toxicity, tachycardia-induced, metabolic/mitochondrial disorders.
- Presents with CHF; management is standard heart-failure therapy (ACE inhibitors, beta-blockers, diuretics, digoxin) ± CRT; **cardiac transplantation** for end-stage disease.

Myocarditis

- Usually **viral** (Coxsackie B, parvovirus B19, adenovirus, HHV-6). Presents with CHF, arrhythmias, or **fulminant cardiogenic shock** mimicking sepsis.
- Diagnosis: elevated **troponin**, echo showing LV dysfunction ± pericardial effusion; **cardiac MRI** (edema/late gadolinium enhancement) is the key noninvasive test; endomyocardial biopsy is the gold standard but rarely done.
- Management: supportive ICU care (inotropes, ventilation), **IVIG** commonly used (evidence mixed), mechanical circulatory support (ECMO) as bridge to recovery or transplant in fulminant cases. **Avoid NSAIDs** in acute myocarditis (worsen myocardial injury in animal models).

Infective Endocarditis

Modified Duke Criteria

- **Major criteria:**
- **Positive blood cultures:** typical organisms (viridans streptococci, *Streptococcus gallolyticus*, HACEK group, *Staphylococcus aureus*, community-acquired enterococci) from **2 separate cultures**, OR persistently positive cultures drawn > 12 hours apart, OR single positive *Coxiella burnetii* culture/phase-I IgG > 1:800.
- **Echo evidence: vegetation**, abscess, new partial dehiscence of prosthetic valve, or **new valvular regurgitation** (worsening of pre-existing murmur is not enough).
- **Minor criteria:** predisposing heart condition or IV drug use; **fever > 38°C**; vascular phenomena (**embolic events, septic pulmonary infarcts, mycotic aneurysm, Janeway lesions**); immunologic phenomena (**Osler nodes, Roth spots, glomerulonephritis, rheumatoid factor**); microbiologic evidence not meeting major criteria.
- **Diagnosis:** 2 major, or 1 major + 3 minor, or 5 minor criteria.
- **Bedside differentiators:** **Janeway lesions** (painless, embolic/vascular) vs **Osler nodes** (painful, immunologic) — "Janeway is painless, Osler hurts."

Prophylaxis (AHA — High-Risk Groups Only)

- Antibiotic prophylaxis is indicated **only** for: **prosthetic valves/materials, previous infective endocarditis, unrepaired cyanotic congenital heart disease** (including palliative shunts/conduits), **repaired CHD with prosthetic material for the first 6 months** post-procedure, and **cardiac transplant recipients with**

valvulopathy — and only before **dental procedures** involving gingival manipulation or oral mucosal perforation.

- Regimen: **amoxicillin 50 mg/kg PO (max 2 g)** single dose 30–60 minutes before the procedure; clindamycin 20 mg/kg if penicillin-allergic. Routine prophylaxis for isolated VSD/ASD/MVP is **not** indicated.

Pulmonary Hypertension and Eisenmenger Syndrome

- **Definition:** Mean PAP > **20 mmHg** at rest on cath. In children with left-to-right shunts, the driver is increased pulmonary blood flow ± elevated PVR.
- **Eisenmenger physiology:** Long-standing large shunt → irreversible pulmonary vascular remodeling (medial hypertrophy, intimal fibrosis, plexiform lesions) → PVR exceeds SVR → **bidirectional then right-to-left shunting** → cyanosis, clubbing, erythrocytosis, hemoptysis risk.
- **Clinical clues: Differential cyanosis and clubbing** (worse in toes than fingers in PDA-Eisenmenger), loud palpable P2, RV heave, exertional dyspnea/syncope.
- **Management principles:**
 - **Never close the defect** — the shunt is a life-preserving pop-off for the failing RV.
 - **Avoid** dehydration, high altitude, pregnancy (maternal mortality ~30–50%), and non-essential surgery.
 - **Pulmonary vasodilators:** **bosentan** (endothelin antagonist), **sildenafil/tadalafil** (PDE-5 inhibitors), prostacyclins (epoprostenol/treprostinil) for advanced disease.
 - **Phlebotomy only for symptomatic hyperviscosity** (headache, visual disturbance) with iron repletion — routine venesection worsens iron-deficiency-related symptoms.
- Definitive: **heart-lung transplantation** (or lung transplant with defect repair) for end-stage disease.

Practice MCQs

Q1. A 6-week-old infant presents with tachypnea, poor feeding, and failure to thrive. Examination reveals a harsh holosystolic murmur at the left lower sternal border with a thrill. Chest X-ray shows cardiomegaly with increased pulmonary vascular markings. The most likely diagnosis is: A) Atrial septal defect B) Ventricular septal defect C) Patent ductus arteriosus D) Tetralogy of Fallot **Answer: B** — A large VSD presents at 4–8 weeks with congestive heart failure as pulmonary vascular resistance falls and left-to-right shunting increases. The harsh holosystolic murmur at the left lower sternal border with thrill is classic for VSD. ASD rarely causes CHF in infancy, and TOF presents with cyanosis, not pulmonary overcirculation.

Q2. A 4-year-old child has a systolic ejection murmur at the left upper sternal border and a fixed widely split S2. ECG shows right axis deviation with incomplete right bundle branch block. The murmur is best explained by: A) Turbulent flow across the atrial septal defect B) Pulmonic stenosis C) Tricuspid regurgitation D) Increased flow across the normal pulmonary valve **Answer: D** — In ASD, the murmur is a flow murmur from increased pulmonary blood flow across a normal pulmonary valve, not from flow across the defect itself (low-pressure gradient, silent). The fixed widely split S2 from RV volume overload and the ECG pattern confirm secundum ASD. True pulmonic stenosis would produce a click and different echo findings.

Q3. A 3-day-old neonate with suspected coarctation of the aorta develops metabolic acidosis, poor perfusion, and absent femoral pulses. The immediate life-saving intervention is: A) Prostaglandin E1 infusion B) Balloon angioplasty C) Furosemide D) Surgical end-to-end anastomosis **Answer: A** — The neonate is duct-dependent; systemic perfusion to the lower body was maintained through the patent ductus arteriosus. Prostaglandin E1 reopens/maintains the ductus as a bridge to definitive surgical repair. Balloon angioplasty is for older children or recoarctation, not for a shocked neonate.

Q4. A 2-month-old with Tetralogy of Fallot develops sudden deep cyanosis and agitation while crying. On examination the previously audible systolic murmur has disappeared. The most appropriate first step is: A) Intravenous propranolol B) Morphine 0.1 mg/kg SC C) Knee-chest positioning with high-flow oxygen D) Emergency BT shunt **Answer: C** — This is a hypercyanotic (tet) spell from infundibular spasm; the disappearing murmur reflects loss of forward flow across the RVOT. Knee-chest positioning (increases SVR and venous return) with oxygen is the immediate first step, followed by fluids, morphine, propranolol, and phenylephrine if the spell persists.

Q5. A cyanotic newborn has an "egg-on-side" cardiac silhouette with a narrow mediastinum on chest X-ray. The most likely diagnosis and the bedside procedure to improve oxygenation are: A) TAPVR; surgical repair B) d-Transposition of great arteries; balloon atrial septostomy C) Truncus arteriosus; prostaglandin E1 D) Tetralogy of Fallot; knee-chest position **Answer: B** — Egg-on-side with narrow mediastinum is classic for d-TGA, in which two parallel circulations require mixing. The Rashkind balloon atrial septostomy tears the atrial septum at the bedside to improve mixing, alongside PGE1 to maintain ductal patency, as a bridge to the arterial switch operation.

Q6. A term neonate presents within hours of birth with profound cyanosis and a "white-out" (ground-glass) appearance of both lung fields on X-ray, without cardiomegaly. The most likely diagnosis is: A) Obstructed infracardiac TAPVR B) Transient tachypnea of the newborn C) d-TGA with intact ventricular septum D) Neonatal pneumonia **Answer: A** — Obstructed TAPVR (classically the infracardiac type draining below the diaphragm) presents at birth with severe cyanosis and pulmonary edema from obstructed pulmonary venous return. The lungs are white from edema while the heart is initially normal-sized. This is a surgical emergency; TTN would improve and show fluid in fissures, not this pattern.

Q7. Cardiac catheterization in a 5-year-old with a large VSD shows: aortic saturation 92%, mixed venous (SVC) saturation 68%, pulmonary venous saturation 98%, pulmonary artery saturation 89%. The calculated Qp:Qs is approximately: A) 1.2:1 B) 1.5:1 C) 2.0:1 D) 2.7:1 **Answer: D** — Using the Fick equation, $Qp:Qs = (SaO_2 - SvO_2)/(SpvO_2 - SpaO_2) = (92 - 68)/(98 - 89) = 24/9 \approx 2.7:1$. This large left-to-right shunt with a significant PA step-up (68% → 89%) confirms a VSD-level shunt that warrants closure, provided pulmonary vascular resistance is in the operable range.

Q8. A 10-year-old with an unrepaired large VSD has a PVRi of 9 Wood units·m² on catheterization with no fall on 100% oxygen and inhaled nitric oxide. The next best step is: A) Urgent surgical VSD closure B) Device closure of the VSD C) Medical management with pulmonary vasodilators; do not close the defect D) Balloon atrial septostomy **Answer: C** — PVRi > 8 WU·m² with no vasoreactivity indicates irreversible pulmonary vascular disease (Eisenmenger physiology). Closing the defect would remove the RV pop-off and precipitate fatal right heart failure. Management is medical: bosentan, sildenafil, avoidance of dehydration/high altitude/pregnancy, with heart-lung transplant as the definitive option.

Q9. A 7-month-old infant presents with paroxysmal SVT at 280 bpm, pale and with poor perfusion but a palpable pulse and measurable blood pressure. After failed vagal maneuvers with an ice-cold cloth to the face, the next step is: A) Synchronized cardioversion at 2 J/kg B) Adenosine 0.1 mg/kg rapid IV push C) Verapamil IV D) Digoxin loading dose **Answer: B** — The infant is stable (palpable pulse, measurable BP), so pharmacologic conversion is preferred over cardioversion. Adenosine 0.1 mg/kg rapid IV push (max 6 mg first dose, then 0.2 mg/kg max 12 mg) with a saline flush is the drug of choice for stable pediatric SVT. Verapamil is contraindicated in infants (risk of cardiovascular collapse), and digoxin is too slow for acute termination.

Q10. A 5-year-old boy has had fever for 7 days with bilateral non-purulent conjunctivitis, strawberry tongue with cracked lips, polymorphous rash, and a 2 cm non-tender cervical lymph node. The most appropriate treatment is: A) IVIG 2 g/kg single infusion plus aspirin B) High-dose corticosteroids alone C) Amoxicillin for 10 days D) Observation until fever subsides **Answer: A** — This child meets complete Kawasaki disease criteria (fever ≥ 5 days + 4/5 features). IVIG 2 g/kg as a single infusion within 10 days of fever onset is the definitive treatment to prevent coronary artery aneurysms, combined with high-dose aspirin (80–100 mg/kg/day) transitioning to low-dose (3–5 mg/kg/day) antiplatelet therapy.

Q11. A 4-month-old infant with fever for 6 days has only conjunctival injection and rash (2 of 5 Kawasaki criteria). Labs show CRP 12 mg/dL, ESR 70 mm/h, platelet count 550,000, and albumin 2.6 g/dL. Echocardiography shows left anterior descending coronary z-score of +3.0. The best management is: A) Withhold treatment since criteria are incomplete B) Start antibiotics for occult bacteremia C) Repeat echo in 4 weeks without treatment D) Treat as incomplete Kawasaki disease with IVIG 2 g/kg **Answer: D** — This is incomplete Kawasaki disease: prolonged fever with 2–3 criteria plus supportive labs (elevated acute-phase reactants, thrombocytosis, hypoalbuminemia) and a positive echo (z-score ≥ 2.5 defines dilation). Infants under 6 months with incomplete KD carry the highest coronary aneurysm risk and must be treated with IVIG 2 g/kg without delay.

Q12. A 9-year-old presents 4 weeks after a mild COVID-19 infection with persistent fever, severe abdominal pain, hypotension requiring inotropes, and an echocardiogram showing LV ejection fraction of 40% with no coronary aneurysm. Labs show lymphopenia, ferritin 1200 ng/mL, and troponin elevation. The most likely diagnosis is: A) Classic Kawasaki disease B) Acute viral myocarditis C) Multisystem inflammatory syndrome in children (MIS-C) D) Toxic shock syndrome **Answer: C** — MIS-C affects older children (median 8–10 years) weeks after SARS-CoV-2 infection, with prominent GI symptoms, shock/myocardial dysfunction, lymphopenia, and markedly elevated ferritin/D-dimer/troponin. Unlike Kawasaki, coronary aneurysms are uncommon and dilation is usually transient. Treatment is IVIG plus upfront corticosteroids with inotropic and anticoagulation support.

Q13. A 14-year-old athlete has a harsh systolic murmur at the left lower sternal border that becomes louder on standing and with Valsalva, but softer with squatting. The most likely diagnosis and inheritance pattern are: A) Hypertrophic cardiomyopathy; autosomal dominant B) Aortic stenosis; autosomal recessive C) Mitral valve prolapse; X-linked D) Ventricular septal defect; sporadic **Answer: A** — Dynamic LVOT obstruction in HCM worsens with decreased preload/afterload (standing, Valsalva) and improves with increased preload/afterload (squatting, handgrip) — the opposite of fixed obstructions like aortic stenosis. HCM is autosomal dominant, most commonly from MYH7 or MYBPC3 sarcomere mutations, and family screening is mandatory.

Q14. A newborn with tricuspid atresia and normally related great arteries is stabilized on prostaglandin E1. The ECG shows left axis deviation with left ventricular hypertrophy. The most appropriate staged surgical pathway is:

A) Arterial switch followed by VSD closure B) BT shunt → bidirectional Glenn → Fontan C) Norwood → Glenn → Fontan D) Primary cardiac transplantation **Answer: B** — Tricuspid atresia is a single-ventricle lesion managed by the Fontan pathway: neonatal BT shunt (or PDA stenting) for pulmonary blood flow, bidirectional Glenn at 4–6 months, and Fontan completion at 2–4 years. The Norwood is specific to HLHS (neoaortic reconstruction), and the ECG pattern of left axis deviation with LVH in a cyanotic infant is itself a classic clue to tricuspid atresia.

Q15. A 6-year-old, 3 years after Fontan completion, presents with generalized edema, hypoalbuminemia (1.8 g/dL), and chronic diarrhea. Fecal alpha-1 antitrypsin is markedly elevated. The most likely diagnosis is: A) Fontan conduit thrombosis B) Postoperative chylothorax C) Nephrotic syndrome D) Protein-losing enteropathy **Answer: D** — Protein-losing enteropathy is a hallmark late Fontan complication caused by chronically elevated systemic venous pressure producing intestinal lymphangiectasia. Elevated fecal alpha-1 antitrypsin confirms enteric protein loss. Management aims to lower venous pressure (fenestration creation, pulmonary vasodilators) and optimize nutrition, with transplant evaluation for refractory cases.

Q16. A 12-year-old with a secundum ASD has right ventricular enlargement on echo and a Qp:Qs of 1.8:1 on catheterization. All rims are adequate on transesophageal echo. The best management is: A) Observation until adulthood B) Surgical ASD closure C) Percutaneous device (Amplatzer) closure D) Pulmonary artery banding **Answer: C** — Closure is indicated when Qp:Qs $\geq 1.5:1$ with RV volume overload. For a secundum ASD with adequate rims, percutaneous device closure is the treatment of choice — less invasive than surgery with excellent outcomes. Surgical closure is reserved for primum/sinus venosus defects, deficient rims, or associated PAPVR requiring baffling.

Q17. A 28-week preterm neonate on day 3 has a continuous murmur, bounding pulses, and increasing ventilator requirements. Serum creatinine is 1.4 mg/dL and platelets are 45,000. The most appropriate pharmacologic choice for ductal closure is: A) Paracetamol 15 mg/kg every 6 hours B) Indomethacin 0.2 mg/kg IV C) Ibuprofen 10 mg/kg IV D) No pharmacologic therapy; observe **Answer: A** — Renal dysfunction (creatinine 1.4 mg/dL) and thrombocytopenia (45,000) are contraindications to both indomethacin and ibuprofen, which worsen renal perfusion and platelet function. Paracetamol (15 mg/kg q6h) closes the ductus via peroxidase inhibition with renal and platelet safety, making it the preferred agent here.

Q18. A 16-year-old collapses while swimming and is resuscitated from torsades de pointes. ECG shows QTc 520 ms. His brother drowned during swim practice at age 12. The most likely genotype and first-line therapy are: A) SCN5A mutation; flecainide B) KCNQ1 mutation; beta-blockers C) KCNH2 mutation; ICD only D) RYR2 mutation; calcium-channel blockers **Answer: B** — Exercise-triggered events, especially swimming, with a family history of exertional death define LQTS type 1 (KCNQ1). Beta-blockers (nadolol/propranolol) are first-line therapy; ICD is reserved for cardiac arrest survivors or breakthrough syncope on therapy. Type 2 (KCNH2) is triggered by auditory/emotional stimuli and type 3 (SCN5A) by rest/sleep events.

Q19. A mother with Sjögren syndrome and positive anti-Ro/SSA antibodies delivers a term infant whose ECG shows complete AV dissociation with a ventricular rate of 50 bpm and a narrow QRS escape. The infant is asymptomatic with normal ventricular function. The most appropriate management is: A) Immediate permanent pacemaker implantation B) Maternal plasmapheresis C) Neonatal IVIG infusion D) Observation with close cardiology follow-up **Answer: D** — Congenital complete heart block from transplacental anti-Ro/La antibodies needs pacing only with defined indications: symptoms, ventricular dysfunction, prolonged QTc, wide-QRS escape, complex ectopy, or heart rate < 55 bpm in infants (< 70 with CHD). An asymptomatic neonate with a

narrow-QRS escape, normal function, and rate ≥ 55 can be observed closely, though many eventually require pacing.

Q20. A 3-week-old with critical aortic stenosis and a peak-to-peak catheter gradient of 70 mmHg is in cardiogenic shock. The ductus is being maintained with PGE1. The definitive urgent intervention is: A) Ross procedure B) Balloon aortic valvuloplasty C) Surgical aortic valve replacement D) Norwood procedure **Answer: B** — Balloon aortic valvuloplasty is the first-line urgent intervention for critical neonatal aortic stenosis, relieving the obstruction while preserving the native valve in a growing child. The Ross procedure or valve replacement is reserved for later childhood if needed; the Norwood is for HLHS, not isolated aortic stenosis.

Q21. A 2-year-old with Down syndrome is found to have a complete atrioventricular septal defect with a large left-to-right shunt and a PVRi of 4 Wood units·m². The optimal timing and reason for surgical planning are: A) Repair at 3–6 months to prevent rapid-onset pulmonary vascular disease B) Repair at 2 years after spontaneous closure is excluded C) Defer repair until PVRi exceeds 8 WU·m² D) Device closure of the defect now **Answer: A** — Complete AVSD, especially in Down syndrome, develops pulmonary vascular obstructive disease unusually early. Repair is indicated at 3–6 months of age; waiting risks inoperability. Device closure is not feasible for complete AV canal defects, which require surgical two-patch repair with reconstruction of the common AV valve.

Q22. A 10-day-old with d-TGA, intact ventricular septum, and a restrictive PFO remains severely cyanotic despite PGE1 infusion. The next best step is: A) Immediate arterial switch operation tonight B) Intravenous propranolol C) Balloon atrial septostomy (Rashkind procedure) D) High-dose oxygen therapy **Answer: C** — In d-TGA, survival depends on mixing between the parallel circulations; a restrictive PFO limits mixing despite an open ductus. The bedside Rashkind balloon atrial septostomy tears the atrial septum to improve mixing immediately, stabilizing the infant for the arterial switch operation, which is optimally performed within the first 2 weeks of life.

Q23. A 15-year-old with repaired Tetralogy of Fallot presents with palpitations. ECG shows a wide-QRS tachycardia and baseline QRS duration of 190 ms. Echocardiography shows severe pulmonary regurgitation with a dilated right ventricle. The most appropriate next step is: A) Reassurance; this is expected after TOF repair B) Start digoxin C) Balloon dilation of the RVOT D) Electrophysiology referral for pulmonary valve replacement evaluation and arrhythmia risk stratification **Answer: D** — Late after TOF repair, chronic pulmonary regurgitation causes progressive RV dilation and dysfunction, and QRS duration > 180 ms is a marker of ventricular tachycardia and sudden death risk. Pulmonary valve replacement (surgical or transcatheter) with concomitant arrhythmia evaluation/ablation is indicated — not reassurance or digoxin.

Q24. A child with a prosthetic mitral valve develops fever of 39°C for 5 days. Blood cultures grow viridans streptococci in 2 separate sets. Transesophageal echo shows a 12 mm vegetation on the prosthetic valve with new paravalvular regurgitation. By modified Duke criteria this is: A) Possible endocarditis B) Rejected endocarditis C) Definite endocarditis D) Culture-negative endocarditis **Answer: C** — Two major Duke criteria are met: (1) persistently positive blood cultures with a typical organism from 2 separate sets, and (2) echocardiographic evidence of vegetation plus new valvular regurgitation. Two major criteria = definite infective endocarditis, requiring prolonged IV antibiotics and surgical evaluation given the prosthetic valve involvement.

Q25. A 30-year-old woman with unrepaired Eisenmenger syndrome due to a large VSD asks about pregnancy. The most accurate counseling is: A) Pregnancy is contraindicated due to ~30–50% maternal mortality; avoid pregnancy and use reliable contraception B) Pregnancy is safe if pulmonary vasodilators are continued C) Vaginal

delivery at term is recommended to avoid surgical stress D) The shunt will reverse to left-to-right during pregnancy, improving cyanosis **Answer: A** — Pregnancy in Eisenmenger syndrome carries prohibitive maternal mortality (30–50%), mostly from peripartum hemodynamic shifts, thromboembolism, and RV failure; it is an absolute contraindication. Patients need firm contraception counseling (progesterone-only or sterilization options, avoiding estrogen-containing methods given thrombotic risk). Pregnancy increases — not reverses — right-to-left shunting as SVR falls.

Pediatric Neurology

Chapter 3: Pediatric Neurology

Neurology is among the highest-yield sections for NEET SS Pediatrics: questions are syndrome-based (age of onset + seizure semiology + EEG pattern = diagnosis), reward MRI pattern recognition (leukodystrophies, neurocutaneous disorders), and test precise drug choices with doses. DM Neurology is also one of the most competitive super-specialities, so this chapter is pitched at that depth — mechanism-linked facts, enzyme names, gene names, and doses, not just lists.

1. Epilepsy Syndromes

- **West syndrome (infantile epileptic spasms syndrome)**: onset 3–12 months (peak 4–6 months). Classic triad — (1) epileptic spasms (brief symmetric flexor, extensor, or mixed jerks occurring in clusters, typically on awakening), (2) **hypsarrhythmia** on EEG (chaotic, high-voltage, disorganized background with multifocal spikes), (3) developmental arrest or regression. Causes: hypoxic-ischemic injury, tuberous sclerosis, cortical malformations, metabolic disorders; many are symptomatic. Treatment is urgent — delay worsens neurodevelopmental outcome.
- Drug of choice: **ACTH** (75–150 IU/m²/day IM; high-dose oral prednisolone 40–60 mg/day is comparably effective) for cryptogenic cases. **Vigabatrin is first-line when spasms occur in tuberous sclerosis** — 50–150 mg/kg/day in two divided doses (start 50 mg/kg/day, titrate). Vigabatrin irreversibly inhibits GABA transaminase, raising brain GABA.
- Vigabatrin toxicity: **irreversible concentric visual field constriction** (retinal toxicity) — monitor with ERG/visual fields; discontinue if spasms persist beyond ~12 weeks, and limit total duration (~6 months) once controlled. ACTH adverse effects: hypertension, immunosuppression, cushingoid facies, hypertrophic cardiomyopathy, electrolyte shifts.
- **Lennox-Gastaut syndrome (LGS)**: onset 2–7 years (peak 3–5), often evolves from West syndrome. Triad — (1) **multiple seizure types**, with **tonic seizures the most characteristic** (especially nocturnal), plus atypical absence, atonic "drop attacks," and myoclonic jerks; (2) EEG **slow spike-wave <2.5 Hz** (1.5–2 Hz) with generalized paroxysmal fast activity in sleep; (3) intellectual disability/cognitive impairment. Drug-resistant by nature.
- Treatment: **valproate first-line**; add-on **rufinamide** (approved for LGS-associated drop attacks), lamotrigine, clobazam, topiramate, cannabidiol; felbamate is effective but restricted (aplastic anemia, hepatotoxicity). **Corpus callosotomy** for intractable drop attacks. Avoid carbamazepine/phenytoin — they may worsen absence and myoclonic seizures.
- **Dravet syndrome (severe myoclonic epilepsy of infancy)**: **SCN1A** loss-of-function mutation (sodium channel Nav1.1); onset 4–8 months with **prolonged febrile hemiclonic seizures**, then afebrile focal/

generalized seizures, myoclonic and atypical absence seizures; developmental plateau/regression after 1–2 years; photosensitivity common.

- **Avoid sodium-channel blockers** — carbamazepine, oxcarbazepine, lamotrigine, phenytoin — they aggravate seizures. Backbone: **valproate + clobazam**; add **stiripentol** (with valproate + clobazam), **fenfluramine**, or **cannabidiol** for refractory cases.
- **Childhood absence epilepsy (CAE)**: onset 4–10 years; brief (5–15 s) staring spells, dozens per day, impaired awareness, no postictal confusion; **hyperventilation precipitates attacks**; EEG **3-Hz generalized spike-and-wave**. **Drug of choice: ethosuximide** (absence seizures only; blocks T-type calcium channels). Valproate if generalized tonic-clonic seizures coexist; lamotrigine is an alternative. Avoid carbamazepine and phenytoin (worsen absence). Excellent prognosis — most outgrow by adolescence.
- **Juvenile myoclonic epilepsy (JME, Janz syndrome)**: onset 12–18 years; **myoclonic jerks on awakening**, generalized tonic-clonic seizures, absence seizures in ~30%; photosensitivity; EEG **generalized polyspike-and-wave at 4–6 Hz**. **Valproate is most effective but teratogenic** (neural tube defects, autism, cognitive impairment) — **avoid in females of childbearing potential**; preferred alternatives: **levetiracetam**, lamotrigine (may slightly worsen myoclonus), topiramate, zonisamide. Usually requires **lifelong treatment** — high relapse on withdrawal. Sleep deprivation and alcohol are triggers.
- **Landau-Kleffner syndrome (acquired epileptic aphasia)**: onset 3–8 years in a previously normal child; **auditory agnosia and language regression** (receptive worse than expressive), seizures in ~70% (often nocturnal focal); EEG shows **continuous spike-wave during slow-wave sleep (CSWS/ESES pattern)**. Hearing is normal — the key distinction from deafness; regression pattern distinguishes it from autism. Treatment: valproate, levetiracetam, **corticosteroids**, high-dose nocturnal diazepam.
- **Benign Rolandic epilepsy (BECTS — benign epilepsy with centrotemporal spikes)**: commonest childhood epilepsy syndrome; onset 3–13 years (peak 7–10); **nocturnal focal seizures** with oropharyngeal features — hemifacial twitching, drooling, guttural sounds, speech arrest; EEG **centrotemporal (Rolandic) spikes activated by sleep** on a normal background. **Remits by mid-adolescence**; many children need no AED. If treated: carbamazepine, oxcarbazepine, or levetiracetam. Rare atypical evolution to Landau-Kleffner/CSWS.

2. Febrile Seizures

- Definition: seizure with fever $\geq 38^{\circ}\text{C}$ in a child **6 months to 5 years**, without CNS infection or prior afebrile seizures.
- **Simple febrile seizure**: **generalized** tonic-clonic, duration **<15 minutes, once in 24 hours**. No workup beyond identifying the fever source; no routine labs, EEG, or neuroimaging.
- **Complex febrile seizure**: any of — **focal features**, duration **>15 minutes, recurrence within 24 hours** (or postictal Todd's paresis). Needs EEG and MRI brain; evaluate for underlying cause.
- **Lumbar puncture (AAP guidance)**: **strongly consider LP in infants <12 months** (meningeal signs may be absent); **consider LP at 12–18 months** if pretreated with antibiotics (may mask meningitis) or Hib/pneumococcal immunization is incomplete. LP is mandatory at any age if meningeal signs are present.
- **EEG is not recommended** after a simple febrile seizure; neuroimaging is not routine for simple febrile seizures.

- **Prophylaxis: not recommended routinely** — neither continuous nor intermittent AED prophylaxis is advised for simple febrile seizures (AAP). Reassure parents: risk of epilepsy after a simple febrile seizure is only ~1–2.5%. Rescue buccal/intranasal midazolam or rectal diazepam is reserved for prolonged or recurrent febrile seizures.
- Recurrence risk factors: onset **<18 months**, family history of febrile seizures, low-grade fever at onset, short duration of fever before the seizure.

3. Status Epilepticus

- **Definition (ILAE operational):** continuous seizure activity **≥5 minutes**, or recurrent seizures without regaining consciousness between them. Treat at 5 minutes (t1); beyond ~30 minutes (t2) the risk of neuronal injury and pharmacoresistance rises steeply.
- **Step 1 — Stabilize:** airway, breathing, circulation; check blood glucose (correct hypoglycemia); cardiac/respiratory monitoring; IV access; send labs (glucose, electrolytes, ABG, AED levels, toxicology as indicated).
- **Step 2 — First-line benzodiazepine: lorazepam 0.1 mg/kg IV (max 4 mg/dose)** — may repeat once after 10–15 minutes. Alternatives: diazepam 0.15–0.2 mg/kg IV (max 10 mg) or 0.5 mg/kg per rectum; **midazolam IM 0.2 mg/kg (max 10 mg)**, buccal 0.3–0.5 mg/kg, or intranasal 0.2 mg/kg (preferred when no IV access).
- **Step 3 — Second-line (established SE): fosphenytoin 20 mg PE/kg IV** (max 1500 mg PE; may give an additional 10 mg PE/kg), **levetiracetam 40–60 mg/kg IV** (max 4500 mg), or **valproate 20–40 mg/kg IV** (max 3000 mg) — avoid valproate in suspected mitochondrial disease, acute liver disease, or children <2 years on polytherapy. Phenobarbital 15–20 mg/kg IV is an alternative second-line agent.
- **Step 4 — Refractory SE (ICU, intubated, continuous EEG): midazolam infusion** — 0.2 mg/kg bolus, then 0.05–0.4 mg/kg/hour; or propofol 1–2 mg/kg bolus then 1–10 mg/kg/hour (watch for **propofol infusion syndrome**); or pentobarbital load 5–15 mg/kg then 0.5–5 mg/kg/hour — **barbiturate coma** titrated to EEG burst suppression.

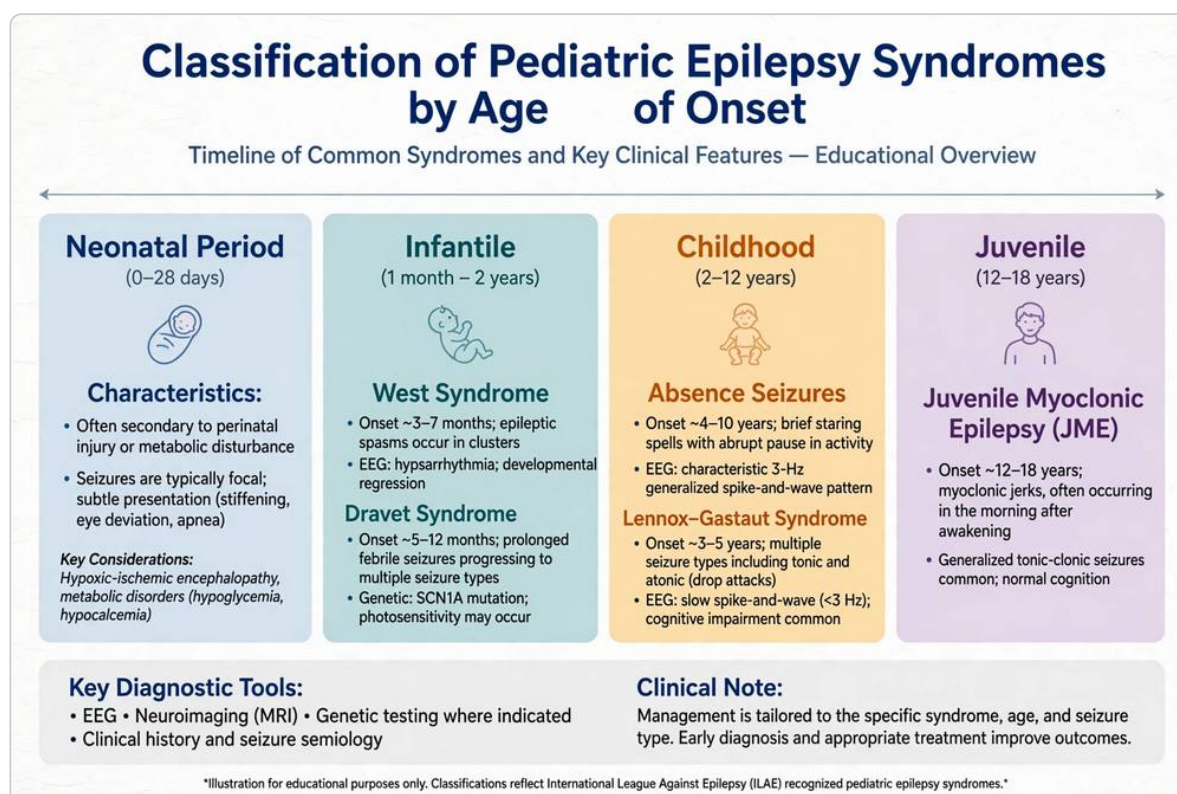


Figure 3.1 — Pediatric epilepsy syndromes by age of onset

4. AED Selection by Seizure Type; Ketogenic Diet

- **Focal-onset seizures:** carbamazepine, oxcarbazepine, levetiracetam, lamotrigine, lacosamide.
- **Generalized tonic-clonic seizures:** valproate, levetiracetam, lamotrigine, topiramate.
- **Absence seizures:** ethosuximide (first-line), valproate, lamotrigine.
- **Myoclonic seizures:** valproate, levetiracetam, topiramate, zonisamide.
- **Golden rule:** carbamazepine and phenytoin can **aggravate absence and myoclonic seizures** — never use them when a generalized epilepsy is suspected.
- **Syndrome-specific choices:** infantile spasms — ACTH/prednisolone (vigabatrin if tuberous sclerosis); Lennox-Gastaut — valproate ± rufinamide/clobazam/lamotrigine; Dravet — valproate + clobazam ± stiripentol/fenfluramine (avoid sodium-channel blockers); childhood absence — ethosuximide; JME — valproate in males, levetiracetam in females of childbearing potential.
- **Ketogenic diet** indications: **drug-resistant epilepsy**, **GLUT1 deficiency (treatment of choice)**, pyruvate dehydrogenase deficiency, Dravet syndrome, Lennox-Gastaut syndrome, infantile spasms, tuberous sclerosis. Mechanism: ketone bodies provide an alternative brain fuel and raise seizure threshold. Contraindications: fatty-acid oxidation defects, pyruvate carboxylase deficiency, porphyria, primary carnitine deficiency. Adverse effects: kidney stones, dyslipidemia, growth slowing, metabolic acidosis, constipation.

5. Neurometabolic Disorders with Neurologic Presentation

- **MELAS** (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes): **maternal inheritance**; commonest mutation **m.3243A>G in MT-TL1**; **stroke-like episodes not conforming to vascular territories** (often occipital), lactic acidosis, myopathy with **ragged-red fibers** on muscle biopsy, short stature, sensorineural hearing loss, diabetes, migraine. Elevated blood and CSF lactate. Acute stroke-like episode: **IV L-arginine**. Supportive: coenzyme Q10, L-carnitine. **Avoid valproate** — it inhibits mitochondrial function and can precipitate fatal hepatotoxicity.
- **Leigh syndrome** (subacute necrotizing encephalomyelopathy): onset infancy/early childhood; developmental regression, hypotonia, brainstem signs (abnormal eye movements, respiratory irregularity), lactic acidosis; MRI shows **symmetric necrotic T2 lesions in the basal ganglia (putamen), thalamus, and brainstem tegmentum**. Caused by mtDNA mutations (complex I genes) or nuclear mutations (**SURF1** is the commonest nuclear cause). Poor prognosis; no curative therapy.
- **Urea cycle disorders: hyperammonemia** (ammonia >100 µmol/L; normal <50) with encephalopathy, vomiting, and poor feeding; **respiratory alkalosis** (ammonia stimulates the medullary respiratory center → central hyperventilation) with **low BUN** — the diagnostic clue cluster; precipitated by protein load, infection, or catabolism. **Ornithine transcarbamylase (OTC) deficiency** is the commonest — X-linked (severe neonatal disease in males; variable phenotype in heterozygous females). Management: stop all protein, IV 10% dextrose (± lipids) to halt catabolism, **nitrogen scavengers** (sodium benzoate/sodium phenylacetate, glycerol phenylbutyrate), arginine supplementation (except in arginase deficiency), **hemodialysis** for severe hyperammonemia; liver transplantation is definitive.
- **Organic acidemias** (maple syrup urine disease, methylmalonic acidemia, propionic acidemia, isovaleric acidemia): **high anion gap metabolic acidosis with ketosis**, mild-to-moderate **hyperammonemia**, **neutropenia/pancytopenia** (marrow suppression), vomiting and lethargy after protein intake. MSUD clue: **maple syrup/burnt-sugar odor** of urine and cerumen with elevated branched-chain amino acids. Acute management: stop protein, IV glucose, carnitine; cobalamin for B12-responsive MMA; dialysis if severe.
- **Biotinidase deficiency**: autosomal recessive; **seizures** (often infantile spasms or myoclonic), **alopecia**, **eczematous rash**, developmental delay, hearing loss, optic atrophy; organic aciduria with mild metabolic acidosis. **Biotin 5–10 mg/day lifelong is dramatically effective** — a classic treatable cause of intractable epilepsy, included in newborn screening in many regions.
- **GLUT1 deficiency syndrome**: **SLC2A1** mutation; impaired glucose transport across the blood-brain barrier; infantile-onset refractory epilepsy, developmental delay, **acquired microcephaly**, paroxysmal movement disorder (exercise-induced dyskinesia). **CSF glucose low** (<40 mg/dL; CSF:blood glucose ratio <0.4) with **normal CSF lactate** — the diagnostic hallmark. **Ketogenic diet is the treatment of choice** (ketones bypass the glucose transport defect).

6. Leukodystrophies: MRI Pattern Recognition

- **Metachromatic leukodystrophy (MLD)**: autosomal recessive; **arylsulfatase A (ARSA)** deficiency → sulfatide accumulation. Late-infantile form (12–24 months) is commonest: gait disturbance, regression, peripheral neuropathy. MRI: **symmetric periventricular white-matter T2 hyperintensity with a tigroid/stripped pattern** (spared perivascular white matter); U-fibers spared early; corpus callosum involved.

Diagnosis: low ARSA activity, elevated urine sulfatides, slowed nerve conduction velocities. HSCT only if presymptomatic; gene therapy (atidarsagene autotemcel) for early-onset forms.

- **Krabbe disease (globoid cell leukodystrophy)**: autosomal recessive; **galactocerebrosidase (GALC)** deficiency → psychosine accumulation. Infantile form (3–6 months): **extreme irritability and hyperesthesia**, opisthotonic posturing, **optic atrophy**, peripheral neuropathy; **CSF protein markedly elevated**. MRI: deep white matter, corticospinal tracts, and cerebellar white matter involvement. HSCT only if presymptomatic.
- **X-linked adrenoleukodystrophy (ALD)**: **ABCD1** mutation → **elevated very-long-chain fatty acids (C26:0)**. Phenotypes: **childhood cerebral form** (4–10 years) — behavioral change and school failure followed by rapid regression; adrenomyeloneuropathy (adult); Addison disease only. MRI: **symmetric parieto-occipital white-matter demyelination with a contrast-enhancing leading edge**; **Loes score (0–34)** quantifies severity — **HSCT is indicated when Loes is <9 and disease is early**. **Adrenal insufficiency is common** — monitor ACTH/cortisol and replace with hydrocortisone/fludrocortisone. Newborn screening via VLCFA is now practiced in several regions.
- **Alexander disease**: autosomal dominant; **GFAP** mutation; infantile form with **megalencephaly**, developmental delay, seizures. MRI: **frontal-predominant** white-matter changes with a periventricular rim; pathology shows **Rosenthal fibers** (astrocytic inclusions).
- **Canavan disease**: autosomal recessive; **aspartoacylase (ASPA)** deficiency → N-acetylaspartate accumulation; **macrocephaly**, severe developmental delay, hypotonia progressing to spasticity. MRI: diffuse spongy white-matter degeneration; **MR spectroscopy shows a markedly elevated NAA peak** — the diagnostic signature. Common in Ashkenazi Jews.
- **Pelizaeus-Merzbacher disease (PMD)**: X-linked; **PLP1** mutation; a **hypomyelinating** (not demyelinating) leukodystrophy. Early **nystagmus/pendular eye movements**, hypotonia, stridor; MRI shows diffuse hypomyelination with a tigroid pattern; MRS NAA is normal (distinguishes it from Canavan).
- **Exam shortcuts**: frontal predominance = Alexander; parieto-occipital + adrenal failure = ALD; tigroid + low arylsulfatase A = MLD; extreme irritability + optic atrophy + very high CSF protein = Krabbe; macrocephaly + high NAA peak on MRS = Canavan; early nystagmus + hypomyelination = Pelizaeus-Merzbacher.

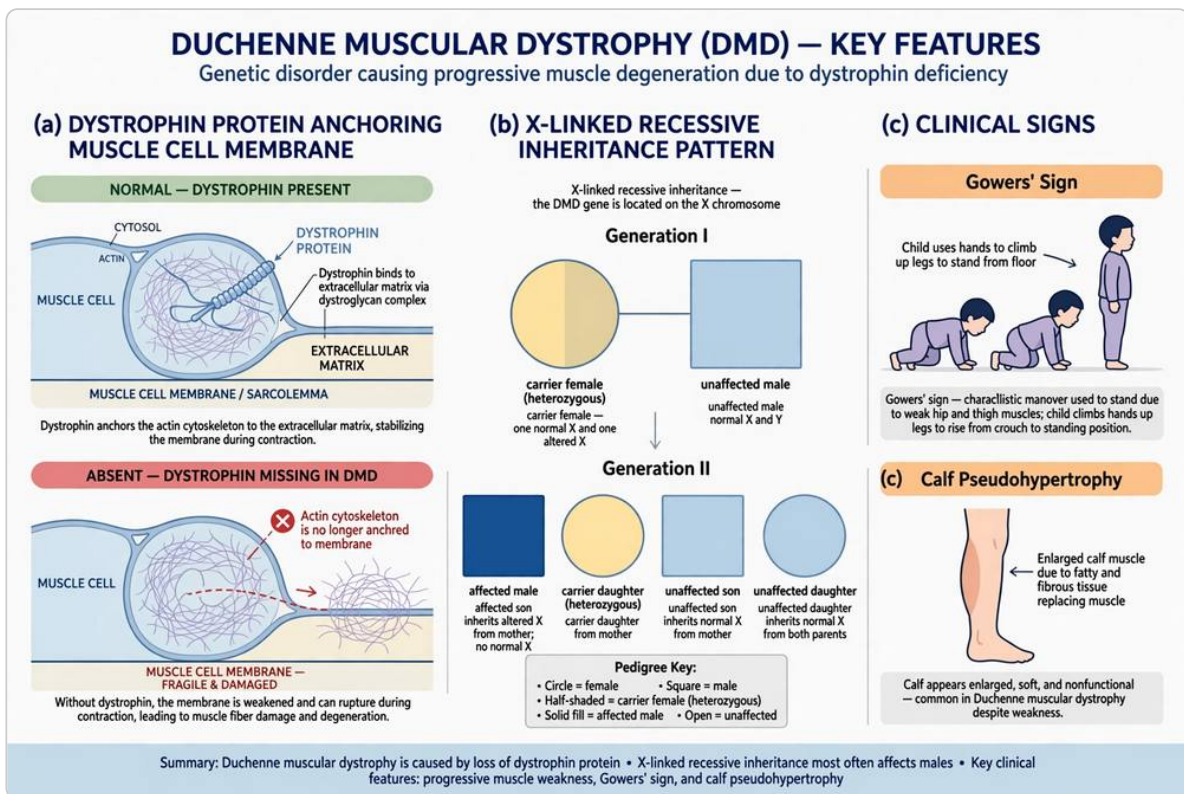


Figure 3.2 — Duchenne muscular dystrophy: dystrophin and inheritance

7. Neuromuscular Disorders

- **Duchenne muscular dystrophy (DMD):** X-linked recessive; **dystrophin** gene (Xp21) — out-of-frame deletions → **absent dystrophin**. Onset 2–5 years: delayed motor milestones, proximal weakness, **Gower sign** (climbing up the legs with the hands to stand), waddling gait, **calf pseudohypertrophy**. **CK massively raised (50–100× normal)** — the screening test. Loss of ambulation ~10–12 years without treatment; death from **dilated cardiomyopathy** and respiratory failure in the 2nd–3rd decade.
- Cornerstone therapy: **corticosteroids** — **prednisone 0.75 mg/kg/day or deflazacort 0.9 mg/kg/day** — prolong ambulation and preserve pulmonary/cardiac function. Mutation-specific: **exon skipping** — eteplirsen (exon 51), golodirsen/viltolarsen (exon 53), casimersen (exon 45); gene therapy **delandistrogene moxeparvovec** for ambulatory young children. Surveillance: annual cardiac imaging, pulmonary function tests, spine (scoliosis), bone health on chronic steroids.
- **Becker muscular dystrophy (BMD):** in-frame mutation → reduced or abnormal dystrophin; ambulation preserved beyond 16 years; milder skeletal course, but cardiomyopathy may dominate — cardiac surveillance is lifelong.
- **Spinal muscular atrophy (SMA):** autosomal recessive; **SMN1** deletion (5q13); **SMN2 copy number** modifies severity (more copies = milder disease). Type 1 (**Werdnig-Hoffmann**): onset <6 months, **never sits**, frog-leg posture, bell-shaped chest with paradoxical breathing, **tongue fasciculations**, absent deep tendon reflexes; fatal before 2 years untreated. Type 2: sits independently, never stands. Type 3 (**Kugelberg-Welander**): stands and walks, proximal weakness. Type 4: adult onset.

- Disease-modifying therapies: **nusinersen** (intrathecal antisense oligonucleotide), **onasemnogene abeparvovec** (one-time IV gene therapy), **risdiplam** (oral SMN2 splicing modifier). Newborn screening enables presymptomatic treatment, which has transformed outcomes.
- **Myasthenia gravis:**
- **Neonatal transient MG:** maternal anti-AChR antibodies cross the placenta; affects 10–15% of infants of myasthenic mothers; onset within hours–days (weak cry, poor suck, hypotonia, ptosis); **resolves spontaneously in 2–3 weeks** as maternal antibodies clear; treat with pyridostigmine/neostigmine plus supportive care.
- **Congenital myasthenic syndromes:** genetic defects of neuromuscular transmission (CHRNE is commonest); no maternal antibodies; onset in infancy with fatigable weakness; some subtypes **worsen with pyridostigmine** (e.g., slow-channel syndrome) — genetic diagnosis guides therapy.
- Juvenile autoimmune MG: pyridostigmine, corticosteroids/immunosuppression, thymectomy in selected cases.
- **Guillain-Barré syndrome:** post-infectious (**Campylobacter jejuni** is the commonest antecedent), ascending **symmetric flaccid paralysis with areflexia**, autonomic instability; **albuminocytologic dissociation** — CSF protein elevated with a normal WBC count (appears after 1–2 weeks; CSF may be normal in the first week). AIDP is the commonest subtype in children. **Miller Fisher variant:** anti-**GQ1b** antibodies; triad of **ophthalmoplegia, ataxia, areflexia**. Treatment: **IVIg 2 g/kg** (over 2–5 days) **or plasmapheresis** — equally effective; **corticosteroids alone are ineffective**. ICU/supportive care: monitor vital capacity and swallowing, manage autonomic dysfunction, DVT prophylaxis.

8. Neurocutaneous Syndromes

- **Neurofibromatosis type 1 (NF1):** autosomal dominant; **NF1 gene (17q11.2)**, neurofibromin (tumor suppressor in the RAS pathway). Diagnosis requires **≥2 of:** **≥6 café-au-lait macules (>5 mm prepubertal, >15 mm postpubertal)**, **≥2 neurofibromas or 1 plexiform neurofibroma**, **axillary/inguinal freckling (Crowe sign)**, **optic pathway glioma**, **≥2 Lisch nodules** (iris hamartomas), distinctive osseous lesion (sphenoid dysplasia, tibial pseudarthrosis), first-degree relative with NF1. (The 2021 revision added choroidal abnormalities and a pathogenic NF1 variant as criteria.) Complications: optic glioma (annual ophthalmology; MRI if symptomatic), **malignant peripheral nerve sheath tumor** (rapid growth or pain in a neurofibroma is a red flag), vasculopathy, learning disabilities. **Selumetinib** (MEK inhibitor) for inoperable plexiform neurofibromas.
- **Tuberous sclerosis complex (TSC):** autosomal dominant; **TSC1 (hamartin)/TSC2 (tuberin)** — mTOR pathway overactivation. Major features (**≥2 major, or 1 major + ≥2 minor, is diagnostic**): **facial angiofibromas (adenoma sebaceum) ≥3**, ungual fibromas **≥2**, **shagreen patch** (connective-tissue nevus), **hypomelanotic macules (ash-leaf spots) ≥3** (best seen with Wood's lamp), cortical tubers/cortical dysplasia, **subependymal giant cell astrocytoma (SEGA)**, cardiac **rhabdomyoma** (often detected on fetal echo), renal **angiomyolipomas ≥2**, retinal hamartomas. Epilepsy occurs in the majority — infantile spasms in ~30% — and **vigabatrin is first-line for spasms in TSC**. **Everolimus** (mTOR inhibitor) for SEGA and angiomyolipomas; epilepsy surgery for a dominant tuber.
- **Sturge-Weber syndrome:** sporadic; **GNAQ** somatic mutation; **port-wine stain (nevus flammeus) in the ophthalmic (V1) trigeminal distribution**, ipsilateral **leptomeningeal angiomas** (pial angioma), **tram-track (gyriform) calcifications** on CT, seizures, hemiparesis, developmental delay, **glaucoma/buphthalmos**.

MRI: leptomeningeal enhancement with underlying cortical atrophy. Manage seizures aggressively; screen for and treat glaucoma; low-dose aspirin is used in some centers; hemispherectomy for refractory epilepsy with established hemiplegia.

9. Hydrocephalus, Chiari Malformations, and Neural Tube Defects

- **Hydrocephalus: communicating** (impaired CSF absorption — post-meningitic, post-hemorrhagic) vs **noncommunicating/obstructive** (blockage of CSF flow — **aqueductal stenosis is the commonest congenital cause**; posterior fossa tumors in older children). Treatment: **ventriculoperitoneal (VP) shunt** (commonest) or **endoscopic third ventriculostomy (ETV)** — preferred for obstructive/aqueductal stenosis since it avoids shunt hardware. Shunt complications: obstruction (commonest), infection (**Staphylococcus epidermidis**), overdrainage/slit-ventricle syndrome, abdominal pseudocyst.
- **Chiari malformations: Type I** — cerebellar **tonsillar herniation ≥ 5 mm** below the foramen magnum; frequently associated with **syringomyelia**; presents with occipital headache, scoliosis, or brainstem signs; posterior fossa decompression if symptomatic or syrinx is progressive. **Type II** — occurs with **myelomeningocele**; small posterior fossa with herniation of tonsils, vermis, and brainstem; prenatal ultrasound clues are the **lemon sign** (frontal bone scalloping) and **banana sign** (cerebellar effacement); hydrocephalus is nearly universal. Type III — with occipital encephalocele (severe, poor prognosis).
- **Neural tube defects**: failure of neural tube closure (days 21–28 of gestation). Spectrum: **anencephaly** (incompatible with life), **myelomeningocele** (commonest open NTD — associated with Chiari II, hydrocephalus, neurogenic bladder, and **latex allergy**), encephalocele. Prevention: **folic acid 0.4 mg/day** for all women of childbearing age; **4 mg/day preconception** for high-risk mothers (prior NTD pregnancy, maternal valproate/carbamazepine use, pregestational diabetes). Screening: **maternal serum AFP is elevated** in open NTDs; detailed anomaly ultrasound for confirmation.

Practice MCQs

Q1. A 7-month-old infant with tuberous sclerosis develops clusters of brief flexor spasms on awakening. EEG shows hypsarrhythmia. The drug of choice is: A) Vigabatrin B) Phenobarbital C) Carbamazepine D) Phenytoin

Answer: A — Vigabatrin is first-line for infantile spasms in tuberous sclerosis (it irreversibly inhibits GABA transaminase, raising brain GABA). Counsel about irreversible concentric visual field constriction and limit treatment duration. ACTH is first-line for non-TSC spasms.

Q2. A 4-year-old with developmental delay has nocturnal tonic seizures, atonic drop attacks, and atypical absences. EEG shows generalized slow spike-wave at 1.5–2 Hz. The most likely syndrome is: A) West syndrome B) Lennox-Gastaut syndrome C) Childhood absence epilepsy D) Dravet syndrome **Answer: B** — Lennox-Gastaut triad: multiple seizure types (tonic most characteristic), slow spike-wave <2.5 Hz, and intellectual disability; onset 2–7 years, often evolving from West syndrome.

Q3. A 9-month-old with an SCN1A mutation has prolonged febrile hemiclonic seizures and developmental slowing. Which drug must be avoided? A) Valproate B) Clobazam C) Carbamazepine D) Stiripentol **Answer: C** — In Dravet syndrome, sodium-channel blockers (carbamazepine, oxcarbazepine, lamotrigine, phenytoin) aggravate seizures. Use valproate + clobazam, adding stiripentol, fenfluramine, or cannabidiol if refractory.

Q4. A 6-year-old has 20–30 daily staring spells lasting ~10 seconds, precipitated by hyperventilation. EEG shows 3-Hz generalized spike-and-wave. The drug of choice is: A) Carbamazepine B) Phenytoin C) Levetiracetam D) Ethosuximide **Answer: D** — Childhood absence epilepsy: ethosuximide (T-type calcium channel blocker) is drug of choice for absence-only seizures. Carbamazepine and phenytoin worsen absence seizures; valproate is preferred if generalized tonic-clonic seizures coexist.

Q5. A 16-year-old girl has early-morning myoclonic jerks and generalized tonic-clonic seizures. EEG shows 4–6 Hz generalized polyspike-wave. She plans pregnancy in the near future. The best initial choice is: A) Levetiracetam B) Valproate C) Carbamazepine D) Phenytoin **Answer: A** — Juvenile myoclonic epilepsy: valproate is most effective but teratogenic (neural tube defects, neurocognitive harm), so levetiracetam is preferred in females of childbearing potential. Carbamazepine worsens myoclonus.

Q6. A 5-year-old with previously normal language develops auditory agnosia and language regression. Seizures occur mostly in sleep. EEG shows continuous spike-wave during slow-wave sleep. The diagnosis is: A) Autism spectrum disorder B) Landau-Kleffner syndrome C) Rett syndrome D) Childhood absence epilepsy **Answer: B** — Landau-Kleffner (acquired epileptic aphasia): language regression at 3–8 years with a CSWS/ESES pattern on sleep EEG. Hearing is normal, distinguishing it from deafness; treat with valproate or corticosteroids.

Q7. An 8-year-old has nocturnal seizures with hemifacial twitching, drooling, and speech arrest. EEG shows centrotemporal spikes activated in sleep on a normal background. The most appropriate advice is: A) Start lifelong valproate therapy B) Urgent epilepsy surgery evaluation C) Benign Rolandic epilepsy — it usually remits by adolescence and often needs no treatment D) Start the ketogenic diet immediately **Answer: C** — Benign Rolandic epilepsy (BECTS) is the commonest childhood epilepsy syndrome, with nocturnal oropharyngeal seizures and an excellent prognosis; many children need no AED and it remits by the mid-teens.

Q8. A 2-year-old has a febrile seizure with focal clonic movements of the right arm lasting 20 minutes. This seizure is classified as complex because of: A) Age under 3 years B) Focal onset and duration >15 minutes C) Fever above 39°C D) It being the first episode **Answer: B** — Complex febrile seizure: focal features, duration >15 minutes, or recurrence within 24 hours. Simple febrile seizures are generalized, <15 minutes, and occur once per 24 hours.

Q9. A 9-month-old presents with a first simple febrile seizure, is now alert, and has an obvious viral source of fever. Regarding lumbar puncture, the next best step is: A) LP is not needed at this age B) Strongly consider LP C) LP only if the seizure recurs D) Defer LP until an EEG is done **Answer: B** — AAP guidance: strongly consider LP in infants <12 months after a febrile seizure because meningeal signs may be absent. Consider LP at 12–18 months if pretreated with antibiotics or under-immunized.

Q10. A 4-year-old is in generalized convulsive status epilepticus. The first-line drug and dose are: A) Lorazepam 0.1 mg/kg IV B) Phenytoin 20 mg/kg IV C) Midazolam infusion 0.1 mg/kg/hour D) Valproate 40 mg/kg IV **Answer: A** — Lorazepam 0.1 mg/kg IV (max 4 mg), repeatable once, is first-line for pediatric status epilepticus (operational definition: ≥5 minutes). Fosphenytoin and levetiracetam are second-line agents.

Q11. The seizure persists after two doses of lorazepam. The next best step is: A) Oral carbamazepine B) Repeat lorazepam indefinitely C) Phenobarbital 5 mg/kg orally D) Fosphenytoin 20 mg PE/kg IV **Answer: D** — Established status epilepticus: second-line IV fosphenytoin 20 mg PE/kg (an additional 10 mg PE/kg may be given), levetiracetam 40–60 mg/kg, or valproate 20–40 mg/kg.

Q12. Status persists despite second-line agents; the child is intubated in the PICU. The next best step is: A) Oral levetiracetam B) Watchful waiting C) Midazolam infusion titrated to EEG burst suppression D) Lumbar puncture
Answer: C — Refractory status epilepticus: continuous midazolam infusion (0.2 mg/kg load, then 0.05–0.4 mg/kg/hour), propofol, or pentobarbital coma with continuous EEG monitoring targeting burst suppression.

Q13. A 2-year-old has refractory epilepsy, developmental delay, and paroxysmal dyskinesia. CSF glucose is 28 mg/dL with blood glucose 95 mg/dL; CSF lactate is normal. The diagnosis and treatment are: A) Mitochondrial disorder — coenzyme Q10 B) GLUT1 deficiency — ketogenic diet C) Urea cycle defect — protein restriction D) Biotinidase deficiency — biotin
Answer: B — GLUT1 (SLC2A1) deficiency: hypoglycorrachia (CSF: blood glucose ratio <0.4) with normal CSF lactate. The ketogenic diet is the treatment of choice because ketones bypass the glucose transport defect.

Q14. A 14-year-old has stroke-like episodes not confined to vascular territories, short stature, sensorineural hearing loss, and lactic acidosis. The most likely mutation is: A) m.3243A>G in MT-TL1 B) SMN1 deletion C) DMPK trinucleotide expansion D) ABCD1 mutation
Answer: A — MELAS: maternal inheritance with the m.3243A>G mutation most common; stroke-like episodes, lactic acidosis, and ragged-red fibers. Treat acute episodes with IV arginine and avoid valproate.

Q15. A 10-month-old shows developmental regression, hypotonia, and abnormal eye movements. MRI shows symmetric T2 hyperintensities in the putamen and brainstem tegmentum; serum lactate is elevated. The diagnosis is: A) Alexander disease B) Canavan disease C) Adrenoleukodystrophy D) Leigh syndrome
Answer: D — Leigh syndrome (subacute necrotizing encephalomyelopathy): symmetric basal ganglia/brainstem necrotic lesions with lactic acidosis, caused by mtDNA or nuclear (e.g., SURF1) mutations.

Q16. A 3-day-old term neonate becomes lethargic with poor feeding after protein feeds. Ammonia is 480 µmol/L with respiratory alkalosis and low BUN. The most likely category is: A) Organic acidemia B) Maple syrup urine disease C) Urea cycle disorder D) Nonketotic hyperglycinemia
Answer: C — Urea cycle defect: marked hyperammonemia with respiratory alkalosis (ammonia-driven central hyperventilation) and low BUN. OTC deficiency is commonest. Stop protein, give IV glucose, start nitrogen scavengers, and dialyze if severe.

Q17. A 6-month-old has intractable seizures, alopecia, and an eczematous rash. Urine organic acids are abnormal. Which treatment is dramatically effective? A) Pyridoxine B) Biotin C) Thiamine D) Folinic acid
Answer: B — Biotinidase deficiency: seizures, alopecia, eczema, and developmental delay; biotin 5–10 mg/day lifelong is dramatically effective, making it a classic treatable cause of intractable epilepsy.

Q18. An 18-month-old with developmental regression and gait disturbance has MRI showing symmetric periventricular white-matter T2 hyperintensity with a tigroid pattern. The deficient enzyme is: A) Galactocerebrosidase B) Aspartoacylase C) Hexosaminidase A D) Arylsulfatase A
Answer: D — Metachromatic leukodystrophy: arylsulfatase A deficiency with sulfatide accumulation; the late-infantile form shows the tigroid MRI pattern from spared perivascular white matter.

Q19. A 5-month-old is extremely irritable with hyperesthesia, opisthotonic posturing, and optic atrophy. CSF protein is markedly elevated. The deficient enzyme is: A) Galactocerebrosidase B) Arylsulfatase A C) β-galactosidase D) α-L-iduronidase
Answer: A — Krabbe disease: galactocerebrosidase (GALC) deficiency with psychosine toxicity; the infantile form presents with extreme irritability, optic atrophy, peripheral neuropathy, and very high CSF protein.

Q20. A 7-year-old boy shows school failure and behavioral change. MRI shows symmetric parieto-occipital white-matter demyelination with a contrast-enhancing leading edge. Labs show elevated very-long-chain fatty acids and low cortisol. The diagnosis is: A) Metachromatic leukodystrophy B) Alexander disease C) X-linked adrenoleukodystrophy D) Pelizaeus-Merzbacher disease **Answer: C** — Childhood cerebral ALD: ABCD1 mutation, elevated VLCFA, parieto-occipital demyelination, and associated adrenal insufficiency. HSCT is indicated if the Loes score is <9 early in the course.

Q21. A 2-year-old with megalencephaly and seizures has MRI showing frontal-predominant white-matter changes. The mutated gene is: A) ASPA B) PLP1 C) ABCD1 D) GFAP **Answer: D** — Alexander disease: GFAP mutation with frontal predominance, megalencephaly, and Rosenthal fibers on pathology.

Q22. A 9-month-old with macrocephaly and developmental delay has MR spectroscopy showing a markedly elevated N-acetylaspartate peak. The diagnosis is: A) Alexander disease B) Krabbe disease C) Metachromatic leukodystrophy D) Canavan disease **Answer: D** — Canavan disease: aspartoacylase (ASPA) deficiency causes NAA accumulation, giving the elevated NAA peak on MRS, with macrocephaly and spongy white-matter degeneration.

Q23. A 4-year-old boy has a Gower sign, calf pseudohypertrophy, and CK of 12,000 IU/L. After confirming a dystrophinopathy, the most specific next step in management is: A) Start corticosteroids (prednisone/deflazacort) B) Start pyridostigmine C) Intravenous immunoglobulin D) Plasmapheresis **Answer: A** — Duchenne muscular dystrophy: corticosteroids (prednisone 0.75 mg/kg/day or deflazacort 0.9 mg/kg/day) prolong ambulation and are the cornerstone of therapy; exon-skipping agents and gene therapy are mutation-specific options.

Q24. A 5-month-old never sits, lies in a frog-leg posture, and has tongue fasciculations with a bell-shaped chest. Genetic testing shows a homozygous SMN1 deletion. The best disease-modifying therapy is: A) Prednisone B) Pyridostigmine C) Nusinersen (or onasemnogene abeparvovec/risdiplam) D) Intravenous immunoglobulin **Answer: C** — SMA type 1 (Werdnig-Hoffmann): SMN1 deletion; nusinersen (intrathecal), onasemnogene abeparvovec (one-time IV gene therapy), or risdiplam (oral) modify the disease course. SMN2 copy number predicts severity.

Q25. A 6-year-old develops ascending symmetric weakness with areflexia two weeks after a diarrheal illness. CSF shows protein 180 mg/dL with 3 WBC/ μ L. The treatment of choice is: A) High-dose corticosteroids alone B) IVIG (2 g/kg) or plasmapheresis C) Pyridostigmine D) Acyclovir **Answer: B** — Guillain-Barré syndrome: albuminocytologic dissociation (elevated protein, normal cell count); IVIG or plasmapheresis hasten recovery, while corticosteroids alone are ineffective.

Pediatric Pulmonology

Chapter 4: Pediatric Pulmonology

Pediatric pulmonology is one of the highest-yield chapters in the NEET SS Pediatrics paper: nearly every session tests asthma management steps, CFTR modulator selection, bronchiolitis "what NOT to do", PFT pattern interpretation, and status asthmaticus drug doses. The questions are vignette-based and assume MD Pediatrics baseline — they probe decisions at the DM level (biologic eligibility, genetic counselling in surfactant disorders, PSG interpretation), not mere recognition.

1. Asthma

Phenotypes and natural history

- **Early transient wheezers** (onset <18 months, remit by 3–6 years): small airways, associated with maternal smoking and viral triggers; no progression to persistent asthma.
- **Persistent wheezers** (onset <3 years, continue past 6 years): atopic — eczema, allergic rhinitis, parental asthma; eosinophilic inflammation; require controller therapy.
- **Late-onset wheezers**: begin 3–6 years, often non-atopic, viral-triggered.
- **Asthma Predictive Index (API)**: stringent — ≥ 3 episodes of wheezing before age 3 PLUS ≥ 1 major criterion (parental asthma, eczema, aeroallergen sensitization) or ≥ 2 minor criteria (food allergy, wheezing without colds, blood eosinophilia $\geq 4\%$); predicts persistent asthma at 6–13 years with $\sim 77\%$ positive predictive value.
- Two pathologic phenotypes in school-age children: **Th2-high (eosinophilic)** — allergen-driven, steroid-responsive, FeNO high; **Th2-low (neutrophilic/non-Th2)** — infection/exercise-triggered, relatively steroid-resistant.

Diagnosis

- Clinical: recurrent wheeze, nocturnal/early-morning cough, exercise- or cold-air-triggered symptoms, personal/family atopy; variable airflow limitation demonstrated by spirometry.
- **Spirometry criteria**: FEV1/FVC < lower limit of normal (<0.90 in children); **bronchodilator reversibility** = $\geq 12\%$ AND ≥ 200 mL increase in FEV1 (in children absolute volume less critical; $\geq 12\%$ accepted).
- FeNO >35 ppb supports eosinophilic airway inflammation; also used to monitor ICS adherence and predict exacerbation risk.
- Methacholine challenge: high negative predictive value (normal challenge essentially excludes current asthma) — see PFT section.

GINA stepwise management (children ≥6 years and adolescents)

- **Step 1** (infrequent symptoms, <twice/month): as-needed low-dose ICS-formoterol (preferred) OR as-needed SABA alone (older GINA only). GINA 2019 onward: **no SABA-only treatment** in anyone with asthma, including children ≥6 — every patient gets an ICS-containing reliever.
- **Step 2** (well-controlled on low-dose ICS or symptoms twice/month): daily low-dose ICS + as-needed ICS-formoterol OR low-dose ICS + SABA as needed.
- **Step 3:** low-dose ICS-LABA (preferred: SMART regimen — budesonide-formoterol as maintenance AND reliever).
- **Step 4:** medium-dose ICS-LABA (or medium-dose ICS + LABA SMART); add tiotropium or high-dose ICS-LABA if uncontrolled.
- **Step 5:** add-on therapy — LAMA (tiotropium), high-dose ICS-LABA, and refer for **biologic evaluation**; add oral corticosteroids only as last resort with monitoring of side effects.
- **Children 5 years and younger:** Step 1: as-needed SABA. Step 2: daily low-dose ICS (preferred controller) + as-needed SABA. Step 3: double low-dose ICS; consider intermittent high-dose ICS at onset of viral URI. Step 4: continue controller and refer to specialist (ICS-LABA use limited evidence in this age group; leukotriene receptor antagonists — montelukast — are an alternative at any step, especially for viral wheeze and allergic rhinitis).
- Low-dose ICS definitions (children 6–11 years): beclometasone HFA 100 mcg/day, budesonide DPI 200 mcg/day, fluticasone propionate DPI 100–200 mcg/day. Step-up only after checking **inhaler technique, adherence, and trigger control** — technique error accounts for most "treatment failures".
- Exacerbation trigger management: short-acting reliever (SABA) every 4 hours; viral URI management; allergen avoidance; influenza vaccination annually.

Severe asthma and biologics (children ≥6 years)

- **Severe asthma:** uncontrolled despite Step 4–5 therapy with correct technique/adherence — phenotype before prescribing.
- **Omalizumab** (anti-IgE): age ≥6 years; moderate-severe allergic asthma; IgE 30–1500 IU/mL and documented perennial aeroallergen sensitization; dosing by weight and IgE every 2–4 weeks subcutaneously; reduces exacerbations and ICS requirement.
- **Mepolizumab** (anti-IL-5): age ≥6 years; severe eosinophilic asthma (blood eosinophils ≥150 cells/μL at initiation or ≥300/μL in prior 12 months); monthly subcutaneous injection; reduces exacerbations.
- **Benralizumab** (anti-IL-5Rα, depletes eosinophils): adolescents/adults. **Dupilumab** (anti-IL-4Rα, blocks IL-4/IL-13): moderate-severe eosinophilic or oral-steroid-dependent asthma, children ≥6; also treats atopic dermatitis/nasal polyps.
- Before biologic: document severe eosinophilic or allergic phenotype, exclude modifiable factors, and note that all biologics reduce exacerbations — choice follows phenotype (allergic → omalizumab; eosinophilic → anti-IL-5 pathway; either/Th2-high → dupilumab).

Status asthmaticus (severe acute exacerbation)

- Recognition of life-threatening features: silent chest, cyanosis, altered sensorium, exhaustion, $\text{SpO}_2 < 90\%$, $\text{PEFR} < 33\%$ predicted, hypercapnia (normalizing CO_2 in a tiring child is ominous — it means impending respiratory arrest, not improvement).
- Management steps:
- **Oxygen:** high-flow to maintain SpO_2 94–98%; treat hypoxemia aggressively — hypoxemia kills in status asthmaticus.
- **Salbutamol:** nebulized 2.5–5 mg (0.15 mg/kg, max 5 mg) every 20 min for 3 doses, then hourly as needed; alternatively continuous nebulization 10–15 mg/hour. Add **ipratropium bromide** 250 mcg (< 20 kg) or 500 mcg (≥ 20 kg) every 20 min $\times$ 3 doses — combination superior to salbutamol alone in moderate-severe attacks.
- **Systemic corticosteroids:** **prednisolone 1–2 mg/kg/day** (max 60 mg) PO divided 1–2 doses, or IV methylprednisolone 1 mg/kg q6h (max 60 mg/day); give within 1 hour of presentation — benefits appear at 2–4 hours. Continue 3–5 days, no taper needed for short courses.
- **Magnesium sulfate: 25–75 mg/kg IV** (max 2 g) over 20 min in severe/refractory attacks — bronchodilator and calcium-channel effect; safe single dose; monitor for hypotension/flushing.
- Escalation: IV aminophylline (5 mg/kg loading if not on theophylline) or terbutaline infusion in ICU; consider noninvasive ventilation; intubation only with senior supervision — risk of air trapping, barotrauma, and cardiovascular collapse; use ketamine for induction.
- What NOT to do: no routine antibiotics, no sedatives (absolute contraindication — mask deterioration), no chest physiotherapy in acute phase, no routine ABG (clinical assessment suffices; ABG only if ICU-level).

2. Cystic Fibrosis

Genetics and pathophysiology

- Autosomal recessive; gene **CFTR** (cystic fibrosis transmembrane conductance regulator) on chromosome 7q31.2 — a cAMP-activated chloride channel also regulating ENaC (sodium) channels.
- **ΔF508 (F508del):** most common mutation worldwide ($\sim 70\%$ of CF chromosomes); class II — defective protein processing, retained in endoplasmic reticulum, degraded. Classes: I (no protein — e.g. G542X), II (trafficking), III (gating — G551D), IV (conductance), V (reduced quantity), VI (reduced stability).
- Pathophysiology: defective chloride secretion + excessive sodium/water absorption $\rightarrow$ dehydrated airway surface liquid $\rightarrow$ impaired mucociliary clearance $\rightarrow$ chronic bacterial infection, neutrophilic inflammation, bronchiectasis; pancreatic duct obstruction $\rightarrow$ exocrine insufficiency; bile duct/sweat gland/vas deferens involvement (congenital bilateral absence of vas deferens — CBAVD — causes male infertility; females fertile but with reduced fertility).

Diagnosis

- **Sweat chloride** is the diagnostic test: ≥ 60 mmol/L diagnostic of CF; 30–59 intermediate (repeat, do CFTR mutation analysis); < 30 normal (in infants < 30 ; < 40 in older children/adults excludes CF in most). Performed by pilocarpine iontophoresis (Gibson-Cooke) after 10 days of age, weight > 2 kg.

- Newborn screening: immunoreactive trypsinogen (IRT) ± DNA panel. Nasal potential difference and intestinal current measurement for equivocal cases.
- Clinical clues: meconium ileus (20% of CF newborns), failure to thrive with steatorrhea, recurrent sinopulmonary infections, nasal polyps in a child, *Pseudomonas aeruginosa* cultured from airway, hypochloremic metabolic alkalosis (Pseudo-Bartter), heat prostration.

Pancreatic insufficiency and nutrition

- 85–90% are pancreatic insufficient: fecal elastase-1 <100 µg/g (severe) or <200 µg/g (insufficient); steatorrhea, failure to thrive.
- **Pancreatic enzyme replacement therapy (PERT)**: lipase 2000–4000 units per gram of dietary fat (or 500–2500 units/kg/meal; max 10,000 units/kg/day to avoid fibrosing colonopathy); give at start of and during meals; add acid suppression (PPI) if poor response. Monitor fat-soluble vitamins A, D, E, K; target BMI ≥50th percentile.
- CF-related diabetes (CFRD): annual OGTT screening from age 10; treat with **insulin** (not oral hypoglycemics — insulin deficiency with insulin resistance); associated with worse pulmonary outcomes.

Pulmonary management and *Pseudomonas*

- Airway clearance: chest physiotherapy, high-frequency chest wall oscillation vest, huff coughing, DNase (dornase alfa) nebulization, hypertonic saline (3–7%).
- First *Pseudomonas aeruginosa* isolation: **eradication protocol** — inhaled tobramycin 300 mg BID for 28 days (TOBI) ± oral ciprofloxacin 14 days; chronic colonization: alternating inhaled tobramycin/colistin cycles, azithromycin 3×/week (anti-inflammatory/anti-quorum sensing).
- Exacerbation: IV antipseudomonal β-lactam (ceftazidime/piperacillin-tazobactam/meropenem) + aminoglycoside for 14 days; *Burkholderia cepacia* complex — strict segregation, poor post-transplant outcomes; MRSA and *Stenotrophomonas* also relevant; **ABPA** below.
- Lung transplantation: FEV1 <30% predicted with exacerbations, or rapid decline; referral when FEV1 <50%.

CFTR modulators (genotype-directed therapy)

- **Ivacaftor** (potentiator): gating mutations (G551D) and residual-function mutations; increases channel open probability.
- **Lumacaftor/ivacaftor**: homozygous F508del; corrector + potentiator — modest FEV1 gain, notable pulmonary exacerbation reduction; significant drug interactions (lumacaftor is a strong CYP3A inducer — reduces efficacy of OCPs, azoles).
- **Tezacaftor/ivacaftor**: homozygous F508del or F508del + residual-function; fewer drug interactions than lumacaftor combo.
- **Elexacaftor/tezacaftor/ivacaftor (ETI, triple therapy)**: F508del homozygous OR heterozygous with minimal-function mutation — the most effective modulator: FEV1 ↑ ~14%, exacerbations ↓ ~63%, sweat chloride falls, BMI rises; approved down to young children; monitor LFTs and cataracts (in young children).

- Modulators do not cure CF: airway clearance and infection surveillance continue; they transform prognosis and eligibility for transplant.

Allergic bronchopulmonary aspergillosis (ABPA)

- Hypersensitivity to *Aspergillus fumigatus* colonizing airways; occurs in CF and asthma.
- Diagnostic criteria (CF): clinical deterioration + total IgE >500 IU/mL (often >1000) + *Aspergillus*-specific IgE positive + precipitating IgG antibodies + new radiographic infiltrates/bronchiectasis; eosinophilia supportive.
- Treatment: systemic corticosteroids (prednisolone 0.5–1 mg/kg/day tapering over 3–6 months) ± **itraconazole** (steroid-sparing); monitor IgE — a 35–50% fall indicates response; relapse common.

3. Bronchiolitis

Etiology and clinical features

- Leading cause: **respiratory syncytial virus (RSV)** (50–80%); others — rhinovirus, human metapneumovirus, parainfluenza 3, adenovirus, bocavirus.
- Peak age 2–18 months (most <12 months); winter seasonality; pathology — necrotizing bronchiolar inflammation, epithelial sloughing, mucus plugging → small-airway obstruction, air trapping, atelectasis.
- Clinical: 2–3 day coryzal prodrome → tachypnea, wheeze, fine crackles, chest hyperinflation, feeding difficulty; apnea may be the presenting feature in young infants (<6 weeks); peak severity day 3–5.
- Risk factors for severe disease: prematurity, age <12 weeks, chronic lung disease (BPD), hemodynamically significant congenital heart disease, immunodeficiency, neuromuscular disease.
- Diagnosis is clinical; routine chest X-ray and viral testing not required in typical cases. Differentiate from: viral wheeze/asthma (recurrent, older infant, atopy), pneumonia (fever >39°C, focal crackles, toxicity), pertussis, foreign body, heart failure.

Supportive management — and what NOT to do

- Mainstays: **oxygen** to keep SpO₂ ≥90% (some guidelines ≥92%), nasal suctioning, IV/NG hydration when feeding <50% of normal or respiratory rate >60–70, minimal handling.
- **High-flow nasal cannula (HFNC)**: heated humidified oxygen at 1–2 L/kg/min; reduces work of breathing and escalation to CPAP/intubation; use in moderate-severe distress or failure to maintain saturation; does not shorten hospital stay vs standard oxygen in mild cases.
- CPAP/intubation for apnea, exhaustion, or refractory hypoxemia.
- **What NOT to do (AAP/NICE — heavily tested)**: NO routine **bronchodilators** (salbutamol trial only in selected cases, stop if no response), NO routine **systemic corticosteroids**, NO routine **antibiotics**, NO routine chest physiotherapy, NO hypertonic saline in the emergency department (may be used in admitted infants but benefit marginal). A single-dose adrenaline trial is no longer recommended routinely.

Palivizumab prophylaxis

- Humanized monoclonal antibody against RSV F protein; monthly IM injections (15 mg/kg) during RSV season (5 doses).
- Criteria (AAP): preterm <29 weeks gestation and <12 months at season start; chronic lung disease of prematurity requiring oxygen/medical therapy in prior 6 months and <24 months; hemodynamically significant CHD and <12 months; anatomic pulmonary/neuromuscular disorders impairing airway clearance and <12 months.
- NOT for healthy term infants, NOT for treatment, NOT beyond the second season except select BPD/CHD cases. Newer long-acting monoclonal **nirsevimab** (single dose per season) is replacing palivizumab in many guidelines — know its existence.

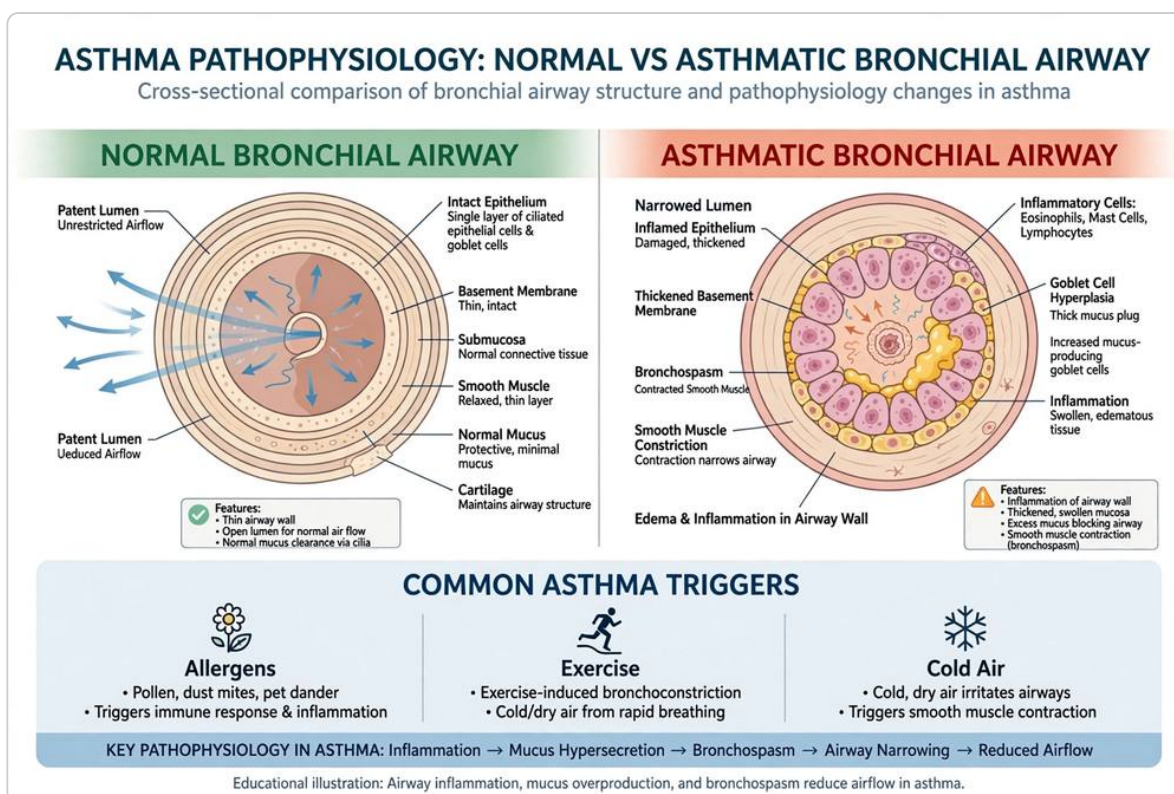


Figure 4.1 — Asthma pathophysiology: normal vs asthmatic airway

4. Pneumonia

Community-acquired pneumonia — organisms by age

- **Neonate (<1 month):** Group B *Streptococcus*, *E. coli*, *Listeria*; consider *Chlamydia trachomatis* (afebrile pneumonitis at 2–12 weeks with eosinophilia and staccato cough).
- **1–3 months:** *S. pneumoniae*, *Chlamydia trachomatis*, *Bordetella pertussis*, RSV/viruses.
- **3 months–5 years:** viruses dominate (RSV, influenza, parainfluenza, adenovirus, rhinovirus); bacterial — *S. pneumoniae* (commonest bacterial), *H. influenzae* (non-typeable), *M. pneumoniae* (increasing after 3 years), *S. aureus* (post-influenza, necrotizing).

- **>5 years:** *Mycoplasma pneumoniae* (commonest in school-age), *S. pneumoniae*, *Chlamydia pneumoniae*.
- Clinical: fever, tachypnea (WHO cutoffs: $\geq 60/\text{min}$ <2 months, $\geq 50/\text{min}$ 2–12 months, $\geq 40/\text{min}$ 1–5 years), cough, crackles, chest indrawing; chest X-ray not routine in mild outpatient cases — obtain if hypoxic, toxic, complicated, or recurrent.

Treatment

- **Amoxicillin first-line** for uncomplicated CAP in children: 80–90 mg/kg/day divided BID/TID for 5–7 days (high dose for penicillin-resistant pneumococcus). Alternatives if β -lactam allergy: macrolide (azithromycin) or levofloxacin.
- Suspected atypical (*Mycoplasma/Chlamydia* — age >5, prolonged low-grade fever, bilateral infiltrates): **azithromycin** 10 mg/kg day 1, then 5 mg/kg days 2–5.
- Neonatal: ampicillin + gentamicin (or cefotaxime). MRSA suspected (necrotizing, pneumatoceles, post-influenza): vancomycin or clindamycin + β -lactam.
- Admission criteria: hypoxemia ($\text{SpO}_2 < 90\%$), severe distress, toxic appearance, dehydration, age <2–6 months, immunocompromise, failed outpatient therapy.

Complicated pneumonia and empyema

- Parapneumonic effusion → fibrinopurulent → organized empyema; suspect with persistent fever >48 h on antibiotics, worsening distress, or dullness with absent breath sounds; confirm with chest ultrasound (septations/loculations) — ultrasound is the investigation of choice for staging.
- Management: IV antibiotics (cover *S. pneumoniae*, *S. aureus* — ceftriaxone + cloxacillin/vancomycin); **chest tube drainage** for frank pus, loculations, or large effusions causing compromise; **intrapleural fibrinolytics** (urokinase/alteplase) reduce need for surgery in loculated empyema; VATS/decortication if organized peel or failed drainage.
- Necrotizing pneumonia: pneumatoceles, bronchopleural fistula — prolonged antibiotics (3–4 weeks), avoid chest tube unless tension/pyopneumothorax; most pneumatoceles resolve spontaneously.

Recurrent pneumonia — workup

- Definition: ≥ 2 episodes in 1 year or ≥ 3 in lifetime with radiographic clearance between episodes; **same lobe** recurrence → local cause; different lobes → systemic cause.
- Same lobe: foreign body (ask!), right middle lobe syndrome, bronchiectasis, congenital anomaly (CPAM, sequestration), extrinsic compression (lymph node, vascular ring).
- Different lobes: aspiration (GERD, swallowing dysfunction, tracheoesophageal fistula), immunodeficiency (hypogammaglobulinemia, CGD), CF, PCD, ciliary dysfunction, asthma misdiagnosed.
- Workup: detailed history (choking episode, feeds, atopy), HRCT chest, sweat chloride, immunoglobulins, bronchoscopy if foreign body suspected, contrast swallow/videofluoroscopy if aspiration suspected, pH-impedance for GERD.

Aspiration syndromes

- Risk: neuromuscular disease, GERD, tracheoesophageal fistula, depressed consciousness, anatomical dysphagia.
- Recurrent right upper lobe (supine aspiration) or superior segment of lower lobe pneumonia; chronic aspiration → bronchiectasis, interstitial changes.
- Diagnosis: videofluoroscopic swallow study, milk scan (radionuclide salivagram), BAL with lipid-laden macrophages (supportive, not specific).
- Management: treat underlying cause, thickened feeds, upright positioning, anti-reflux therapy, gastrostomy if unsafe swallow; consider fundoplication in severe GERD with aspiration.

5. Childhood Interstitial Lung Disease (chILD)

- Heterogeneous group of diffuse parenchymal lung diseases; classification (ATS/ERS): disorders of infancy (developmental, surfactant dysfunction), disorders of older children (immune-mediated, systemic disease-associated), and exposure-related.
- Red flags: tachypnea/hypoxemia out of proportion to X-ray, failure to thrive, clubbing, crackles, family history of neonatal respiratory deaths, consanguinity.
- HRCT patterns: ground-glass opacification, septal thickening, cysts; lung biopsy (surgical) remains gold standard in ambiguous cases; genetic testing increasingly first-line when surfactant disorder suspected.

Neuroendocrine cell hyperplasia of infancy (NEHI)

- Presents <2 years with persistent tachypnea, hypoxemia, crackles, failure to thrive — but affected infants are usually **not severely ill**; insidious onset after an apparently normal neonatal period.
- HRCT: characteristic **ground-glass opacification in the right middle lobe, lingula, and paramediastinal regions** — so specific that biopsy can be avoided.
- Histology: increased bombesin-immunopositive neuroendocrine cells in distal airways without inflammation or fibrosis; diagnosis now clinical-radiological.
- Course: generally good prognosis — symptoms improve over years, most outgrow oxygen need by 2–3 years; management is supportive (oxygen, nutrition, avoid over-immunosuppression — steroids do NOT help).

Surfactant protein disorders

- **SFTPB (surfactant protein B)**: autosomal recessive; presents with severe RDS in a **term** infant, refractory to surfactant and ventilation; **lethal** — death in weeks-months without lung transplant; most common mutation 121ins2.
- **ABCA3**: autosomal recessive (most common genetic cause of surfactant dysfunction); spectrum — fatal neonatal RDS to chronic ILD in older children; consanguinity clue.
- **SFTPC**: autosomal **dominant** (de novo common); variable — neonatal RDS to adult-onset pulmonary fibrosis; family history of ILD across generations.

- NKX2-1 (TTF-1): triad of chILD + congenital hypothyroidism + chorea (brain-lung-thyroid syndrome), autosomal dominant.
- Management: genetic diagnosis, supportive care, hydroxychloroquine/azithromycin tried with limited evidence; **lung transplantation** is definitive for severe SFTP/ABCA3 neonatal disease; counsel families — 25% recurrence risk for recessive forms.

6. Sleep-Disordered Breathing and OSA

- Spectrum: primary snoring → upper airway resistance syndrome → **obstructive sleep apnea (OSA)** → obstructive hypoventilation.
- Commonest cause in children: **adenotonsillar hypertrophy** (peak 3–7 years); others — obesity (adolescents), craniofacial anomalies (Pierre Robin, Down syndrome, achondroplasia), neuromuscular disease, sickle cell disease.
- Clinical: habitual loud snoring ≥3 nights/week, witnessed apneas, mouth breathing, restless sleep, enuresis, daytime somnolence/poor school performance, hyperactivity (children present with **inattention/hyperactivity rather than sleepiness**), growth failure, morning headache; examination — adenoid facies, tonsillar hypertrophy (Brodsky grading), midface hypoplasia.
- Complications: neurocognitive deficits, behavioral problems, systemic/pulmonary hypertension, cor pulmonale (severe), metabolic syndrome.

Polysomnography (PSG) — indications

- **Gold standard** for diagnosis of OSA; AHI (apnea-hypopnea index): ≥1.5–2 events/hour abnormal in children (adult cutoff 5 does not apply); OSA severity — mild AHI 1–5, moderate 5–10, severe >10.
- Indications: habitual snoring with risk factors, equivocal clinical picture before adenotonsillectomy in high-risk children (<3 years, severe OSA, comorbidities — Down syndrome, craniofacial anomalies, neuromuscular disease, obesity, sickle cell), persistent symptoms after surgery, central apnea suspicion.
- Overnight oximetry is a screening tool only — normal oximetry does not exclude OSA.

Management

- **Adenotonsillectomy is first-line** for OSA due to adenotonsillar hypertrophy — curative in ~80% of otherwise healthy children.
- Mild OSA or mild adenotonsillar hypertrophy: trial of intranasal corticosteroids ± montelukast for 6–12 weeks.
- Residual/persistent OSA (obesity, Down syndrome, craniofacial): **CPAP**; maxillofacial surgery/orthodontic expansion in selected adolescents; weight management.
- Perioperative caution: children with severe OSA (AHI >10), age <3 years, or comorbidities need postoperative inpatient monitoring — heightened opioid sensitivity and risk of postoperative respiratory compromise; avoid routine opioids, use multimodal analgesia.

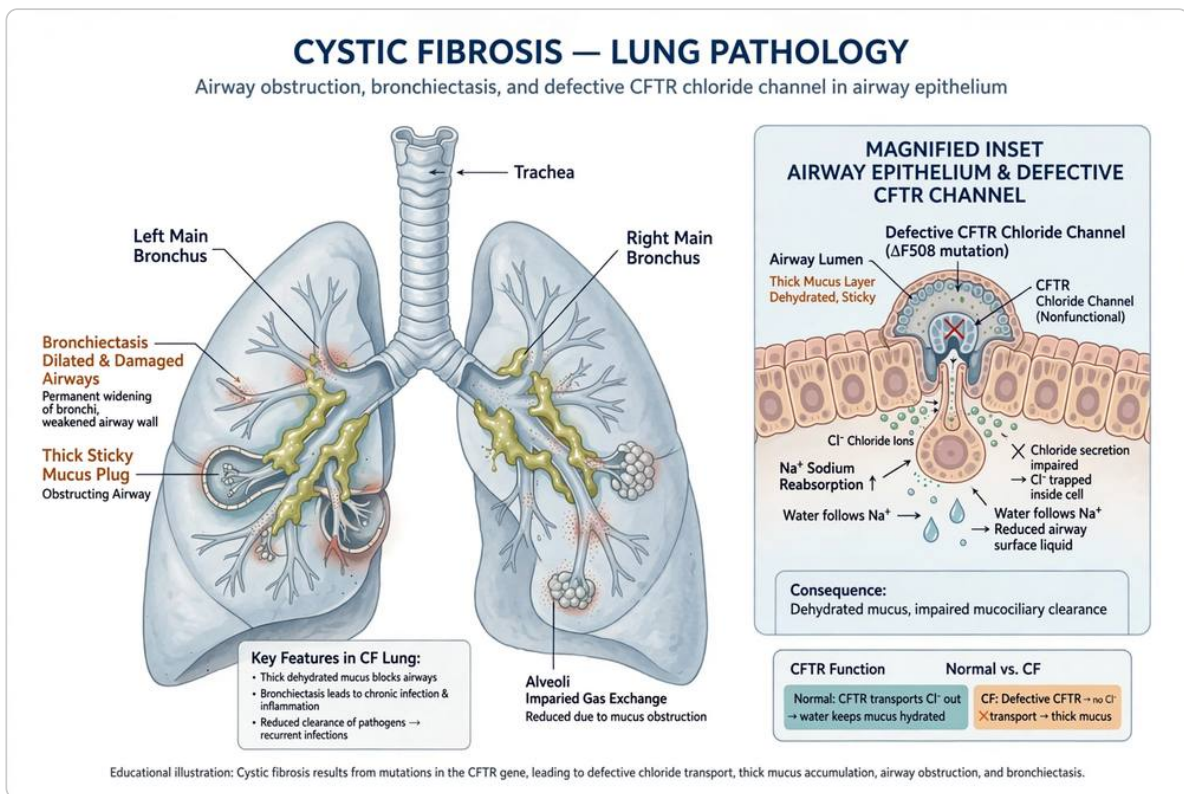


Figure 4.2 — Cystic fibrosis lung disease

7. Pulmonary Function Test Interpretation

Obstructive vs restrictive patterns

- **Obstructive:** FEV1/FVC **reduced** (< lower limit of normal; <0.85–0.90 in children); FEV1 reduced; FVC normal or reduced (air trapping); **TLC normal or increased** (hyperinflation); RV increased; DLCO normal or increased (asthma) — reduced in emphysema.
- **Restrictive:** FEV1/FVC **normal or increased**; FVC reduced; **TLC reduced** (<80% predicted) — TLC is required to confirm true restriction (a low FVC with normal TLC is "pseudo-restriction" from air trapping or suboptimal effort); DLCO reduced (interstitial disease) or normal (chest wall/neuromuscular disease with normal parenchyma).
- Mixed pattern: both FEV1/FVC and TLC reduced.
- **Bronchodilator reversibility:** ≥12% AND ≥200 mL increase in FEV1 (or FVC) — supports asthma; lack of reversibility does not exclude it.

Flow-volume loops

- **Obstructive:** scooped/coved expiratory limb, reduced peak flow, prolonged expiration.
- **Restrictive:** tall narrow loop — reduced volumes but normal shape, steep slopes.
- **Variable extrathoracic obstruction** (vocal cord dysfunction, laryngomalacia): flattened **inspiratory** limb.
- **Variable intrathoracic obstruction** (tracheomalacia, mediastinal mass): flattened **expiratory** limb.

- **Fixed obstruction** (tracheal stenosis, foreign body): flattening of **both** limbs — box-shaped loop.

DLCO and lung volumes

- **DLCO** (diffusing capacity for carbon monoxide): reduced in interstitial disease, emphysema, pulmonary vascular disease, anemia (correct for hemoglobin); increased in asthma, obesity, pulmonary hemorrhage, left-to-right shunt/polycythemia.
- Elevated RV/TLC ratio indicates air trapping (asthma, CF, bronchiolitis obliterans).

Methacholine challenge

- Indication: suspected asthma with **normal baseline spirometry**; inhaled methacholine in doubling concentrations; positive if FEV1 falls $\geq 20\%$ (PC20).
- **High negative predictive value** — a negative challenge essentially rules out current asthma; positive test is nonspecific (also positive in CF, allergic rhinitis, COPD, post-viral hyperreactivity).
- Contraindications: FEV1 $< 60\text{--}70\%$ predicted, recent MI/stroke, uncontrolled hypertension, pregnancy, current respiratory infection.

8. Bronchiectasis, Primary Ciliary Dyskinesia, Foreign Body Aspiration

Bronchiectasis

- Definition: irreversible abnormal dilatation of bronchi with chronic productive cough; causes in children — CF (commonest in West), post-infectious (measles, pertussis, adenovirus, TB), immunodeficiency, PCD, aspiration, ABPA.
- **HRCT is the gold standard**: signet-ring sign (bronchus larger than accompanying artery — broncho-arterial ratio > 1), lack of tapering, bronchial wall thickening, mucus plugging; cylindrical $>$ varicose $>$ cystic (Reid classification).
- Clinical: chronic wet cough, recurrent infections, hemoptysis, clubbing, coarse crackles; sputum culture — *H. influenzae*, *S. pneumoniae*, *Pseudomonas* (CF/non-CF).
- Workup: HRCT, sweat chloride, immunoglobulins (IgG, IgA, IgM, IgE), nasal NO/ciliary studies if PCD suspected, sputum cultures, consider bronchoscopy.
- Management: airway clearance physiotherapy (cornerstone), prompt antibiotics for exacerbations (guided by sputum culture; *Pseudomonas* — ciprofloxacin $\pm$ inhaled tobramycin), long-term azithromycin in frequent exacerbators, treat underlying cause (immunoglobulin replacement, PERT in CF), influenza/pneumococcal vaccination; surgery (lobectomy) only for localized disease failing medical therapy.

Primary ciliary dyskinesia (PCD)

- Autosomal recessive (mostly); defective dynein arms/ultrastructure → impaired mucociliary clearance.

- Classic triad (**Kartagener syndrome**): chronic sinusitis, bronchiectasis, **situs inversus** (50% — dextrocardia); neonatal RDS in term infant, chronic wet cough from day 1, chronic otitis media with hearing loss, male infertility (immotile sperm).
- **Nasal nitric oxide (nNO)**: markedly **low** (<77 nL/min) — best screening test; confirm with high-speed video microscopy of ciliary beat and transmission electron microscopy of ciliary ultrastructure; genetics (DNAH5, DNAI1 most common).
- Differentiate from CF: PCD has normal sweat chloride, earlier otitis/sinus disease, situs anomalies, low nasal NO (nasal NO is normal-to-high in CF).
- Management: like non-CF bronchiectasis — airway clearance, aggressive antibiotics, avoid smoking; lung function declines slower than CF; genetic counselling.

Foreign body aspiration

- Peak age 1–3 years; organic (peanut — commonest, seeds) vs inorganic; right main bronchus commonest site (more vertical), but in small children either side.
- **Ball-valve (check-valve) effect**: air enters on inspiration but cannot exit on expiration → obstructive emphysema of affected segment/lobe — **expiratory chest X-ray or decubitus film shows air trapping** with mediastinal shift away; complete obstruction → atelectasis; chronic → recurrent same-lobe pneumonia/bronchiectasis.
- Clinical: sudden choking/gagging (may be unwitnessed), then asymptomatic interval, then cough/wheeze; unilateral wheeze or decreased breath sounds is the red flag.
- **Rigid bronchoscopy is the gold standard** — diagnostic AND therapeutic (removal); flexible bronchoscopy for distal or uncertain cases; do not attempt blind finger sweeps; back blows/chest thrusts (Heimlich in older children) only for complete obstruction.
- Prevention counselling: no peanuts/whole grapes/popcorn before age 4, supervised eating.

9. Congenital Lung Anomalies (brief)

Congenital pulmonary airway malformation (CPAM, formerly CCAM)

- Hamartomatous lesion from abnormal branching morphogenesis; Stocker types: 0 (lethal), **I (commonest — large cysts >2 cm, good prognosis)**, II (small cysts, associated anomalies), III (microcystic, poor prognosis), IV (large cyst, pneumothorax risk).
- Antenatal ultrasound diagnosis; CVR (CPAM volume ratio) >1.6 predicts hydrops risk; most regress partially in third trimester.
- Postnatal: CT chest for delineation; asymptomatic lesions — elective lobectomy debated (infection/malignancy risk — pleuropulmonary blastoma association in type IV); symptomatic (respiratory distress, infection) → surgical resection (lobectomy preferred over segmentectomy).

Congenital diaphragmatic hernia (CDH)

- Posterolateral (Bochdalek, 90% — left-sided 85%) defect → herniation of abdominal contents → **pulmonary hypoplasia** (ipsilateral worse, contralateral also affected) + persistent pulmonary hypertension of the newborn (PPHN).
 - Presentation: respiratory distress at birth, scaphoid abdomen, barrel chest, bowel sounds in thorax, mediastinal shift.
 - Management principles: **avoid bag-mask ventilation** (inflates bowel, worsens compression) — immediate **endotracheal intubation**, NG tube decompression; gentle ventilation (permissive hypercapnia, PIP <25 cm H₂O), treat PPHN (inhaled nitric oxide, ECMO if needed); **delayed surgical repair** after cardiopulmonary stabilization (24–48 h, not a neonatal emergency); associated anomalies — cardiac, chromosomal (trisomy 18).
 - Prognostic markers: lung-to-head ratio (LHR) on antenatal ultrasound, observed/expected LHR <25% severe; liver herniation ("liver up") — poor prognosis.
-

Practice MCQs

Q1. A 7-year-old boy with moderate persistent asthma on low-dose budesonide has had 4 exacerbations in the past year requiring oral steroids. His IgE is 450 IU/mL with positive skin prick to house dust mite. Inhaler technique and adherence are confirmed good. The most appropriate next step is: A) Double the budesonide dose and continue SABA as needed B) Add montelukast and continue current therapy C) Refer for omalizumab eligibility assessment D) Start daily oral prednisolone **Answer: C** — This is severe allergic asthma in a child ≥6 years with IgE 30–1500 IU/mL and perennial aeroallergen sensitization, uncontrolled despite controller therapy. Omalizumab (anti-IgE) is the indicated add-on biologic. Daily oral steroids are a last resort, and technique/adherence are already optimized.

Q2. A 3-month-old term infant presents with coryza for 2 days followed by tachypnea (RR 68/min), wheeze, and fine crackles. SpO₂ is 93% on room air. Chest X-ray shows hyperinflation with peribronchial thickening. The most appropriate management includes: A) Nebulized salbutamol every 4 hours and oral prednisolone B) IV ceftriaxone and azithromycin C) Supplemental oxygen, nasal suctioning, and maintenance of hydration D) High-dose inhaled corticosteroids via spacer **Answer: C** — Typical RSV bronchiolitis is managed supportively: oxygen to keep SpO₂ ≥90%, suctioning, and hydration. Routine bronchodilators, systemic steroids, and antibiotics are NOT recommended by AAP/NICE guidelines.

Q3. A 10-year-old girl with cystic fibrosis (F508del homozygous) has chronic *Pseudomonas aeruginosa* colonization with declining FEV1. Which CFTR modulator combination offers the greatest expected FEV1 improvement for her genotype? A) Ivacaftor alone B) Lumacaftor/ivacaftor C) Tezacaftor/ivacaftor D) Elexacaftor/tezacaftor/ivacaftor **Answer: D** — Elexacaftor/tezacaftor/ivacaftor (triple therapy) is the most effective modulator for F508del homozygous patients, improving FEV1 by ~14% and reducing exacerbations by ~63%. Ivacaftor alone works only for gating/residual-function mutations.

Q4. Spirometry in a 12-year-old shows FVC 68% predicted, FEV1 70% predicted, FEV1/FVC 0.92, and TLC 65% predicted. Bronchodilator produces a 6% FEV1 increase. The pattern indicates: A) Obstructive defect with

significant reversibility B) Restrictive defect, likely parenchymal C) Mixed obstructive-restrictive defect D) Normal study with poor effort **Answer: B** — FVC is reduced with a normal/high FEV1/FVC ratio and a reduced TLC (<80% predicted), which confirms true restriction. TLC is required to distinguish true restriction from pseudo-restriction due to air trapping. The 6% BD response is not significant (needs $\geq 12\%$ and ≥ 200 mL).

Q5. A 2-year-old with sudden onset choking while eating peanuts, followed by persistent cough and unilateral wheeze on the right, has a chest X-ray showing hyperinflation of the right lung on the expiratory film with mediastinal shift to the left. The pathophysiology and gold-standard management are: A) Complete bronchial obstruction causing atelectasis; flexible bronchoscopy B) Aspiration pneumonitis; IV antibiotics and chest physiotherapy C) Ball-valve effect causing obstructive emphysema; rigid bronchoscopy D) Reactive airway disease; nebulized adrenaline **Answer: C** — The peanut creates a check-valve (ball-valve) obstruction: air enters on inspiration but cannot escape on expiration, causing obstructive emphysema visible on expiratory films. Rigid bronchoscopy is the gold standard for both diagnosis and therapeutic removal.

Q6. Parents of a 28-week preterm infant now 8 months old (chronological) with bronchopulmonary dysplasia requiring home oxygen ask about RSV prevention for the upcoming winter season. The correct advice is: A) Monthly palivizumab 15 mg/kg IM for the RSV season B) Palivizumab is not indicated since the infant is over 6 months old C) Single dose of nirsevimab is contraindicated in BPD D) Oral ribavirin prophylaxis for 5 days each month **Answer: A** — Infants with chronic lung disease of prematurity requiring medical therapy within 6 months of the season start qualify for palivizumab prophylaxis up to 24 months of age. The dose is 15 mg/kg IM monthly (5 doses per season). Nirsevimab (long-acting monoclonal) is an emerging single-dose alternative, not contraindicated.

Q7. A 14-year-old with severe asthma on high-dose ICS-LABA has blood eosinophils of 420 cells/ μ L, IgE 80 IU/mL, and negative aeroallergen testing. He continues to have frequent exacerbations. The most appropriate biologic is: A) Omalizumab B) Ivacaftor C) Palivizumab D) Mepolizumab **Answer: D** — This is a severe eosinophilic (non-allergic) phenotype: eosinophils ≥ 150 cells/ μ L at initiation with negative allergy workup. Mepolizumab (anti-IL-5) is indicated for severe eosinophilic asthma in children ≥ 6 years. Omalizumab requires allergic sensitization with IgE 30–1500 IU/mL.

Q8. A 6-year-old with cystic fibrosis develops worsening cough, new infiltrates on chest X-ray, total serum IgE of 1200 IU/mL, and positive Aspergillus-specific IgE. The most likely diagnosis and first-line treatment are: A) Pseudomonas exacerbation; IV ceftazidime and tobramycin B) Allergic bronchopulmonary aspergillosis; systemic corticosteroids C) ABPA; itraconazole monotherapy D) CF-related diabetes; insulin therapy **Answer: B** — Total IgE >500 IU/mL (here 1200) with Aspergillus-specific IgE and new infiltrates in a CF patient meets ABPA criteria. First-line treatment is systemic corticosteroids (prednisolone taper over months); itraconazole is an adjunct steroid-sparing agent, not monotherapy.

Q9. An 8-year-old with recurrent pneumonia of the right middle lobe (3 episodes in 2 years, clearing between episodes) undergoes HRCT showing bronchiectasis localized to the right middle lobe. Sweat chloride and immunoglobulins are normal. The next best step is: A) Start long-term azithromycin B) Lobectomy of the right middle lobe C) CFTR modulator therapy D) Bronchoscopy to exclude foreign body **Answer: D** — Recurrent pneumonia in the SAME lobe points to a local cause, and an aspirated foreign body is the classic etiology in this age group. Bronchoscopy is both diagnostic and therapeutic. Surgery is reserved for localized disease failing medical therapy after the cause is addressed.

Q10. A 5-year-old with loud habitual snoring, witnessed apneas, and daytime hyperactivity undergoes polysomnography showing an AHI of 8 events/hour. Examination reveals Brodsky grade 3 tonsils. The most appropriate management is: A) Adenotonsillectomy B) Intranasal steroids for 12 months C) CPAP titration D) Reassurance and watchful waiting **Answer: A** — AHI 8/hour is moderate-to-severe pediatric OSA (pediatric thresholds: mild 1–5, moderate 5–10, severe >10), and adenotonsillar hypertrophy is the commonest cause. Adenotonsillectomy is first-line and curative in ~80% of otherwise healthy children. CPAP is reserved for residual/persistent OSA.

Q11. In status asthmaticus, a 9-year-old weighing 30 kg remains severely distressed after 3 salbutamol-ipratropium nebulizations and IV methylprednisolone. The appropriate dose of IV magnesium sulfate and its rationale are: A) 10 mg/kg; calcium channel blockade reduces mucus viscosity B) 25–75 mg/kg (max 2 g); bronchodilation via calcium antagonism and membrane stabilization C) 100 mg/kg; direct mast cell degranulation D) Magnesium is contraindicated in children with asthma **Answer: B** — IV magnesium sulfate 25–75 mg/kg (max 2 g) over 20 minutes is indicated in severe/refractory status asthmaticus. It acts as a physiologic calcium antagonist producing bronchial smooth-muscle relaxation. It is safe as a single dose; monitor for hypotension and flushing.

Q12. A term neonate develops severe respiratory distress within hours of birth, refractory to surfactant and mechanical ventilation. The infant's older sibling died of similar neonatal respiratory failure. The most likely diagnosis is: A) Surfactant protein B deficiency B) Transient tachypnea of the newborn C) Meconium aspiration syndrome D) Congenital diaphragmatic hernia **Answer: A** — Severe RDS in a TERM infant refractory to surfactant, with a family history of neonatal respiratory deaths (autosomal recessive), is classic for SFTPB deficiency (most common mutation 121ins2). It is lethal without lung transplantation. TTN resolves within 24–72 hours and MAS occurs with meconium-stained liquor.

Q13. A 16-month-old with persistent tachypnea, crackles, and failure to thrive since 3 months of age is growing along a low but steady curve and is not severely ill. HRCT shows ground-glass opacification in the right middle lobe, lingula, and paramediastinal regions. The most likely diagnosis is: A) Surfactant protein C deficiency B) Hypersensitivity pneumonitis C) Cystic fibrosis D) Neuroendocrine cell hyperplasia of infancy **Answer: D** — NEHI presents in infancy with persistent tachypnea and hypoxemia in a child who is not severely ill, with highly characteristic HRCT ground-glass changes in the right middle lobe, lingula, and paramediastinal areas. This radiologic pattern is diagnostic enough to avoid lung biopsy. Prognosis is good with supportive care; steroids do not help.

Q14. A 12-year-old boy has had a chronic wet cough since infancy, recurrent otitis media, and chronic sinusitis. Chest X-ray shows dextrocardia. Nasal nitric oxide is markedly reduced. The most likely diagnosis and confirmatory test are: A) Primary ciliary dyskinesia; ciliary ultrastructure on electron microscopy B) Cystic fibrosis; sweat chloride C) Immunodeficiency; serum immunoglobulins D) Asthma; methacholine challenge **Answer: A** — The triad of chronic sinopulmonary disease, otitis media, and situs inversus (Kartagener syndrome) with very low nasal NO indicates primary ciliary dyskinesia. Confirmation is by high-speed video microscopy of ciliary beat or transmission electron microscopy showing dynein arm defects. Sweat chloride is normal in PCD.

Q15. A 4-year-old with known asthma presents with SpO₂ 88% on room air, silent chest, drowsiness, and a PaCO₂ of 55 mmHg. The most critical immediate actions are: A) Reassurance, as normalizing CO₂ indicates improvement B) High-flow oxygen, continuous salbutamol-ipratropium nebulization, IV steroids, ICU transfer C) Oral prednisolone and discharge with inhaler technique check D) Chest physiotherapy and IV antibiotics **Answer:**

B — Silent chest, altered sensorium, hypoxemia, and hypercapnia define life-threatening asthma; a "normalizing" CO₂ in a tiring child signals impending respiratory arrest, not improvement. Management is high-flow oxygen (target SpO₂ 94–98%), continuous bronchodilators, systemic steroids within the hour, magnesium if refractory, and ICU care. Sedatives are absolutely contraindicated.

Q16. The parents of a child with newly diagnosed cystic fibrosis and pancreatic insufficiency ask about enzyme replacement. The correct counselling is: A) Give lipase 200–400 units/kg/meal with no upper limit B) Enzymes are only needed when steatorrhea is visible C) Replace with adult-dose proton pump inhibitor alone D) Give 2000–4000 lipase units per gram of dietary fat, not exceeding 10,000 units/kg/day, to avoid fibrosing colonopathy
Answer: D — PERT dosing is 2000–4000 lipase units per gram of dietary fat (or 500–2500 units/kg/meal), capped at 10,000 units/kg/day because excessive doses cause fibrosing colonopathy. Enzymes are given with every meal/snack containing fat, and a PPI may be added if response is poor — not as monotherapy.

Q17. A 7-year-old with community-acquired pneumonia has low-grade fever for 10 days, bilateral perihilar infiltrates, and a normal WBC count. The child is 8 years old and attends school. The most likely organism and treatment are: A) *Mycoplasma pneumoniae*; azithromycin B) *Streptococcus pneumoniae*; high-dose amoxicillin C) *Staphylococcus aureus*; vancomycin D) Respiratory syncytial virus; supportive care **Answer: A** — In school-aged children (>5 years), *Mycoplasma pneumoniae* is the commonest cause of CAP, presenting with prolonged low-grade fever and bilateral infiltrates ("walking pneumonia"). Treatment is azithromycin (10 mg/kg day 1, then 5 mg/kg days 2–5). Amoxicillin is first-line for typical pneumococcal pneumonia.

Q18. A 6-year-old with left-sided empyema has persistent fever after 72 hours of IV ceftriaxone and cloxacillin. Chest ultrasound shows multiple septations and loculations. The next best step is: A) Switch to oral amoxicillin and observe B) Immediate open thoracotomy and decortication C) Add nebulized hypertonic saline D) Chest tube drainage with intrapleural fibrinolytics **Answer: D** — Loculated/septated empyema with persistent fever requires drainage: chest tube plus intrapleural fibrinolytics (urokinase/alteplase), which break septations and reduce the need for surgery. Ultrasound is the investigation of choice for staging parapneumonic effusions. Surgery (VATS/decortication) is reserved for organized peel or failed drainage.

Q19. Flow-volume loop in a 10-year-old shows flattening of both the inspiratory and expiratory limbs with normal lung volumes. The most likely cause is: A) Asthma exacerbation B) Vocal cord dysfunction C) Fixed upper airway obstruction such as subglottic stenosis D) Chest wall restriction **Answer: C** — Flattening of BOTH limbs indicates a fixed obstruction (e.g., tracheal/subglottic stenosis, retained foreign body). Variable extrathoracic obstruction flattens only the inspiratory limb; variable intrathoracic obstruction flattens only the expiratory limb; asthma shows a scooped expiratory limb.

Q20. A 9-year-old with suspected asthma has normal baseline spirometry. Methacholine challenge is performed and FEV₁ falls by 22% at the lowest concentration. Which statement is correct? A) The test confirms asthma with 100% specificity B) Methacholine challenge is contraindicated in all children C) A negative challenge would essentially exclude current asthma due to high negative predictive value D) A positive result is diagnostic of cystic fibrosis **Answer: C** — Methacholine challenge has a high negative predictive value: a normal result essentially rules out current asthma. A positive result (PC20 — 20% FEV₁ fall) is sensitive but nonspecific, also seen in CF, allergic rhinitis, and post-viral hyperreactivity. It is contraindicated when FEV₁ <60–70% predicted.

Q21. A newborn with antenatally diagnosed left-sided congenital diaphragmatic hernia is delivered. The immediate resuscitation steps include: A) Bag-mask ventilation with high pressures and immediate surgical repair

B) Endotracheal intubation, orogastric decompression, and gentle ventilation with delayed repair after stabilization C) High-frequency ventilation and emergency thoracotomy in the delivery room D) Surfactant administration and prone positioning **Answer: B** — Bag-mask ventilation must be avoided as it inflates herniated bowel and worsens lung compression. Immediate endotracheal intubation with orogastric tube decompression, gentle ventilation (permissive hypercapnia, low PIP), PPHN management, and delayed surgical repair after cardiopulmonary stabilization (not a delivery-room emergency) is standard.

Q22. A 5-year-old with cystic fibrosis (F508del/G551D compound heterozygote) is started on a CFTR modulator. Which agent specifically targets the G551D gating defect? A) Lumacaftor B) Tezacaftor C) Ivacaftor D) Elexacaftor **Answer: C** — Ivacaftor is a potentiator that increases the open probability of the CFTR channel, specifically effective for gating (class III) mutations like G551D and residual-function mutations. Lumacaftor, tezacaftor, and elexacaftor are correctors that aid F508del protein trafficking.

Q23. A sweat chloride test in a 3-week-old infant with meconium ileus returns 68 mmol/L. The interpretation is: A) Normal; CF excluded B) Intermediate; repeat after 6 months C) Diagnostic of cystic fibrosis D) Suggestive of primary ciliary dyskinesia **Answer: C** — Sweat chloride ≥ 60 mmol/L is diagnostic of CF at any age (performed after 10 days of life). Meconium ileus is a classic CF presentation (20% of CF newborns). Values 30–59 are intermediate; <30 normal. PCD has normal sweat chloride.

Q24. A 13-year-old with severe persistent asthma on medium-dose ICS-LABA is being considered for step-up. Inhaler technique is poor and he admits missing doses frequently. GINA recommends before stepping up: A) Add tiotropium immediately B) Correct inhaler technique and address adherence first C) Start omalizumab D) Switch to daily oral prednisolone **Answer: B** — GINA mandates checking and correcting inhaler technique, adherence, and trigger exposure before any step-up, as most "treatment failures" are technique/adherence failures. Stepping up without this wastes therapy and exposes the child to unnecessary drug burden.

Q25. DLCO is reduced in a 15-year-old with interstitial lung disease pattern on HRCT. In which of the following conditions would DLCO instead be INCREASED? A) Pulmonary hemorrhage B) Emphysema C) Pulmonary vascular disease D) Anemia **Answer: A** — DLCO is increased when there is more hemoglobin available to bind CO in the alveoli: pulmonary hemorrhage (intra-alveolar blood), asthma, obesity, polycythemia, and left-to-right shunts. It is reduced in interstitial disease, emphysema (loss of alveolar-capillary surface), pulmonary vascular disease, and anemia.

Pediatric Gastroenterology

Chapter 5: Pediatric Gastroenterology

NEET SS questions on pediatric gastroenterology increasingly mirror DM Gastroenterology entrance material: IBD biologics, VEO-IBD genetics, biliary atresia timing, Wilson disease workup, and acute liver failure transplant criteria. A superficial "general pediatrics" reading will miss the diagnostic thresholds and drug doses examiners now ask for. This chapter gives you those numbers — thresholds, criteria, drug doses, and gold-standard investigations — in one dense pass.

Inflammatory Bowel Disease (IBD)

- Two major forms: **Crohn disease (CD)** — transmural, any site from mouth to anus, skip lesions, stricturing/fistulizing; and **ulcerative colitis (UC)** — mucosal, colon-only, continuous from rectum proximally, pseudopolyps, toxic megacolon.
- **Crohn vs UC — clinical:** CD → perianal disease, oral ulcers, growth failure, right lower quadrant mass, fistulae/strictures; UC → bloody diarrhea with tenesmus/urgency, continuous rectal involvement, higher risk of toxic megacolon and colon cancer (extent/duration dependent).
- **Endoscopic:** CD → aphthous ulcers, skip lesions, cobblestoning, strictures, perianal tags/fistulae; UC → continuous erythema/friability from rectum, loss of vascular pattern, contact bleeding, pseudopolyps.
- **Histologic:** CD → transmural inflammation, **non-caseating granulomas** (pathognomonic but seen in <30% of biopsies), lymphoid aggregates; UC → mucosal-only inflammation, cryptitis, **crypt abscesses**, goblet cell depletion, crypt distortion (chronicity).
- **Paris classification (pediatric IBD, Montreal adaptation):** CD — Age: A1a (0–<10 y), A1b (10–<17 y), A2 (17–40 y); Location: L1 (distal 1/3 ileum ± limited cecal), L2 (colonic), L3 (ileocolonic), L4a (upper disease proximal to ligament of Treitz), L4b (upper disease distal to Treitz, proximal to distal 1/3 ileum); Behavior: B1 (nonstricturing/nonpenetrating), B2 (stricturing), B3 (penetrating), B2B3 (both), p (perianal modifier); Growth: G0 (no growth delay), G1 (growth delay). UC — Extent: E1 (ulcerative proctitis), E2 (left-sided, distal to splenic flexure), E3 (extensive, proximal to splenic flexure but distal to hepatic flexure), E4 (pancolitis); Severity: S0 (never severe), S1 (ever severe).
- **Extraintestinal manifestations:** erythema nodosum, pyoderma gangrenosum (more UC), uveitis/episcleritis, arthritis (type 1 pauciarticular mirrors bowel activity; type 2 polyarticular independent), **primary sclerosing cholangitis** (strongly UC-associated), growth failure/delayed puberty (more CD), nephrolithiasis (oxalate stones in CD with ileal disease), oral aphthae, osteoporosis.
- **Workup:** CBC, ESR/CRP, albumin (nutritional marker), iron studies; **fecal calprotectin** — sensitive screen for intestinal inflammation; distinguishes IBD from functional pain/IBS (calprotectin >50–150 µg/g suggests

organic disease; >250 µg/g strongly favors IBD). Serology: **ASCA positive** favors Crohn; **pANCA positive** favors UC — neither is diagnostic alone, used adjunctively in indeterminate colitis.

- **Imaging/endoscopy:** ileocolonoscopy with segmental biopsies = gold standard for diagnosis; MR enterography for small-bowel Crohn (strictures, fistulae); video capsule endoscopy for small-bowel mucosal disease when ileocolonoscopy + MRE are negative (avoid if stricture suspected).
- **Treatment ladder — Crohn:** mild luminal → exclusive enteral nutrition (first-line in children, induces remission + mucosal healing without steroids); moderate-severe → systemic steroids (prednisolone 1–2 mg/kg/day, max 40–60 mg) for induction; **azathioprine** (2–2.5 mg/kg/day) or 6-mercaptopurine as steroid-sparing maintenance (check TPMT status first); **anti-TNF:** **infliximab 5 mg/kg IV** at weeks 0, 2, 6 then every 8 weeks, or **adalimumab** (160 mg, then 80 mg, then 40 mg every 2 weeks — weight-based in children) for moderate-severe/refractory, fistulizing, or perianal disease; **vedolizumab** (gut-selective anti-α4β7 integrin) for anti-TNF failure/intolerance; surgery for strictures, fistulae, medically refractory disease (ileocecal resection).
- **Treatment ladder — UC:** 5-ASA (mesalamine, topical + oral) for mild-moderate; oral steroids for flares; azathioprine/6-MP maintenance; anti-TNF (infliximab/adalimumab) for steroid-refractory; **tacrolimus/cyclosporine** as rescue in acute severe colitis; colectomy (curative) for medically refractory disease, dysplasia, toxic megacolon.
- **Acute severe colitis (Truelove–Witts):** ≥6 bloody stools/day + tachycardia, fever, anemia, ESR >30 — needs IV steroids; assess response at day 3 (Oxford/Lindgren criteria); rescue with infliximab or cyclosporine by day 3–5 if no response.
- **VEO-IBD (very early onset, <6 years; infantile <2 years):** suspect monogenic immunodeficiency when severe, refractory, consanguinity, recurrent infections, perianal disease. Key defects: **IL-10 and IL-10 receptor (IL10RA/IL10RB)** mutations — severe infantile enterocolitis with perianal fistulae, treatment = hematopoietic stem cell transplant (curative); also XIAP, FOXP3 (IPEX), TTC7A, chronic granulomatous disease (CYBB/NCF) — colitis resembling Crohn.

Celiac Disease

- Autoimmune enteropathy triggered by gluten (gliadin) in genetically susceptible children; targets tissue transglutaminase.
- **Screening:** **anti-tTG IgA** is the first-line screen — but always order **total serum IgA** simultaneously (selective IgA deficiency causes false-negative tTG-IgA; if IgA-deficient, use tTG-IgG or deamidated gliadin peptide-IgG).
- Confirmatory: duodenal biopsy with **Marsh classification** — Marsh 0 (normal), Marsh 1 (increased intraepithelial lymphocytes >25/100 enterocytes), Marsh 2 (IEL + crypt hyperplasia), Marsh 3a/3b/3c (partial/subtotal/total **villous atrophy**), Marsh 4 (hypoplastic atrophic lesion, rare).
- **HLA-DQ2/DQ8:** necessary but not sufficient; negative HLA-DQ2/DQ8 essentially **excludes** celiac disease (high negative predictive value) — useful in equivocal cases or to rule out disease in at-risk relatives.
- **ESPGHAN no-biopsy pathway:** symptomatic child with tTG-IgA >10× upper limit of normal + positive endomysial antibody (EMA-IgA) on a second sample + positive HLA-DQ2/DQ8 → diagnosis without biopsy.

- **Treatment:** strict lifelong **gluten-free diet** (wheat, barley, rye excluded; oats allowed only if certified gluten-free) — villous recovery, antibody normalization; monitor tTG-IgA at 6–12 months. Involve dietitian; screen first-degree relatives.
- **Complications of untreated disease:** iron-deficiency anemia, short stature/growth failure, delayed puberty, dermatitis herpetiformis, dental enamel defects, osteoporosis; malignancy risk — **enteropathy-associated T-cell lymphoma** and small-bowel adenocarcinoma; refractory celiac disease (type II with aberrant IELs) is pre-lymphomatous.
- Differentials of villous atrophy: giardiasis, cow's milk protein allergy, autoimmune enteropathy, tropical sprue, immunodeficiency.

GERD vs Eosinophilic Esophagitis (EoE)

- **GERD in children:** regurgitation, irritability, feeding refusal, arching (Sandifer syndrome), chronic cough/wheeze, erosive esophagitis; responds to PPI; pH-impedance monitoring is the gold standard for correlating symptoms with reflux.
- **EoE:** immune-mediated, food-antigen driven; presents with **dysphagia, food impaction**, vomiting, feeding difficulties, atopy history (asthma, eczema, allergic rhinitis).
- **Endoscopy: esophageal rings (trachealization), linear furrows, white exudates/papules, strictures, crepe-paper mucosa** — take multiple biopsies from proximal and distal esophagus.
- **Histology: >15 eosinophils per high-power field** — diagnostic threshold; basal zone hyperplasia, eosinophilic microabscesses. Note: PPI trial is no longer required to exclude PPI-responsive eosinophilia (PPI is now considered a treatment, not a diagnostic criterion).
- **Treatment:** swallowed topical steroids — **fluticasone** (swallowed, not inhaled) or **budesonide slurry/viscous**; dietary elimination (6-food elimination or targeted); **dupilumab** (anti-IL-4R α) approved for EoE ≥ 12 years; esophageal dilation for fibrostenotic strictures. Monitor for candidiasis with swallowed steroids.

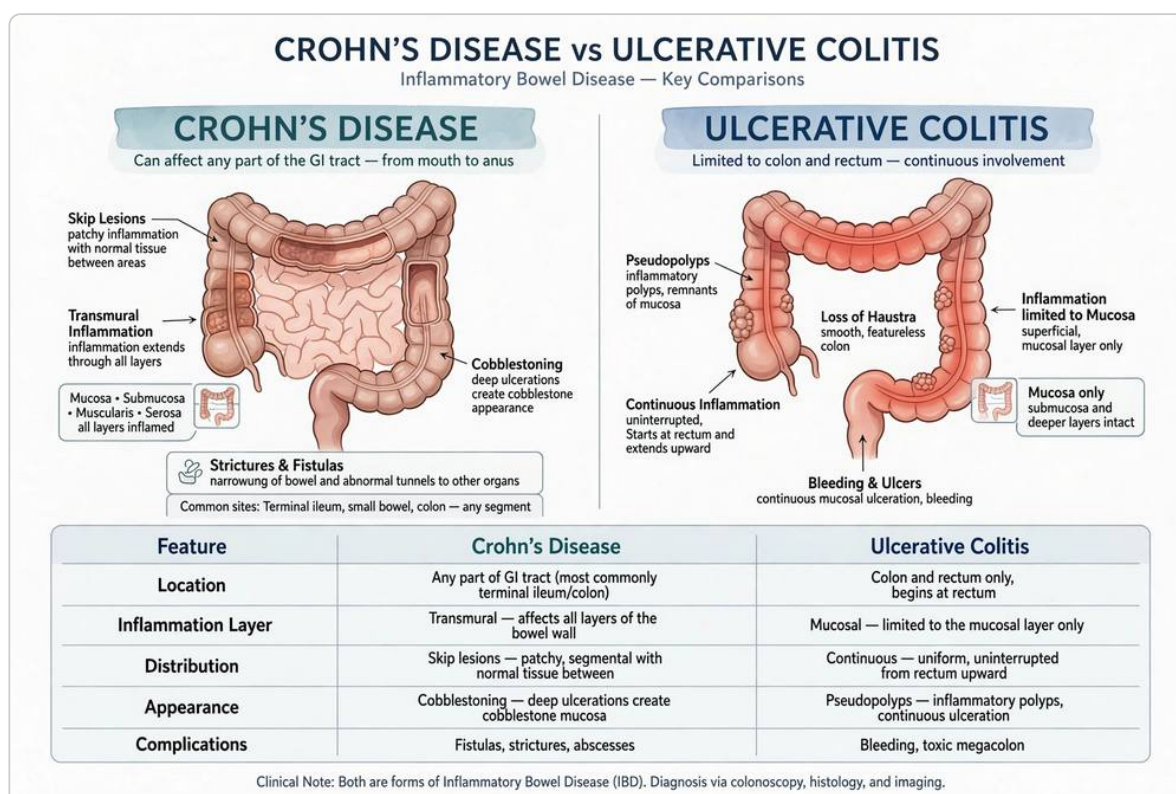


Figure 5.1 — Crohn's disease vs ulcerative colitis

Acute Liver Failure (ALF)

- **Definition (pediatric):** acute liver injury with **coagulopathy uncorrectable by vitamin K** (INR ≥ 1.5 with encephalopathy, or INR ≥ 2.0 without encephalopathy) + no known chronic liver disease. Encephalopathy may be subtle/absent in young children — do not wait for it.
- **Etiologies by age:** neonate/infant → **metabolic** (galactosemia, tyrosinemia type 1, mitochondrial disorders, Niemann-Pick C), **neonatal hemochromatosis (gestational alloimmune liver disease)**, HLH; child → **viral** (hepatitis A/E, EBV, adenovirus), **paracetamol (acetaminophen) toxicity**, autoimmune hepatitis; adolescent → **Wilson disease** (acute hemolytic presentation with Coombs-negative hemolysis + low ALP/bilirubin ratio), paracetamol, viral, Budd-Chiari.
- **Clues:** paracetamol → very high transaminases (>3500 IU/L), history/level; Wilson → Coombs-negative hemolytic anemia, low ceruloplasmin, **ALP:bilirubin ratio <2** , AST:ALT >2 ; autoimmune → high IgG, autoantibodies.
- **Management:** ICU; correct coagulopathy only if bleeding or invasive procedure planned (routine FFP correction masks INR as a prognostic marker); **N-acetylcysteine (NAC)** — IV protocol: 150 mg/kg over 1 hour, then 50 mg/kg over 4 hours, then 100 mg/kg over 16 hours — benefits paracetamol AND non-paracetamol ALF; treat cerebral edema (head elevation, hypertonic saline, avoid fluid overload); monitor glucose, ammonia; broad workup including paracetamol level, viral serologies, autoimmune panel, metabolic screen, Wilson workup, Doppler USG.
- **King's College criteria (paracetamol):** arterial pH <7.30 after resuscitation, OR all three of: INR >6.5 , creatinine >300 $\mu\text{mol/L}$ (>3.4 mg/dL), grade III–IV encephalopathy. **Non-paracetamol:** INR >6.5 , OR any three of: age <10 or >40 years, unfavorable etiology (non-A/non-B hepatitis, idiosyncratic drug reaction),

jaundice-to-encephalopathy interval >7 days, INR >3.5, bilirubin >300 µmol/L (>17.5 mg/dL). Meeting criteria → list for **urgent liver transplant** (status 1A / super-urgent).

- Contraindications to transplant: uncontrolled sepsis, severe brain injury/raised ICP unresponsive to therapy, multisystem failure.

Biliary Atresia

- Obliterative cholangiopathy of extrahepatic (and intrahepatic) bile ducts; commonest indication for pediatric liver transplant worldwide.
- **Presentation:** persistent **neonatal cholestasis** beyond 2 weeks — **acholic (pale/clay) stools**, dark urine, **direct (conjugated) hyperbilirubinemia** (direct bilirubin >1 mg/dL if total <5 mg/dL, or >20% of total), hepatomegaly; infant otherwise well initially, then failure to thrive, progressive fibrosis.
- **Workup:** fractionated bilirubin; abdominal USG (absent/small gallbladder, triangular cord sign); **HIDA (hepatobiliary iminodiacetic acid) scan** — non-excretion into bowel after 24 hours suggests biliary atresia (phenobarbital priming improves specificity); liver biopsy (bile duct proliferation, portal fibrosis, bile plugs).
- **Gold standard: intraoperative cholangiogram** — non-visualization of extrahepatic ducts confirms diagnosis.
- **Treatment: Kasai portoenterostomy** (hepatic portoenterostomy) — excise atretic ducts at porta hepatis, Roux-en-Y jejunal loop anastomosis. Timing is everything: **optimal <60 days of age** (best outcomes <30–45 days); success falls sharply after 90 days.
- **Post-Kasai:** ursodeoxycholic acid, fat-soluble vitamin supplementation (A, D, E, K), prophylactic antibiotics (cotrimoxazole) — **ascending cholangitis** (fever, worsening jaundice, acholic stools) is the commonest early complication, treat aggressively with IV broad-spectrum antibiotics; monitor for portal hypertension; most children ultimately need liver transplant even after successful Kasai — refer early to transplant center.
- Differentials of neonatal cholestasis: Alagille syndrome, PFIC, α1-antitrypsin deficiency, choledochal cyst, inspissated bile syndrome.

Wilson Disease

- Autosomal recessive defect in **ATP7B** (chromosome 13) — impaired copper incorporation into ceruloplasmin + impaired biliary copper excretion → copper deposition in liver, basal ganglia, cornea, kidneys.
- **Presentation:** hepatic (chronic hepatitis, cirrhosis, acute hemolytic ALF in adolescents), neurologic (tremor, parkinsonism, dysarthria — typically >10 years), psychiatric, renal tubular dysfunction, Coombs-negative hemolytic anemia.
- **Diagnosis: Kayser-Fleischer rings** (corneal copper deposits — slit-lamp exam, also seen in cholestasis so interpret with context), **low serum ceruloplasmin** (<20 mg/dL), **elevated 24-hour urinary copper** (>100 µg/24 h; >40 µg after penicillamine challenge in equivocal cases), elevated hepatic copper on biopsy (>250 µg/g dry weight), ATP7B mutation analysis. Leipzig score ≥4 = diagnosis established.
- **Treatment:** copper chelators — **D-penicillamine** (watch for nephrotic syndrome, bone marrow suppression, pyridoxine supplementation needed) or **trientine** (fewer side effects, preferred in many centers); **zinc salts**

block intestinal copper absorption — used for maintenance and in presymptomatic patients; lifelong therapy; low-copper diet adjunct. Treat presymptomatic siblings identified by family screening.

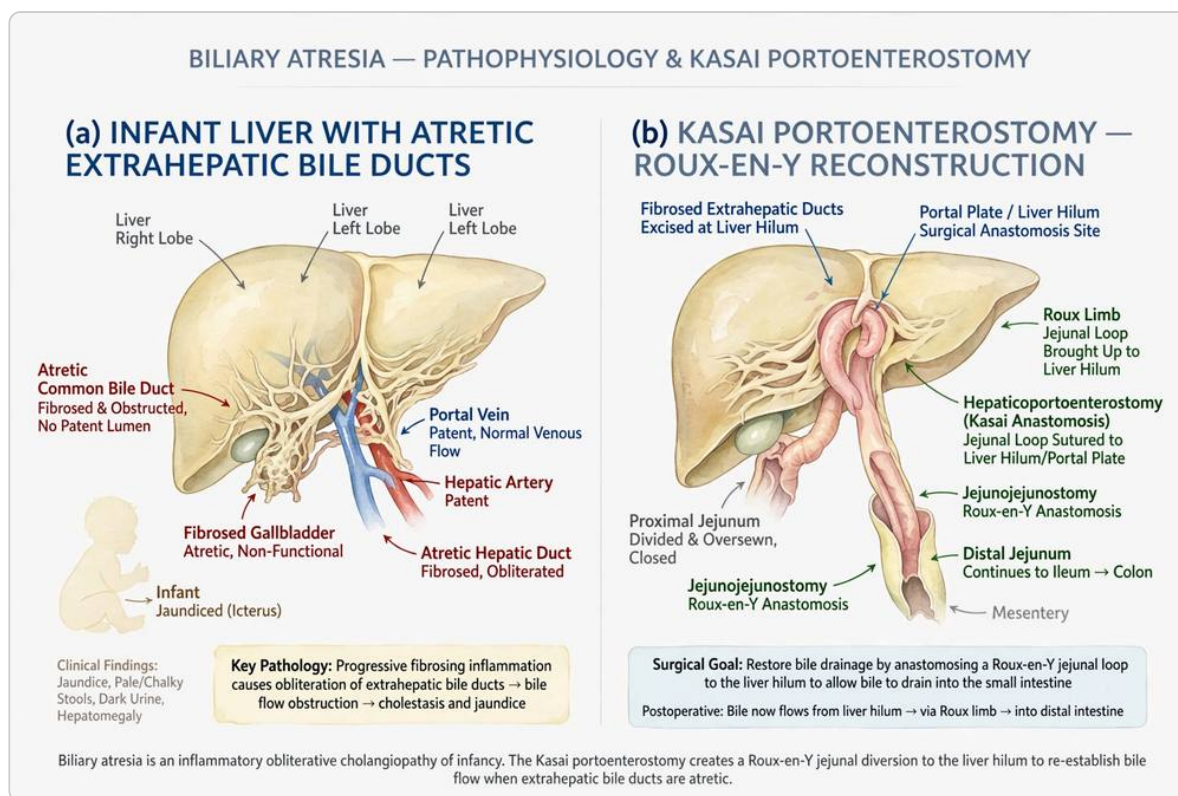


Figure 5.2 — Biliary atresia and Kasai portoenterostomy

Autoimmune Hepatitis, Sclerosing Cholangitis, Alagille Syndrome

- **Autoimmune hepatitis (AIH): Type 1** — anti-smooth muscle antibody (ASMA) and **ANA** positive, any age, raised IgG; **Type 2** — **anti-LKM1** (liver-kidney microsome) positive, younger children, more aggressive/relapse-prone. Diagnosis: raised transaminases + hypergammaglobulinemia (IgG) + autoantibodies + interface hepatitis with plasma cells on biopsy (exclude viral/Wilson). Treatment: **prednisolone** induction + **azathioprine** maintenance; relapse common on withdrawal.
- **Primary sclerosing cholangitis (PSC):** chronic cholestatic disease with beaded intra/extrahepatic ducts on MRCP; strongly associated with **ulcerative colitis** (screen all PSC children with colonoscopy); pANCA often positive; risk of cholangiocarcinoma (adults) and colon cancer; no proven medical therapy — UDCA used, transplant for end-stage.
- **Alagille syndrome:** autosomal dominant **JAG1** mutation (Notch signaling; rarely NOTCH2) — paucity of interlobular bile ducts. Features: chronic cholestasis, characteristic facies (broad forehead, deep-set eyes, pointed chin), **butterfly (hemivertebrae) vertebrae**, **posterior embryotoxon** (eye), peripheral pulmonary stenosis, renal dysplasia. Diagnosis: clinical criteria + JAG1 testing; liver biopsy shows bile duct paucity. Management: supportive (cholestasis care, fat-soluble vitamins, pruritus control with cholestyramine/rifampicin), transplant for end-stage.

GI Bleeding in Children

- **Upper GI bleeding (proximal to ligament of Treitz):** hematemesis, melena; causes — **esophageal varices** (portal hypertension: extrahepatic portal venous obstruction is commonest cause of pediatric variceal bleed in India), gastritis, peptic ulcer (H. pylori, NSAIDs), Mallory-Weiss tear.
- **Variceal bleed management (numbered steps):** 1. Resuscitate — airway, large-bore IV access, type & crossmatch; restrictive transfusion (Hb target ~7–8 g/dL). 2. **Octreotide** infusion — bolus 1–2 µg/kg then 1–2 µg/kg/hour (splanchnic vasoconstriction); vasopressin/terlipressin alternatives. 3. Urgent endoscopy — **variceal band ligation** preferred over sclerotherapy in children. 4. Antibiotic prophylaxis (ceftriaxone) — reduces rebleed/infection. 5. Secondary prophylaxis — non-selective beta-blocker (propranolol) ± repeat banding; definitive — shunt surgery or transplant per etiology.
- **Non-variceal upper bleed:** high-dose IV PPI, endoscopic hemostasis (adrenaline injection, clips, thermal), H. pylori testing/treatment.
- **Lower GI bleeding:** hematochezia; causes by age — neonate: swallowed maternal blood (Apt test), NEC, malrotation/volvulus; infant: **Meckel's diverticulum** (painless rectal bleeding), intussusception (red currant jelly stools); child: **juvenile polyps** (commonest cause of painless rectal bleeding in 2–10 y — solitary hamartomatous), IBD, infectious colitis, Henoch-Schönlein purpura.
- **Meckel's diverticulum:** rule of 2s — 2% population, 2 feet from ileocecal valve, 2 inches long, 2% symptomatic, 2:1 male predominance, presents by age 2; ectopic gastric mucosa ulcerates adjacent ileum. **Tc-99m pertechnetate (Meckel's) scan** — detects ectopic gastric mucosa (gold standard imaging); false negatives with brisk bleeding — enhance with pentagastrin/cimetidine pre-treatment. Treatment: surgical resection.
- **Bleeding algorithm:** 1. ABCs, vitals, IV access, CBC, type & crossmatch. 2. Localize — history (hematemesis/melena vs hematochezia), NG aspirate if unclear. 3. Upper source → endoscopy within 24 h (urgent if variceal/unstable). 4. Lower source → stabilize, colonoscopy after bowel prep; Meckel's scan if painless bleeding in young child; tagged RBC scan/angiography if unstable and source unknown. 5. Ongoing bleeding despite resuscitation → surgical/ IR consultation.

Diarrhea: Chronic Workup, Pancreatitis, Choledochal Cyst, MASLD

- **Chronic diarrhea** (>14 days): classify as osmotic (stops with fasting, acidic stools — e.g., carbohydrate malabsorption), secretory (persists fasting — e.g., neuroendocrine tumors, congenital chloride diarrhea), inflammatory (blood/mucus — IBD, infection), or fatty/malabsorptive (greasy stools — pancreatic insufficiency, celiac).
- **Toddler's diarrhea** (chronic nonspecific diarrhea): 1–3 years, 4–6 loose stools/day with undigested food, thriving child, excessive juice intake (sorbitol/fructose); benign — reassure, reduce juice, ensure fat intake; diagnosis of exclusion.
- **Celiac vs cystic fibrosis (CF) in chronic diarrhea:** celiac → tTG-IgA positive, villous atrophy, responds to gluten-free diet; CF → pancreatic insufficiency (low fecal elastase <100 µg/g), recurrent chest infections, **sweat chloride >60 mmol/L** diagnostic, CFTR mutations; both cause failure to thrive and fat-soluble vitamin deficiency.

- **Acute pancreatitis — revised Atlanta criteria:** need 2 of 3 — (1) characteristic epigastric pain radiating to back, (2) **serum lipase (or amylase) >3× upper limit of normal** (lipase more specific), (3) characteristic imaging (CT/MRI/USG). Severity: mild (no organ failure/complications), moderately severe (transient organ failure <48 h or local complications), severe (persistent organ failure >48 h). Management: aggressive IV fluids, analgesia, early enteral nutrition, no routine antibiotics; ERCP only for choledocholithiasis with cholangitis.
- **Choledochal cyst — Todani classification:** Type I (fusiform dilation of common bile duct — commonest, ~80–90%), Type II (saccular diverticulum), Type III (choledochoceles), Type IVa (multiple intra- + extrahepatic cysts), Type IVb (multiple extrahepatic only), Type V (Caroli disease — intrahepatic only). Presentation: classic triad of abdominal pain, jaundice, palpable mass (uncommon complete); cholangitis, pancreatitis. Treatment: complete cyst excision + Roux-en-Y hepaticojejunostomy (excision mandatory — malignancy risk in retained cyst).
- **NAFLD/MASLD in obese children:** commonest chronic liver disease in children now; screen overweight/obese children ≥9–10 years with ALT; diagnosis of exclusion (rule out viral, Wilson, autoimmune, α1-antitrypsin); USG shows fatty liver; biopsy (steatosis, ballooning, fibrosis) is gold standard but reserved. Management: **lifestyle — diet + exercise + weight loss** is first-line (no approved drug; vitamin E/pioglitazone evidence is adult); monitor for progression to steatohepatitis/fibrosis.

Practice MCQs

Q1. A 12-year-old boy has chronic abdominal pain, perianal fistula, and growth failure. Colonoscopy shows skip lesions with cobblestoning; biopsy reveals non-caseating granulomas. Serology is ASCA-positive, pANCA-negative. The most likely diagnosis is: A) Ulcerative colitis B) Crohn disease C) Eosinophilic colitis D) Intestinal tuberculosis **Answer: B** — Transmural skip lesions, cobblestoning, perianal fistulae, non-caseating granulomas, and ASCA positivity define Crohn disease; UC is continuous, mucosal, and pANCA-associated.

Q2. A 9-year-old girl with bloody diarrhea has a colonoscopy showing continuous erythema from the rectum with crypt abscesses on biopsy. According to the Paris classification, pancolitis is designated as: A) E1 B) E2 C) E4 D) L3 **Answer: C** — Paris UC extent: E1 proctitis, E2 left-sided, E3 extensive, E4 pancolitis; L-designations apply to Crohn disease location, not UC.

Q3. A 3-year-old with severe infantile-onset enterocolitis, perianal fistulae, and consanguineous parents is refractory to steroids and anti-TNF therapy. The most likely underlying defect and definitive treatment are: A) IL-10/IL-10 receptor defect — hematopoietic stem cell transplant B) NOD2 mutation — infliximab C) FOXP3 mutation — lifelong steroids D) HLA-DQ2 — gluten-free diet **Answer: A** — VEO-IBD with severe infantile perianal disease suggests IL-10 pathway defects, which are curable only by HSCT; anti-TNF is typically ineffective in these monogenic cases.

Q4. A 7-year-old with chronic diarrhea and failure to thrive has a positive anti-tTG IgA at 12× the upper limit of normal, positive EMA-IgA on repeat sampling, and HLA-DQ2 positivity. As per ESPGHAN guidance, the next step is: A) Duodenal biopsy to confirm Marsh grade B) Gluten-free diet without biopsy C) Trial of pancreatic enzyme replacement D) Colonoscopy to exclude IBD **Answer: B** — The ESPGHAN no-biopsy pathway allows diagnosis when tTG-IgA exceeds 10× ULN with confirmatory EMA-IgA and HLA-DQ2/DQ8 positivity; biopsy is not mandatory in this scenario.

Q5. The earliest histologic change in celiac disease (Marsh 1 lesion) is: A) Partial villous atrophy B) Crypt hyperplasia C) Subtotal villous atrophy D) Increased intraepithelial lymphocytes (>25 per 100 enterocytes)

Answer: D — Marsh 1 is the infiltrative lesion: increased intraepithelial lymphocytes with normal villous architecture; crypt hyperplasia (Marsh 2) and villous atrophy (Marsh 3a/3b/3c) come later.

Q6. A 30-year-old man diagnosed with celiac disease in childhood admits to poor dietary compliance. He now presents with weight loss, nocturnal diarrhea, and ulcerative jejunitis. The most feared long-term complication is:

A) Colorectal carcinoma B) Hepatocellular carcinoma C) Enteropathy-associated T-cell lymphoma D) Gastric MALToma

Answer: C — Untreated/refractory celiac disease predisposes to enteropathy-associated T-cell lymphoma (and small-bowel adenocarcinoma); refractory celiac type II with aberrant IELs is pre-lymphomatous.

Q7. A 14-year-old with atopic dermatitis presents with recurrent food impaction. Endoscopy shows esophageal rings, linear furrows, and white exudates. Biopsy shows 40 eosinophils/hpf. The diagnostic threshold and first-line therapy are: A) >5 eos/hpf — PPI alone B) >10 eos/hpf — esophageal dilation C) >25 eos/hpf — systemic steroids D) >15 eos/hpf — swallowed topical steroids **Answer: D** — EoE is defined by >15 eosinophils/hpf with compatible endoscopic features (rings, furrows); first-line therapy is swallowed fluticasone or budesonide slurry, not systemic steroids.

Q8. A 16-year-old girl presents with acute liver failure after a paracetamol overdose. Arterial pH is 7.25 after resuscitation. As per King's College criteria, the indication for urgent transplant listing here is:

A) pH <7.30 after resuscitation B) INR >3.5 alone C) Bilirubin >17.5 mg/dL alone D) Encephalopathy grade II alone

Answer: A — For paracetamol-induced ALF, arterial pH <7.30 after resuscitation alone mandates urgent listing; alternatively all three of INR >6.5, creatinine >3.4 mg/dL, and grade III–IV encephalopathy are required.

Q9. A 15-year-old boy presents with acute liver failure, Coombs-negative hemolytic anemia, low serum ceruloplasmin, and an ALP-to-bilirubin ratio <2. The most likely diagnosis is: A) Autoimmune hepatitis B)

Wilson disease C) Acute hepatitis E D) Budd-Chiari syndrome **Answer: B** — The combination of acute hemolytic ALF with Coombs-negative hemolysis, very low ALP:bilirubin ratio, and AST:ALT >2 is classic for fulminant Wilson disease in an adolescent.

Q10. In the management of acute liver failure, N-acetylcysteine is indicated in: A) Paracetamol toxicity only B)

Viral hepatitis only C) Both paracetamol and non-paracetamol ALF D) Wilsonian ALF only

Answer: C — NAC benefits both paracetamol-induced and non-paracetamol ALF (improves transplant-free survival); the IV protocol is 150 mg/kg over 1 h, then 50 mg/kg over 4 h, then 100 mg/kg over 16 h.

Q11. A 6-week-old infant has persistent jaundice, acholic stools, dark urine, and a conjugated bilirubin of 6 mg/dL. HIDA scan shows no excretion into bowel at 24 hours. The gold-standard confirmatory investigation is: A)

Repeat HIDA after phenobarbital priming B) MRCP C) Intraoperative cholangiogram D) Liver biopsy

Answer: C — Intraoperative cholangiogram demonstrating non-visualization of extrahepatic ducts is the gold standard for biliary atresia; HIDA non-excretion is suggestive but not definitive.

Q12. A 45-day-old infant is diagnosed with biliary atresia on intraoperative cholangiogram. The optimal surgical management and its timing are: A) Kasai portoenterostomy, ideally before 60 days of age B) Primary liver

transplant, ideally before 60 days C) Choledochal cyst excision at 6 months D) ERCP with stenting immediately

Answer: A — Kasai portoenterostomy is the first-line surgery, with best outcomes when performed before 60 days (ideally <30–45 days); success falls sharply after 90 days.

Q13. A 2-month-old post-Kasai infant develops fever, worsening jaundice, and pale stools. The most likely complication and its management are: A) Bile leak — percutaneous drainage B) Ascending cholangitis — IV broad-spectrum antibiotics C) Portal vein thrombosis — anticoagulation D) Anastomotic stricture — ERCP
Answer: B — Ascending cholangitis is the commonest early post-Kasai complication and is treated aggressively with IV broad-spectrum antibiotics; prophylactic cotrimoxazole is often continued.

Q14. A 12-year-old with chronic liver disease has Kayser-Fleischer rings on slit-lamp exam, serum ceruloplasmin 12 mg/dL, and 24-hour urinary copper of 180 µg. The gene mutated and first-line chelator options are: A) ATP7A — zinc only B) JAG1 — penicillamine C) HFE — phlebotomy D) ATP7B — penicillamine or trientine **Answer: D** — Wilson disease is caused by ATP7B mutations; treatment is with copper chelators (D-penicillamine or trientine), with zinc for maintenance and presymptomatic patients.

Q15. A 10-year-old girl presents with fluctuating jaundice, markedly elevated IgG, ANA and anti-smooth muscle antibody positivity, and interface hepatitis with plasma cells on biopsy. The diagnosis and maintenance therapy are: A) Type 2 autoimmune hepatitis — interferon B) Primary sclerosing cholangitis — UDCA alone C) Type 1 autoimmune hepatitis — azathioprine maintenance after steroid induction D) Wilson disease — zinc monotherapy
Answer: C — ANA/ASMA positivity with raised IgG defines type 1 AIH (anti-LKM1 defines type 2); standard therapy is prednisolone induction followed by azathioprine maintenance.

Q16. A 6-year-old with ulcerative colitis develops progressive cholestasis; MRCP shows beaded intra- and extrahepatic bile ducts. The most likely associated diagnosis is: A) Primary sclerosing cholangitis B) Biliary atresia C) Choledochal cyst type I D) Alagille syndrome **Answer: A** — PSC is strongly associated with ulcerative colitis and shows characteristic multifocal strictures ("beading") on MRCP; all children with PSC need colonoscopic screening for IBD.

Q17. A neonate with cholestasis has a broad forehead, deep-set eyes, pointed chin, butterfly vertebrae on spine X-ray, and posterior embryotoxon. The mutated gene is: A) ATP8B1 B) JAG1 C) ABCB4 D) SERPINA1 **Answer: B** — Alagille syndrome is caused by JAG1 (Notch signaling) mutations, with bile duct paucity plus characteristic facies, butterfly vertebrae, posterior embryotoxon, and peripheral pulmonary stenosis.

Q18. A 7-year-old with known extrahepatic portal venous obstruction presents with massive hematemesis. After resuscitation, the preferred vasoactive drug and definitive endoscopic therapy are: A) Vasopressin bolus — sclerotherapy B) Somatostatin — TIPSS C) Propranolol IV — glue injection D) Octreotide infusion — variceal band ligation **Answer: D** — Octreotide (1–2 µg/kg bolus then 1–2 µg/kg/h infusion) reduces splanchnic flow, and variceal band ligation is preferred over sclerotherapy in children; add ceftriaxone prophylaxis.

Q19. A 2-year-old boy presents with painless, massive rectal bleeding. The most likely diagnosis and gold-standard investigation are: A) Juvenile polyp — colonoscopy B) Intussusception — ultrasound C) Meckel's diverticulum — Tc-99m pertechnetate scan D) Anal fissure — clinical examination **Answer: C** — Painless rectal bleeding in a toddler is classic for Meckel's diverticulum with ectopic gastric mucosa; the Tc-99m pertechnetate (Meckel's) scan detects ectopic gastric mucosa.

Q20. A 2-year-old thriving child passes 5 loose stools daily containing undigested food particles and drinks large volumes of fruit juice. Growth and examination are normal. The next best step is: A) Start a gluten-free diet B) Sweat chloride test C) Colonoscopy with biopsy D) Reassurance, reduce fruit juice, ensure adequate dietary fat
Answer: D — This is toddler's diarrhea (chronic nonspecific diarrhea of childhood), a benign diagnosis of

exclusion in thriving 1–3-year-olds with excessive juice intake; management is reassurance and dietary modification, not invasive workup.

Q21. An 8-year-old with failure to thrive, greasy stools, and recurrent chest infections has a fecal elastase of 60 µg/g. The confirmatory test for the underlying disease is: A) Sweat chloride test B) Anti-tTG IgA C) Fecal calprotectin D) Hydrogen breath test **Answer: A** — Pancreatic insufficiency with recurrent respiratory infections suggests cystic fibrosis; sweat chloride >60 mmol/L is diagnostic, confirmed by CFTR mutation analysis.

Q22. A 12-year-old presents with severe epigastric pain radiating to the back, serum lipase 1200 IU/L (normal <160), and bulky pancreas on ultrasound. As per the revised Atlanta criteria, the diagnosis of acute pancreatitis requires: A) Lipase >3× ULN alone B) Pain plus imaging only C) All three criteria D) Any two of the three criteria **Answer: D** — Revised Atlanta requires 2 of 3: characteristic pain, lipase/amylase >3× ULN, and characteristic imaging; this child meets all three.

Q23. A 5-year-old presents with intermittent abdominal pain, jaundice, and a palpable right upper quadrant mass. Ultrasound shows fusiform dilation of the common bile duct. The Todani type and definitive treatment are: A) Type III — endoscopic sphincterotomy B) Type I — complete cyst excision with Roux-en-Y hepaticojejunostomy C) Type V — liver transplant D) Type II — observation **Answer: B** — Fusiform CBD dilation is Todani type I (commonest); complete excision with Roux-en-Y hepaticojejunostomy is mandatory because of the malignancy risk in retained cyst tissue.

Q24. A 13-year-old obese boy (BMI >95th percentile) has ALT 96 IU/L and a fatty liver on ultrasound. Viral, Wilson, and autoimmune workups are negative. The first-line management is: A) Vitamin E supplementation B) Pioglitazone C) Lifestyle modification with diet and exercise D) Liver biopsy followed by steroids **Answer: C** — Pediatric MASLD/NAFLD is managed first-line with lifestyle modification (diet, exercise, weight loss); no drug is approved for children, and biopsy is reserved for atypical or advanced cases.

Q25. A 14-year-old with Crohn disease has moderate-to-severe ileocolonic disease refractory to steroids and azathioprine. The next step in the treatment ladder and its standard induction dose is: A) Infliximab 5 mg/kg IV at weeks 0, 2, and 6 B) Mesalamine 4 g/day C) Exclusive enteral nutrition for 2 weeks D) Immediate ileocecal resection **Answer: A** — Anti-TNF therapy is next for steroid/immunomodulator-refractory pediatric Crohn disease; infliximab is dosed at 5 mg/kg IV at weeks 0, 2, 6, then every 8 weeks.

Pediatric Nephrology

Chapter 6: Pediatric Nephrology

Nephrology is disproportionately high-yield for NEET SS Pediatrics: a single vignette can test steroid-response definitions, complement patterns, dialysis indications, tubular physiology, or the HUS–TTP distinction in one stem. The examiner's favourite traps are the entities that look alike — SSNS vs SRNS, Bartter vs Gitelman, typical vs atypical HUS, PSGN vs C3 glomerulopathy — so this chapter is built around those contrasts, with doses and cut-offs stated exactly as guidelines define them.

1. Nephrotic Syndrome

- **Definition (all four):** nephrotic-range proteinuria (>40 mg/m²/hour, or >50 mg/kg/day, or spot urine protein:creatinine ratio >2 mg/mg [>200 mg/mmol]), serum albumin <2.5 g/dL, edema, hyperlipidemia. Lipiduria with fatty casts/oval fat bodies is supportive, not required.
- **Minimal change disease (MCD)** causes 85–90% of childhood nephrotic syndrome. Selective albuminuria (selectivity index [clearance IgG/clearance transferrin] <0.2), normal complements, no hematuria/hypertension/renal failure. Light microscopy normal; EM shows diffuse foot-process effacement. Steroid-sensitive in $>90\%$.
- **FSGS** is the commonest cause of steroid-resistant nephrotic syndrome (SRNS) in children. LM: segmental sclerosis starting at the vascular pole (tip variant) or perihilar; EM shows foot-process effacement. Variants: tip (best prognosis), cellular, perihilar, collapsing (HIV-associated nephropathy, APOL1 risk alleles), NOS. Presents with non-selective proteinuria, often hypertension, hematuria, renal insufficiency.
- **Membranous nephropathy** is rare in children — always look for secondary causes: SLE (class V), hepatitis B, drugs, malignancy. Adults: anti-PLA2R antibodies; "spike and dome" on silver stain, subepithelial deposits.
- **MPGN pattern** on biopsy is now split: **C3 glomerulopathy** (dense deposit disease, C3GN — complement-driven, persistently low C3) vs **immune-complex MPGN** (infections, lupus, cryoglobulinemia). Tram-track/duplication of GBM on LM.
- **Congenital nephrotic syndrome** (onset <3 months): Finnish type (NPHS1/nephrin, autosomal recessive), Denys-Drash (WT1), Pierson (LAMB2). Presents with massive proteinuria, usually steroid-resistant — biopsy/genetics, not prolonged steroids.
- **Response definitions (IPNA 2020 — memorize verbatim):**
 - Remission: urine protein negative/trace (dipstick) or UPCR <0.2 mg/mg for 3 consecutive days.
 - Relapse: 3+ proteinuria (or UPCR >2) for 3 consecutive days.
 - **SRNS:** failure to achieve complete remission after **4 weeks of daily prednisolone 2 mg/kg/day**.

- **SDNS (steroid-dependent):** 2 consecutive relapses during alternate-day steroids or within 14 days of stopping.
- **FRNS (frequently relapsing):** ≥ 2 relapses within 6 months of initial response, or ≥ 4 relapses in any 12-month period.
- **First-episode treatment:** prednisolone **60 mg/m²/day or 2 mg/kg/day (max 60 mg/day)** single daily dose for **4–6 weeks**, then **40 mg/m²/day or 1.5 mg/kg on alternate days** for 4–6 weeks, then taper. Relapse: 2 mg/kg/day until 3 days of remission, then 1.5 mg/kg alternate days for 4 weeks.
- **Biopsy indications:** age <1 year or >12 years at onset; SRNS; atypical features (gross hematuria, low C3, renal failure, sustained hypertension, extrarenal signs — rash, arthritis, purpura); before starting calcineurin inhibitors or cyclophosphamide. Not needed in classic SSNS aged 1–12 years.
- **Steroid-sparing agents (for SDNS/FRNS/SRNS):**
 - Levamisole 2.5 mg/kg on alternate days (watch neutropenia).
 - Cyclophosphamide 2 mg/kg/day PO for 8–12 weeks; keep cumulative dose <168 mg/kg (gonadal toxicity, hemorrhagic cystitis — MESNA/hydration).
 - Cyclosporine 4–6 mg/kg/day in 2 divided doses (trough 80–120 ng/mL; gum hyperplasia, hirsutism, nephrotoxicity) or tacrolimus 0.1–0.15 mg/kg/day in 2 doses (trough 5–10 ng/mL; diabetogenic, neurotoxicity).
 - Mycophenolate mofetil 1200 mg/m²/day in 2 divided doses (GI upset, leukopenia).
 - **Rituximab** 375 mg/m² IV per dose, given as 1–4 weekly infusions (commonly 2 doses); depletes CD20+ B cells — monitor CD19 counts; premedicate, screen for hepatitis B; choice agent for SDNS/FRNS to avoid chronic CNIs, and increasingly used in SRNS.
- **Complications:**
 - Infections: urinary loss of immunoglobulins/complement factor B + immunosuppression → **S. pneumoniae peritonitis** (commonest life-threatening infection), cellulitis, varicella. Give pneumococcal and varicella vaccines in remission; penicillin prophylaxis during relapse in unimmunized children; hold live vaccines while on daily steroids/CNIs.
 - Thrombosis: urinary loss of antithrombin III, protein C/S + hepatic overproduction of fibrinogen → **renal vein thrombosis** (flank pain, gross hematuria, enlarged kidney, declining function), sagittal sinus thrombosis, DVT. Treat with heparin/warfarin; consider prophylactic anticoagulation if albumin <2 g/dL with additional risk factors.
 - AKI (prerenal from intravascular depletion), hypovolemic shock, hyperlipidemia, steroid toxicity (growth failure, cataract, hypertension, AVN).

2. Nephritic Syndrome

- **Definition:** hematuria with RBC casts/dysmorphic RBCs, sub-nephrotic proteinuria, hypertension, oliguria, periorbital/pedal edema. Low C3 narrows the differential: PSGN, C3 glomerulopathy/MPGN, lupus nephritis, shunt nephritis. Normal complements: IgA nephropathy, ANCA vasculitis, anti-GBM disease, Henoch-Schönlein (IgA vasculitis).

- **Post-streptococcal GN (PSGN):** follows group A streptococcal pharyngitis (latent period 1–3 weeks; nephritogenic M types 1, 12) or skin infection (3–6 weeks; M types 49, 55). ASO titre rises after pharyngitis; anti-DNase B after skin infection. **C3 low, C4 normal; C3 normalizes by 6–8 weeks.** Natural history: >95% children recover fully with supportive care alone. Antibiotics treat active streptococcal infection but do not alter the nephritis. Persistent low C3 beyond 8–12 weeks, or nephrotic-range proteinuria, or RPGN course → renal biopsy (suspect C3GN, lupus, or MPGN).
- **IgA nephropathy (Berger disease):** recurrent episodes of gross hematuria **1–2 days after an upper respiratory infection** (synpharyngitic — vs 1–3 weeks in PSGN). Normal complements. Mesangial IgA deposits on immunofluorescence. Most common GN worldwide. Manage proteinuria/hypertension with ACEi/ARB; Oxford MEST-C score (mesangial/endocapillary hypercellularity, segmental sclerosis, tubular atrophy, crescents) predicts prognosis. Fish-oil and tonsillectomy have no proven role in children.
- **C3 glomerulopathy:** dense deposit disease (type II MPGN; C3 nephritic factor stabilizes C3 convertase) and C3GN. Dominant C3 staining with minimal immunoglobulin; **persistently low C3** that does not normalize. Poor prognosis; consider eculizumab in selected cases.
- **Lupus nephritis (ISN/RPS classes):** I — minimal mesangial; II — mesangial proliferative; III — focal (<50% glomeruli); IV — diffuse (≥50%, worst prognosis, wire-loop lesions); V — membranous; VI — advanced sclerosing (≥90% globally sclerosed). "Full house" immunofluorescence (IgG, IgA, IgM, C3, C1q). Class III/IV: induction with **mycophenolate mofetil or cyclophosphamide + pulse methylprednisolone**, then maintenance MMF or azathioprine. Class V with nephrotic proteinuria: add calcineurin inhibitor. Hydroxychloroquine for all SLE.
- **ANCA vasculitis:** GPA (Wegener) — **PR3-ANCA (c-ANCA)**, upper airway granulomas, sinusitis, pulmonary nodules/cavities; MPA — **MPO-ANCA (p-ANCA)**, no granulomas. Both cause pauci-immune crescentic GN (no/few immune deposits). Pulmonary hemorrhage + RPGN = emergency. Induction: rituximab or cyclophosphamide + steroids; maintenance rituximab/azathioprine.
- **Anti-GBM disease (Goodpasture):** linear IgG along GBM on immunofluorescence; circulating anti-GBM antibodies; pulmonary alveolar hemorrhage + RPGN. Treatment: **urgent plasmapheresis + cyclophosphamide + corticosteroids**. Smoking/hydrocarbon exposure precipitates hemorrhage.
- **Rapidly progressive GN (RPGN):** >50% glomeruli with crescents, renal function lost over days–weeks. Type I — anti-GBM; Type II — immune-complex (lupus, PSGN, IgA); Type III — pauci-immune (ANCA). All need urgent biopsy and immunosuppression.

3. Acute Kidney Injury

- **KDIGO definition:** creatinine rise ≥ 0.3 mg/dL within 48 h, or $\geq 1.5\times$ baseline within 7 days, or urine output < 0.5 mL/kg/h for 6 h.
- **Prerenal vs intrinsic vs postrenal:**
- Prerenal: FENa $< 1\%$, BUN:creatinine ratio $> 20:1$, urine osmolality > 500 mOsm/kg, urine Na < 20 mEq/L, bland sediment; responds to fluids. Causes: dehydration, hemorrhage, cardiac failure, hepatorenal physiology.
- Intrinsic (ATN): FENa $> 2\%$, BUN:creatinine $< 20:1$, urine osmolality < 350 , urine Na > 40 , **muddy brown granular casts**, tubular epithelial cells. Causes: prolonged ischemia, aminoglycosides, amphotericin B, contrast, rhabdomyolysis (pigment nephropathy), tumor lysis syndrome.

- Postrenal: anuria/oliguria with hydronephrosis on USG; PUV in boys, stones, neurogenic bladder. Post-obstructive diuresis after relief — watch electrolytes.
- $\text{FENa} = (\text{urine Na} \times \text{plasma creatinine}) / (\text{plasma Na} \times \text{urine creatinine}) \times 100$. Unreliable if on diuretics — use $\text{FEUrea} < 35\%$ instead.
- **ATN course:** oliguric phase → diuretic phase (tubules recover filtration before concentration — risk of dehydration/electrolyte loss) → recovery. Manage conservatively: restrict fluids to insensible + output, correct hyperkalemia/acidosis, stop nephrotoxins, dose-adjust drugs.
- **Dialysis indications — AEIOU:** **A**cidosis (refractory metabolic acidosis), **E**lectrolyte disturbances (hyperkalemia unresponsive to medical therapy), **I**ngestions (salicylates, lithium, methanol, ethylene glycol, theophylline), **O**verload (fluid overload with pulmonary edema/hypertension refractory to diuretics), **U**remia (pericarditis, encephalopathy, bleeding, severe anorexia).
- **Modality choice:** **Peritoneal dialysis** — preferred in neonates/infants (no vascular access needed, hemodynamically gentle); **intermittent hemodialysis** — fastest solute/fluid removal (poisonings, severe hyperkalemia); **CRRT** — hemodynamically unstable children, precise fluid control in ICU. Peritoneal dialysis is contraindicated with diaphragmatic hernia or recent abdominal surgery.
- **Tumor lysis syndrome:** hyperuricemia, hyperkalemia, hyperphosphatemia with **hypocalcemia**; prevention with hydration + allopurinol; rasburicase for established hyperuricemia (avoid in G6PD deficiency).

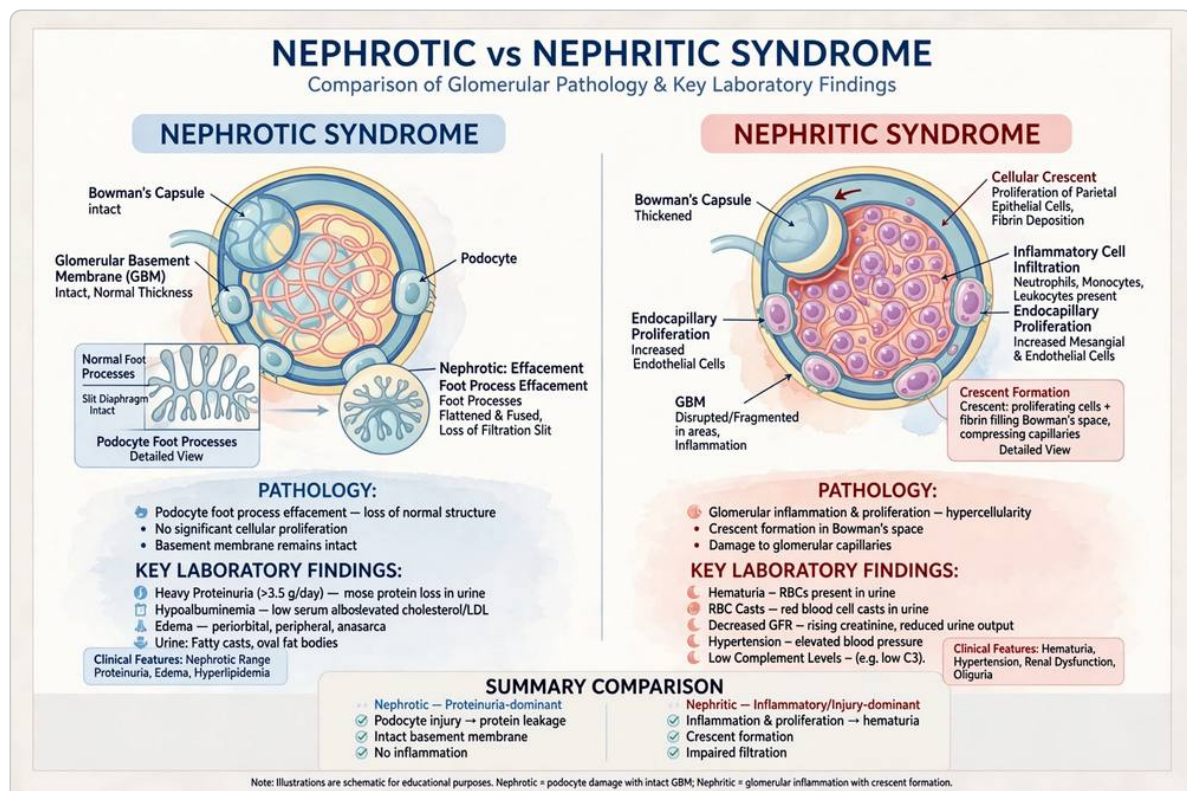


Figure 6.1 — Nephrotic vs nephritic syndrome

4. Chronic Kidney Disease

- **Definition:** kidney damage (albuminuria, abnormal imaging/histology) or GFR <60 mL/min/1.73 m² persisting ≥3 months.
- **KDIGO staging by GFR:** G1 ≥90 (normal/high, with damage), G2 60–89, G3a 45–59, G3b 30–44, G4 15–29 (severe decrease), G5 <15 (kidney failure). Albuminuria categories: A1 <30 mg/g, A2 30–300, A3 >300 mg/g creatinine.
- **eGFR in children — bedside Schwartz:** $eGFR = 0.413 \times \text{height(cm)} / \text{serum creatinine (mg/dL)}$. Cystatin C-based equations when muscle mass is abnormal.
- **Common pediatric causes:** congenital anomalies of kidney and urinary tract (CAKUT — obstructive uropathy, dysplasia, reflux nephropathy) dominate in young children; glomerular diseases (FSGS, lupus) dominate in adolescents.
- **Complications and management:**
 - **Anemia:** erythropoietin deficiency (+ iron deficiency, blood loss). Treat iron deficiency first (IV iron if on dialysis), then **erythropoiesis-stimulating agents** (epoetin alfa, darbepoetin); target Hb 10–12 g/dL, not normalization (higher targets increase cardiovascular risk).
 - **CKD–mineral and bone disorder (CKD-MBD):** phosphate retention → secondary hyperparathyroidism, vitamin D deficiency, renal osteodystrophy, growth failure. Restrict dietary phosphate; **phosphate binders with meals** (calcium carbonate/acetate in early CKD; sevelamer or lanthanum when calcium load is a concern); active vitamin D (**calcitriol/alfacalcidol**); cinacalcet (calcimimetic) for refractory hyperparathyroidism in dialysis patients. Monitor Ca, PO₄, PTH, alkaline phosphatase, 25-OH vitamin D.
 - **Metabolic acidosis:** supplement sodium bicarbonate to keep HCO₃ ≥22 mEq/L (acidosis worsens bone disease and growth).
 - **Growth failure:** optimize nutrition, correct acidosis, then **recombinant human growth hormone** if height <3rd percentile with open epiphyses despite correction — the only intervention proven to improve final height in CKD.
 - **Hypertension:** ACEi/ARB first line (also reduce proteinuria and slow progression); avoid hyperkalemia and monitor creatinine (rise >30% → suspect renal artery stenosis/volume depletion).
 - **Hyperkalemia:** low-potassium diet, loop diuretics, sodium bicarbonate; kayexalate only short-term (bowel necrosis risk in neonates).
 - **Slowing progression:** control BP, minimize proteinuria (ACEi/ARB), avoid nephrotoxins (NSAIDs, aminoglycosides), treat UTIs promptly in reflux nephropathy, correct obstruction early. Refer for transplant evaluation at G4; preemptive transplantation gives the best graft and growth outcomes in children.

5. Renal Tubular Acidosis, Bartter and Gitelman Syndromes

- **All RTAs share:** hyperchloremic (normal anion gap) metabolic acidosis. Distinguish by serum potassium, urine pH, and associated features.
- **Type 1 (distal) RTA:** collecting-duct failure to secrete H⁺ → **urine pH >5.5 despite systemic acidosis**, hypokalemia, hypercalciuria, hypocitraturia → **nephrocalcinosis and calcium stones**, rickets/growth failure.

Causes in children: obstructive uropathy, Sjögren syndrome, amphotericin B, toluene. Treatment: lifelong alkali as **potassium citrate** (corrects acidosis and hypokalemia, raises urinary citrate to prevent stones).

- **Type 2 (proximal) RTA:** impaired proximal bicarbonate reabsorption → bicarbonate wasting until serum HCO_3 falls to a new threshold, then **urine pH <5.5**; **Fanconi syndrome** (phosphaturia, glucosuria with normal blood sugar, aminoaciduria, low-molecular-weight proteinuria), hypokalemia, rickets. Commonest inherited cause in children: **cystinosis** (CTNS gene; corneal cystine crystals, treat with cysteamine). Also Dent disease, Lowe syndrome, drugs (ifosfamide, valproate). Treatment: large alkali doses + phosphate + active vitamin D; thiazides reduce bicarbonaturia.
- **Type 4 RTA:** aldosterone deficiency or resistance → **hyperkalemia**, mild acidosis, **urine pH <5.5** (acidification intact). Causes: obstructive uropathy, diabetic nephropathy, adrenal insufficiency, calcineurin inhibitors. Treatment: fludrocortisone (if adrenal insufficiency), loop diuretics, low-potassium diet, treat hyperkalemia; alkali if HCO_3 very low.

• **Lab pattern table (memorize):**

Feature	Type 1 (distal)	Type 2 (proximal)	Type 4
Urine pH during acidosis	>5.5	<5.5	<5.5
Serum K^+	Low	Low	High
Nephrocalcinosis	Yes	No	No
Fanconi features	No	Yes	No
Anion gap	Normal	Normal	Normal

- **Bartter syndrome:** defect in the **thick ascending limb of Henle** (furosemide-like) — NKCC2 (type I), ROMK (type II), ClC-Kb (type III), barttin (type IV + sensorineural deafness), CaSR activating (type V + hypocalcemia). Antenatal types present with **polyhydramnios and prematurity**. Labs: hypokalemic metabolic alkalosis, **hypercalciuria** → **nephrocalcinosis**, normal magnesium, high renin/aldosterone with **normal/low blood pressure**. Treatment: KCl supplements, NSAIDs (indomethacin reduces polyuria), spironolactone.
- **Gitelman syndrome:** defect in the **distal convoluted tubule** Na-Cl cotransporter (thiazide-like). Later onset (adolescents/adults), milder. Labs: hypokalemic metabolic alkalosis, **hypomagnesemia**, **hypocalciuria** (opposite of Bartter), normal BP, high renin/aldosterone. Treatment: lifelong magnesium and potassium replacement; amiloride/spironolactone.
- **Bartter vs Gitelman one-liner:** Bartter = loop-diuretic mimic with hypercalciuria and nephrocalcinosis, normal Mg, presents early; Gitelman = thiazide mimic with hypomagnesemia and hypocalciuria, presents late. Both have metabolic alkalosis, high renin/aldosterone, and normal blood pressure — unlike primary hyperaldosteronism/Liddle (hypertensive).

6. Urinary Tract Infection and Vesicoureteral Reflux

- **Febrile UTI workup:** urine culture is mandatory — catheterized or suprapubic sample in non-toilet-trained infants (bag specimens are unacceptable for culture). **E. coli** causes >80%. Treat febrile UTI for 7–10 days; infants <2 months need parenteral therapy and sepsis workup.

- **Imaging after first febrile UTI: renal-bladder ultrasound** for all infants (detects hydronephrosis, duplex systems, ureterocele, bladder wall thickening). **VCUG (MCU)** is not routine — reserve for abnormal USG, atypical organisms, poor urinary stream, recurrent febrile UTIs, or known antenatal hydronephrosis. **DMSA scan** (3–6 months after infection) detects cortical scarring and split function.
- **VUR grading (International I–V):** I — reflux into ureter only; II — reflux into ureter, pelvis and calyces without dilation; III — mild dilation of ureter/pelviccalyceal system, no tortuosity; IV — moderate dilation/tortuosity with blunting of fornices; V — gross dilation and tortuosity with loss of papillary impressions. Grades I–II usually resolve spontaneously; grades IV–V often need intervention.
- **Continuous antibiotic prophylaxis (CAP):** indicated for VUR grades III–V, recurrent febrile UTIs, or high-grade reflux awaiting surgery; agents: nitrofurantoin or trimethoprim-sulfamethoxazole (avoid TMP-SMX <2 months; avoid nitrofurantoin with GFR <30). RIVUR trial: CAP reduces recurrent febrile UTI but does not reduce renal scarring. Stop CAP when reflux resolves, the child is toilet-trained with normal voiding, and no breakthrough infections.
- **Surgical options:** endoscopic **Deflux** (dextranomer/hyaluronic acid) subureteric injection — day-care, lower success in grade V; **ureteral reimplantation** (Cohen cross-trigonal technique) — gold standard for high-grade VUR, failed Deflux, or breakthrough febrile UTIs on prophylaxis.
- **Dysfunctional voiding** (holding maneuvers, constipation) must be treated (timed voiding, laxatives) — it causes "pseudo-reflux" persistence and recurrent UTI despite anatomically low-grade VUR.

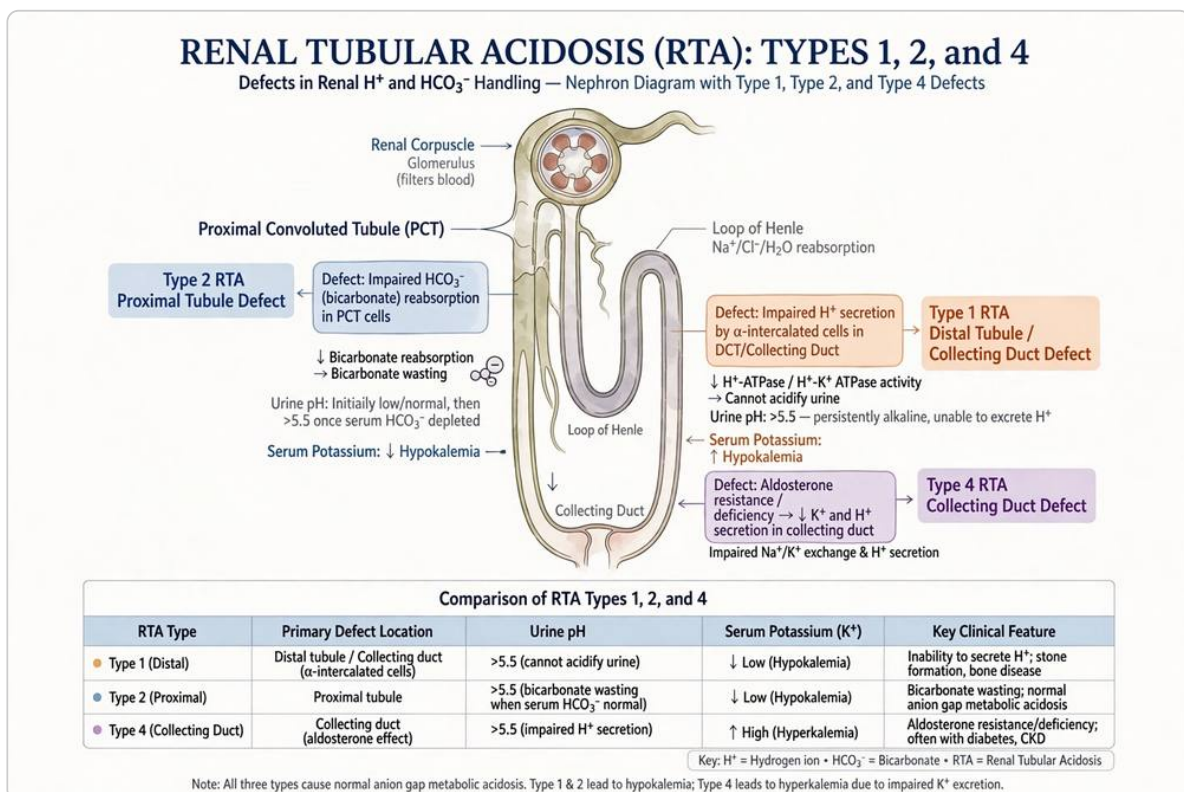


Figure 6.2 — Renal tubular acidosis types and nephron defect sites

7. HUS vs TTP

- **Typical (STEC) HUS:** Shiga toxin-producing **E. coli O157:H7** (undercooked beef, unpasteurized milk); bloody diarrhea prodrome 5–7 days before the triad of **microangiopathic hemolytic anemia (schistocytes, high LDH, low haptoglobin, negative Coombs), thrombocytopenia, and AKI**. Peak age 1–5 years. Treatment is **supportive only** — fluids, dialysis as needed; **do NOT give antibiotics or antimotility agents** (increase toxin release and HUS risk). Plasma exchange has no role. Most recover; ~5% mortality, some progress to CKD.
- **Atypical HUS:** complement-mediated (mutations in CFH, CFI, MCP/CD46, C3, CFB; anti-factor H antibodies). **No diarrheal prodrome**, recurrent episodes, worse renal prognosis, can present in infancy. Low C3 with normal C4 suggests alternative-pathway activation. Treatment: **eculizumab** — terminal complement (C5) inhibitor, weight-based IV dosing (adult reference: 900 mg weekly × 4, then 1200 mg every 2 weeks); **vaccinate against meningococcus (and ideally pneumococcus/Hib) at least 2 weeks before starting**, with penicillin prophylaxis if vaccination is delayed. Plasma exchange is a bridge only.
- **TTP:** severe **ADAMTS13 deficiency (<10% activity)** — congenital (Upshaw-Schulman) or acquired autoantibody. Classic pentad: MAHA, thrombocytopenia, **fluctuating neurological symptoms**, renal impairment, fever — but the dyad of MAHA + thrombocytopenia without another cause is enough to treat. PLASMIC score predicts severe deficiency. Treatment: **urgent therapeutic plasma exchange + corticosteroids**; caplacizumab (vWF inhibitor) and rituximab for refractory/acquired cases. **Do not transfuse platelets** unless life-threatening bleeding or urgent surgery — it fuels microthrombi.
- **HUS vs TTP one-liner:** HUS = Shiga toxin/complement, kidney-predominant, supportive care or eculizumab; TTP = ADAMTS13 <10%, neuro-predominant, plasma exchange is life-saving and platelets are contraindicated.

8. Nephrolithiasis, Posterior Urethral Valves, Wilms vs Hydronephrosis

- **Nephrolithiasis:** commonest metabolic abnormality in children is **idiopathic hypercalciuria**; also hypocitraturia, hyperoxaluria, hyperuricosuria. Calcium oxalate stones predominate. **Cystinuria** (autosomal recessive, dibasic amino acids) → hexagonal crystals, staghorn calculi, positive cyanide-nitroprusside test. **Struvite** (magnesium ammonium phosphate) stones form in alkaline urine with urease-positive organisms (Proteus) — "coffin-lid" crystals. Workup: stone analysis, 24-hour urine (calcium, oxalate, citrate, uric acid, cystine), serum Ca/PO4/PTH. Management: high fluid intake, **thiazides for hypercalciuria**, potassium citrate for hypocitraturia, low salt; cystine stones need aggressive hydration + alkalinization ± tiopronine.
- **Posterior urethral valves (PUV):** commonest cause of bladder outlet obstruction in **boys**; presents with poor urinary stream, dribbling, palpable bladder, recurrent UTI, and bilateral hydroureteronephrosis. VCUG shows the **"keyhole" sign** (dilated posterior urethra). Antenatal: oligohydramnios, bilateral hydronephrosis — may need vesicoamniotic shunting. Treatment: **endoscopic valve ablation**; vesicostomy if the infant is unstable. Long-term risk of CKD from renal dysplasia and "valve bladder" dysfunction — lifelong nephrology follow-up.
- **Wilms tumor vs hydronephrosis:** Wilms — solid **intrarenal mass that does not cross the midline**, "claw sign" of renal parenchyma around the mass, peak age 2–3 years, hypertension, hematuria uncommon, associated with WAGR, Beckwith-Wiedemann, Denys-Drash (WT1). Hydronephrosis — dilated anechoic

collecting system **without a solid mass**. Neuroblastoma — the mimicker that **crosses the midline**, calcifies, and encases vessels. Never biopsy a suspected Wilms before nephrectomy workup (upstages the tumor).

9. Hypertension in Children

- **Definition (AAP 2017):** average of 3 readings **≥95th percentile for age, sex, and height**. Stage 1: 95th percentile to <95th + 12 mmHg; Stage 2: ≥95th + 12 mmHg (or ≥140/90, whichever is lower). Adolescents ≥13 years use adult cut-offs: elevated 120–129/<80, stage 1 130–139/80–89, stage 2 ≥140/90. Confirm with ambulatory BP monitoring to exclude white-coat hypertension.
- **Etiology:** younger/prepubertal children → **secondary causes dominate**, commonest being **renal parenchymal disease**, then renovascular disease, **coarctation of aorta** (check 4-limb BP and femoral pulses), endocrine (pheochromocytoma, hyperthyroidism, CAH due to 11β- or 17α-hydroxylase deficiency), drugs (steroids, decongestants, stimulants). Adolescents → primary/essential hypertension with obesity and family history.
- **Workup:** urinalysis, basic metabolic panel, renal ultrasound, fasting lipids and glucose/HbA1c if overweight, TSH; echocardiography at initiation of drug therapy (LVH assessment). Renovascular hypertension: renal Doppler → CTA/MRA; fibromuscular dysplasia is the commonest pediatric cause (string-of-beads).
- **Management:** lifestyle modification first (DASH diet, exercise, weight control, salt restriction). Drugs when stage 2, symptomatic, diabetic/CKD, or persistent stage 1: **ACE inhibitors or ARBs first line** (especially with proteinuria, CKD, diabetes); amlodipine (CCB) or thiazide diuretics as alternatives/add-ons. Avoid ACEi/ARB in bilateral renal artery stenosis and pregnancy; beta-blockers are not first line in children.
- **Hypertensive emergency** (severe HTN + end-organ damage — encephalopathy, seizures, AKI, heart failure): IV therapy in ICU — **nicardipine or sodium nitroprusside** infusion; lower mean arterial pressure by **no more than 25% in the first 8 hours** (rapid drops cause cerebral/coronary ischemia). Sublingual nifedipine is obsolete and dangerous. Hypertensive urgency (no end-organ damage): oral agents, gradual control.

Practice MCQs

Q1. A 4-year-old boy with nephrotic syndrome receives prednisolone 2 mg/kg/day. After 4 weeks, his urine protein is still 3+ and serum albumin is 1.8 g/dL. The most appropriate next step is: A) Continue daily steroids for another 4 weeks B) Start cyclophosphamide immediately C) Add albumin infusions and continue steroids D) Label as steroid-resistant NS and obtain a renal biopsy **Answer: D** — Failure to achieve remission after 4 weeks of daily prednisolone 2 mg/kg/day defines SRNS (IPNA 2020). The next step is renal biopsy to identify the histology (commonly FSGS) before starting calcineurin inhibitors or other second-line agents.

Q2. A 9-year-old HIV-positive boy presents with nephrotic-range proteinuria, normal complements, and rapidly rising creatinine. Biopsy is most likely to show: A) Membranous nephropathy B) Minimal change disease C) IgA nephropathy D) Collapsing FSGS **Answer: D** — HIV-associated nephropathy manifests as the collapsing variant of FSGS, with glomerular tuft collapse, podocyte hypertrophy, and microcystic tubular dilatation. It presents with heavy proteinuria and rapid progression to renal failure, typically with normal complements.

Q3. A 13-year-old girl presents with new-onset nephrotic syndrome: BP 140/90, creatinine 1.4 mg/dL, C3 62 mg/dL (low), urine shows RBC casts. The best next step is: A) Renal biopsy B) Start prednisolone 2 mg/kg/day empirically C) Check ASO titre and wait 8 weeks D) Start rituximab **Answer: A** — Onset after 12 years with atypical features (hypertension, renal failure, low C3, RBC casts) mandates biopsy before steroids. This presentation suggests MPGN/C3 glomerulopathy or lupus nephritis, not classic minimal change disease.

Q4. A 6-year-old with growth failure has arterial pH 7.28, HCO₃ 15 mEq/L, K⁺ 2.9 mEq/L, Cl⁻ 115 mEq/L, urine pH 6.8, and bilateral nephrocalcinosis on ultrasound. The most likely diagnosis is: A) Type 2 RTA B) Type 4 RTA C) Type 1 (distal) RTA D) Bartter syndrome **Answer: C** — Normal anion gap metabolic acidosis with hypokalemia, inability to acidify urine below pH 5.5, and nephrocalcinosis from hypercalciuria/hypocitraturia is classic distal (type 1) RTA. Bartter causes metabolic alkalosis, not acidosis.

Q5. A 7-year-old develops periorbital edema and cola-colored urine 2 weeks after streptococcal pharyngitis. Labs: C3 45 mg/dL (low), C4 normal, ASO 800 IU/mL, creatinine 0.9 mg/dL. The expected natural history is: A) Progression to ESRD within 5 years without immunosuppression B) Spontaneous recovery with supportive care; C3 normalizes in 6–8 weeks C) Lifelong low C3 requiring eculizumab D) Mandatory renal biopsy to exclude lupus **Answer: B** — This is classic PSGN: latent period 1–3 weeks post-pharyngitis, low C3 with normal C4, elevated ASO. Over 95% of children recover fully with supportive care alone; C3 normalizes by 6–8 weeks. Persistent low C3 beyond 8–12 weeks warrants biopsy.

Q6. A 14-year-old girl has recurrent muscle cramps and tetany. Labs: K⁺ 2.8 mEq/L, Mg²⁺ 1.1 mg/dL (low), HCO₃ 32 mEq/L, urinary calcium excretion low, BP 100/60. The most likely diagnosis is: A) Gitelman syndrome B) Bartter syndrome C) Liddle syndrome D) Primary hyperaldosteronism **Answer: A** — Hypokalemic metabolic alkalosis with hypomagnesemia, hypocalciuria, normal BP, and adolescent onset defines Gitelman syndrome (thiazide-like DCT defect). Bartter has hypercalciuria with nephrocalcinosis and normal magnesium; Liddle and hyperaldosteronism cause hypertension.

Q7. A 10-year-old with AKI (creatinine 4.2 mg/dL) has K⁺ 5.1 mEq/L, HCO₃ 20 mEq/L, is euvolemic, making 1 mL/kg/h urine, and is alert with a normal ECG. Which finding would NOT be an indication for urgent dialysis? A) Pericardial friction rub B) Pulmonary edema refractory to furosemide C) K⁺ 5.1 mEq/L responsive to medical therapy D) Uremic encephalopathy **Answer: C** — AEIOU indications are refractory acidosis, refractory electrolyte disturbance, ingestions, refractory overload, and uremia (pericarditis, encephalopathy). A K⁺ of 5.1 that responds to medical therapy is not a dialysis indication; pericarditis, refractory overload, and encephalopathy are.

Q8. A 3-year-old develops bloody diarrhea after eating undercooked beef; 6 days later he has pallor, petechiae, LDH 1800 IU/L, platelets 45,000/μL, schistocytes on smear, creatinine 2.1 mg/dL, Coombs negative. The most appropriate management is: A) Start ciprofloxacin and loperamide B) Urgent plasma exchange C) Supportive care with fluids and dialysis as needed; avoid antibiotics D) Eculizumab immediately **Answer: C** — This is typical STEC-HUS (O157:H7). Management is supportive; antibiotics and antimotility agents increase toxin release and worsen outcomes. Plasma exchange has no role in STEC-HUS, and eculizumab is reserved for atypical (complement-mediated) HUS.

Q9. A 12-year-old girl with SLE has proteinuria 3.5 g/day, active urinary sediment, and biopsy showing diffuse proliferative glomerulonephritis involving >50% of glomeruli with wire-loop lesions. The ISN class and preferred induction therapy are: A) Class III; rituximab alone B) Class IV; mycophenolate mofetil or cyclophosphamide

with corticosteroids C) Class V; ACE inhibitor alone D) Class II; hydroxychloroquine alone **Answer: B** — Involvement of $\geq 50\%$ of glomeruli with diffuse proliferation defines ISN class IV lupus nephritis. Induction is MMF or cyclophosphamide plus corticosteroids (with pulse methylprednisolone), followed by maintenance immunosuppression.

Q10. A VCUG in a 5-year-old with recurrent febrile UTIs shows reflux into a moderately dilated, tortuous ureter with blunting of the calyceal fornices but preserved papillary impressions. The VUR grade is: A) Grade II B) Grade III C) Grade V D) Grade IV **Answer: D** — Grade IV VUR shows moderate ureteral dilation and tortuosity with blunting of fornices but retained papillary impressions. Grade V has gross dilation with loss of papillary impressions; grade III has only mild dilation without tortuosity.

Q11. A dehydrated 8-year-old has BUN 48 mg/dL, creatinine 1.2 mg/dL, urine Na 12 mEq/L, FENa 0.6%. The most likely category of AKI and best initial management are: A) Prerenal AKI; isotonic fluid resuscitation B) Acute tubular necrosis; urgent dialysis C) Postrenal obstruction; bladder catheterization D) Glomerulonephritis; pulse steroids **Answer: A** — FENa $< 1\%$, BUN:creatinine ratio $> 20:1$ ($48/1.2 = 40$), and low urine sodium indicate prerenal AKI from volume depletion, which responds to isotonic fluid resuscitation. ATN would show FENa $> 2\%$ with muddy brown casts.

Q12. A 6-year-old with steroid-dependent nephrotic syndrome has relapsed twice on alternate-day prednisolone and developed cataracts and growth failure. The agent that depletes CD20+ B cells and allows steroid withdrawal is: A) Cyclosporine B) Levamisole C) Rituximab D) Cyclophosphamide **Answer: C** — Rituximab is an anti-CD20 monoclonal antibody (375 mg/m² per dose, 1–4 weekly infusions) that depletes B cells, monitored via CD19 counts. It is increasingly preferred for SDNS/FRNS to achieve prolonged remission while withdrawing steroids and avoiding chronic calcineurin-inhibitor nephrotoxicity.

Q13. A 2-year-old presents with MAHA, thrombocytopenia, and AKI without any diarrheal prodrome; this is his second episode. C3 is low, C4 normal. Genetic testing is pending. The most appropriate disease-targeted therapy is: A) Plasma exchange B) Eculizumab after meningococcal vaccination C) High-dose steroids alone D) Platelet transfusion **Answer: B** — Recurrent HUS without diarrhea and with low C3/normal C4 indicates atypical (complement-mediated) HUS. Eculizumab, a terminal C5 complement inhibitor, is the targeted therapy; meningococcal vaccination (≥ 2 weeks prior, with penicillin bridge) is mandatory due to the risk of meningococemia.

Q14. A 10-year-old boy develops gross hematuria 1 day after a sore throat. BP is 110/70, C3 and C4 are normal, creatinine is 0.7 mg/dL, and urine shows dysmorphic RBCs without casts. The most likely diagnosis is: A) IgA nephropathy B) Post-streptococcal GN C) Alport syndrome D) Thin basement membrane disease **Answer: A** — Synpharyngitic hematuria (1–2 days after URI) with normal complements is classic Berger disease (IgA nephropathy). PSGN has a 1–3 week latent period with low C3; Alport presents with sensorineural deafness and a family history of renal failure.

Q15. A 9-year-old with CKD stage 4 has phosphate 7.2 mg/dL, calcium 8.1 mg/dL, PTH 480 pg/mL, and 25-OH vitamin D 14 ng/mL. The most appropriate initial management of his mineral bone disorder is: A) Cinacalcet alone B) High-dose calcium supplements C) Parathyroidectomy D) Dietary phosphate restriction, phosphate binder with meals, and active vitamin D **Answer: D** — CKD-MBD management starts with dietary phosphate restriction, phosphate binders taken with meals (calcium-based or sevelamer), and active vitamin D (calcitriol) for

secondary hyperparathyroidism. Cinacalcet is reserved for refractory hyperparathyroidism on dialysis; parathyroidectomy is a last resort.

Q16. A newborn boy has a poor urinary stream, dribbling, a palpable bladder, and bilateral hydronephrosis on antenatal scans. VCUG shows dilation of the posterior urethra with a characteristic "keyhole" appearance. The definitive treatment is: A) Vesicoamniotic shunt B) Endoscopic valve ablation C) Bilateral ureteral reimplantation D) Chronic peritoneal dialysis **Answer: B** — The keyhole sign on VCUG is diagnostic of posterior urethral valves, the commonest bladder outlet obstruction in boys. Definitive treatment is endoscopic valve ablation; vesicostomy is reserved for unstable infants, and these children need lifelong nephrology follow-up for CKD.

Q17. A 14-year-old girl presents with confusion, petechiae, LDH 2200 IU/L, platelets 28,000/ μ L, schistocytes, creatinine 1.3 mg/dL, and ADAMTS13 activity 6%. The most urgent, life-saving intervention is: A) Eculizumab B) Platelet transfusion C) High-dose IVIG D) Therapeutic plasma exchange with corticosteroids **Answer: D** — ADAMTS13 <10% with MAHA and thrombocytopenia defines TTP. Urgent therapeutic plasma exchange plus corticosteroids is life-saving; platelet transfusion is contraindicated (fuels microthrombi) unless there is life-threatening bleeding.

Q18. A 7-year-old with obstructive uropathy has pH 7.30, HCO_3^- 18 mEq/L, K^+ 6.1 mEq/L, Cl^- 112 mEq/L, and urine pH 5.2. The most likely diagnosis and appropriate therapy are: A) Type 4 RTA; fludrocortisone, loop diuretic, and low-potassium diet B) Type 1 RTA; potassium citrate C) Type 2 RTA; bicarbonate and phosphate D) Bartter syndrome; indomethacin **Answer: A** — Hyperkalemia with mild normal-anion-gap acidosis and intact urinary acidification (urine pH <5.5) defines type 4 RTA from aldosterone deficiency/resistance, common in obstructive uropathy. Treatment targets hyperkalemia: fludrocortisone (if mineralocorticoid-deficient), loop diuretics, and potassium restriction.

Q19. A 5-year-old with relapsing nephrotic syndrome (albumin 1.6 g/dL, unimmunized) develops fever and abdominal pain with rebound tenderness. Ascitic tap shows 900 neutrophils/ μ L. Beyond empiric ceftriaxone, the important preventive measure for future relapses is: A) Prophylactic heparin during every relapse B) Pneumococcal vaccination in remission (penicillin prophylaxis during relapse if unvaccinated) C) Lifelong daily albumin infusions D) Splenectomy **Answer: B** — Spontaneous bacterial peritonitis from *S. pneumoniae* is the classic life-threatening infection in nephrotic syndrome due to urinary immunoglobulin/complement loss. Prevention is pneumococcal (and varicella) vaccination given during remission, with penicillin prophylaxis during relapses in unimmunized children.

Q20. A 15-year-old boy has chronic sinusitis, epistaxis, pulmonary nodules with cavitation, and rapidly rising creatinine with an active urinary sediment. c-ANCA (anti-PR3) is strongly positive. The expected renal biopsy finding is: A) Linear IgG along the GBM B) Subepithelial "spike and dome" deposits C) Pauci-immune crescentic glomerulonephritis D) Mesangial IgA deposits **Answer: C** — Upper airway granulomatous disease with PR3/c-ANCA positivity defines granulomatosis with polyangiitis (GPA), which causes pauci-immune (few/no immune deposits) crescentic GN. Linear IgG indicates anti-GBM disease; spikes and domes indicate membranous nephropathy.

Q21. A 4-month-old girl presents with her first febrile UTI; urine culture grows *E. coli* >100,000 CFU/mL from a catheterized sample. After completing antibiotics, the most appropriate next imaging study is: A) Renal-bladder ultrasound B) VCUG immediately C) DMSA scan within 1 week D) CT urography **Answer: A** — Guidelines recommend renal-bladder ultrasound after the first febrile UTI in infants to detect hydronephrosis, duplex

systems, or bladder abnormalities. VCUG is reserved for abnormal USG, atypical organisms, or recurrent infections; DMSA for scarring is done 3–6 months later.

Q22. A 3-year-old (15 kg) presents with first-episode nephrotic syndrome: generalized edema, albumin 1.9 g/dL, cholesterol 340 mg/dL, urine protein 4+. The correct initial prednisolone regimen is: A) 1 mg/kg/day for 2 weeks B) Pulse methylprednisolone 30 mg/kg for 3 days then stop C) 2 mg/kg alternate days for 8 weeks D) 2 mg/kg/day (30 mg) daily for 4–6 weeks, then 1.5 mg/kg alternate days for 4–6 weeks **Answer: D** — The standard first-episode regimen is prednisolone 60 mg/m²/day or 2 mg/kg/day (max 60 mg/day) daily for 4–6 weeks, followed by 40 mg/m²/day or 1.5 mg/kg on alternate days for 4–6 weeks, then taper. For a 15 kg child, 2 mg/kg/day = 30 mg daily. Daily (not alternate-day) therapy is required for the initial phase.

Q23. A 16-year-old boy presents with hemoptysis, falling hemoglobin, and creatinine rising from 0.9 to 3.4 mg/dL over 10 days. Urine shows RBC casts; anti-GBM antibodies are positive. Renal biopsy immunofluorescence will most likely show: A) Granular IgG and C3 along capillary walls B) Linear IgG along the glomerular basement membrane C) Dominant mesangial IgA D) "Full house" immunoglobulin deposition **Answer: B** — Pulmonary hemorrhage with RPGN and positive anti-GBM antibodies defines Goodpasture (anti-GBM) disease, whose hallmark is linear IgG deposition along the GBM. Treatment is urgent plasmapheresis plus cyclophosphamide and steroids.

Q24. A 12-year-old with known CKD presents with seizures; BP is 190/120 mmHg, and funduscopy shows papilledema. The most appropriate immediate management is: A) Sublingual nifedipine and discharge on oral amlodipine B) Oral labetalol and outpatient follow-up in 1 week C) ICU admission with IV nicardipine infusion, lowering MAP by ≤25% in the first 8 hours D) Immediate hemodialysis regardless of labs **Answer: C** — Seizures with papilledema indicate hypertensive emergency with end-organ damage, requiring ICU-based IV therapy (nicardipine or nitroprusside). MAP must not fall more than 25% in the first 8 hours to avoid cerebral ischemia; sublingual nifedipine causes precipitous, dangerous drops.

Q25. A 3-year-old boy presents with an abdominal mass. Ultrasound shows a large solid intrarenal mass that does not cross the midline, with a "claw" of renal parenchyma around it and no calcifications. The most likely diagnosis is: A) Wilms tumor B) Neuroblastoma C) Hydronephrosis D) Autosomal recessive polycystic kidney disease **Answer: A** — A solid intrarenal mass not crossing the midline with the claw sign and no calcifications in a 2–3-year-old is classic Wilms tumor. Neuroblastoma crosses the midline, calcifies, and encases vessels; hydronephrosis shows a dilated collecting system without a solid mass.

Pediatric Endocrinology

Chapter 7: Pediatric Endocrinology

Endocrinology punches above its weight in NEET SS Pediatrics: the vignettes are short, the numbers are exact, and the examiner rewards whoever memorized the dose, the cut-off, and the distinguishing lab value rather than the story. DKA fluid/insulin/potassium sequencing, the MODY gene that responds to sulfonylureas, the 10–15 mcg/kg/day levothyroxine rule, and the SIADH-versus-cerebral-salt-wasting split are classic single-best-answer territory. This chapter is built around those contrasts, with every critical dose stated the way the question will ask it.

1. Type 1 Diabetes Mellitus

- **Pathophysiology:** T-cell-mediated autoimmune destruction of pancreatic beta cells in a genetically susceptible child (HLA-DR3/DR4, especially DR3-DQ2/DR4-DQ8). Islet autoantibodies — **anti-GAD65** (most persistent), anti-IA-2, anti-insulin (IAA, first to appear in young children), anti-ZnT8 — may precede clinical disease by years. Clinical diabetes appears when ~80–90% of beta-cell mass is lost. Environmental triggers: enteroviral infections, early cow's-milk exposure, vitamin D deficiency (associations, none proven causal).
- **Diagnosis (ADA/ISPAD criteria):** fasting glucose ≥ 126 mg/dL, 2-hour OGTT ≥ 200 mg/dL, random glucose ≥ 200 mg/dL **with classic symptoms** (polyuria, polydipsia, polyphagia, weight loss), or HbA1c $\geq 6.5\%$. DKA at presentation occurs in 25–40% of new pediatric cases.
- **Honeymoon (partial remission) phase:** weeks to months after insulin initiation, residual beta cells recover transiently and insulin requirements fall dramatically (sometimes <0.5 U/kg/day total). It is temporary — ongoing autoimmunity destroys remaining beta cells — so insulin must never be stopped; counsel families that rising requirements signal the end of the honeymoon, not treatment failure.
- **Insulin regimens:**
 - **Basal-bolus (MDI — multiple daily injections):** long-acting basal (glargine/detemir once daily, or degludec) supplying ~40–50% of total daily dose + rapid-acting bolus (lispro, aspart, glulisine) with each meal covering ~50–60%. Standard of care for most children.
 - **Insulin pump (CSII — continuous subcutaneous insulin infusion):** rapid-acting insulin only, delivered as programmable basal rates plus meal/correction boluses. Advantages: flexibility, lower hypoglycemia, precise micro-dosing for toddlers; disadvantages: DKA risk if infusion interrupted (no long-acting depot), cost, site infections.
- **Dosing rules of thumb:** total daily dose (TDD) ~0.5–1.0 U/kg/day in prepubertal children, up to 1.5 U/kg/day during puberty (growth hormone-driven insulin resistance). **Insulin-to-carbohydrate ratio:** $500/\text{TDD} =$ grams of carbohydrate covered by 1 unit (450 rule also used in young children). **Correction (insulin**

sensitivity) factor: $1800/\text{TDD} = \text{mg/dL fall in glucose per 1 unit of rapid-acting insulin}$ (1500 rule in small children).

- **DKA — diagnostic criteria:** hyperglycemia (usually $>200\text{--}250\text{ mg/dL}$), venous pH <7.3 , bicarbonate $<15\text{ mEq/L}$, ketonemia/ketonuria, elevated anion gap. Severity: mild (pH $7.2\text{--}7.3$), moderate ($7.1\text{--}7.2$), severe (<7.1).
- **DKA management (ISPAD sequence — know the order):**
 - **Assess and resuscitate:** ABCs, weight, dehydration, mental status (Glasgow coma scale — cerebral edema watch). Correct shock with **isotonic fluid (normal saline) $10\text{--}20\text{ mL/kg bolus}$** , repeatable.
 - **Fluids:** after shock resuscitation, replace deficit + maintenance with **isotonic crystalloid (NS)** over 24–48 hours. Avoid hypotonic fluids early (cerebral edema risk); switch to NS with dextrose (D5-NS) when glucose falls to $\sim 250\text{--}300\text{ mg/dL}$ so insulin can continue while preventing hypoglycemia. Do not correct glucose faster than $\sim 50\text{--}100\text{ mg/dL/hour}$.
 - **Insulin:** start **$0.05\text{--}0.1\text{ U/kg/hour IV infusion}$** (0.05 preferred in young children) **after** initial fluid expansion — no routine bolus. Continue until anion gap closes and bicarbonate normalizes, then transition to subcutaneous insulin with a 30–60 minute overlap (give the first SC dose before stopping the infusion).
 - **Potassium:** total-body potassium is depleted despite normal/high measured K (acidosis shifts K extracellularly). **If K $<3.3\text{ mEq/L}$ — hold insulin and replace K first.** If K $3.3\text{--}5.3\text{ mEq/L}$ with adequate urine output, add **$20\text{--}40\text{ mEq/L potassium}$** (half KCl, half KPhos) to IV fluids. If K >5.5 , recheck in 2 hours. Monitor ECG for peaked T waves / prolonged QT.
 - **Do NOT give bicarbonate** routinely — reserved for pH <6.9 with compromised cardiac contractility; it worsens intracellular acidosis and hypokalemia.
 - **Treat the precipitant:** infection (most common trigger — do not give antibiotics blindly; look), missed insulin doses, new-onset diabetes, pump failure.
 - **Cerebral edema — the DKA killer:** occurs in $\sim 0.5\text{--}1\%$ of pediatric DKA, mortality $\sim 25\%$, mostly in young children with severe acidosis. **Warning signs:** headache, irritability then drowsiness, altered consciousness, incontinence, bradycardia, hypertension, cranial nerve palsies, pupillary changes. Risk factors: severe acidosis, low pCO_2 , high BUN, aggressive/hypotonic fluids, bicarbonate use.
 - **Treatment (act before imaging):** elevate head of bed 30° , restrict fluids to two-thirds maintenance, hyperosmolar therapy — **mannitol $0.25\text{--}1\text{ g/kg IV}$** (20% solution) or **3% hypertonic saline $5\text{--}10\text{ mL/kg IV}$** (1 mL/kg raises serum Na by $\sim 1\text{ mEq/L}$). Intubate with controlled hyperventilation only if herniation is imminent; get CT head but never delay treatment for it.
 - **Hypoglycemia management:** alert value $<70\text{ mg/dL}$. Mild (conscious): **15-15 rule** — 15 g fast-acting carbohydrate (glucose tablets, juice), recheck in 15 minutes, repeat; then a snack with complex carbohydrate. Severe (altered consciousness/seizure): **IV dextrose $0.5\text{--}1\text{ g/kg}$** (D25W $2\text{--}4\text{ mL/kg}$) or **glucagon IM/SC — 0.5 mg if $<25\text{ kg}$, 1 mg if $\geq 25\text{ kg}$** (intranasal glucagon 3 mg also available). Never give oral carbohydrate to an unconscious child (aspiration). Every family must have a glucagon emergency kit.
 - **Glycemic targets (ISPAD/ADA):** HbA1c $<7.0\%$ for children and adolescents on modern therapy; time-in-range ($70\text{--}180\text{ mg/dL}$) $>70\%$; minimize severe hypoglycemia and DKA. Individualize upward in hypoglycemia-unaware or very young children.
 - **Screening in T1DM:** at diagnosis — thyroid function + anti-TPO/anti-thyroglobulin (autoimmune thyroid disease), tissue transglutaminase IgA + total IgA (celiac), lipids. Annual: ACR (albumin:creatinine ratio) and

dilated eye exam starting at puberty or after 5 years' duration; blood pressure each visit. Sick-day rules: never stop basal insulin, check ketones with every illness, give extra rapid-acting per ketone-correction plan.

2. Monogenic Diabetes — MODY and Neonatal Diabetes

- **When to suspect monogenic diabetes:** diabetes <6 months of age (always genetic — never call it type 1), strong autosomal-dominant family history across ≥ 3 generations, mild fasting hyperglycemia with near-normal HbA1c, absence of islet autoantibodies, low insulin requirement, or extrapancreatic features (renal cysts, deafness, macrosomia).
- **HNF1A-MODY (MODY3):** commonest MODY in adolescents/adults. Progressive beta-cell dysfunction; marked sensitivity to **low-dose sulfonylureas** — patients often transfer off insulin to sulfonylurea with better control. Low renal glucose threshold → glycosuria at normal blood glucose (exam trap). Microvascular complications occur like type 1 — treat to target.
- **GCK-MODY (MODY2):** heterozygous glucokinase mutation resets the glucose-sensing threshold upward. **Mild, stable fasting hyperglycemia (100–150 mg/dL), HbA1c 5.8–7.6%** from birth, no progression, microvascular complications essentially absent. **No treatment needed** — do not start insulin or oral agents; the commonest exam error is over-treating. Reassure; screen family members.
- **HNF4A-MODY (MODY1):** macrosomia and **neonatal hyperinsulinemic hypoglycemia** (fetal hyperinsulinism), later progressing to diabetes; sulfonylurea-sensitive like HNF1A.
- **HNF1B-MODY (MODY5): renal cysts and diabetes (RCAD)** — renal malformations, hypomagnesemia, hyperuricemia, genital tract anomalies; diabetes often requires insulin (not sulfonylurea-responsive).
- **Neonatal diabetes (<6 months):**
 - **KCNJ11 / ABCC8** (Kir6.2 / SUR1 — K-ATP channel subunits): commonest cause of permanent neonatal diabetes. Activating mutations keep the K-ATP channel open → no insulin release. **Treatment: switch from insulin to high-dose sulfonylurea (glibenclamide/glyburide)** — sulfonylureas close the channel independent of ATP and restore endogenous insulin, often dramatically improving control. KCNJ11 can also cause **DEND syndrome** (developmental delay, epilepsy, neonatal diabetes) — sulfonylurea may improve neurodevelopmental features.
 - **INS gene mutations:** misfolded proinsulin → beta-cell ER stress; requires lifelong insulin.
 - **6q24 imprinting abnormalities (ZAC/HYMAI overexpression): transient neonatal diabetes (TNDM)** — presents in first weeks, resolves by ~18 months, may relapse in adolescence/adulthood as type 2–like diabetes.
 - Others: EIF2AK3 (Wolcott-Rallison — skeletal dysplasia, recurrent hepatitis), FOXP3 (IPEX — immune dysregulation, enteropathy, eczema), GATA6/PDX1 (pancreatic agenesis).
- **Exam rule:** any infant diagnosed with "type 1 diabetes" under 6 months → send monogenic diabetes gene panel; KCNJ11/ABCC8 positivity → attempt sulfonylurea transfer.

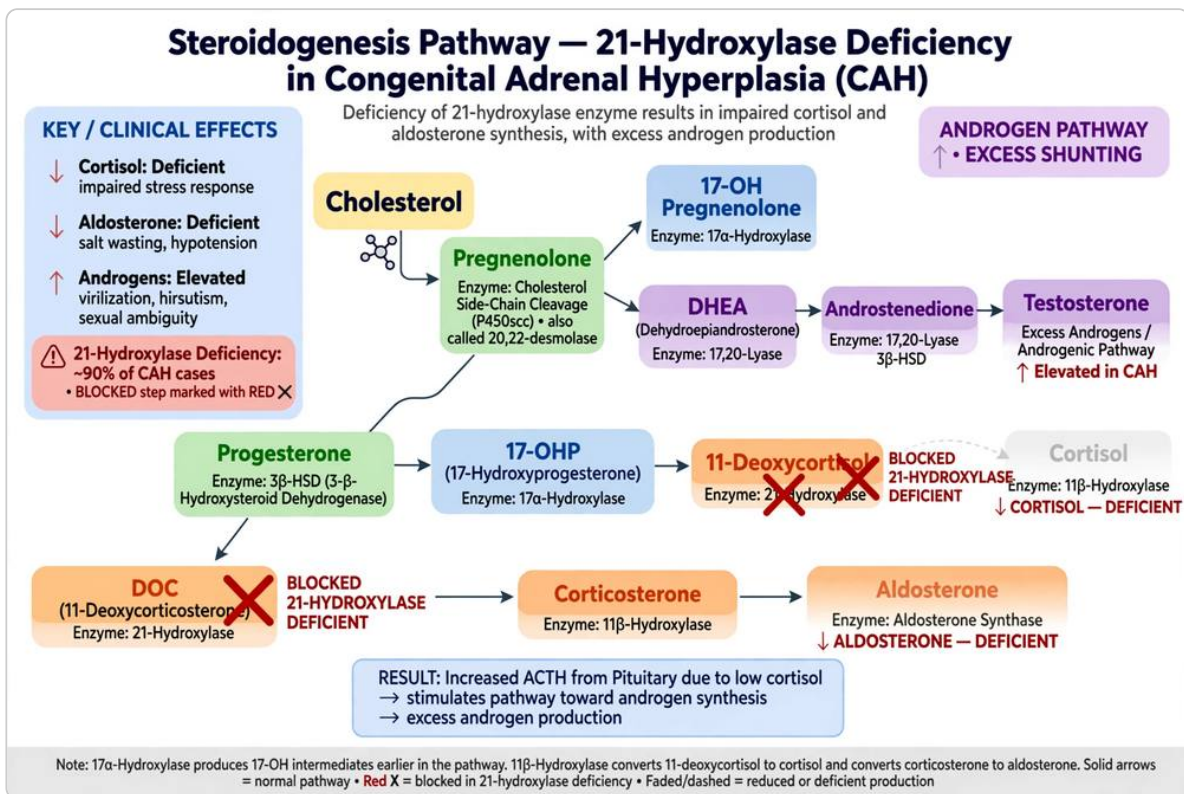


Figure 7.1 — Steroidogenesis: 21-hydroxylase deficiency in CAH

3. Thyroid Disorders

- **Congenital hypothyroidism (CH):** commonest preventable cause of intellectual disability — newborn screening exists precisely because untreated CH causes irreversible cognitive damage within weeks.
- **Causes:** thyroid **dysgenesis** (agenesis, hypoplasia, ectopia — commonest, usually sporadic) > **dysmorphogenesis** (autosomal recessive enzyme defects — goiter present, e.g., TPO, thyroglobulin, NIS defects) > transient causes (maternal TSH-receptor blocking antibodies, iodine excess/deficiency, maternal antithyroid drugs).
- **Screening:** heel-prick dried blood spot, usually **primary TSH** (with T4 backup) at 48–72 hours of life. A high TSH → confirmatory serum TSH + free T4; do not wait for the confirmatory result if strongly positive — start treatment.
- **Treatment: levothyroxine 10–15 mcg/kg/day PO once daily, started within the first 2 weeks of life** (ideally days). Give on empty stomach, crushed if needed; avoid soy formula, iron, and calcium at the same time. Goals: normalize free T4 within 2 weeks and TSH within 1 month; monitor TSH/free T4 at 2 and 4 weeks, then periodically. Continue through the critical first 3 years of brain development; trial off therapy at age 3 if etiology unclear (transient vs permanent).
- **Clinical clues if missed:** prolonged physiological jaundice, poor feeding, lethargy, constipation, hoarse cry, large posterior fontanelle, umbilical hernia, dry skin, macroglossia, hypotonia.
- **Graves disease:** commonest cause of pediatric hyperthyroidism; autoimmune, **TSH-receptor stimulating antibodies (TRAb/TSI)** positive. Goiter, ophthalmopathy (less severe than adults), pretibial myxedema rare in children; associated with other autoimmune diseases (type 1 DM, celiac).

- **Treatment: carbimazole/methimazole** (carbimazole is a prodrug of methimazole; methimazole dose ~0.5–1 mg/kg/day in divided doses) as first-line for 12–24 months aiming for remission. Warn about **agranulocytosis** (sore throat/fever → urgent CBC) and hepatotoxicity. **Propylthiouracil is avoided in children** (black-box hepatotoxicity risk) except in thyroid storm/first-trimester pregnancy. **Beta-blockers (propranolol)** control adrenergic symptoms (tremor, tachycardia) while thionamides take effect. Definitive therapy for relapse/large goiter: **radioactive iodine or total thyroidectomy** (surgery preferred in <5 years or very large glands).
- **Neonatal Graves:** transplacental TRAb from a mother with Graves (active or treated) → fetal/neonatal thyrotoxicosis — monitor all infants of TRAb-positive mothers; treat the neonate with methimazole + propranolol; self-limited as maternal antibodies clear over weeks–months.
- **Hashimoto thyroiditis:** commonest cause of acquired hypothyroidism and goiter in children/adolescents; **anti-TPO antibodies** (and anti-thyroglobulin) positive, lymphocytic infiltration, firm rubbery goiter. Euthyroid → subclinical → overt hypothyroidism. Treat overt hypothyroidism (high TSH + low free T4) with levothyroxine; observe subclinical (high TSH, normal T4) unless goiter/symptoms/antibodies strongly positive. Associated with Turner and Down syndromes — screen them.
- **Thyroid storm:** life-threatening decompensation, usually precipitated by infection, surgery, or abrupt thionamide withdrawal in untreated Graves. **Burch-Wartofsky score** ≥45 = highly suggestive. Fever, marked tachycardia, agitation/delirium, GI upset, heart failure.
- **Management (order matters):** 1) **Beta-blocker** (propranolol or esmolol infusion) for adrenergic blockade; 2) **thionamide** (methimazole/carbimazole; PTU historically used in storm for T4 → T3 blockade but avoided in children — high-dose methimazole is the pediatric choice) to block new hormone synthesis; 3) **inorganic iodine (Lugol's solution or SSKI) ≥1 hour AFTER the thionamide** to block hormone release (given first, iodine fuels more synthesis — classic trap); 4) **hydrocortisone** (blocks T4 → T3 conversion and covers relative adrenal insufficiency); 5) cooling, fluids, treat precipitant. Cholestyramine can bind thyroid hormone in the gut.

4. Congenital Adrenal Hyperplasia (CAH)

- **21-hydroxylase deficiency (CYP21A2):** ~90–95% of CAH, autosomal recessive. Blocks cortisol (and aldosterone) synthesis → ACTH-driven adrenal hyperplasia and shunting of precursors into **androgen excess**.
- **Salt-wasting (severe, ~75% of classic):** aldosterone deficiency → **hyponatremia, hyperkalemia, metabolic acidosis, hypovolemia, hypotension/shock** in the first 1–3 weeks of life, plus virilization. Life-threatening adrenal crisis if missed.
- **Simple virilizing (~25% of classic):** cortisol deficiency + androgen excess without salt loss → **ambiguous genitalia in 46,XX newborns** (clitoromegaly, fused labia, urogenital sinus — internal Müllerian structures normal since no AMH issue), tall early growth with **advanced bone age and premature adrenarche/precocious puberty** in boys, short adult stature.
- **Non-classic (late-onset):** mild enzyme defect → premature pubarche, hirsutism, acne, menstrual irregularity in adolescent girls; often misdiagnosed as PCOS.
- **Diagnosis: markedly elevated 17-hydroxyprogesterone (17-OHP)** — the screening and diagnostic hallmark (newborn screening measures 17-OHP on the heel-prick card). Confirm with ACTH stimulation (cosyntropin)

test: exaggerated 17-OHP rise. Supporting labs: low cortisol, high ACTH, high androstenedione/testosterone/DHEA-S; in salt-wasters — low aldosterone, **high plasma renin**, hyponatremia/hyperkalemia.

- **Treatment: hydrocortisone 10–15 mg/m²/day PO in 3 divided doses** (preferred in growing children — shortest half-life, least growth suppression; avoid dexamethasone/prednisolone long-term in childhood). **Fludrocortisone 0.05–0.2 mg/day** (typically 0.1 mg) + **sodium chloride supplementation (1–2 g/day)** in salt-wasting infants. Monitor: growth velocity, bone age, 17-OHP and androstenedione (aim upper-normal — overtreatment stunts growth, undertreatment advances bone age), blood pressure, electrolytes, plasma renin.
- **Stress dosing (exam favourite):** double or triple oral hydrocortisone for minor febrile illness; **major stress/surgery/vomiting** → **hydrocortisone 50–100 mg/m² IV** (or ~25 mg <1 yr, 50 mg 1–5 yrs, 100 mg >5 yrs IM) plus isotonic fluids and dextrose. Families carry an emergency injection kit and a steroid card. Never stop glucocorticoid abruptly.
- **11 β -hydroxylase deficiency (CYP11B1):** second commonest CAH. Blocks cortisol synthesis distal to DOC → **DOC (deoxycorticosterone) excess** → **hypertension, hypokalemia, suppressed renin**, plus virilization. Lab hallmark: **elevated 11-deoxycortisol** (and DOC); 17-OHP may be mildly raised but far less than in 21-OH deficiency. Treatment is glucocorticoid alone (hydrocortisone) — suppressing ACTH removes the DOC drive; **no fludrocortisone** (mineralocorticoid excess is the problem).
- **Other rare forms:** 3 β -HSD (salt-wasting + incomplete virilization in males), 17 α -hydroxylase (hypertension + hypokalemia + **absent puberty/sexual infantilism** — no sex steroids), StAR/lipoid CAH (most severe, salt-wasting in both sexes, males undervirilized), POR deficiency.
- **Prenatal dexamethasone** for at-risk 46,XX fetuses is experimental/controversial and not standard care — know it only to reject it as an option.

5. Growth Disorders

- **Definitions:** short stature = height <3rd percentile (or <-2 SD) for age/sex; growth failure = **growth velocity <25th percentile** (roughly <4–5 cm/year in childhood) or crossing percentiles downward. Always plot on a growth chart with mid-parental (target) height: boys = (father + mother + 13)/2 cm; girls = (father + mother – 13)/2 cm; target range ± 8.5 cm.
- **Constitutional delay of growth and puberty (CDGP) vs pathologic short stature:** CDGP ("late bloomers") — bone age delayed **equal to height age**, growth velocity normal, family history of delayed puberty, predicted adult height normal; reassure, observe. Pathologic — **growth velocity low**, bone age delayed more than height age would predict (or advanced in precocious puberty/CAH), height falling off the curve → full workup. Bone age (Greulich-Pyle left-hand X-ray) is the single most useful first test.
- **Growth hormone deficiency (GHD):**
- **Causes:** idiopathic (commonest), septo-optic dysplasia, pituitary hypoplasia/ectopic posterior pituitary, craniopharyngioma, cranial irradiation, trauma, Langerhans cell histiocytosis. Neonatal clues: hypoglycemia, prolonged jaundice, micropenis.
- **Workup:** auxology (height <3rd percentile, low growth velocity, delayed bone age, chubby "cherubic" facies with frontal bossing), **low IGF-1 and IGFBP-3** (screening — but normal IGF-1 does not exclude GHD in young children), **GH stimulation tests** — two provocative tests (clonidine, arginine, insulin tolerance, glucagon, L-DOPA); peak GH **<10 ng/mL = deficient** (<7 ng/mL severe by stricter cut-offs). Exclude mimics

first: hypothyroidism (TFT), celiac (tTG-IgA), chronic kidney disease, Turner syndrome (karyotype in every short girl), skeletal dysplasia. **MRI brain/pituitary** in confirmed GHD — look for ectopic posterior pituitary bright spot, thin/interrupted stalk, pituitary hypoplasia, craniopharyngioma.

- **Treatment: recombinant human GH (somatropin) ~0.16–0.24 mg/kg/week (≈25–35 mcg/kg/day) subcutaneously, given daily at bedtime** (mimics physiologic nocturnal pulsatility). Monitor growth velocity every 3–6 months, IGF-1 (keep within normal range), bone age annually, thyroid function and HbA1c. Stop when growth velocity <2 cm/year or bone age fused (girls ~14–15, boys ~16–17 years).
- **Turner syndrome (45,X0 and mosaics):**
 - **Features:** short stature (SHOX haploinsufficiency — the one universal feature), **webbed neck, low posterior hairline, shield (broad) chest with widely spaced nipples, cubitus valgus**, lymphedema of hands/feet at birth, **coarctation of the aorta and bicuspid aortic valve**, horseshoe kidney, recurrent otitis media, **streak gonads → hypergonadotropic hypogonadism** (high FSH/LH, low estradiol), primary amenorrhea, infertility. Increased risk: hypothyroidism (Hashimoto), celiac disease, diabetes, aortic dissection.
 - **Diagnosis:** karyotype — indicated in every girl with unexplained short stature. Baseline: echocardiography, renal ultrasound, TFT, celiac screen, audiometry, blood pressure in both arms.
 - **Treatment: GH (≈0.33 mg/kg/week in divided daily doses)** started early for height; **estrogen replacement at 11–12 years** (low-dose estradiol, titrated up over 2–3 years) then add cyclic progesterone for withdrawal bleeding and uterine maturation. Growth + puberty induction are the two therapeutic pillars.
 - **Noonan syndrome (PTPN11 and other RASopathies):** short stature, webbed neck, pectus deformity, **pulmonic stenosis / hypertrophic cardiomyopathy**, cryptorchidism, bleeding diathesis, characteristic facies; GH therapy FDA-approved for Noonan short stature.
 - **Small for gestational age (SGA) without catch-up:** GH approved if no catch-up growth by **2–4 years of age** (dose 0.33–0.48 mg/kg/week).
 - **Other GH indications:** chronic kidney disease, Prader-Willi syndrome, SHOX deficiency.

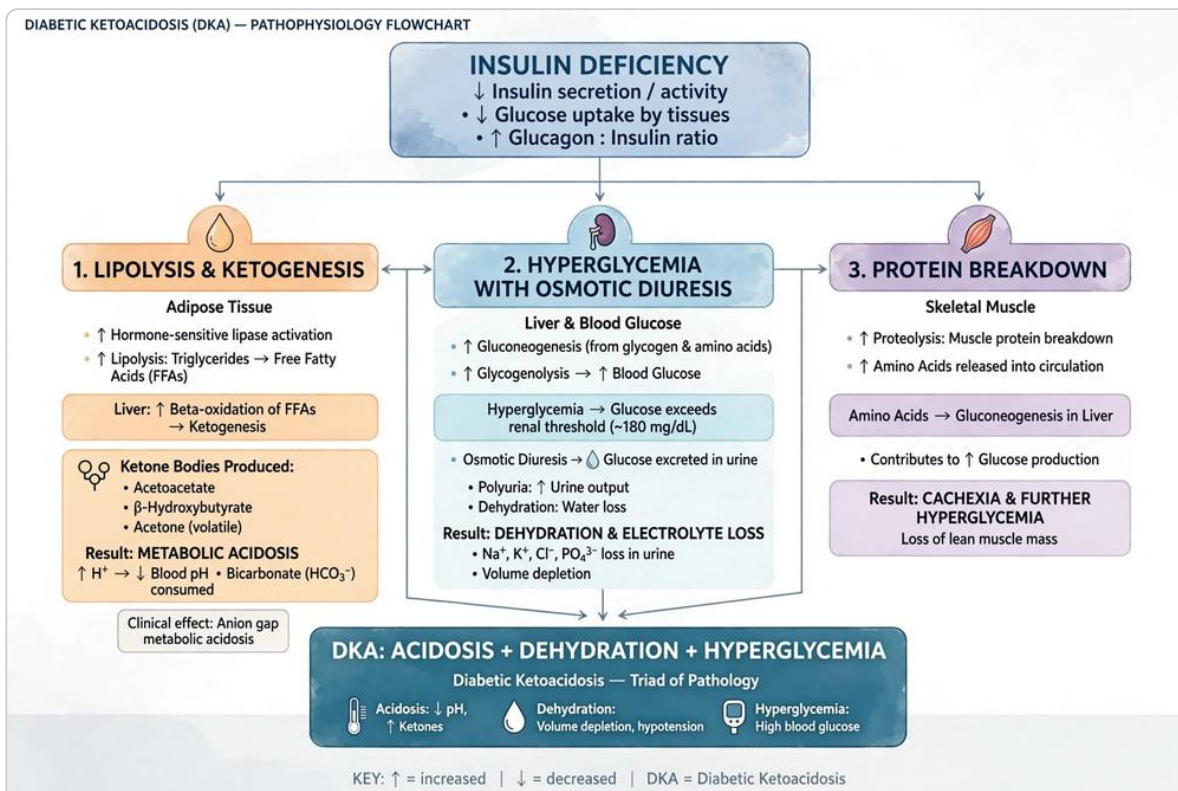


Figure 7.2 — Diabetic ketoacidosis pathophysiology

6. Disorders of Puberty

- **Normal timing:** thelarche 8–13 years (girls), testicular enlargement (≥ 4 mL) 9–14 years (boys); puberty complete within ~4 years. **Precocious puberty** = secondary sexual characteristics before **8 years (girls) / 9 years (boys)**. **Delayed puberty** = no thelarche by 13 (girls) or no testicular enlargement by 14 (boys), or >5 years to complete.
- **Central (GnRH-dependent) precocious puberty (CPP):** premature activation of the hypothalamic-pituitary-gonadal axis — puberty is complete and sequential, just early. **Idiopathic in most girls; in boys always exclude CNS pathology** (hypothalamic hamartoma — classic cause with gelastic seizures, optic glioma, craniopharyngioma, hydrocephalus). Labs: pubertal **basal LH (>0.3 IU/L)** and LH-predominant response on GnRH stimulation test; bone age advanced; pelvic US shows pubertal uterus/ovaries. MRI brain mandatory in boys and in girls <6 years (or with neurologic signs).
- **Treatment: long-acting GnRH analogues (leuprolide depot monthly/3-monthly, triptorelin, histrelin implant)** — continuous GnRH desensitizes pituitary gonadotrophs, halting puberty and preserving adult height. Indicated when puberty is rapidly progressive, bone age markedly advanced, or predicted adult height compromised.
- **Peripheral (GnRH-independent) precocious puberty:** sex steroids from a non-HPG source — puberty is often incomplete/sequential-disordered. **LH/FSH suppressed** (key discriminator), GnRH stimulation test flat.
- **McCune-Albright syndrome:** GNAS activating mutation (mosaic) — triad of **irregular "coast of Maine" café-au-lait macules + polyostotic fibrous dysplasia + autonomous endocrine hyperfunction** (recurrent estrogen-secreting ovarian cysts → episodic vaginal bleeding/precocious puberty in girls; also

hyperthyroidism, GH excess, Cushing). Treat the cysts/bleeding (aromatase inhibitors, SERMs) — GnRH analogues do NOT work (axis is not the driver).

- **CAH (simple virilizing, undertreated):** androgen-driven heterosexual precocity in boys.
- **Testotoxicosis (familial male-limited precocious puberty):** activating **LHCGR** mutation — autosomal dominant, boys only, testosterone high with prepubertal testes.
- Others: ovarian granulosa-cell or testicular Leydig-cell tumors, hCG-secreting tumors (hepatoblastoma, germ-cell tumors — stimulate Leydig cells in boys), severe untreated hypothyroidism (**Van Wyk-Grumbach syndrome** — precocious puberty + delayed bone age + galactorrhea; treat the hypothyroidism).
- **Delayed puberty workup:**
 - **High LH/FSH (hypergonadotropic):** gonadal failure — Turner (45,X0), **Klinefelter (47,XXY)**, gonadal dysgenesis, chemotherapy/radiation, autoimmune oophoritis.
 - **Low LH/FSH (hypogonadotropic):** CDGP (commonest — bone age = height age, normal growth velocity, family history; reassure or brief low-dose sex-steroid "jump-start"), Kallmann syndrome (anosmia/hyposmia — KAL1/anosmin defect, micropenis/cryptorchidism in boys), chronic systemic disease, anorexia, excessive exercise, pituitary lesions, isolated GnRH deficiency.
- Karyotype when hypergonadotropic; MRI pituitary when hypogonadotropic with red flags; smell testing for Kallmann.
- **Klinefelter syndrome (47,XXY):** tall stature with long legs, **small firm testes (<4 mL)**, **gynecomastia**, sparse body hair, **azoospermia/infertility**, high FSH/LH with low-normal testosterone, mild learning difficulties. **Testosterone replacement** from puberty for virilization, bone health, and mood; fertility options via TESE/micro-TESE.

7. Pituitary, Diabetes Insipidus, and Sodium Disorders

- **Hypopituitarism — causes: craniopharyngioma** (adamantinomatous, calcified suprasellar mass in children — bitemporal hemianopia, short stature from GH deficiency, **diabetes insipidus**, obesity from hypothalamic damage), **septo-optic dysplasia** (optic nerve hypoplasia + absent septum pellucidum + pituitary hormone deficiencies), pituitary aplasia/hypoplasia, Langerhans cell histiocytosis, germinoma, trauma, post-surgical, PROP1/POU1F1 genetic defects.
- **Neonatal red flags:** hypoglycemia, micropenis with undescended testes, prolonged unconjugated jaundice, midline defects (cleft lip/palate, single central incisor). Evaluate cortisol and thyroid axes before GH — **replace cortisol before levothyroxine** (thyroxine accelerates cortisol metabolism and can precipitate adrenal crisis).
- **Diabetes insipidus (DI):** polyuria (>2 L/m²/day), polydipsia, hypernatremia with dilute urine.
- **Central DI:** ADH deficiency — craniopharyngioma/surgery, LCH, trauma, septo-optic dysplasia, germinoma, idiopathic/autoimmune. Treat with **desmopressin (DDAVP)** — oral, intranasal, or sublingual.
- **Nephrogenic DI:** renal resistance to ADH — **X-linked AVPR2 mutations** (commonest congenital), AQP2 mutations, lithium, hypercalcemia, hypokalemia, obstructive uropathy. Treat with **thiazide diuretics + low-salt diet** (paradoxical antidiuresis via volume contraction) ± amiloride/NSAIDs; desmopressin ineffective.

- **Water deprivation test (the discriminator):** withhold water and track urine osmolality/weight/serum Na. In DI, urine stays dilute (<300 mOsm/kg) with rising serum osmolality; then give desmopressin — **central DI concentrates urine (>50% rise in osmolality)**, nephrogenic DI does not. Stop the test if weight loss >5% or Na >150 mEq/L. Primary polydipsia concentrates urine during deprivation alone.
- **SIADH vs cerebral salt wasting (CSW):** both cause hyponatremia after CNS insult (meningitis, head injury, post-neurosurgery) — but treatment is opposite, so this distinction is heavily examined.
- **SIADH:** euvolemic (or mildly hypervolemic) — ADH excess → water retention, concentrated urine (osmolality >100), high urine Na (>40), low serum uric acid, **low BUN**. Treatment: **fluid restriction**; severe symptomatic (seizures/coma) → 3% saline.
- **CSW:** hypovolemic — renal salt wasting driven by natriuretic peptides → true volume depletion, high urine Na, **high BUN/hematocrit**, orthostatic hypotension, weight loss. Treatment: **isotonic saline / salt replacement** — fluid restriction here is dangerous.
- **Bedside discriminator:** volume status and BUN — euvolemia + low BUN = SIADH (restrict fluids); hypovolemia + high BUN = CSW (give salt and water).

8. Adrenal Insufficiency and Cushing Syndrome

- **Primary adrenal insufficiency (Addison disease):** autoimmune adrenalitis commonest in children (isolated or APS-1/APECED — with mucocutaneous candidiasis and hypoparathyroidism; APS-2 — with type 1 DM and Hashimoto); **X-linked adrenoleukodystrophy in boys** (check very-long-chain fatty acids — progressive neurologic disease, treatable if caught early); TB, adrenal hemorrhage (Waterhouse-Friderichsen in meningococcemia), congenital adrenal hypoplasia.
- **Clinical:** chronic — fatigue, weight loss, **hyperpigmentation** (ACTH/MSH excess — knuckles, gums, scars, palmar creases), salt craving, hypotension, **hyponatremia, hyperkalemia, hypoglycemia, metabolic acidosis**. High ACTH + low cortisol confirms primary; low ACTH + low cortisol = secondary (no hyperpigmentation, no salt-wasting — aldosterone intact).
- **Adrenal crisis:** vomiting, abdominal pain, shock, hypoglycemia, hyponatremia/hyperkalemia — precipitated by infection, surgery, or abrupt steroid withdrawal.
- **Crisis management: hydrocortisone 50–100 mg/m² IV bolus** (practically: 25 mg <1 yr, 50 mg 1–5 yrs, 100 mg >5 yrs IM/IV), then **50–100 mg/m²/day divided every 6 hours**, aggressive **isotonic fluid resuscitation**, dextrose for hypoglycemia. Then taper to maintenance: **hydrocortisone ~8 mg/m²/day in 3 divided doses + fludrocortisone 0.05–0.1 mg/day**; stress-dose education as in CAH.
- **Cushing syndrome:** commonest cause in children is **iatrogenic (exogenous steroids)** — always exclude first. Endogenous: **Cushing disease (ACTH-secreting pituitary adenoma)** commonest endogenous cause in children >5 years; adrenal adenoma/carcinoma in infants and young children; ectopic ACTH rare in pediatrics.
- **Clinical:** weight gain with **growth failure** (the pediatric hallmark — height velocity drops while weight rises), moon facies, buffalo hump, violaceous striae, hypertension, glucose intolerance, hirsutism/acne.
- **Workup (sequence):** 1) confirm hypercortisolism — **loss of diurnal rhythm (elevated late-night salivary cortisol), 24-hour urinary free cortisol elevated, failure to suppress on low-dose dexamethasone** (1-mg overnight test: morning cortisol >1.8 mcg/dL is abnormal); 2) measure **ACTH** — high/normal = ACTH-dependent (pituitary vs ectopic), suppressed = adrenal source; 3) localize — pituitary MRI; **high-dose**

dexamethasone suppression (pituitary adenomas usually suppress, ectopic/ adrenal do not); inferior petrosal sinus sampling in equivocal ACTH-dependent cases.

- **Treatment: transsphenoidal selective adenomectomy** for Cushing disease; adrenalectomy for adrenal tumors; ketoconazole/metyrapone/etomidate for medical control or when surgery delayed.

Practice MCQs

Q1. A 7-year-old boy presents with 3 weeks of polyuria, polydipsia, weight loss of 3 kg, and 2 days of vomiting and abdominal pain. Labs: glucose 480 mg/dL, venous pH 7.18, bicarbonate 9 mEq/L, urine ketones strongly positive, K 4.8 mEq/L. What is the most appropriate FIRST step in management? A) Normal saline 10–20 mL/kg IV bolus B) Insulin infusion 0.1 U/kg/hour IV C) Sodium bicarbonate infusion D) Potassium chloride replacement

Answer: A — This is moderate-to-severe DKA. ISPAD sequencing mandates volume resuscitation with isotonic fluid before insulin; starting insulin in a shocked, volume-depleted child worsens perfusion and risks cerebral edema. Insulin follows after initial fluid expansion, potassium is handled per protocol, and bicarbonate is not routinely indicated.

Q2. A 10-year-old girl with known type 1 diabetes presents in DKA: pH 7.12, glucose 520 mg/dL, K 2.9 mEq/L on admission labs. She has received a 20 mL/kg normal saline bolus. What is the next best step? A) Start insulin infusion 0.1 U/kg/hour immediately B) Give sodium bicarbonate C) Switch fluids to half-normal saline D) Give IV potassium replacement and hold insulin until K normalizes **Answer: D** — With K <3.3 mEq/L, insulin must be held because insulin drives potassium intracellularly and can precipitate fatal arrhythmia; replace potassium first (20–40 mEq/L with urine output established), then start insulin once K is ≥3.3. Bicarbonate is not indicated, and hypotonic fluids early increase cerebral edema risk.

Q3. During DKA treatment of a 6-year-old boy, 8 hours into therapy he develops severe headache, becomes drowsy, and his heart rate drops from 120 to 70/min with rising blood pressure. What is the most appropriate immediate treatment? A) Increase IV fluid rate B) IV mannitol or 3% hypertonic saline C) Sodium bicarbonate D) Lumbar puncture **Answer: B** — Headache, altered consciousness, bradycardia, and hypertension during DKA treatment signal cerebral edema — treat immediately with hyperosmolar therapy (mannitol 0.25–1 g/kg or 3% saline 5–10 mL/kg), elevate the head, and restrict fluids; never delay treatment for imaging. Increasing fluids worsens edema, and bicarbonate is contraindicated.

Q4. A 12-year-old boy with type 1 diabetes on an insulin pump is found unconscious at home with a blood glucose of 32 mg/dL. His parents have a glucagon emergency kit. He weighs 40 kg. What is the correct glucagon dose? A) 0.25 mg IM B) 0.5 mg IM C) 1 mg IM D) Oral glucose gel **Answer: C** — Severe hypoglycemia with unconsciousness requires parenteral therapy — never oral carbohydrate (aspiration risk). Glucagon dosing is 0.5 mg IM/SC for children <25 kg and 1 mg for ≥25 kg; at 40 kg he receives 1 mg. IV dextrose 0.5–1 g/kg is the alternative in a facility.

Q5. A 16-year-old girl diagnosed with diabetes at age 14 has negative islet autoantibodies, a father and paternal grandmother with diabetes diagnosed in their 20s, and glycosuria despite blood glucose of 130 mg/dL. Genetic testing is most likely to reveal a mutation in which gene, and what is the preferred treatment? A) HNF1A; low-dose sulfonylurea B) GCK; no treatment needed C) INS; lifelong insulin D) HNF1B; insulin therapy **Answer: A** — Autosomal-dominant diabetes across three generations with absent autoantibodies suggests MODY; HNF1A-

MODY (MODY3) is the commonest adolescent form and is exquisitely sensitive to low-dose sulfonylureas, often allowing transfer off insulin. The low renal glucose threshold (glycosuria at normal glycemia) is a classic HNF1A clue.

Q6. A 10-year-old boy is found on school screening to have fasting glucose 118 mg/dL. HbA1c is 6.2%, islet antibodies negative, BMI normal, father has similar lifelong mild hyperglycemia never requiring medication. What is the most appropriate management? A) Start basal insulin B) Start metformin C) Reassurance; no pharmacologic treatment D) Start sulfonylurea **Answer: C** — This is classic GCK-MODY (MODY2); lifelong mild stable fasting hyperglycemia (100–150 mg/dL), HbA1c 5.8–7.6%, autosomal-dominant pattern, and negligible microvascular risk. No glucose-lowering treatment is indicated — the commonest exam trap is over-treating; reassure and screen family members.

Q7. A 3-month-old infant presents with hyperglycemia (glucose 380 mg/dL), no ketosis, negative islet autoantibodies. Genetic testing reveals an activating KCNJ11 mutation. What is the best long-term treatment? A) Lifelong basal-bolus insulin B) Metformin C) Dietary management alone D) High-dose sulfonylurea (glibenclamide) **Answer: D** — Diabetes under 6 months is monogenic until proven otherwise. Activating KCNJ11 mutations keep the beta-cell K-ATP channel open; sulfonylureas close the channel independent of ATP, restoring endogenous insulin secretion — most patients transfer off insulin with superior control. KCNJ11 may also cause DEND syndrome, where sulfonylurea can improve neurodevelopmental features.

Q8. A newborn screening report shows TSH 68 mIU/L (normal <20) on day 3 of life. Confirmatory serum TSH is 85 mIU/L with low free T4. The infant is 4 days old, weight 3.2 kg. What is the correct management? A) Repeat screening in 2 weeks B) Start low-dose levothyroxine and recheck at 3 months C) Thyroid ultrasound before any treatment D) Start levothyroxine 10–15 mcg/kg/day immediately **Answer: D** — Confirmed congenital hypothyroidism requires levothyroxine 10–15 mcg/kg/day started within the first 2 weeks of life (ideally days) to protect brain development; do not delay treatment for imaging. Goals are normal free T4 within 2 weeks and TSH within a month, with continuation through the first 3 years.

Q9. A 13-year-old girl presents with a 6-month history of weight loss, tremor, palpitations, and a diffuse goiter with a bruit. Labs: suppressed TSH, elevated free T4, positive TRAb. What is the most appropriate initial treatment? A) Carbimazole/methimazole plus propranolol B) Propylthiouracil alone C) Radioactive iodine ablation D) Total thyroidectomy **Answer: A** — This is Graves disease (TRAb positive). First-line pediatric therapy is a thionamide — carbimazole or methimazole for 12–24 months aiming for remission — with a beta-blocker for adrenergic symptom control. Propylthiouracil is avoided in children due to hepatotoxicity; radioactive iodine and surgery are definitive options reserved for relapse or large goiters.

Q10. A 15-year-old boy with known Graves disease, noncompliant with carbimazole, presents with fever 40°C, heart rate 160/min, agitation, vomiting, and heart failure after an upper respiratory infection. Burch-Wartofsky score is 60. After starting propranolol and high-dose methimazole, what is the next step? A) Lugol's iodine immediately along with methimazole B) Lugol's iodine at least 1 hour after the thionamide C) Radioactive iodine D) Stop methimazole and observe **Answer: B** — This is thyroid storm. Inorganic iodine (Lugol's/SSKI) blocks thyroid hormone release but must be given ≥ 1 hour AFTER the thionamide; given first, iodine provides substrate for new hormone synthesis and worsens the storm. The sequence is beta-blocker → thionamide → iodine → hydrocortisone → supportive care.

Q11. A 12-year-old girl has a firm, rubbery, nontender goiter. Labs: TSH 28 mIU/L, free T4 low-normal, strongly positive anti-TPO antibodies. What is the most likely diagnosis and appropriate management? A) Graves disease; carbimazole B) Toxic adenoma; surgery C) Hashimoto thyroiditis; levothyroxine replacement D) Subacute thyroiditis; NSAIDs **Answer: C** — Anti-TPO–positive goiter with hypothyroidism in an adolescent is Hashimoto thyroiditis, the commonest cause of acquired pediatric hypothyroidism; overt hypothyroidism is treated with levothyroxine replacement. Graves would show suppressed TSH with TRAb, and subacute thyroiditis presents with a painful tender gland.

Q12. A 10-day-old 46,XX infant with ambiguous genitalia (clitoromegaly, fused labia) presents with vomiting, poor feeding, and shock. Labs: Na 122 mEq/L, K 7.1 mEq/L, glucose 38 mg/dL, metabolic acidosis. 17-OHP is markedly elevated. What is the most likely diagnosis? A) 11 β -hydroxylase deficiency B) 17 α -hydroxylase deficiency C) 21-hydroxylase deficiency, salt-wasting type D) 21-hydroxylase deficiency, simple virilizing type **Answer: C** — Virilized 46,XX infant plus hyponatremia, hyperkalemia, hypoglycemia, and shock in the first weeks of life with markedly elevated 17-OHP is classic salt-wasting 21-hydroxylase deficiency (aldosterone + cortisol deficiency). Simple virilizing CAH has no salt loss; 11 β -hydroxylase deficiency causes hypertension, not salt wasting.

Q13. The infant in Q12 is stabilized. For long-term maintenance, which regimen is most appropriate? A) Hydrocortisone 10–15 mg/m²/day in 3 divided doses + fludrocortisone daily B) Dexamethasone once daily alone C) Fludrocortisone alone D) Prednisolone once daily alone **Answer: A** — Salt-wasting CAH requires physiologic glucocorticoid replacement (hydrocortisone 10–15 mg/m²/day TID — preferred in growing children for least growth suppression) PLUS mineralocorticoid replacement (fludrocortisone 0.05–0.2 mg/day) with salt supplementation in infancy. Long-acting steroids like dexamethasone suppress growth and are avoided for chronic childhood therapy; mineralocorticoid cannot be omitted in salt-wasters.

Q14. A 6-year-old boy with tall stature, advanced bone age, and precocious puberty has blood pressure 140/95 mmHg, hypokalemia (K 2.8 mEq/L), and suppressed plasma renin. 11-deoxycortisol is markedly elevated. What is the diagnosis and correct treatment? A) 21-hydroxylase deficiency; hydrocortisone + fludrocortisone B) 17 α -hydroxylase deficiency; sex-steroid replacement C) Primary hyperaldosteronism; spironolactone D) 11 β -hydroxylase deficiency; hydrocortisone alone **Answer: D** — Hypertension with hypokalemia, suppressed renin, virilization/precocious puberty, and elevated 11-deoxycortisol define 11 β -hydroxylase deficiency (DOC excess drives mineralocorticoid effects). Treatment is glucocorticoid alone to suppress ACTH-driven DOC — fludrocortisone is contraindicated since mineralocorticoid excess is the problem.

Q15. A 5-year-old boy has height <3rd percentile, growth velocity 3 cm/year, delayed bone age, frontal bossing, and a chubby "cherubic" appearance. IGF-1 is low. TFT and celiac screen are normal. What is the next best step to confirm the diagnosis? A) Start rhGH empirically B) GH stimulation (provocative) testing C) Karyotype D) Pituitary MRI **Answer: B** — The auxology and low IGF-1 suggest GH deficiency, but confirmation requires provocative GH stimulation testing (two agents; peak <10 ng/mL = deficient), since IGF-1 alone is insufficiently sensitive in young children. MRI follows confirmation to look for structural causes (ectopic posterior pituitary, stalk interruption, craniopharyngioma); karyotype is for short girls (Turner).

Q16. A 14-year-old girl presents with short stature (<3rd percentile), webbed neck, shield chest with widely spaced nipples, and primary amenorrhea. Labs: FSH 68 IU/L, LH 32 IU/L, estradiol undetectable. Echocardiography is most important to screen for which lesion? A) Tetralogy of Fallot B) Atrial septal defect C) Patent ductus arteriosus D) Coarctation of the aorta **Answer: D** — This is Turner syndrome (45,X0): short stature,

webbed neck, shield chest, streak gonads with hypergonadotropic hypogonadism. The characteristic cardiac lesion is coarctation of the aorta (plus bicuspid aortic valve), with risk of aortic dissection — echocardiography (and BP in both arms) is mandatory at diagnosis, alongside renal ultrasound, TFT, and celiac screening.

Q17. A 14-year-old boy has no pubertal development, height at the 10th percentile but previously at the 50th, growth velocity 5.5 cm/year, bone age 12 years, and a father who attained puberty at 16. Testicular volume is 3 mL. What is the most likely diagnosis? A) Constitutional delay of growth and puberty B) Klinefelter syndrome C) Kallmann syndrome D) Craniopharyngioma **Answer: A** — Bone age delayed equal to height age, preserved normal growth velocity, prepubertal testes, and a family history of delayed puberty define constitutional delay of growth and puberty — the commonest cause of delayed puberty; reassure (a brief low-dose testosterone "jump-start" is optional). Klinefelter shows hypergonadotropic labs with small firm testes; Kallmann includes anosmia.

Q18. A 6-year-old girl presents with breast development and vaginal bleeding. Labs: LH 4.2 IU/L (pubertal), FSH pubertal range, estradiol elevated, bone age 9 years. MRI brain is normal. What is the diagnosis and best treatment? A) McCune-Albright syndrome; aromatase inhibitor B) Idiopathic central precocious puberty; GnRH analogue C) Ovarian tumor; oophorectomy D) Premature thelarche; observation **Answer: B** — Pubertal LH with a pubertal LH-predominant pattern, sequential complete puberty, and advanced bone age indicate GnRH-dependent (central) precocious puberty; with a normal MRI in a 6-year-old girl this is idiopathic CPP. Long-acting GnRH analogues (leuprolide depot) desensitize the axis, halting progression and preserving adult height. McCune-Albright would show suppressed gonadotropins with café-au-lait macules.

Q19. A 4-year-old girl has episodic vaginal bleeding, irregular "coast of Maine" café-au-lait macules, and X-ray shows polyostotic fibrous dysplasia. Labs: estradiol high, LH/FSH suppressed. What is the diagnosis? A) Idiopathic central precocious puberty B) Ovarian granulosa cell tumor C) McCune-Albright syndrome D) Van Wyk-Grumbach syndrome **Answer: C** — The triad of irregular café-au-lait macules + polyostotic fibrous dysplasia + autonomous endocrine hyperfunction (here, estrogen-secreting ovarian cysts causing peripheral precocious puberty with suppressed gonadotropins) is McCune-Albright syndrome (mosaic GNAS activation). GnRH analogues are ineffective since the HPG axis is not the driver; bleeding is managed with aromatase inhibitors/SERMs.

Q20. A 16-year-old boy is evaluated for delayed puberty: tall with long legs, gynecomastia, testes 3 mL and firm, sparse facial hair. Labs: FSH 38 IU/L, LH 22 IU/L, testosterone 180 ng/dL (low). What is the most likely karyotype? A) 45,X0 B) 47,XY Y C) 46,XX male D) 47,XXY **Answer: D** — Small firm testes, gynecomastia, tall stature, and hypergonadotropic hypogonadism (high FSH/LH, low testosterone) in an adolescent boy define Klinefelter syndrome (47,XXY). Management is testosterone replacement from puberty for virilization and bone health; fertility may be salvageable via micro-TESE.

Q21. A 9-year-old boy post-craniopharyngioma resection develops polyuria (4 L/day), polydipsia, serum Na 152 mEq/L, and urine osmolality 150 mOsm/kg. After a supervised water deprivation test, urine osmolality remains 180 mOsm/kg; following desmopressin administration, urine osmolality rises to 650 mOsm/kg. What is the diagnosis? A) Central diabetes insipidus B) Nephrogenic diabetes insipidus C) Primary polydipsia D) SIADH **Answer: A** — Failure to concentrate urine during water deprivation with a >50% rise in urine osmolality after desmopressin confirms central DI (ADH deficiency) — expected after craniopharyngioma surgery damaging the posterior pituitary/stalk. Nephrogenic DI would not respond to desmopressin; treatment is desmopressin (DDAVP) replacement.

Q22. A 7-year-old girl on day 3 after meningitis develops seizures. Labs: Na 118 mEq/L, serum osmolality 245 mOsm/kg, urine osmolality 520 mOsm/kg, urine Na 68 mEq/L. She appears clinically euvolemic with normal blood pressure, BUN 8 mg/dL, weight unchanged. What is the diagnosis and best immediate management? A) Cerebral salt wasting; isotonic saline infusion B) Adrenal insufficiency; hydrocortisone C) SIADH; fluid restriction D) Nephrogenic DI; thiazide diuretic **Answer: C** — Hyponatremia with concentrated urine, high urine sodium, euvolemia, low BUN, and no weight loss after CNS insult is SIADH; management is fluid restriction (3% saline only if severely symptomatic/seizing). Cerebral salt wasting would show hypovolemia, weight loss, and elevated BUN — and requires salt/water repletion, the opposite treatment.

Q23. A 12-year-old boy with known Addison disease develops vomiting, abdominal pain, and hypotension (BP 70/40) during a febrile illness after his parents stopped his steroids for 2 days. Labs: Na 120 mEq/L, K 6.4 mEq/L, glucose 42 mg/dL. What is the most appropriate immediate management? A) Oral hydrocortisone double dose B) IV hydrocortisone 50–100 mg/m² bolus + isotonic fluids + dextrose C) Fludrocortisone alone D) IV insulin for hyperkalemia **Answer: B** — This is an adrenal crisis (volume depletion, hyponatremia, hyperkalemia, hypoglycemia, shock). Immediate treatment is stress-dose hydrocortisone IV (50–100 mg/m² bolus, then divided doses), aggressive isotonic fluid resuscitation, and dextrose for hypoglycemia — oral steroids are inadequate in shock with vomiting.

Q24. An 8-year-old girl has 1 year of weight gain with a fall in height velocity from the 50th to the 10th percentile, moon facies, violaceous striae, and hypertension. Overnight 1-mg dexamethasone suppression test shows morning cortisol 8.2 mcg/dL. ACTH is 78 pg/mL (high). What is the next best step to localize the source? A) Adrenal CT B) Inferior petrosal sinus sampling immediately C) Start ketoconazole D) Pituitary MRI **Answer: D** — Growth failure with weight gain is the pediatric hallmark of Cushing syndrome; failed low-dose dexamethasone suppression confirms hypercortisolism, and elevated ACTH indicates ACTH-dependent disease — in children this is overwhelmingly Cushing disease (pituitary adenoma). Pituitary MRI is the next localization step; petrosal sinus sampling is reserved for equivocal cases, and adrenal CT is for ACTH-independent (suppressed ACTH) disease.

Q25. A 4-year-old girl newly diagnosed with type 1 diabetes weighs 16 kg. Her total daily insulin requirement is estimated at 0.8 U/kg/day. Using a basal-bolus regimen, what is the most appropriate insulin plan? A) NPH twice daily alone B) Glargine ~5 units once daily + lispro ~2–3 units with each meal C) Regular insulin sliding scale alone D) Insulin pump with NPH **Answer: B** — TDD = $0.8 \times 16 \approx 13$ units; basal (glargine) supplies ~40–50% (~5–6 units once daily) and rapid-acting lispro covers meals (~2–3 units per meal). Basal-bolus MDI is the standard pediatric regimen; sliding-scale regular insulin alone and NPH-only regimens give inferior control with more hypoglycemia, and pumps use rapid-acting insulin only (never NPH).

Pediatric Hematology & Oncology

Chapter 8: Pediatric Hematology-Oncology

Hematology and oncology form one of the highest-yield sections in NEET SS Pediatrics, cutting across neonatology, genetics, and emergency care. Questions focus on diagnostic algorithms (smear + red-cell indices + Coombs), molecular risk stratification of leukemias, and standard-of-care protocols rather than rare trivia. Master the criteria, staging systems, and first-line therapies — that is where the marks are.

1. Iron Deficiency Anemia (IDA)

- Commonest nutritional anemia worldwide; peak at 6–24 months (rapid growth, cow's milk, delayed weaning foods).
- Pathophysiology: depleted iron → restricted heme synthesis → microcytic hypochromic RBCs.
- Clinical: pallor, pica, koilonychia, angular cheilitis, irritability, developmental delay; Plummer-Vinson triad (adults, not pediatric focus).
- Labs (diagnostic pattern): low ferritin (<12 ng/mL in children; <30 ng/mL if inflammation), low serum iron, high TIBC, low transferrin saturation (<16%), **high RDW (earliest change)**, low MCV/MCH/MCHC, high platelet count (reactive thrombocytosis). Mentzer index (MCV/RBC) >13 favors IDA over thalassemia trait (<13).
- Treatment: oral elemental iron 3–6 mg/kg/day in 1–2 divided doses, between meals (with vitamin C; avoid milk/antacids). Reticulocyte rise in 3–5 days, Hb rise ~1–2 g/dL per month; continue 2–3 months after Hb normalizes to replenish stores. Parenteral iron (iron sucrose, ferric carboxymaltose) for malabsorption, intolerance, or ongoing blood loss.
- NEET SS pearl: ferritin is an acute-phase reactant — a "normal" ferritin with CRP elevation does not exclude IDA; check transferrin saturation.

2. Vitamin B12 and Folate Deficiency (Megaloblastic Anemia)

- B12 deficiency: strict vegetarian maternal diet → deficient breastfed infant; pernicious anemia (anti-intrinsic factor), ileal resection/Crohn, Imerslund-Gräsbeck syndrome. Neurologic signs (subacute combined degeneration — dorsal/lateral column signs, irritability, developmental regression) occur with B12, NOT folate deficiency.
- Folate deficiency: goat's milk feeding, chronic hemolysis, anticonvulsants (phenytoin), methotrexate.
- Labs: macrocytosis (MCV >100 fL), hypersegmented neutrophils (>5 lobes), low B12 (<200 pg/mL) or low RBC folate; high LDH, indirect hyperbilirubinemia (ineffective erythropoiesis); pancytopenia in severe cases.

- Treatment: B12 1000 mcg IM (or high-dose oral 1000–2000 mcg/day) — always correct B12 BEFORE folate; giving folate alone to a B12-deficient child corrects the anemia but precipitates/worsens irreversible neurologic damage.
- Management steps: 1) Confirm macrocytosis + low B12/folate. 2) Check diet, drugs, GI history. 3) Replace B12 first if deficient. 4) Monitor reticulocyte response and neurologic recovery.

3. Hemolytic Anemias

3.1 Hereditary Spherocytosis (HS)

- Commonest inherited red-cell membrane defect (Northern European ancestry); AD inheritance (75%), most commonly spectrin or ankyrin mutations.
- Mechanism: membrane protein defect → loss of membrane surface → spherocytes → trapped and destroyed in spleen.
- Clinical: anemia, intermittent jaundice, splenomegaly; gallstones (pigment), aplastic crisis with parvovirus B19 (reticulocytopenia), hemolytic crisis with infections, megaloblastic crisis (folate consumption).
- Labs: **MCHC elevated** (classic — spherocytes are dense), high RDW, reticulocytosis; smear shows spherocytes without central pallor. **Increased osmotic fragility** (gold standard historically); EMA binding test and ektacytometry are modern confirmatory tests. Coombs negative.
- Management: folic acid supplementation; **splenectomy** for moderate-severe disease (usually after age 5–6 years to reduce post-splenectomy sepsis risk) with partial splenectomy preferred in children to preserve immune function; vaccinate against pneumococcus, Hib, meningococcus ≥2 weeks before elective splenectomy; lifelong penicillin prophylaxis post-splenectomy in young children.

3.2 G6PD Deficiency

- X-linked recessive; commonest enzyme defect of RBCs; Mediterranean, African, Asian variants. Mediterranean variant = severe chronic; African A- variant = episodic.
- Mechanism: defective hexose monophosphate shunt → NADPH deficiency → oxidant stress → **Heinz bodies** (denatured Hb precipitates) → bite/blister cells on smear.
- Triggers: oxidant drugs (primaquine, dapson, nitrofurantoin, rasburicase, methylene blue, sulfonamides), fava beans (favism), infections, diabetic ketoacidosis. Neonatal jaundice is a classic presentation.
- Labs: acute hemolysis with bite cells and Heinz bodies (supravital stain); G6PD assay is falsely normal during acute hemolysis (young RBCs have higher enzyme) — repeat after 2–3 months.
- Management: avoid oxidant triggers; supportive care, transfusion if severe. Never give methylene blue for methemoglobinemia in G6PD deficiency.

3.3 Autoimmune Hemolytic Anemia (AIHA)

- Warm AIHA (IgG, extravascular, spleen): associated with SLE, immunodeficiency, CLL/lymphoma (adults), post-viral in children.

- Cold AIHA (IgM, complement-mediated, intravascular): post-Mycoplasma pneumoniae, EBV; cold agglutinins.
- Paroxysmal cold hemoglobinuria: Donath-Landsteiner antibody, post-viral in children.
- Labs: **Direct Coombs (DAT) positive** (warm: IgG $\pm$ C3; cold: C3 only), spherocytes, reticulocytosis, high LDH, low haptoglobin, indirect hyperbilirubinemia.
- Management steps: 1) Confirm DAT-positive hemolysis; classify warm vs cold. 2) Treat underlying cause; keep cold AIHA patients warm. 3) Warm AIHA: **corticosteroids first-line** (prednisolone 2 mg/kg/day, taper over weeks-months). 4) Refractory/relapsing: **rituximab** (anti-CD20) second-line; splenectomy for chronic warm AIHA; transfuse "least incompatible" blood if life-threatening anemia — never withhold transfusion for serologic incompatibility alone.

4. Thalassemia Syndromes

4.1 Alpha Thalassemia

- Gene deletion on chromosome 16 (normal: 4 alpha genes, $\alpha\alpha/\alpha\alpha$).
- 1-gene deletion: silent carrier; 2-gene deletion: alpha trait (microcytosis); 3-gene deletion: **HbH disease** (β_4 tetramers, HbH inclusions on supravital stain, chronic hemolysis); **4-gene deletion: hydrops fetalis** (Hb Bart's, γ_4 — high oxygen affinity, fatal in utero/neonatal without intrauterine transfusion).
- Cis deletion (α^-/α^-) in Asian ancestry → risk of hydrops; trans deletion ($\alpha^-/-\alpha$) in African ancestry → no hydrops risk.
- Labs: microcytosis with normal/high RBC count, normal RDW, normal HbA2 (vs beta trait where HbA2 is high).

4.2 Beta Thalassemia

- Point mutations on chromosome 11; β^+ (reduced) vs β^0 (absent) synthesis.
- Beta-major (Cooley anemia): presents at 6+ months as HbF → HbA switch completes; severe anemia, hepatosplenomegaly, chipmunk facies (frontal bossing, maxillary hyperplasia from marrow expansion), growth failure.
- Labs: HbF markedly elevated, HbA2 elevated ($>3.5\%$), HbA reduced/absent; microcytic hypochromic, target cells, nucleated RBCs; Mentzer index <13 .
- Management steps: 1) Regular transfusions to maintain pre-transfusion Hb 9–10.5 g/dL (suppresses ineffective erythropoiesis). 2) **Iron chelation** once ferritin >1000 ng/mL or after ~ 10 – 20 transfusions: **deferoxamine** (IV/SC infusion, 8–12 h, ototoxicity/retinopathy), **deferiprone** (oral, agranulocytosis risk — weekly CBC), **deferasirox** (oral once daily, renal/hepatic monitoring). 3) HbF induction with **hydroxyurea** (mainly intermedia/sickle; modest role in major). 4) Splenectomy if transfusion requirement excessive. 5) Curative: allogeneic HSCT (best with matched sibling donor, young age, low iron load); gene therapy (betibeglogene) emerging.
- Beta-intermedia: milder, later presentation, may not need regular transfusions; beta-minor (trait): asymptomatic microcytosis, HbA2 $>3.5\%$, no treatment needed — counsel, do not give iron.

4.3 HbE and HbE/Beta-Thalassemia

- HbE ($\beta 26 \text{ Glu} \rightarrow \text{Lys}$): commonest hemoglobinopathy in Southeast Asia/NE India; HbE trait is benign with mild microcytosis.
- HbE/beta-thalassemia: highly variable — from intermedia-like to transfusion-dependent major-like phenotype; commonest severe thalassemia syndrome in India/SE Asia.
- HbE homozygotes: mild hemolytic anemia, usually no transfusions.

5. Sickle Cell Disease (HbSS)

- Point mutation $\beta 6 \text{ Glu} \rightarrow \text{Val}$; polymerization under deoxygenation $\rightarrow$ sickling, vaso-occlusion, hemolysis.
- Newborn screening: HbSS on HPLC/IEF; confirm by 6 months (HbF predominant at birth masks disease).
- Complications: **vaso-occlusive pain crisis** (dactylitis/hand-foot syndrome in infants — first presentation), **acute chest syndrome** (fever, chest pain, new infiltrate — leading cause of death; treat with oxygen, antibiotics, transfusion/exchange), **splenic sequestration** (sudden splenomegaly + Hb drop $\geq 2 \text{ g/dL}$ + reticulocytosis; may need splenectomy after recurrences), **stroke** (overt or silent infarcts), aplastic crisis (parvovirus B19), priapism, avascular necrosis, gallstones, delayed puberty.
- **Stroke prevention: annual transcranial Doppler (TCD) from age 2–16 years**; abnormal high velocity $\rightarrow$ chronic transfusion program (STOP trial) or HSCT.
- Infection prevention: **penicillin prophylaxis from birth to at least age 5** (125 mg BD $< 3 \text{ yr}$, 250 mg BD $\geq 3 \text{ yr}$); **pneumococcal vaccination** (conjugate + polysaccharide), Hib, meningococcal, annual influenza; prompt fever workup (blood culture + ceftriaxone) — functional asplenia by age 5.
- Disease-modifying therapy: **hydroxyurea** (increases HbF, reduces pain crises, ACS, transfusions; monitor CBC/retics for myelosuppression); L-glutamine, voxelotor, crizanlizumab (newer agents); curative: HSCT, gene therapy.
- Management steps for acute chest syndrome: 1) Oxygen to keep $\text{SpO}_2 \geq 95\%$. 2) Broad-spectrum antibiotics (including macrolide). 3) Simple or exchange transfusion if hypoxic/deteriorating. 4) Bronchodilators, incentive spirometry, analgesia. 5) ICU if progressive.

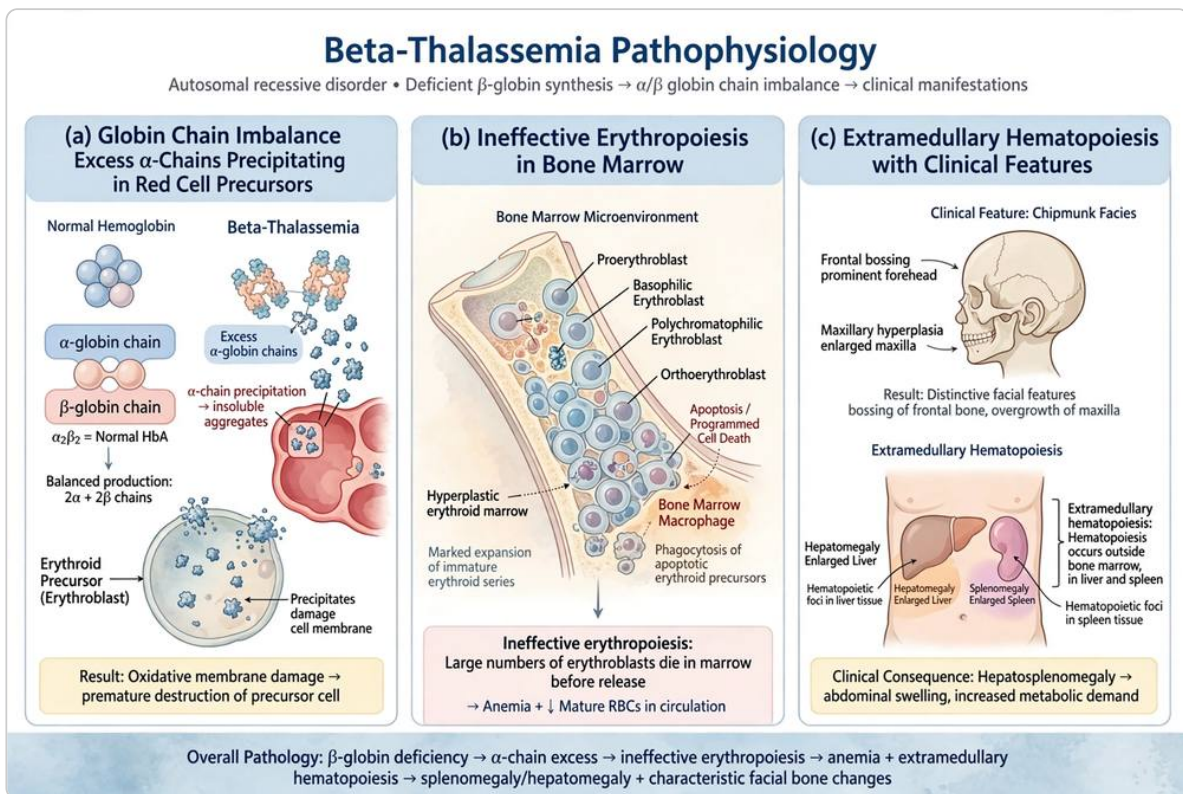


Figure 8.1 — Beta-thalassemia pathophysiology

6. Immune Thrombocytopenia (ITP)

- Autoimmune platelet destruction (anti-GPIIb/IIIa); post-viral in children.
- **Acute ITP**: 1–10 years, abrupt bruising/petechiae 1–3 weeks after viral illness, self-limited (resolves in 3–6 months in 80%).
- **Chronic ITP**: >12 months duration; adolescent girls, insidious onset; check ANA, consider Evans syndrome/CVID/ALPS.
- Labs: isolated thrombocytopenia ($<100 \times 10^9/L$), normal Hb/WBC, large young platelets on smear; antiplatelet antibodies not routinely needed.
- **Bone marrow examination**: NOT routine in typical acute ITP; do it if atypical features — anemia/leukopenia, organomegaly, lymphadenopathy, poor steroid response, before splenectomy, or to exclude leukemia/aplasia.
- Treatment thresholds: treat bleeding, not numbers. Observe if platelets $>20\text{--}30 \times 10^9/L$ with only skin bleeding. Treat if: active mucosal bleeding, platelets $<20 \times 10^9/L$ with high bleeding risk, or pre-procedure.
- First-line: **corticosteroids** (prednisolone $2 \text{ mg/kg/day} \times 2\text{--}3$ weeks or dexamethasone pulses) or **IVIg** ($0.8\text{--}1 \text{ g/kg}$) for rapid rise (severe bleeding, pre-surgery). Anti-D for Rh-positive non-splenectomized children.
- Persistent/chronic: **thrombopoietin receptor agonists** — **romiplostim** (weekly SC) or **eltrombopag** (oral); rituximab; splenectomy deferred as long as possible (ideally >5 years, after vaccines + counseling).
- Emergency (intracranial bleed): platelet transfusion + IVIG + high-dose methylprednisolone.

7. Hemophilia A and B

- X-linked recessive; Hemophilia A = **factor VIII** deficiency (commoner), Hemophilia B = **factor IX** deficiency (Christmas disease).
- Labs: **isolated prolonged aPTT** with normal PT, normal platelets, normal bleeding time; low factor VIII or IX assay; vWF normal (distinguishes from vWD).
- Severity: <1% severe (spontaneous hemarthrosis), 1–5% moderate, 5–40% mild (bleeding with trauma/surgery).
- Clinical: hemarthrosis (ankle/knee/elbow), muscle hematomas, prolonged bleeding after circumcision/venipuncture; intracranial bleed risk; pseudotumor in severe disease.
- **Factor replacement dosing:** Dose (IU) = weight (kg) × desired rise (%) × 0.5 for factor VIII; × 1.0 for factor IX (larger volume of distribution). Factor VIII: 1 IU/kg raises level ~2%; half-life 8–12 h. Factor IX: 1 IU/kg raises ~1%; half-life 18–24 h. Target: 50% for hemarthrosis, 80–100% for CNS bleed/surgery.
- Desmopressin (DDAVP) for mild hemophilia A (releases endogenous vWF/FVIII stores); no role in hemophilia B or severe A.
- **Inhibitors:** alloantibodies (mostly hemophilia A, severe) rendering replacement ineffective; suspect when bleeding fails to respond. **Bethesda assay** quantifies inhibitor titer (BU). Low titer: high-dose factor; high titer: **bypassing agents** — recombinant factor VIIa or activated prothrombin complex concentrate (FEIBA); emicizumab (bispecific VIII-mimetic) for prophylaxis in inhibitor patients.
- Management steps for acute hemarthrosis: 1) Factor replacement immediately (do not wait for imaging). 2) Rest, ice, compression, elevation. 3) Physiotherapy after pain subsides. 4) Consider prophylaxis (regular factor infusions) in severe disease to prevent arthropathy.

8. von Willebrand Disease (vWD)

- Commonest inherited bleeding disorder; mostly AD; quantitative (type 1, 3) or qualitative (type 2) vWF defect. vWF carries factor VIII and mediates platelet adhesion.
- Clinical: mucocutaneous bleeding — epistaxis, menorrhagia, easy bruising, post-procedural bleeding; hemarthrosis rare except type 3.
- Labs: prolonged bleeding time/PFA-100, **low ristocetin cofactor activity**, low vWF antigen, variably low factor VIII; aPTT may be prolonged if FVIII low.
- Types: Type 1 (partial quantitative — commonest, mild), Type 2A (defective platelet binding, loss of high-molecular-weight multimers), Type 2B (gain-of-function — increased platelet binding → thrombocytopenia; **desmopressin contraindicated**), Type 2M, Type 2N (Normandy — defective FVIII binding, mimics hemophilia A), Type 3 (severe quantitative, AR).
- Treatment: **desmopressin (DDAVP)** first-line for type 1 (test response with DDAVP challenge); vWF-containing factor VIII concentrates for type 2/3, severe bleeding, or DDAVP non-responders; tranexamic acid as adjunct for mucosal bleeding. Avoid NSAIDs.

9. Acute Lymphoblastic Leukemia (ALL)

- Commonest childhood malignancy (peak 2–5 years); 80–85% B-ALL, ~15% T-ALL.
- Presentation: bone marrow failure (anemia, thrombocytopenia, neutropenia with fever), bone pain/limp, lymphadenopathy, hepatosplenomegaly; T-ALL: anterior mediastinal mass, SVC syndrome, hyperleukocytosis; CNS involvement at diagnosis uncommon but sanctuary site.
- Diagnosis: blasts on smear; bone marrow >25% lymphoblasts; **immunophenotyping by flow cytometry**: B-ALL (CD19, CD10/CALLA, CD79a, TdT+), T-ALL (CD3, CD7, TdT+). Cytochemistry: PAS-positive blasts, myeloperoxidase negative. Cytogenetics/FISH: **hyperdiploidy (>50 chromosomes) and t(12;21)/ETV6-RUNX1 — favorable; BCR-ABL t(9;22) (Ph+), KMT2A/MLL rearrangement (infants), hypodiploidy — unfavorable.**
- Risk stratification: favorable — age 1–10 years, WBC <50,000/ μ L, hyperdiploidy, ETV6-RUNX1, rapid early response, **MRD negativity**; unfavorable — age <1 or >10 years, WBC >50,000, Ph+, MLL, CNS/testicular disease, MRD positive at end of induction. **MRD (minimal residual disease) by flow/PCR is the strongest prognostic factor.**
- Phases of therapy (total ~2–3 years): 1) **Induction** (4–6 weeks: vincristine, steroids, asparaginase $\pm$ anthracycline) — goal remission. 2) **Consolidation/intensification** (high-dose methotrexate, mercaptopurine). 3) **Maintenance** (daily 6-mercaptopurine + weekly methotrexate, ~2 years). Ph+ ALL: add tyrosine kinase inhibitor (imatinib/dasatinib).
- **CNS prophylaxis: intrathecal methotrexate** ($\pm$ cytarabine, hydrocortisone) for all; cranial irradiation now reserved for CNS3/high-risk T-ALL (late effects).
- Relapse: marrow (commonest), CNS, testicular; treat with intensive re-induction, blinatumomab/inotuzumab, CAR-T cell therapy (tisagenlecleucel), HSCT.
- Late effects: growth, neurocognitive, cardiotoxicity (anthracyclines), second malignancy.

10. Tumor Lysis Syndrome (TLS)

- Massive release of intracellular contents from rapid tumor breakdown (Burkitt lymphoma, T-ALL, AML with high WBC).
- Labs (Cairo-Bishop): **hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia** (calcium-phosphate precipitation), rising creatinine. ECG: peaked T waves (K^+), prolonged QT (Ca^{2+}).
- Prevention: aggressive **IV hydration** (3 L/ m^2 /day, maintain urine output), avoid potassium/calcium in fluids, urinary alkalization is obsolete.
- **Rasburicase** (recombinant urate oxidase) 0.15–0.2 mg/kg IV single dose for high-risk/established TLS — converts uric acid to soluble allantoin; check G6PD status (hemolysis risk), send uric acid samples on ice. Allopurinol (xanthine oxidase inhibitor) for low-intermediate risk — prevents new uric acid formation but does not clear existing.
- Management steps: 1) Risk-stratify before chemotherapy. 2) Hyperhydrate + rasburicase if high risk. 3) Monitor K, uric acid, phosphate, calcium, creatinine every 6–12 h. 4) Treat hyperkalemia (calcium, insulin-glucose, kayexalate, dialysis). 5) Dialysis for refractory electrolyte derangement, oliguria, or fluid overload.

11. Acute Myeloid Leukemia and Related Disorders

- **AML:** 15–20% of childhood leukemia; Auer rods, myeloperoxidase positive blasts; associated with Down syndrome (transient abnormal myelopoiesis → AMKL), Fanconi anemia.
- **APL (M3, t(15;17) PML-RARA):** presents with **DIC/bleeding** — medical emergency. Treatment: **ATRA (all-trans retinoic acid) 45 mg/m²/day** (25 mg/m²/day in children per some protocols) + **arsenic trioxide** — start ATRA on clinical suspicion before genetic confirmation. Beware differentiation (retinoic acid) syndrome: fever, dyspnea, infiltrates, effusions — treat with dexamethasone. Avoid leukapheresis.
- **CML:** rare in children; **BCR-ABL t(9;22)**, massive leukocytosis with basophilia, low LAP score; chronic phase → treat with **imatinib** (TKI) — excellent response; HSCT for resistant/advanced disease. Distinguish from leukemoid reaction (high LAP).
- **JMML** (juvenile myelomonocytic leukemia): <4 years, often with NF1/CBL/PTPN11 mutations, monosomy 7; presents with hepatosplenomegaly, monocytosis, elevated HbF; only curative therapy is HSCT; GM-CSF hypersensitivity of progenitors is characteristic.

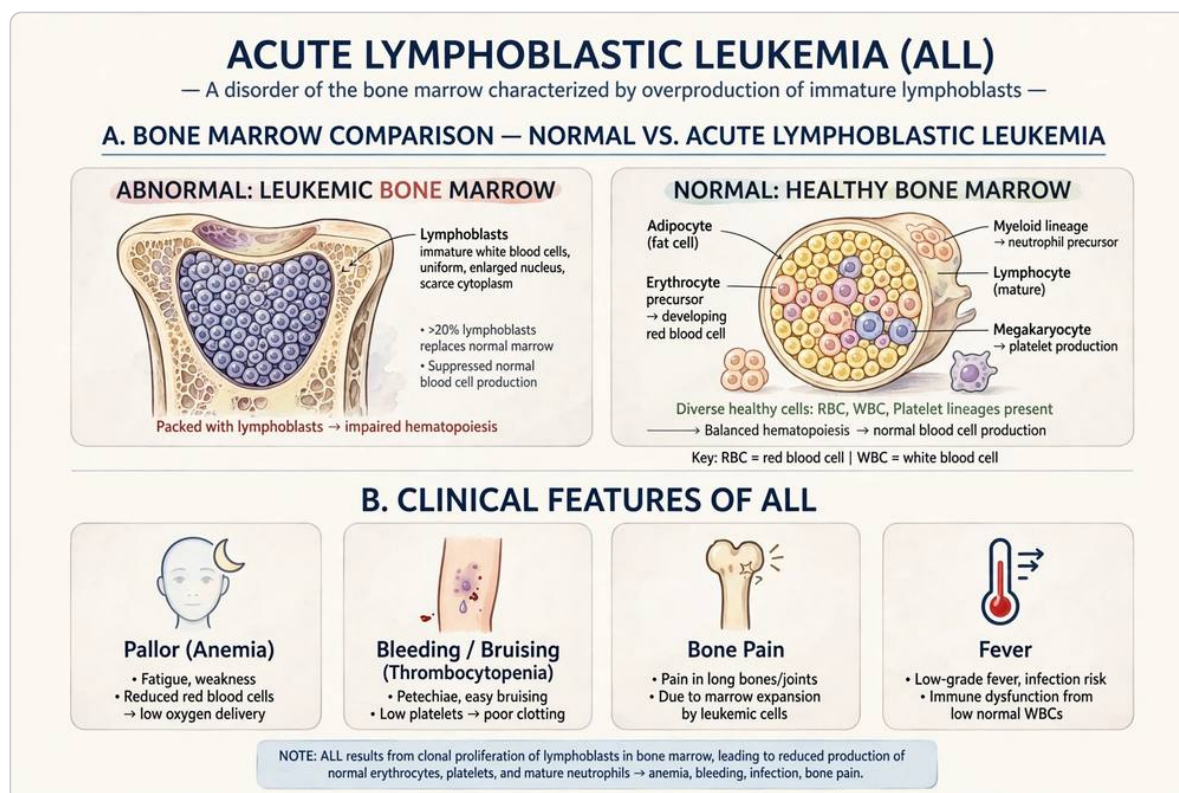


Figure 8.2 — Acute lymphoblastic leukemia: marrow and clinical features

12. Neuroblastoma

- Commonest extracranial solid tumor of childhood; median age 18 months; arises from neural crest (adrenal medulla 40%, paraspinal sympathetic chain).
- Presentation: **abdominal mass** (firm, crosses midline — vs Wilms which does not), **opsoclonus-myoclonus** ("dancing eyes, dancing feet" paraneoplastic), **Horner syndrome** (cervical/thoracic tumor), periorbital

ecchymosis ("raccoon eyes" — orbital mets), bone pain, hypertension, chronic diarrhea (VIP secretion), spinal cord compression.

- Labs: elevated urine **VMA/HVA** (catecholamine metabolites); **MIBG scan** (metaiodobenzylguanidine — taken up by sympathetic tissue) for staging and response; bone marrow biopsy for mets.
- Biology: **N-myc (MYCN) amplification — poor prognosis**; 1p deletion, 11q deletion unfavorable; hyperdiploidy favorable in infants; ALK mutations targetable.
- INSS staging: Stage 1 (localized, complete resection), 2 (localized, incomplete resection), 3 (unresectable, crosses midline), 4 (distant mets), 4S (infants <12–18 months with mets limited to liver/skin/marrow — often spontaneously regresses).
- INRG risk groups guide therapy: low (surgery ± observation), intermediate (moderate chemo), high (intensive multiagent chemo, surgery, myeloablative therapy + stem-cell rescue, radiation, isotretinoin, **anti-GD2 immunotherapy — dinutuximab**).
- Screening note: urinary catecholamine screening of infants was abandoned — detected mostly favorable tumors that would regress, without mortality benefit.

13. Wilms Tumor (Nephroblastoma)

- Commonest pediatric renal tumor; peak 2–4 years; **WT1** (11p13) and WT2 (11p15) loci.
- Presentation: **asymptomatic abdominal mass** discovered by parent/bath (does not cross midline — confined by Gerota fascia); hypertension (renin), hematuria, fever.
- Associations: **WAGR** (Wilms, Aniridia, Genitourinary anomalies, mental Retardation — WT1 deletion), **Denys-Drash** (WT1 mutation: Wilms + gonadal dysgenesis + nephropathy), **Beckwith-Wiedemann** (11p15 overgrowth: hemihypertrophy, macroglossia, omphalocele — Wilms + hepatoblastoma risk).
- NWTs/COG staging (post-surgical): I (confined to kidney, completely resected), II (extends beyond kidney, completely resected), III (residual disease/spillage/lymph nodes), IV (distant mets — lung commonest), V (bilateral).
- Treatment: **upfront nephrectomy (no pre-op biopsy — unlike neuroblastoma, to avoid spillage/upstaging)** + chemotherapy (vincristine, actinomycin-D ± doxorubicin by stage); flank radiation for stage III/IV. SIOP (European) protocol uses pre-op chemotherapy instead — know the COG vs SIOP difference.
- Prognosis: >90% 5-year survival for favorable histology; anaplasia (diffuse) is unfavorable — needs intensified therapy.

14. Hemophagocytic Lymphohistiocytosis (HLH)

- Hyperinflammatory syndrome from defective NK/T-cell cytotoxicity → uncontrolled macrophage activation and cytokine storm.
- Primary (familial): **PRF1 (perforin)** most common, UNC13D, STX11, STXBP2; XLP (SH2D1A), Griscelli, Chédiak-Higashi.
- Secondary: **EBV** commonest infectious trigger, malignancy (lymphoma), autoimmune (macrophage activation syndrome in SJIA).

- **HLH-2004 diagnostic criteria — 5 of 8 required:** 1) fever, 2) splenomegaly, 3) cytopenias ≥ 2 lineages (Hb < 9 , platelets $< 100k$, neutrophils < 1000), 4) hypertriglyceridemia (≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 150 mg/dL), 5) **ferritin ≥ 500 ng/mL** (often $> 10,000$ in HLH), 6) hemophagocytosis in marrow/spleen/lymph node, 7) low/absent **NK cell activity**, 8) elevated **soluble CD25 (sIL-2R) ≥ 2400 U/mL**. (Molecular diagnosis alone also suffices.)
- Distinguish from sepsis: extreme ferritin, cytopenias, splenomegaly, low fibrinogen with high triglycerides.
- Treatment (HLH-94/2004 protocol): 1) **Dexamethasone** (crosses blood-brain barrier) + **etoposide** + intrathecal methotrexate if CNS involvement. 2) Treat trigger (rituximab for EBV-driven). 3) **Allogeneic HSCT** for primary/familial, relapsed, or refractory disease — only curative option. 4) Supportive: IVIG, transfusions. Emapalumab (anti-IFN- γ) for refractory primary HLH.

15. Langerhans Cell Histiocytosis (LCH)

- Clonal proliferation of Langerhans-type dendritic cells; MAPK pathway mutations (BRAF-V600E ~50%).
- Pathology: **Birbeck granules** (tennis-racket granules on EM); IHC: **CD1a+ and CD207 (langerin)+**, S100+.
- Clinical spectrum: single bone lesion (eosinophilic granuloma — skull "punched-out" lesions), Hand-Schüller-Christian triad (skull lesions, **diabetes insipidus**, exophthalmos), Letterer-Siwe (multisystem infants — skin rash, hepatosplenomegaly, cytopenias).
- Risk organs: liver, spleen, bone marrow, lung — multisystem with risk-organ involvement has worse prognosis. **Diabetes insipidus** (pituitary stalk infiltration) and neurodegeneration are key sequelae.
- Treatment: single-system — curettage/observation; multisystem — vinblastine + prednisolone; BRAF/MEK inhibitors (dabrafenib, trametinib) for refractory/BRAF-mutated disease.

16. Pediatric Brain Tumors

- Brain tumors are the commonest solid tumors of childhood and the leading cause of cancer death in children; 60% are infratentorial (posterior fossa) — opposite of adults.
- **Medulloblastoma:** commonest malignant brain tumor; posterior fossa/cerebellar vermis in children; presents with ataxia, morning headache/vomiting (raised ICP), hydrocephalus. **CSF dissemination** is characteristic — stage with spine MRI + CSF cytology. Molecular subgroups: WNT (best prognosis), SHH, Group 3 (MYC — worst), Group 4. Treatment: maximal safe resection, craniospinal irradiation (avoided < 3 years — use chemotherapy), adjuvant chemo.
- **Pilocytic astrocytoma:** commonest benign/low-grade glioma; cerebellar; **BRAF fusion (KIAA1549-BRAF)** or V600E; cystic lesion with enhancing mural nodule; gross total resection often curative.
- **Ependymoma:** posterior fossa (4th ventricle) or supratentorial; "plastic" tumor extruding through foramina; surgery + focal radiation; CSF spread possible.
- **Craniopharyngioma:** suprasellar; **adamantinomatous** type in children (CTNNB1/ β -catenin); **calcification** on CT is classic; presents with visual field defects (bitemporal hemianopia), short stature/GH deficiency, **diabetes insipidus**; treatment: surgery (often subtotal to preserve hypothalamus/pituitary) + radiation; cystic recurrences managed with intracystic interferon/bleomycin.

- **Diffuse midline glioma (H3 K27M)**: pontine (DIPG); worst prognosis; radiation only, no surgical role.
- Posterior fossa surgery complication: **cerebellar mutism** (posterior fossa syndrome) after medulloblastoma resection.
- Workup steps for suspected brain tumor: 1) MRI brain with contrast (CT if unstable). 2) Spine MRI + CSF cytology for embryonal tumors. 3) Endocrine workup for suprasellar lesions. 4) Maximal safe resection for histology/molecular profiling. 5) Risk-adapted chemo-radiation.

Practice MCQs

Q1. A 14-month-old boy presents with pallor and pica. Labs: Hb 8.2 g/dL, MCV 62 fL, RDW 18.5%, ferritin 8 ng/mL, TIBC elevated. Peripheral smear shows microcytic hypochromic RBCs with pencil cells. What is the most appropriate initial treatment? A) Oral elemental iron 3–6 mg/kg/day B) Packed red cell transfusion C) Vitamin B12 injections D) Folic acid supplementation **Answer: A** — This is classic iron deficiency anemia (low ferritin, high RDW, microcytosis). Oral elemental iron 3–6 mg/kg/day is first-line; transfusion is reserved for hemodynamic instability or Hb <7 with symptoms. B12/folate treat megaloblastic, not microcytic, anemia.

Q2. A 4-year-old girl with known hereditary spherocytosis develops sudden pallor and fatigue after a febrile illness. Labs: Hb 4.5 g/dL (baseline 10), reticulocyte count 0.1%, WBC normal. What is the most likely cause? A) Hemolytic crisis B) Splenic sequestration C) Parvovirus B19-induced aplastic crisis D) Megaloblastic crisis **Answer: C** — Parvovirus B19 infects erythroid precursors causing transient red cell aplasia; in chronic hemolysis (HS, sickle cell) this produces severe anemia with reticulocytopenia. Hemolytic crisis would show reticulocytosis; sequestration occurs in sickle cell disease.

Q3. A 6-year-old boy develops acute hemolytic anemia with jaundice 2 days after starting primaquine for malaria. Smear shows bite cells and Heinz bodies on supravital stain. G6PD assay done today is normal. What is the next best step? A) Accept the normal result and look for another cause B) Start methylene blue C) Splenectomy D) Repeat G6PD assay after 2–3 months **Answer: D** — During acute hemolysis, older G6PD-deficient RBCs are destroyed, leaving young RBCs with falsely normal enzyme levels. The assay must be repeated after 2–3 months. Methylene blue is contraindicated in G6PD deficiency; splenectomy has no role.

Q4. A 3-year-old presents with pallor, jaundice, and splenomegaly. Labs: Hb 7.8 g/dL, reticulocytes 12%, LDH elevated, haptoglobin low, Direct Coombs test positive for IgG. What is the first-line treatment? A) Splenectomy B) Rituximab C) Corticosteroids D) IVIG alone **Answer: C** — DAT-positive (IgG) hemolysis indicates warm autoimmune hemolytic anemia, for which corticosteroids (prednisolone 2 mg/kg/day) are first-line. Rituximab is second-line for refractory disease; splenectomy is reserved for chronic relapsing warm AIHA.

Q5. A newborn of Southeast Asian parents develops hydrops fetalis and dies shortly after birth. Hemoglobin electrophoresis of cord blood shows predominantly Hb Bart's. How many alpha-globin genes are deleted? A) One B) Two C) Three D) Four **Answer: D** — Four-gene alpha deletion (α^-/α^- on both chromosomes) produces Hb Bart's (γ_4 tetramers) and hydrops fetalis, which is fatal without intrauterine transfusion. Three-gene deletion causes HbH disease; one/two-gene deletions are silent carrier/trait.

Q6. An 8-month-old boy presents with severe anemia, hepatosplenomegaly, and frontal bossing. Hb 6.5 g/dL, MCV 64 fL, HbF 92%, HbA2 5%, HbA 3%. What is the most appropriate long-term management? A) Oral iron supplementation B) Regular transfusions with iron chelation C) Hydroxyurea alone D) Splenectomy alone

Answer: B — Beta-thalassemia major (Cooley anemia) requires regular transfusions to maintain pre-transfusion Hb 9–10.5 g/dL plus iron chelation (deferoxamine/deferiprone/deferiasirox) once iron overload develops. Iron is contraindicated; hydroxyurea has limited role in major.

Q7. A 16-year-old girl with beta-thalassemia major on chronic transfusions has ferritin 2400 ng/mL. She develops neutropenia (ANC 800/ μ L) while on an oral chelator. Which chelator is she most likely taking, and what is the required monitoring? A) Deferoxamine — audiometry B) Deferiprone — weekly CBC C) Deferiasirox — serum creatinine D) Deferiprone — ophthalmology exam **Answer: B** — Deferiprone causes agranulocytosis/neutropenia, requiring weekly CBC monitoring. Deferoxamine causes ototoxicity/retinopathy (audiometry/ophthalmology); deferiasirox causes renal/hepatic toxicity.

Q8. A 2-year-old boy with sickle cell disease presents with fever, cough, chest pain, and a new right lower lobe infiltrate with SpO₂ 91%. What is the most appropriate immediate management step? A) Oxygen, broad-spectrum antibiotics including macrolide, and transfusion evaluation B) Outpatient oral antibiotics C) Exchange transfusion only D) High-dose steroids alone **Answer: A** — This is acute chest syndrome, the leading cause of death in sickle cell disease. Management is oxygen to keep SpO₂ $\geq$ 95%, broad-spectrum antibiotics (ceftriaxone + macrolide for atypical cover), bronchodilators, and simple or exchange transfusion if hypoxic or deteriorating.

Q9. A 4-year-old with sickle cell anemia has a transcranial Doppler showing time-averaged mean velocity of 210 cm/s in the middle cerebral artery. What is the next best step? A) Repeat TCD in 1 year B) Start chronic transfusion program C) Start hydroxyurea only D) Reassurance **Answer: B** — TCD velocity $\geq$ 200 cm/s is abnormal and indicates high stroke risk (STOP trial); the child should start a chronic transfusion program to keep HbS <30%. Annual TCD screening is done from age 2–16 years; conditional velocities (170–199) are repeated sooner.

Q10. A 3-year-old boy with ITP has platelet count 18,000/ μ L with only petechiae and bruising, no mucosal bleeding. He is otherwise well. What is the most appropriate management? A) Immediate platelet transfusion B) Emergency splenectomy C) Observation with precautions D) Bone marrow aspiration **Answer: C** — In childhood acute ITP, treatment is guided by bleeding, not platelet number. With only cutaneous bleeding and platelets >20,000/ μ L (close), observation is appropriate. Bone marrow is not routine in typical ITP; splenectomy is deferred.

Q11. A 9-year-old girl has had thrombocytopenia for 14 months (platelets 25,000–40,000/ μ L) with intermittent epistaxis. ANA positive. Bone marrow was normal at presentation. What is the most appropriate next therapy given inadequate response to steroids? A) Splenectomy immediately B) Platelet transfusion C) High-dose IVIG monthly lifelong D) Thrombopoietin receptor agonist (romiplostim) **Answer: D** — Chronic ITP (>12 months) refractory to steroids is managed with thrombopoietin receptor agonists (romiplostim/eltrombopag) or rituximab before considering splenectomy, which is deferred as long as possible in children. The positive ANA warrants follow-up for evolving SLE.

Q12. A 5-year-old boy with hemophilia A (factor VIII <1%) presents with a swollen, painful right knee after minor trauma. His weight is 20 kg. What dose of factor VIII concentrate should be given to achieve ~50% level? A) 250 IU B) 1000 IU C) 500 IU D) 2000 IU **Answer: C** — Factor VIII dose (IU) = weight (kg) $\times$ desired rise (%) $\times$ 0.5 = 20 $\times$ 50 $\times$ 0.5 = 500 IU. For hemarthrosis the target is ~50%; CNS bleeds and surgery need 80–100%.

Q13. A 12-year-old with severe hemophilia A on prophylaxis develops a muscle hematoma that fails to improve despite adequate factor VIII replacement. aPTT remains prolonged after factor infusion. What is the next best investigation? A) Platelet function test B) vWF antigen level C) Factor IX level D) Bethesda assay for factor VIII inhibitor **Answer: D** — Failure to respond to adequate factor replacement suggests an inhibitor (alloantibody); the Bethesda assay quantifies the inhibitor titer. High-titer inhibitors require bypassing agents (rFVIIa or FEIBA) or emicizumab prophylaxis.

Q14. A 14-year-old girl presents with menorrhagia and recurrent epistaxis since menarche. Labs: normal platelets, prolonged bleeding time, low ristocetin cofactor activity, factor VIII 35%. Her younger brother has normal coagulation studies. What is the most likely diagnosis and first-line treatment? A) Hemophilia A — factor VIII concentrate B) vWD type 1 — desmopressin C) vWD type 2B — desmopressin D) ITP — steroids **Answer: B** — Mucocutaneous bleeding with low ristocetin cofactor activity and reduced FVIII indicates von Willebrand disease; the mild quantitative pattern and dominant inheritance fit type 1, treated first-line with desmopressin (DDAVP). Type 2B is a contraindication to desmopressin (worsens thrombocytopenia).

Q15. A 4-year-old boy presents with 3 weeks of fever, bone pain, pallor, and cervical lymphadenopathy. CBC: Hb 7.2 g/dL, WBC 48,000/ μ L with 60% blasts, platelets 35,000/ μ L. Flow cytometry: CD19+, CD10+, CD79a+, TdT+. Cytogenetics: hyperdiploidy with 55 chromosomes. What is his prognostic category? A) High risk — infant MLL B) High risk — Ph positive C) Standard risk — favorable cytogenetics D) T-ALL high risk **Answer: C** — This is B-ALL (CD19/CD10/CD79a) in a 4-year-old with WBC <50,000 and hyperdiploidy (>50 chromosomes) — all favorable features placing him in the standard-risk group with >90% cure rate. Ph+ and MLL rearrangements are unfavorable; T-ALL would express CD3/CD7.

Q16. A 7-year-old girl with B-ALL completes induction therapy. End-of-induction MRD by flow cytometry is 0.5%. What does this signify? A) Positive MRD — higher relapse risk, treatment intensification needed B) Excellent prognosis, de-escalate therapy C) Normal finding, continue maintenance D) Indicates CNS relapse **Answer: A** — MRD $\geq 0.01\%$ at end of induction is positive and is the strongest adverse prognostic factor, mandating treatment intensification (and consideration of HSCT/blinatumomab per protocol). MRD negativity (<0.01%) predicts excellent outcome.

Q17. A 10-year-old boy with newly diagnosed T-ALL and WBC 180,000/ μ L develops oliguria 24 hours after starting chemotherapy. Labs: K+ 6.8 mEq/L, uric acid 14 mg/dL, phosphate 8.5 mg/dL, calcium 6.9 mg/dL, creatinine 2.1 mg/dL. ECG shows peaked T waves. What is the single most important immediate therapy in addition to hydration? A) Allopurinol B) Sodium bicarbonate infusion C) Calcium gluconate alone D) Rasburicase **Answer: D** — Established tumor lysis syndrome with hyperuricemia and AKI requires rasburicase (0.15–0.2 mg/kg IV), which directly converts existing uric acid to allantoin. Allopurinol only prevents new uric acid formation. Check G6PD status before rasburicase (hemolysis risk).

Q18. A 6-year-old girl presents with epistaxis, gum bleeding, and fatigue. CBC: WBC 35,000/ μ L with abnormal promyelocytes containing multiple Auer rods (faggot cells), platelets 28,000/ μ L, fibrinogen low, D-dimer markedly elevated. What is the most appropriate immediate treatment? A) ATRA immediately, before genetic confirmation B) Leukapheresis C) Standard AML induction only D) Heparin infusion **Answer: A** — Acute promyelocytic leukemia (M3, t(15;17)) with DIC is a medical emergency; ATRA (45 mg/m²/day; 25 mg/m²/day in children per some protocols) plus arsenic trioxide must start on clinical suspicion without waiting for PML-RARA confirmation. Leukapheresis worsens coagulopathy; watch for differentiation syndrome (treat with dexamethasone).

Q19. A 13-year-old boy presents with fatigue, massive splenomegaly, WBC 220,000/ μ L with basophilia and the full spectrum of myeloid maturation, LAP score low. What is the defining molecular abnormality and first-line therapy? A) PML-RARA — ATRA B) BCR-ABL t(9;22) — imatinib C) JAK2 mutation — hydroxyurea D) MLL rearrangement — HSCT **Answer: B** — Chronic myeloid leukemia in chronic phase: BCR-ABL t(9;22), leukocytosis with basophilia, low LAP score (distinguishes from leukemoid reaction). First-line therapy is the tyrosine kinase inhibitor imatinib, with excellent responses; HSCT reserved for resistant/advanced disease.

Q20. An 18-month-old boy presents with a firm abdominal mass crossing the midline, periorbital ecchymosis, and ataxia with chaotic eye movements. Urine VMA/HVA elevated. MIBG scan shows uptake in the adrenal mass and multiple bone lesions. What finding confers the worst prognosis? A) Age <18 months B) Hyperdiploidy C) Stage 4S disease D) N-myc (MYCN) amplification **Answer: D** — N-myc (MYCN) amplification is the key adverse biologic marker in neuroblastoma, mandating high-risk therapy (intensive chemo, transplant, radiation, isotretinoin, anti-GD2 dinutuximab). Opsoclonus-myoclonus itself is paraneoplastic and associated with favorable biology; 4S disease in infants often regresses spontaneously.

Q21. A 3-year-old girl's mother notices an asymptomatic abdominal swelling while bathing her. Examination reveals a large, firm, non-tender flank mass that does not cross the midline. BP 130/85 mmHg. Ultrasound shows a solid renal mass. What is the next best step? A) Upfront nephrectomy followed by chemotherapy B) Percutaneous biopsy of the mass C) Preoperative chemotherapy per all protocols D) Observation with repeat ultrasound **Answer: A** — Classic Wilms tumor: asymptomatic abdominal mass not crossing the midline in a 2–4-year-old, with hypertension. Per COG/NWTS, upfront nephrectomy without pre-op biopsy is standard (biopsy risks spillage and upstaging) — unlike neuroblastoma where biopsy is routine. SIOP (Europe) uses pre-op chemo, but the COG approach is tested here.

Q22. The child in Q21 is found to also have aniridia and developmental delay. Which gene deletion explains this association? A) RB1 B) WT1 (11p13) C) TP53 D) APC **Answer: B** — WAGR syndrome (Wilms tumor, Aniridia, Genitourinary anomalies, mental Retardation) results from deletion at 11p13 involving WT1. Denys-Drash is WT1 mutation (gonadal dysgenesis + nephropathy); Beckwith-Wiedemann is 11p15 (hemihypertrophy, macroglossia, omphalocele).

Q23. A 2-year-old boy presents with 10 days of high fever, splenomegaly, Hb 7.5 g/dL, platelets 60,000/ μ L, neutrophils 800/ μ L, triglycerides 320 mg/dL, fibrinogen 110 mg/dL, ferritin 18,000 ng/mL. Bone marrow shows hemophagocytosis. EBV PCR positive. How many HLH-2004 criteria does he meet, and what is the definitive treatment for familial disease? A) 4 criteria — steroids alone B) 3 criteria — IVIG alone C) 5 criteria — splenectomy D) 6 criteria — dexamethasone + etoposide, then allogeneic HSCT **Answer: D** — He meets 6 of 8 HLH-2004 criteria (fever, splenomegaly, cytopenias in 3 lineages, hypertriglyceridemia + hypofibrinogenemia, ferritin $\geq$ 500, hemophagocytosis). Treatment per HLH-94/2004 is dexamethasone + etoposide ($\pm$ intrathecal MTX), with allogeneic HSCT as the only curative therapy for primary/familial HLH (e.g., PRF1 mutations).

Q24. A 5-year-old boy presents with a "punched-out" lytic skull lesion, polyuria, polydipsia, and exophthalmos. Biopsy shows cells with reniform nuclei that stain positive for CD1a and langerin (CD207). What ultrastructural finding is characteristic? A) Birbeck granules B) Auer rods C) Neurosecretory granules D) Michaelis-Gutmann bodies **Answer: A** — Langerhans cell histiocytosis: CD1a+/CD207 (langerin)+ dendritic cells with tennis-racket-shaped Birbeck granules on electron microscopy. The triad of skull lesions, diabetes insipidus, and exophthalmos is Hand-Schüller-Christian disease. BRAF-V600E is found in ~50%.

Q25. A 6-year-old boy presents with 3 weeks of morning headache, vomiting, and new-onset gait ataxia. MRI shows a midline posterior fossa mass in the cerebellar vermis with homogeneous enhancement. What is the most likely diagnosis, and what staging workup is mandatory? A) Pilocytic astrocytoma — no further staging B) Ependymoma — MIBG scan C) Medulloblastoma — spine MRI and CSF cytology for dissemination D) Craniopharyngioma — urine VMA/HVA **Answer: C** — Vermian posterior fossa mass in a child with ataxia and raised ICP is classic medulloblastoma, the commonest malignant pediatric brain tumor. Because medulloblastoma disseminates through CSF, staging requires contrast spine MRI plus CSF cytology. Pilocytic astrocytoma is typically a cystic cerebellar hemispheric lesion with mural nodule; craniopharyngioma is suprasellar with calcification.

Infectious Diseases & Immunology

Chapter 9: Infectious Diseases & Immunology

Infectious diseases and immunology together form one of the highest-yield domains in NEET SS Pediatrics: pattern-recognition vignettes of primary immunodeficiencies, drug-of-choice and regimen questions in TB/HIV/tropical infections, and vaccine-schedule traps appear in nearly every paper. This chapter is built for that exam — dense, pattern-driven, and anchored to standard regimens and doses you will be tested on.

1. Primary Immunodeficiencies: Pattern Recognition

NEET SS tests PIDs as clinical vignettes. Learn each by its **signature triad/pattern**, the **gene**, the **confirmatory test**, and the **definitive treatment**. Age of onset is itself a clue: SCID presents in early infancy, XLA after 6 months (when maternal IgG wanes), CVID after early childhood.

Severe Combined Immunodeficiency (SCID) — the pediatric emergency

- **Definition:** Profound defect of T-cell development ($\pm$ B/NK defects); the most severe PID. Presents in the first months of life with failure to thrive, chronic diarrhea, persistent oral thrush/candidiasis, **Pneumocystis jirovecii pneumonia**, and severe/recurrent viral infections.
- **Red flags:** Absolute lymphocyte count $< 2,500/\text{mm}^3$ in an infant (normal infant ALC is 4,000–9,000), **absent thymic shadow on chest X-ray**, absent tonsils/lymph nodes, graft-vs-host-like rash from transplacental maternal T cells.
- **Variants by lymphocyte pattern (must memorize):**
 - **T–B–NK–:** X-linked SCID — **IL2RG** (common γ -chain) mutation, most common form; also **JAK3** deficiency (autosomal recessive, identical phenotype).
 - **T–B–NK+:** **RAG1/RAG2** deficiency and **Artemis (DCLRE1C)** deficiency (defective VDJ recombination; Artemis also causes radiosensitivity).
 - **T–B–NK–:** Adenosine deaminase (ADA) deficiency (also causes skeletal/rib abnormalities — "ADA-SCID").
- **Management:** **Hematopoietic stem cell transplant (HSCT)** is curative — best done before 3.5 months and before infections set in; gene therapy for ADA and X-linked SCID. Bridge with **IVIG**, PCP prophylaxis (cotrimoxazole), and antifungals.
- **Absolute contraindications:** **No live vaccines** (BCG, OPV, MMR, varicella, rotavirus) — they cause disseminated vaccine-strain disease. Give only **irradiated blood products** (to prevent transfusion-associated GVHD).

X-Linked Agammaglobulinemia (Bruton) — XLA

- **Gene:** **BTK** (Bruton's tyrosine kinase), X-linked recessive; arrest of B-cell maturation at the pre-B stage → **near-absent circulating B cells (CD19/CD20)** and profoundly low all immunoglobulin isotypes.
- **Timing clue:** Healthy for the first 6 months (protected by maternal IgG), then **recurrent sinopulmonary infections** with encapsulated bacteria — *Streptococcus pneumoniae*, *Haemophilus influenzae*.
- **Signature organisms:** Also susceptible to **Giardia lamblia** (chronic diarrhea), **enteroviruses** (chronic meningoencephalitis from echovirus — may be fatal), and *Mycoplasma/Ureaplasma* arthritis.
- **Examination clue:** Absent/scant tonsils and impalpable lymph nodes.
- **Treatment:** Lifelong **IVIG 400–600 mg/kg/month** (trough IgG > 500–800 mg/dL); prompt antibiotics for breakthrough infections. No HSCT needed (unlike SCID).

Common Variable Immunodeficiency (CVID)

- **Definition:** **Low IgG plus low IgA and/or low IgM**, with **poor specific antibody response to vaccines**, onset usually after 2 years (often adolescence/adulthood) — the most common symptomatic PID.
- **Pattern:** Recurrent sinopulmonary infections like XLA, but B cells are present (dysfunctional). Distinguish from XLA by age of onset and detectable B cells.
- **Associated features:** Autoimmune cytopenias, granulomatous disease, lymphadenopathy/splenomegaly, increased risk of lymphoma.
- **Treatment:** IVIG replacement; monitor for autoimmunity and chronic lung disease (bronchiectasis).

Chronic Granulomatous Disease (CGD) — phagocyte killing defect

- **Defect:** **NADPH oxidase** failure → phagocytes cannot generate reactive oxygen species (respiratory burst) to kill **catalase-positive organisms** (catalase destroys the microbe's own H₂O₂, which CGD phagocytes parasitically rely on).
- **Genes:** **gp91phox (CYBB)** — X-linked, most common and most severe; **p47phox (NCF1)** — autosomal recessive, milder.
- **Signature organisms:** *Aspergillus* (pneumonia, most common cause of death), *Burkholderia cepacia*, *Serratia marcescens*, *Staphylococcus aureus*, *Nocardia*. Recurrent skin/soft-tissue abscesses, suppurative lymphadenitis, liver abscesses, and **granuloma formation** (gastric outlet/GU obstruction).
- **Tests:** **NBT (nitroblue tetrazolium)** reduction test and the more sensitive **DHR (dihydrorhodamine) flow cytometry** — absent oxidative burst confirms.
- **Treatment:** Prophylactic **TMP-SMX + itraconazole**, **interferon-gamma** (reduces serious infections), and **HSCT** is curative.

Leukocyte Adhesion Deficiency (LAD)

- **LAD-1: CD18 (β2-integrin)** defect — neutrophils cannot adhere to endothelium and migrate to infection sites.

- **Signature:** **Delayed umbilical cord separation (> 3 weeks)**, **omphalitis**, severe periodontitis, poor wound healing, and skin/soft-tissue infections **without pus formation** despite **marked leukocytosis** (WBC 30,000–100,000 with neutrophilia).
- **LAD-2:** Defective selectin ligand (SLC35C1); milder, with dysmorphic facies and developmental delay.
- **Treatment:** HSCT; aggressive antibiotics; no pus + high WBC is the exam giveaway.

DiGeorge Syndrome (22q11.2 Deletion)

- **Mnemonic CATCH-22:** **C**ardiac (conotruncal: truncus arteriosus, tetralogy of Fallot, interrupted aortic arch type B), **A**bnormal facies, **T**hymic aplasia (T-cell defect), **C**left palate, **H**ypocalcemia (hypoparathyroidism → neonatal tetany/seizures).
- **Immunology:** Variable T-cell deficiency from thymic hypoplasia; humoral immunity usually intact. Severe (complete) DiGeorge behaves like SCID — no live vaccines, irradiated blood.
- **Test:** FISH for 22q11.2 deletion; low CD3 counts, low PTH, low calcium.

Wiskott-Aldrich Syndrome (WAS)

- **Gene:** **WASP**, X-linked recessive; defective actin polymerization in hematopoietic cells.
- **Classic triad:** **Eczema + thrombocytopenia with SMALL platelets (low MPV)** + recurrent infections (sinopulmonary, otitis). The small platelet size distinguishes it from ITP (large platelets).
- **Other clues:** Bloody diarrhea in infancy, elevated IgE with low IgM, autoimmune disease, increased lymphoma risk.
- **Treatment:** IVIG, HSCT (curative); splenectomy improves platelet counts but mandates lifelong penicillin prophylaxis and vaccines.

Hyper-IgE Syndrome (Job Syndrome)

- **AD form:** **STAT3** mutation. **AR forms:** **DOCK8** (severe viral skin infections, worse prognosis), **TYK2**.
- **Signature:** Newborn rash → severe **eczema**, **recurrent "cold" staphylococcal skin abscesses** (minimal inflammation), **pneumatocoles** after staphylococcal pneumonias, **retained primary teeth**, coarse facies, fractures/scoliosis from skeletal fragility.
- **Lab:** Markedly elevated **IgE (> 2,000 IU/mL)**, eosinophilia.
- **Treatment:** Prophylactic TMP-SMX/antistaphylococcal antibiotics; HSCT less established than in SCID — supportive care dominates.

Complement Deficiencies — the Neisseria clue

- **Early classical pathway (C1, C2, C4):** SLE-like autoimmune disease; C2 deficiency is the most common complement deficiency.
- **C3 deficiency:** Recurrent severe pyogenic (encapsulated bacterial) infections.
- **Terminal pathway (C5–C9):** **Recurrent disseminated Neisseria infections** — meningococcemia/meningitis and gonococcemia. **Properdin** (X-linked) deficiency → fulminant meningococcal disease.

- **Tests:** **CH50** (screens classical pathway), **AH50** (alternative pathway); low CH50 with normal AH50 → classical/terminal defect.
- **Management:** Meningococcal vaccines (MenACWY + MenB), penicillin prophylaxis, urgent antibiotics for febrile illness.

2. PID Workup: From Suspicion to Confirmation

When to suspect — the 10 warning signs (Jeffrey Modell Foundation)

- ≥ 4 ear infections in one year; ≥ 2 serious sinus infections in one year; ≥ 2 **pneumonias in one year**; ≥ 2 **deep-seated infections including sepsis**; recurrent deep skin/organ abscesses; persistent thrush or fungal skin infection after 1 year of age; need for IV antibiotics to clear infections; failure to thrive; **family history of PID** or early infant deaths.

Stepwise laboratory evaluation

1. **CBC with differential:** Lymphopenia suggests SCID/T-cell defect; neutropenia suggests cyclic neutropenia or Chediak-Higashi; **small platelets (low MPV)** suggest Wiskott-Aldrich; neutrophilia without pus suggests LAD.
2. **Immunoglobulin levels by age:** IgG reaches adult levels by ~6 years, IgA by adolescence. Very low IgG/IgA/IgM with absent B cells → XLA; low IgG + low IgA/IgM with poor vaccine responses after age 2 → CVID; isolated high IgE → Job syndrome or allergy.
3. **Lymphocyte subsets (flow cytometry):** CD3/CD4/CD8 (T cells), CD19/CD20 (B cells), CD16/CD56 (NK cells). Defines the SCID variant (T-B+NK- vs T-B-NK+).
4. **Phagocyte function:** **NBT** and **DHR** tests for CGD; neutrophil oxidative burst absent.
5. **Complement:** **CH50/AH50** when Neisseria or autoimmune patterns dominate.
6. **Specific antibody responses:** Measure pre- and post-vaccination titers (tetanus, pneumococcal) to document functional antibody failure in suspected CVID.
7. **Genetic confirmation:** Targeted gene panels (BTK, IL2RG, RAG1/2, CYBB, WASP, STAT3) guide family counseling and HSCT donor decisions.

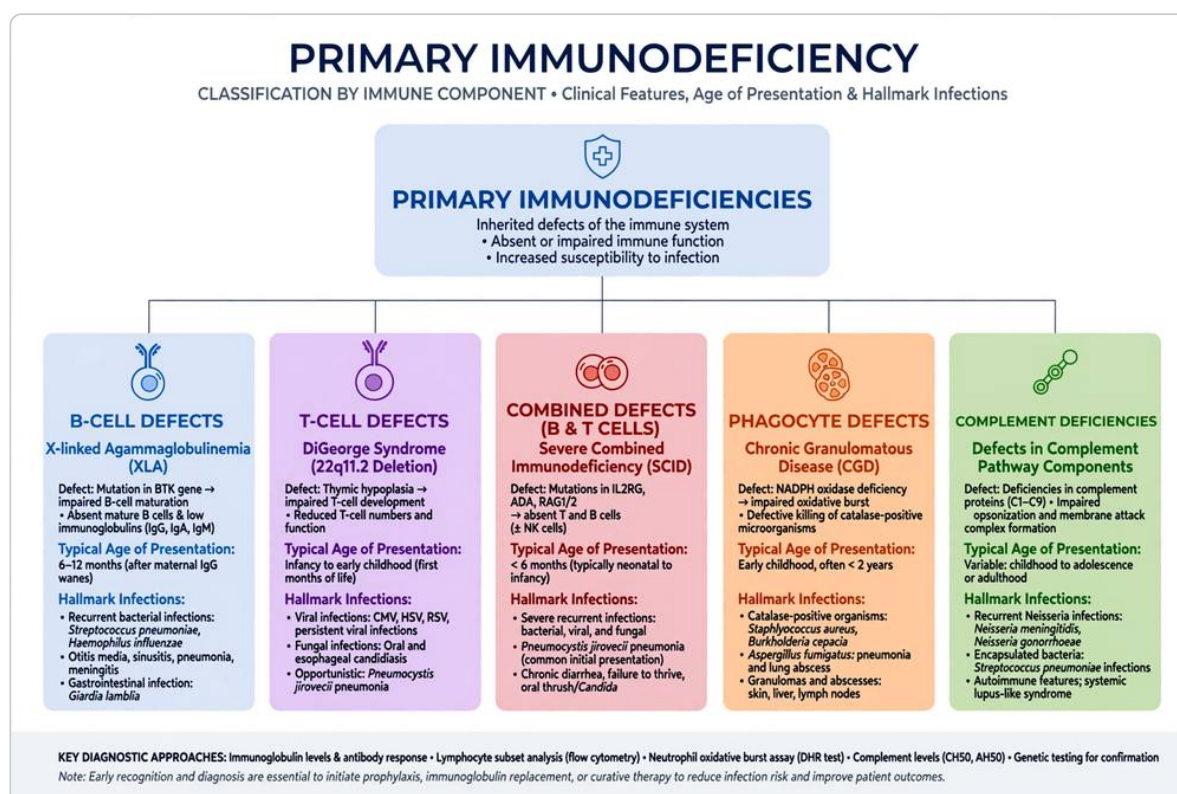


Figure 9.1 — Primary immunodeficiency classification

3. HIV Infection in Children

Prevention of perinatal transmission

- **Maternal ART:** All pregnant women with HIV receive lifelong triple ART regardless of CD4 count ("treat all") — the single most effective intervention; target undetectable viral load by delivery.
- **Infant prophylaxis:** **Nevirapine daily for 6 weeks** from birth (extended to 12 weeks if high risk — maternal viral load > 1,000 copies/mL near delivery, no maternal ART, or breastfeeding infant of untreated mother). High-risk: dual prophylaxis with AZT + NVP.
- **Delivery:** Elective caesarean section if maternal viral load > 1,000 copies/mL near term; avoid invasive fetal monitoring and prolonged rupture of membranes.
- **Feeding:** Where safe replacement feeding is not feasible, **exclusive breastfeeding for 6 months with continued maternal ART** (per WHO/NACO); never mixed feeding in the first 6 months.
- **Early infant diagnosis:** HIV DNA PCR at **6 weeks** of age (antibody tests are unreliable until 18 months due to maternal antibody).

Opportunistic infection prophylaxis

- **PCP prophylaxis:** **Cotrimoxazole from 6 weeks of age** for all HIV-exposed infants until HIV infection is excluded and no longer at risk; all HIV-infected infants < 1 year regardless of CD4. Dose: TMP **5 mg/kg/day** (single daily dose) or thrice-weekly regimen. Continue in older children if CD4 < 15% (< 200 cells/mm³ in older children).

- Also protects against toxoplasmosis and severe bacterial infections.

WHO clinical staging (children) — exam favorite

- **Stage 1:** Asymptomatic or persistent generalized lymphadenopathy.
- **Stage 2:** Unexplained persistent hepatosplenomegaly, papular pruritic eruptions, extensive warts/molluscum, herpes zoster, recurrent upper respiratory infections.
- **Stage 3:** Unexplained moderate malnutrition, persistent diarrhea > 14 days, persistent fever > 37.5°C for > 1 month, **oral candidiasis beyond the neonatal period**, acute necrotizing ulcerative gingivitis, pulmonary TB, severe recurrent bacterial pneumonia.
- **Stage 4:** Unexplained severe wasting, **PCP**, extrapulmonary TB, cryptococcal meningitis, toxoplasmosis, HIV encephalopathy, Kaposi sarcoma, extrapulmonary cryptococcosis.

ART regimens

- **Principle:** Treat all HIV-infected children regardless of CD4 count or clinical stage, with viral load monitoring.
- **First-line (WHO/NACO): Dolutegravir-based** triple therapy — **ABC + 3TC + DTG** (abacavir + lamivudine + dolutegravir) for children; neonates: AZT + 3TC + NVP. Adolescents/adults: TLD (tenofovir + lamivudine + dolutegravir).
- **Monitoring:** Viral load at 6 months, 12 months, then annually; CD4 for staging and OI prophylaxis decisions. Treatment failure: two consecutive viral loads > 1,000 copies/mL → adherence counseling, then switch.

4. Tuberculosis in Children

Latent TB infection (LTBI)

- **Diagnosis: TST (Mantoux)** — ≥ 10 mm induration positive in normal children, ≥ **5 mm in HIV-infected or close contacts**; BCG cross-reacts. **IGRA (Quantiferon-TB Gold)** — not affected by BCG, preferred in BCG-vaccinated children; cannot distinguish latent from active disease (neither can TST).
- **Treatment (preventive therapy):** Isoniazid **10 mg/kg/day for 6 months (6H)**; or **3 months of daily rifampicin + isoniazid (3HR)**; or weekly rifapentine + INH for 12 weeks (3HP). Give to under-5 household contacts and HIV-infected children after ruling out active TB.

Active TB — diagnosis

- **CBNAAT/GeneXpert MTB/RIF:** First-line test — detects *M. tuberculosis* DNA **and rifampicin resistance** within 2 hours from sputum, gastric aspirate, or lymph node aspirate. A negative Xpert does not rule out TB in children (paucibacillary disease).
- **Culture (LJ or MGIT):** Gold standard but slow (2–6 weeks). Sputum AFB smear is insensitive in children.
- **Chest X-ray clues:** Hilar lymphadenopathy, miliary mottling, pleural effusion, cavitation (adolescents).

Treatment regimens (NTEP)

- **Drug-sensitive TB: 2HRZE/4HR** — 2 months of isoniazid + rifampicin + pyrazinamide + ethambutol (intensive phase), then 4 months of isoniazid + rifampicin (continuation phase), given daily as weight-band fixed-dose combinations.
- **CNS TB (meningitis):** Longer course — **2HRZE/10HR (12 months total)** plus **adjunctive corticosteroids** (dexamethasone or prednisolone with taper over 6–8 weeks) to reduce mortality and neurological sequelae. Never omit steroids in TB meningitis.
- **MDR/RR-TB:** Regimens built around **bedaquiline**, **delamanid**, linezolid, clofazimine, and moxifloxacin; shorter 9–12-month all-oral regimens for eligible patients. Bedaquiline prolongs QT — monitor ECG.
- **Pyridoxine (vitamin B6)** with isoniazid in malnourished, HIV-infected, or adolescent patients to prevent peripheral neuropathy.

BCG

- Given at birth; protects against **miliary and meningeal TB** in young children, not reliably against pulmonary TB.
- **Disseminated BCG disease ("BCG-osis")** occurs in SCID and other severe T-cell defects — a live vaccine, so absolutely contraindicated in known immunodeficiency. Suspect PID in any infant with disseminated BCG.

5. Tropical Infections

Dengue

- **Agent/vector:** Flavivirus transmitted by **Aedes aegypti** (day-biting). Incubation 4–7 days. Four serotypes — second infection with a different serotype risks severe dengue (antibody-dependent enhancement).
- **Diagnosis:** **NS1 antigen** (days 1–5 of fever), **IgM** (after day 5); rising hematocrit with falling platelets tracks plasma leakage.
- **Warning signs (memorize):** Severe abdominal pain/tenderness, **persistent vomiting**, clinical fluid accumulation, **mucosal bleeding**, lethargy/restlessness, liver enlargement > 2 cm, and **rising hematocrit with rapid platelet fall**.
- **Severe dengue:** Shock (dengue shock syndrome), severe bleeding, organ impairment (AST/ALT $\geq$ 1,000, myocarditis, encephalopathy).
- **Fluid management:** Isotonic crystalloids (Ringer's lactate/NS) — 20 mL/kg bolus for shock, then titrate to urine output and hematocrit; avoid fluid overload in the recovery phase (watch for respiratory distress from reabsorption).
- **Do NOT give:** **NSAIDs** (bleeding risk), **steroids** (no benefit), prophylactic platelet transfusions (only for active major bleeding or planned invasive procedures with very low counts).

Malaria

- ***P. falciparum* — severe malaria:** Drug of choice is **IV artesunate 2.4 mg/kg at 0, 12, and 24 hours, then once daily** (minimum 24 hours IV) followed by a full oral ACT course. Superior to quinine (fewer deaths, less hypoglycemia). Cerebral malaria, severe anemia, blackwater fever, and ARDS are falciparum complications.
- **Uncomplicated falciparum:** Artemisinin combination therapy — **artemether-lumefantrine**.
- ***P. vivax*:** Chloroquine (25 mg/kg over 3 days) for blood stages plus **primaquine 0.25 mg/kg/day for 14 days** for radical cure of liver hypnozoites — **check G6PD status first** (primaquine causes hemolysis in G6PD deficiency; avoid or use weekly regimen under supervision).
- **Diagnosis:** Peripheral smear (gold standard — species identification and parasite index) or rapid diagnostic test (HRP-2 for falciparum).

Enteric (typhoid) fever

- **Gold standard: Blood culture** (highest yield in the first week); bone marrow culture most sensitive overall. Widal is unreliable — never the answer.
- **Treatment: Ceftriaxone** (75 mg/kg/day IV) or **azithromycin** (10–20 mg/kg/day PO) for uncomplicated disease; XDR typhoid (Pakistan clone) — azithromycin ± meropenem. Defervescence typically in 3–5 days; treat for 7–14 days.
- **Complications:** Intestinal perforation/hemorrhage (3rd week), encephalopathy, hepatitis.

Leptospirosis

- Exposure to water contaminated with rat urine; biphasic illness. **Weil disease:** jaundice + renal failure + hemorrhage (conjunctival suffusion is a clue).
- **Treatment:** Mild — **doxycycline**; severe — IV penicillin G or ceftriaxone. Diagnosis by MAT serology or PCR.

Scrub typhus

- **Agent:** *Orientia tsutsugamushi*, transmitted by **chiggers (trombiculid mites)**.
- **Signature: Eschar** (cigarette-burn-like necrotic lesion at the bite site — search axillae, groin, genitalia), fever, lymphadenopathy, maculopapular rash.
- **Drug of choice: Doxycycline** — endorsed as safe in children of all ages for rickettsial diseases (short courses do not cause meaningful dental staining); defervescence within 24–48 hours confirms the diagnosis clinically. Azithromycin is the alternative in pregnancy.

Kala-azar (visceral leishmaniasis)

- **Agent:** *Leishmania donovani*, sandfly vector; prolonged fever, massive splenomegaly, pancytopenia, hypergammaglobulinemia.
- **Diagnosis:** Demonstration of amastigotes (LD bodies) in splenic/bone marrow aspirate; **rK39 rapid test** for screening.

- **Treatment (India): Single-dose liposomal amphotericin B 10 mg/kg IV** (national elimination program regimen); multi-dose schedules use **3 mg/kg/day**. Alternatives: miltefosine, paromomycin. Post-kala-azar dermal leishmaniasis (PKDL) follows treated disease.

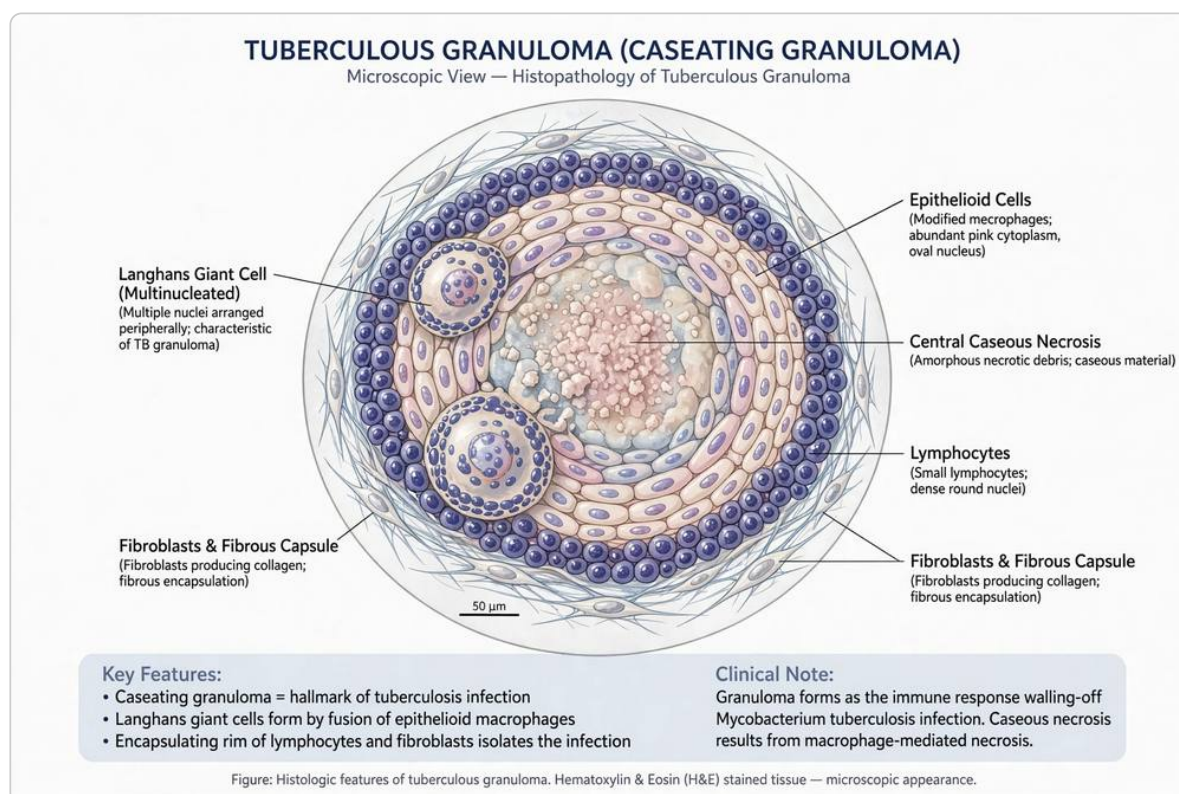


Figure 9.2 — Tuberculous granuloma

6. Immunization: IAP Schedule and Special Situations

IAP routine schedule — high-yield anchors

- **Birth:** BCG, OPV-0, Hepatitis B (birth dose within 24 hours).
- **6, 10, 14 weeks:** Pentavalent (DPT + HepB + Hib), OPV, Rotavirus; **IPV at 6 and 14 weeks**; PCV at 6 and 10 weeks.
- **9 months:** **MMR-1**, PCV booster, Typhoid conjugate vaccine (TCV, single dose at 9–12 months).
- **12 months:** Hepatitis A-1; **15 months:** MMR-2, Varicella-1; **16–18 months:** DPT booster-1, Hib booster, OPV booster.
- **4–6 years:** DPT booster-2, OPV, MMR-3, Varicella-2; **10–12 years:** Tdap, **HPV (9–14 years, 2 doses 6 months apart)**.
- **Influenza:** Annually from 6 months of age (single dose < 9 years first year needs 2 doses 4 weeks apart).

Special situations — frequently tested

- **Asplenia (sickle cell, splenectomy):** **Pneumococcal (PCV + PPSV-23), meningococcal (MenACWY), Hib**, annual influenza; plus **penicillin prophylaxis** (especially under-5s). Vaccinate 2 weeks before elective splenectomy.
- **Complement deficiency: Meningococcal MenACWY + MenB** vaccines and penicillin prophylaxis — recurrent *Neisseria* is the threat.
- **HIV:** Inactivated vaccines per schedule; **avoid live vaccines (MMR, varicella, BCG, OPV)** if severe immunosuppression ($CD4 < 15\%$).
- **Preterm infants:** Vaccinate by **chronological age** (not corrected), except hold HepB birth dose until weight ≥ 2 kg if mother is HBsAg-negative.
- **Post-HSCT:** Revaccinate as per transplant protocol starting ~6–12 months post-transplant; no live vaccines until immune reconstitution.
- **Corticosteroid therapy:** Live vaccines deferred if on ≥ 2 mg/kg/day prednisolone (≥ 20 mg/day) for ≥ 2 weeks — wait 1 month after stopping.

7. FUO, Kawasaki vs MIS-C, Endocarditis Prophylaxis, and Congenital Infections

Fever of unknown origin (FUO)

- **Definition (Petersdorf):** Fever $> 38.3^{\circ}\text{C}$ on several occasions, lasting ≥ 3 weeks, with no diagnosis after 1 week of intensive workup. Pediatric practice often uses ≥ 8 days of unexplained fever.
- **Big three categories: Infections** (TB, EBV/CMV, enteric fever, UTI, endocarditis, occult abscess, osteomyelitis), **collagen vascular** (systemic-onset JIA, SLE, Kawasaki), **malignancy** (leukemia, lymphoma, neuroblastoma). Miscellaneous: drug fever, factitious fever, IBD, HLH.
- **Workup sequence:** Detailed history/examination → CBC, ESR/CRP, **blood cultures $\times 3$** , urine culture, chest X-ray, TST/IGRA → EBV/CMV serologies, ANA, abdominal ultrasound → bone marrow examination if cytopenias or suspected malignancy/HLH → FDG-PET/CT for elusive cases.

Kawasaki disease vs MIS-C (cross-reference)

- **Kawasaki:** Fever ≥ 5 days plus **4 of 5**: bilateral non-purulent conjunctivitis, oral mucosal changes (strawberry tongue, cracked lips), polymorphous rash, extremity changes (edema/erythema, periungual desquamation), cervical lymphadenopathy ≥ 1.5 cm. Peak age **6 months–5 years**. **IVIG 2 g/kg single infusion** + high-dose aspirin; echo at diagnosis, 2 weeks, 6–8 weeks for **coronary aneurysms**.
- **MIS-C:** Typically **6–12 years**, 2–6 weeks after SARS-CoV-2 infection; prominent **GI symptoms, shock/myocardial dysfunction, lymphopenia and thrombocytopenia** (Kawasaki shows thrombocytosis), very high CRP/ferritin/D-dimer. Treatment: **IVIG + methylprednisolone**.
- **Exam discriminator:** Older child + shock + GI pain + cytopenias after COVID → MIS-C; under-5 with mucocutaneous criteria → Kawasaki.

Infective endocarditis prophylaxis (AHA)

- **Who needs it:** Prosthetic valves/material, **previous endocarditis**, unrepaired cyanotic CHD (including palliative shunts), repaired CHD with prosthetic material **within 6 months**, repaired CHD with residual defects at prosthetic sites.
- **Procedures covered:** Dental procedures with gingival/periapical manipulation or mucosal perforation; respiratory tract procedures with mucosal incision.
- **Regimen:** Amoxicillin 50 mg/kg PO (max 2 g) 30–60 minutes before; penicillin-allergic: **clindamycin 20 mg/kg (max 600 mg)** or azithromycin.

Congenital infections (TORCH) — essentials

- **CMV** (most common congenital infection): Microcephaly, **periventricular calcifications**, sensorineural hearing loss, petechiae/"blueberry muffin" rash, chorioretinitis. **Treatment:** Symptomatic infants with CNS involvement — **valganciclovir 16 mg/kg/dose PO twice daily for 6 months** (improves hearing and neurodevelopmental outcomes); IV ganciclovir 6 mg/kg/dose q12h for severe disease.
- **Toxoplasmosis:** Hydrocephalus + **diffuse intracranial calcifications** + **chorioretinitis** triad. Treatment: **pyrimethamine + sulfadiazine + leucovorin for 12 months**. Spiramycin for maternal infection to reduce transmission.
- **Rubella:** Cataract, **PDA**, sensorineural deafness, "salt-and-pepper" retinopathy, blueberry muffin rash. Prevention by MMR vaccination.
- **HSV:** SEM (skin-eye-mouth), CNS, or disseminated disease — **IV acyclovir** promptly; caesarean if active genital lesions at delivery.
- **Syphilis:** Snuffles, rash, Hutchinson teeth, saber shins, mulberry molars — **penicillin**; screen all pregnancies with VDRL/RPR.

Practice MCQs

Q1. A 3-month-old boy presents with failure to thrive, chronic diarrhea, persistent oral thrush, and Pneumocystis pneumonia. Absolute lymphocyte count is 700/mm³ and chest X-ray shows absent thymic shadow. The most likely diagnosis is: A) X-linked agammaglobulinemia B) Severe combined immunodeficiency C) Common variable immunodeficiency D) Chronic granulomatous disease **Answer: B** — Early infancy onset with PJP, thrush, lymphopenia (normal infant ALC 4,000–9,000) and absent thymic shadow is classic SCID. XLA presents after 6 months when maternal IgG wanes; CGD has normal lymphocyte counts.

Q2. An 8-month-old boy has had 5 episodes of otitis media and 2 pneumonias since 6 months of age. Tonsils are absent and lymph nodes impalpable. Serum IgG, IgA, and IgM are all profoundly low. The underlying genetic defect is in: A) BTK B) IL2RG C) WASP D) STAT3 **Answer: A** — Onset after 6 months, absent tonsils/lymph nodes, absent B cells with panhypogammaglobulinemia points to X-linked agammaglobulinemia caused by BTK mutation. IL2RG causes X-linked SCID (T-B+NK⁻, early infancy).

Q3. A 4-year-old boy with recurrent *Aspergillus* pneumonia, liver abscess, and cervical lymphadenitis is evaluated. The confirmatory test for the suspected immunodeficiency is: A) CH50 assay B) Lymphocyte subset analysis C) DHR flow cytometry D) Serum IgE level **Answer: C** — Recurrent catalase-positive organism infections (*Aspergillus*) with granulomas indicate chronic granulomatous disease (NADPH oxidase defect), confirmed by absent oxidative burst on NBT or the more sensitive DHR test.

Q4. A neonate's umbilical cord separates at 4 weeks. He develops omphalitis and recurrent skin infections without pus formation, with a WBC count of 45,000/mm³. The defect is in: A) NADPH oxidase B) Common gamma chain C) WASP protein D) CD18 integrin **Answer: D** — Delayed cord separation (>3 weeks), omphalitis, infections without pus despite marked leukocytosis is leukocyte adhesion deficiency type 1, caused by CD18 (β2-integrin) defect preventing neutrophil migration.

Q5. A 2-year-old boy presents with severe eczema, bloody diarrhea in infancy, and recurrent sinopulmonary infections. Platelet count is 40,000/mm³ with low MPV. The most likely diagnosis is: A) Wiskott-Aldrich syndrome B) Immune thrombocytopenia C) Hyper-IgE syndrome D) Atopic dermatitis with sepsis **Answer: A** — Eczema + thrombocytopenia with characteristically small platelets (low MPV) + recurrent infections is the Wiskott-Aldrich triad (WASP mutation). ITP has large platelets and no eczema/infection pattern.

Q6. A newborn with truncus arteriosus develops hypocalcemic seizures on day 3. He has a cleft palate and recurrent viral infections with low CD3 counts. The most appropriate confirmatory test is: A) BTK gene sequencing B) FISH for 22q11.2 deletion C) NBT test D) Serum IgA level **Answer: B** — Conotruncal cardiac anomaly + neonatal hypocalcemia (hypoparathyroidism) + cleft palate + T-cell deficiency is DiGeorge syndrome (CATCH-22), confirmed by FISH demonstrating the 22q11.2 deletion.

Q7. A 6-year-old girl has severe eczema, recurrent cold staphylococcal abscesses, pneumatoceles after pneumonia, and retained primary teeth. Serum IgE is 5,000 IU/mL. The mutated gene is: A) DOCK8 B) IL2RG C) STAT3 D) RAG1 **Answer: C** — Eczema, cold abscesses, pneumatoceles, retained primary teeth, and very high IgE define autosomal dominant hyper-IgE (Job) syndrome caused by STAT3 mutation. DOCK8 causes the AR form with severe viral infections.

Q8. A 14-year-old boy has had three episodes of meningococcal meningitis. Immunoglobulin levels and lymphocyte subsets are normal. The most likely deficiency involves: A) C1q B) C3 C) Mannose-binding lectin D) C5–C9 **Answer: D** — Recurrent disseminated *Neisseria* infections with normal humoral and cellular immunity point to terminal complement pathway (C5–C9) deficiency. Screen with CH50/AH50 and vaccinate with MenACWY + MenB.

Q9. A term neonate is born to an HIV-positive mother with viral load 800 copies/mL on ART near delivery. The recommended infant prophylaxis is: A) Nevirapine daily for 6 weeks B) Zidovudine for 12 months C) Single-dose nevirapine only D) No prophylaxis needed **Answer: A** — Standard infant prophylaxis for HIV-exposed neonates is daily nevirapine for 6 weeks from birth (extended to 12 weeks or dual therapy only if high risk: maternal VL >1,000, no maternal ART). Early infant diagnosis by DNA PCR at 6 weeks.

Q10. An HIV-exposed 2-month-old infant's DNA PCR is pending. When should cotrimoxazole prophylaxis for *Pneumocystis* have been started? A) At 6 months of age B) At 6 weeks of age C) Only after confirmed HIV infection D) Only if CD4 < 200 **Answer: B** — Cotrimoxazole (TMP 5 mg/kg/day) is started at 6 weeks of age for

all HIV-exposed infants until HIV is excluded and exposure risk ends; all HIV-infected infants under 1 year receive it regardless of CD4 count.

Q11. A 7-year-old child with drug-sensitive pulmonary tuberculosis is started on treatment under NTEP. The correct regimen is: A) 2HRZE/7HR thrice weekly B) 6 months of HR only C) 2HRZE/4HR daily D) 2HRZ/4HR with steroids **Answer: C** — Drug-sensitive TB is treated with 2 months of isoniazid, rifampicin, pyrazinamide, ethambutol followed by 4 months of isoniazid + rifampicin (2HRZE/4HR), given daily as weight-band fixed-dose combinations.

Q12. A 12-year-old with rifampicin-resistant pulmonary TB needs an all-oral regimen. The drug most associated with QT prolongation that is now a backbone of MDR-TB treatment is: A) Linezolid B) Clofazimine C) Pyrazinamide D) Bedaquiline **Answer: D** — Bedaquiline is a cornerstone of modern MDR/RR-TB regimens (with delamanid, linezolid, clofazimine, moxifloxacin) and characteristically prolongs the QT interval, requiring ECG monitoring.

Q13. A 9-year-old with dengue fever on day 4 develops severe abdominal pain, persistent vomiting, and restlessness. Hematocrit has risen 25% from baseline with platelets of 40,000/mm³. The next step is: A) Start isotonic crystalloid IV fluids B) Transfuse platelets immediately C) Start IV steroids D) Give an NSAID for pain **Answer: A** — These are dengue warning signs with plasma leakage; management is judicious isotonic crystalloid resuscitation titrated to hematocrit and urine output. NSAIDs and steroids are contraindicated; prophylactic platelet transfusion is not indicated.

Q14. A 5-year-old with confirmed falciparum malaria presents with coma, severe anemia, and 12% parasitemia. The drug of choice is: A) IV quinine B) IV artesunate 2.4 mg/kg C) Oral chloroquine D) IM artemether only **Answer: B** — Severe falciparum malaria (cerebral malaria) is treated with IV artesunate 2.4 mg/kg at 0, 12, and 24 hours then daily, which reduces mortality compared with quinine, followed by a full oral ACT course.

Q15. A child treated for vivax malaria needs radical cure of liver hypnozoites. Before prescribing primaquine, the mandatory test is: A) Reticulocyte count B) Liver function tests C) G6PD status D) Hemoglobin electrophoresis **Answer: C** — Primaquine (0.25 mg/kg/day for 14 days) eradicates vivax hypnozoites but causes hemolysis in G6PD deficiency, so G6PD testing is mandatory before starting radical cure.

Q16. A 10-year-old presents with 2 weeks of step-ladder fever, relative bradycardia, and rose spots. The gold standard diagnostic test is: A) Widal test B) Typhi dot IgM C) Stool culture D) Blood culture **Answer: D** — Blood culture (highest yield in the first week; bone marrow culture most sensitive overall) is the gold standard for enteric fever. Widal is unreliable due to poor sensitivity and specificity.

Q17. An 8-year-old with 6 days of high fever has a cigarette-burn-like necrotic lesion in the axilla, generalized lymphadenopathy, and maculopapular rash. The drug of choice is: A) Doxycycline B) Amoxicillin C) Azithromycin as first choice D) Ceftriaxone **Answer: A** — Eschar with fever and rash is scrub typhus (*Orientia tsutsugamushi*, chigger bite); doxycycline is the drug of choice and is endorsed as safe in children of all ages for rickettsial diseases, with defervescence in 24–48 hours.

Q18. A 6-year-old from Bihar has 3 months of fever, massive splenomegaly, and pancytopenia. rK39 is positive. The recommended treatment under the national program is: A) Sodium stibogluconate for 30 days B) Single-dose liposomal amphotericin B 10 mg/kg C) Miltefosine for 7 days D) Fluconazole for 6 weeks **Answer: B** — Visceral

leishmaniasis (kala-azar) in India is treated with single-dose liposomal amphotericin B 10 mg/kg IV under the elimination program; multi-dose schedules use 3 mg/kg/day.

Q19. A boy with suspected phagocyte defect has recurrent Serratia lymphadenitis. His neutrophils fail to reduce nitroblue tetrazolium. The inheritance of the most common form of this disease is: A) Autosomal recessive B) Autosomal dominant C) X-linked recessive D) Mitochondrial **Answer: C** — Absent NBT reduction confirms chronic granulomatous disease (NADPH oxidase defect); the most common and severe form is X-linked recessive due to gp91phox (CYBB) mutation, while p47phox disease is autosomal recessive and milder.

Q20. A 16-year-old girl has recurrent sinusitis and bronchiectasis. Labs show low IgG, low IgA, normal B-cell numbers, and poor pneumococcal vaccine response. The most likely diagnosis is: A) X-linked agammaglobulinemia B) Selective IgA deficiency C) Transient hypogammaglobulinemia of infancy D) Common variable immunodeficiency **Answer: D** — Low IgG plus low IgA/IgM with poor specific antibody responses, present (dysfunctional) B cells, and onset after early childhood define CVID — the most common symptomatic PID. XLA has absent B cells and earlier onset.

Q21. Parents of a 2-month-old diagnosed with SCID ask about vaccination of the baby. The correct advice is: A) Withhold all live vaccines including BCG, OPV, MMR, and rotavirus B) Give BCG but withhold OPV C) Give all routine vaccines on schedule D) Give only killed vaccines after 1 year **Answer: A** — Live vaccines are absolutely contraindicated in SCID as they cause disseminated vaccine-strain disease; the infant needs HSCT, IVIG bridging, PCP prophylaxis, and only irradiated blood products.

Q22. A 9-year-old presents 4 weeks after COVID-19 with persistent fever, severe abdominal pain, hypotension, and myocardial dysfunction. Labs show lymphopenia, thrombocytopenia, CRP 220 mg/L, and ferritin 1,800 ng/mL. The most likely diagnosis is: A) Classic Kawasaki disease B) Multisystem inflammatory syndrome in children C) Toxic shock syndrome D) Systemic-onset JIA **Answer: B** — Older child, post-COVID timing, prominent GI symptoms, shock with myocardial dysfunction, and lymphopenia/thrombocytopenia (Kawasaki shows thrombocytosis) define MIS-C, treated with IVIG plus methylprednisolone.

Q23. A 7-year-old with unrepaired tetralogy of Fallot needs a dental extraction. The recommended endocarditis prophylaxis is: A) No prophylaxis needed B) IV vancomycin 1 hour before C) Amoxicillin 50 mg/kg PO 30–60 minutes before D) Azithromycin for 5 days after **Answer: C** — Unrepaired cyanotic CHD is a high-risk condition for endocarditis; dental procedures with gingival manipulation need single-dose amoxicillin 50 mg/kg (max 2 g) 30–60 minutes before the procedure.

Q24. A neonate born to a mother with primary CMV infection in pregnancy has microcephaly, periventricular calcifications, and failed hearing screening. The evidence-based treatment to improve hearing outcomes is: A) Oral acyclovir for 6 months B) IVIG monthly C) Ganciclovir for 2 weeks only D) Valganciclovir 16 mg/kg twice daily for 6 months **Answer: D** — Symptomatic congenital CMV with CNS involvement is treated with valganciclovir 16 mg/kg/dose twice daily for 6 months, which improves hearing and neurodevelopmental outcomes compared with shorter courses.

Q25. A 4-year-old undergoes splenectomy after trauma. Besides pneumococcal vaccine, the additional vaccines and prophylaxis indicated are: A) Meningococcal, Hib, annual influenza vaccines plus penicillin prophylaxis B) BCG and OPV only C) MMR booster and varicella only D) No additional measures needed **Answer: A** —

Asplenia mandates pneumococcal (PCV + PPSV-23), meningococcal (MenACWY), Hib, and annual influenza vaccines plus penicillin prophylaxis against overwhelming post-splenectomy sepsis from encapsulated organisms.

Critical Care & Emergency

Chapter 10: Critical Care & Emergency Medicine

Critical care and emergency medicine is among the highest-yield chapters for NEET SS Pediatrics — it is algorithm-driven, dose-heavy, and directly tests decision-making under time pressure. PALS protocols, shock resuscitation, DKA management, status epilepticus ladders, poisoning antidotes, and trauma survey steps are tested repeatedly, often as "next best step" or "first-line drug with dose" vignettes. This chapter is written to be memorized, not read.

1. Shock in Children

- **Definition:** Shock is acute circulatory failure — inadequate tissue perfusion and oxygen delivery relative to metabolic demand, with resultant cellular and organ dysfunction. Hypotension is a LATE sign in children (compensated shock); early diagnosis rests on clinical assessment of perfusion.
- **Clinical recognition (before BP falls):** Tachycardia (earliest sign), delayed capillary refill >2 sec, weak/thready pulses, mottled or pale extremities, altered sensorium (irritability → lethargy), decreased urine output (<1 mL/kg/h), tachypnea, metabolic (lactic) acidosis.

1.1 Types of shock and clinical differentiation

- **Hypovolemic shock:** Loss of intravascular volume — dehydration (diarrhea, vomiting), hemorrhage, burns, third-spacing. Cold extremities, delayed cap refill, weak pulses, dry mucous membranes, sunken eyes/fontanelle, history of fluid/blood loss. Jugular veins flat; CVP low. Responds to fluid boluses.
- **Cardiogenic shock:** Pump failure — myocarditis, congenital heart disease, cardiomyopathy, post-arrest, arrhythmia, drug toxicity. Cold extremities, delayed cap refill, weak pulses BUT with hepatomegaly, gallop rhythm, crackles/pulmonary edema, raised JVP, cardiomegaly on CXR. Fluids must be given CAUTIOUSLY (small aliquots, 5-10 mL/kg) — fluid challenge can precipitate pulmonary edema. Requires inotropes early.
- **Distributive shock:** Abnormal vasomotor tone with maldistribution — septic shock (commonest cause in children), anaphylaxis, neurogenic shock, adrenal insufficiency. Two phenotypes:
 - **Warm shock (vasodilatory):** Bounding pulses, flash cap refill, wide pulse pressure, warm extremities, low SVR, high cardiac output. Classic of early septic shock in children is less common than cold shock — but in older children/adolescents warm shock predominates.
 - **Cold shock:** Delayed cap refill, weak/thready pulses, narrow pulse pressure, cool mottled extremities, low cardiac output, high SVR. More common in children than warm shock.
- **Obstructive shock:** Impaired cardiac filling or outflow despite adequate volume and pump — tension pneumothorax, cardiac tamponade, massive pulmonary embolism, duct-dependent congenital lesions with

closed ductus. Key features: distended neck veins, muffled heart sounds (tamponade), unilateral absent breath sounds with tracheal shift (tension pneumothorax), pulsus paradoxus. Management is relief of obstruction (needle decompression, pericardiocentesis, thrombolysis/anticoagulation) — fluids and pressors alone fail.

- **Exam pearl:** Narrow pulse pressure (diastolic maintained, systolic falling) = cold shock/hypovolemic/cardiogenic. Wide pulse pressure = warm/distributive shock.

1.2 Fluid resuscitation

- **Agent:** Isotonic crystalloid — Normal Saline (0.9%) or Ringer's Lactate. RL is increasingly preferred (balanced, less hyperchloremic acidosis); avoid hypotonic fluids in shock.
- **Dose:** **20 mL/kg IV/IO bolus**, pushed rapidly. Repeat up to **40-60 mL/kg in the first hour** of septic shock, with **reassessment after EVERY bolus**.
- **Reassess for:** Improvement (HR ↓, cap refill <2 sec, pulses stronger, sensorium better, urine output, BP) vs. fluid overload — new/worsening hepatomegaly, crackles, increased work of breathing, gallop. If overload signs appear → stop fluids, start vasoactive support.
- **If still hypotensive after 40-60 mL/kg** (fluid-refractory shock) → start vasoactive drug; consider central access but do NOT delay pressors for line placement (peripheral epinephrine/norepinephrine is acceptable short-term).
- **Blood:** Give blood early in hemorrhagic shock (do not persist with crystalloids alone); in septic shock, transfuse if Hb <7 g/dL (restrictive strategy) or ongoing hypoperfusion.

1.3 Vasoactive drugs — doses to memorize

- **Epinephrine:** First-line for **cold shock** (low cardiac output). Dose **0.05–0.3 mcg/kg/min** IV infusion. At low doses predominantly inotropic/chronotropic (β_1); higher doses add vasoconstriction (α). Also the pressor of choice in anaphylaxis and cardiac arrest.
- **Norepinephrine:** First-line for **warm shock** (low SVR, vasodilatory). Potent α vasoconstrictor with some β_1 . Dose **0.05–0.3 mcg/kg/min** (titrate; some protocols start 0.1). Preferred in fluid-refractory warm septic shock and in adolescents/adults.
- **Dopamine:** 5–20 mcg/kg/min (historical first-line; now second-line — more arrhythmogenic, higher mortality signal in adult sepsis vs norepinephrine). Dose-dependent: 2–5 "renal" (no proven benefit — abandoned concept), 5–10 inotropic, >10 vasopressor.
- **Dobutamine:** 2–20 mcg/kg/min. Pure inotrope (β_1) with mild vasodilation — for cardiogenic shock / low cardiac output with normal or high SVR (e.g., myocarditis, post-cardiotomy). Often combined with norepinephrine.
- **Milrinone:** PDE-3 inhibitor — inodilator ($\uparrow$ contractility + $\downarrow$ SVR + $\downarrow$ PVR). Loading 50 mcg/kg then **0.25–0.75 mcg/kg/min**. Useful in cold shock with high SVR and pulmonary hypertension, and in decompensated heart failure. Causes hypotension — often needs concomitant norepinephrine; long half-life in renal dysfunction.
- **Vasopressin:** 0.01–0.03 U/min (adolescent/adult dosing; pediatric 0.2–0.4 mU/kg/min) — adjunct in catecholamine-resistant vasodilatory shock. Monitor for digital/mesenteric ischemia and hyponatremia.

- **Exam pearl:** Cold shock (poor perfusion, narrow pulse pressure) → **epinephrine**. Warm shock (flash refill, wide pulse pressure) → **norepinephrine**. Failing heart (gallop, hepatomegaly) → **dobutamine/milrinone**, fluids cautiously.

1.4 Septic shock bundle (Surviving Sepsis — pediatric adaptation)

- **Within 1 hour of recognition:** (1) Blood cultures BEFORE antibiotics (do not delay antibiotics for cultures), (2) **Broad-spectrum empiric antibiotics IV within 1 hour**, (3) Begin fluid resuscitation 20 mL/kg boluses with reassessment, (4) Start vasoactive if fluid-refractory, (5) Source control.
- **Empiric antibiotics (community-acquired, previously healthy child):** Ceftriaxone + vancomycin (covers pneumococcus, meningococcus, MRSA). Neonate: ampicillin + cefotaxime (or gentamicin) ± acyclovir if HSV suspected. Immunocompromised/neutropenic: antipseudomonal β -lactam (piperacillin-tazobactam or cefepime/meropenem) + vancomycin.
- **Adjuncts:** Stress-dose hydrocortisone ONLY if fluid- and catecholamine-resistant shock with suspected/confirmed adrenal insufficiency (50 mg/m²/day divided q6h); IVIG not routine; tight glucose control not recommended (avoid hypoglycemia — target <180 mg/dL).
- **Targets:** Cap refill <2 sec, normal pulses, warm extremities, urine output ≥ 1 mL/kg/h, normal sensorium, lactate clearance, ScvO₂ >70%.

2. Diabetic Ketoacidosis (DKA)

2.1 Diagnostic criteria (all three required)

- **Hyperglycemia:** Blood glucose >200 mg/dL (note: euglycemic DKA possible with SGLT2 inhibitors, pregnancy, starvation — check ketones anyway).
- **Metabolic acidosis:** Venous pH <7.3 and/or bicarbonate <15–18 mEq/L.
- **Ketonemia/ketonuria:** Positive serum/urine ketones (β -hydroxybutyrate ≥ 3 mmol/L is the preferred marker).
- **Severity:** Mild pH 7.2–<7.3; Moderate 7.1–<7.2; Severe <7.1. Severity guides ICU admission and cerebral edema vigilance.

2.2 Management — stepwise

1. **ABCs and assessment:** Airway, breathing (Kussmaul respirations — do NOT intubate solely for Kussmaul breathing if the child is protecting airway; intubation in severe acidosis is high-risk), circulation, dehydration %, weight, neurological status (GCS), precipitating cause (infection, missed insulin, new-onset).
2. **Fluids — deficit replacement over 48 hours:** Assume ~5–10% dehydration (shock: give 20 mL/kg NS bolus first and subtract from total).
3. Use **isotonic fluids** (NS or RL) — never hypotonic initially.
4. Calculate: Maintenance (Holliday-Segar) + deficit (weight $\times$ %dehydration $\times 10 =$ mL), minus boluses, spread evenly over **48 hours** (slower than standard dehydration correction — rapid shifts precipitate cerebral edema).

5. When glucose falls to ~250–300 mg/dL, add dextrose (D5 in 0.45–0.9% saline) — **do NOT stop insulin**; continue insulin with dextrose-containing fluids until acidosis resolves.
6. **Insulin:** Start **after ~1 hour of fluid resuscitation** (never as a bolus in children). Regular insulin infusion **0.05–0.1 U/kg/hr** (0.05 preferred in younger children to reduce hypoglycemia/cerebral edema risk). Target glucose fall 50–100 mg/dL/hr. Continue until pH >7.3, bicarbonate >15, anion gap closed, and child eating — then transition to subcutaneous basal-bolus with a 30–60 min overlap.
7. **Potassium:** Total-body K⁺ is depleted despite normal/high initial serum K⁺ (acidosis shifts K⁺ out). **Do NOT start insulin if K⁺ <3.3 mEq/L** — replace K⁺ first. Once K⁺ 3.3–5.2 and urine output established, add **20–30 mEq/L K⁺** ($\frac{2}{3}$ KCl + $\frac{1}{3}$ KPhos) to maintenance fluids. If K⁺ >5.2, hold K⁺ and recheck. Monitor ECG (peaked T, wide QRS = hyperkalemia; U waves, flat T = hypokalemia).
8. **Bicarbonate:** NOT routine — only if pH <6.9 with compromised cardiac contractility/vasopressor response. It worsens intracellular acidosis and hypokalemia.
9. **Monitoring:** Hourly vitals, neuro checks (GCS), glucose; 2–4 hourly electrolytes, blood gas, osmolality; strict input/output; ECG monitoring. Watch phosphate and magnesium (replace if symptomatic).

2.3 Cerebral edema — the killer complication

- **Incidence/risk:** ~0.5–1% of pediatric DKA; mortality ~20–25%. Risk factors: young age (<5 years), new-onset diabetes, severe acidosis (low pCO₂), high BUN, rapid fluid administration, bicarbonate use, failure of sodium to rise as glucose falls.
- **Warning signs: Headache** (earliest), altered sensorium/drowsiness, irritability, incontinence, vomiting, bradycardia, hypertension, unequal/pinpoint pupils, seizures, respiratory pattern change. Typically occurs 4–12 hours into treatment, often as glucose/acidosis is improving — a deteriorating neuro status in an "improving" DKA child = cerebral edema until proven otherwise.
- **Treatment (do not wait for imaging):**
 - **Mannitol 0.5–1 g/kg IV** over 20 min (first-line) OR **3% hypertonic saline 5–10 mL/kg** — equally effective; hypertonic saline preferred if hypotensive.
 - **Reduce IV fluid rate** to $\sim\frac{2}{3}$ maintenance; raise head of bed 30°.
 - Elevate head, keep neck midline (jugular drainage), treat pain/fever/agitation.
 - Hyperventilation ONLY as temporary bridge to herniation control — avoid prophylactic hyperventilation (cerebral vasoconstriction worsens ischemia).
 - Urgent neuroimaging AFTER stabilization; involve PICU/neurosurgery.
 - **Exam pearl:** Headache + drowsiness in a child on DKA treatment = cerebral edema → mannitol/hypertonic saline immediately. Bedside glucose improving does not rule it out.

3. Status Epilepticus

- **Definition:** **≥5 minutes of continuous seizure activity OR recurrent seizures without regaining consciousness between them.** (Operational definition — treat at 5 min; the older 30-min definition marked the point of neuronal injury risk.)

- **Refractory status epilepticus:** Seizures persist despite adequate first- and second-line therapy (i.e., after a benzodiazepine + one second-line agent).
- **Super-refractory status epilepticus:** Persists ≥ 24 hours after initiation of anesthetic therapy, or recurs on weaning anesthetics.

3.1 Stepwise management (time-critical — the longer it lasts, the harder to stop)

1. **0–5 min — Stabilize:** ABCs, position lateral, suction, O₂, check glucose (treat hypoglycemia), vitals, IV/IO access, brief history (fever? trauma? known epilepsy? drug levels?).
2. **First-line (5–20 min) — Benzodiazepine:**
3. **Lorazepam 0.1 mg/kg IV** (max 4 mg), may repeat once after 5–10 min — drug of choice (longer seizure control than diazepam).
4. If no IV access: **buccal/intranasal midazolam 0.2 mg/kg** (max 10 mg) OR **per-rectal diazepam 0.5 mg/kg** (max 20 mg).
5. **Second-line (20–40 min) — one of:**
6. **Fosphenytoin 20 mg PE/kg IV** (max 1500 mg PE) — give slowly; monitor BP/ECG (hypotension, arrhythmia). Prodrug of phenytoin, safer/faster than phenytoin.
7. **Levetiracetam 40–60 mg/kg IV** (max 4500 mg) — preferred if hemodynamically unstable or cardiac disease (no cardiac toxicity).
8. Alternatives: valproate 20–40 mg/kg IV (avoid in suspected mitochondrial disease, liver dysfunction, <2 years), phenobarbital 15–20 mg/kg IV.
9. **Refractory (beyond 40 min) — continuous infusion in PICU with EEG monitoring:**
10. **Midazolam infusion:** 0.2 mg/kg bolus, then 0.05–0.4 mg/kg/hr titrated to burst suppression.
11. If fails → **propofol** (1–2 mg/kg bolus, 2–10 mg/kg/hr; watch propofol infusion syndrome — metabolic acidosis, rhabdomyolysis, cardiac failure) or **thiopental/pentobarbital** load then infusion.
12. **Super-refractory:** Continue anesthetic 24–48 h with continuous EEG; consider ketamine, inhalational agents, immunotherapy (if autoimmune encephalitis suspected), epilepsy surgery evaluation, ketogenic diet.
13. **Exam pearls:** Lorazepam 0.1 mg/kg is THE first-line IV drug and dose. Fosphenytoin dose is in **mg PE (phenytoin equivalents)/kg**. Always check/correct glucose, and give thiamine before dextrose in a malnourished/adolescent patient. Febrile status epilepticus in a child 6 mo–5 yr: treat seizure first, then evaluate fever source (LP if meningitis suspected after stabilization).

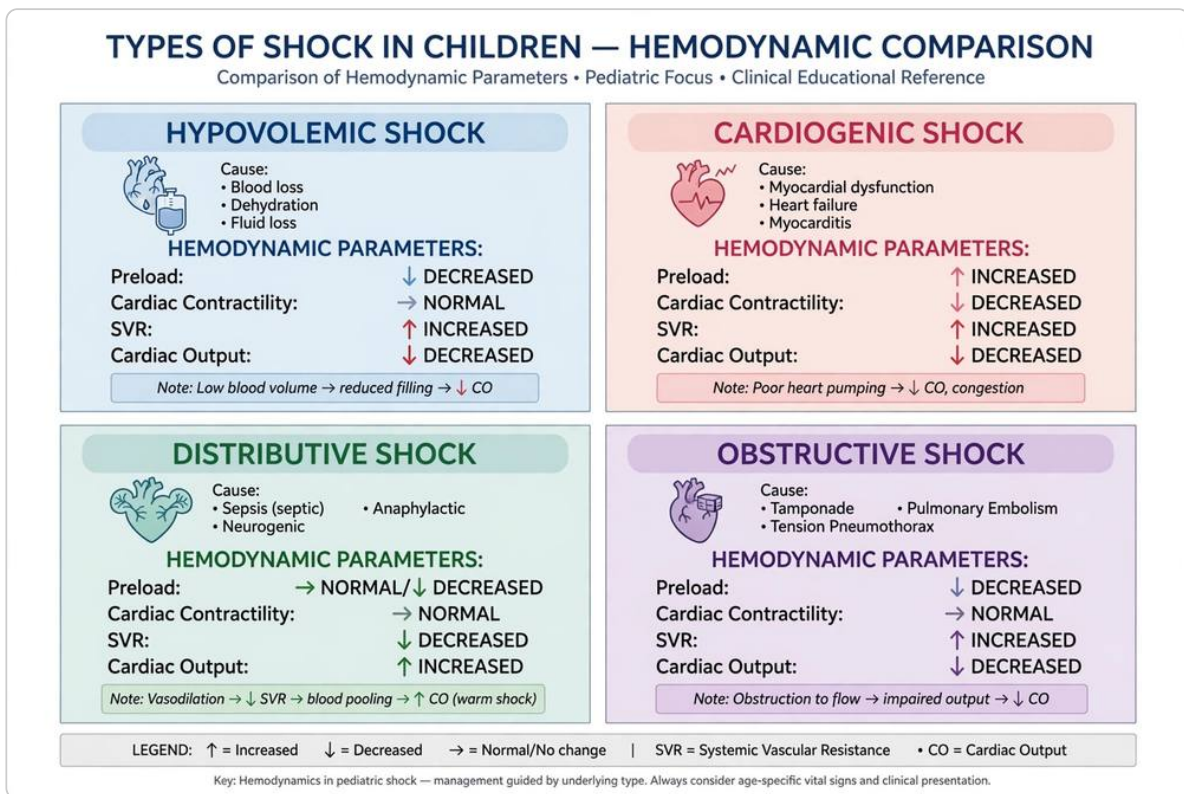


Figure 10.1 — Types of shock: hemodynamic profiles

4. Poisoning

- **General approach:** ABCs → decontamination decision → antidote → enhanced elimination → supportive care. **Activated charcoal 1 g/kg** (max 50 g) within 1 hour of ingestion if airway protected and poison adsorbs to charcoal — NOT for iron, lithium, alcohols, hydrocarbons, caustics, or button batteries. **Gastric lavage** rarely indicated (only within 1 hour of life-threatening ingestion with protected airway). **Ipecac-induced emesis is obsolete — never use.** Whole-bowel irrigation (PEG) for sustained-release drugs, iron, lead, drug packets.

4.1 Paracetamol (acetaminophen)

- **Toxic dose:** >150 mg/kg single ingestion (or >75 mg/kg in high-risk: chronic alcohol, malnutrition, enzyme inducers). Hepatotoxicity from NAPQI metabolite depleting glutathione.
- **Clinical phases:** I (0–24 h): nausea, vomiting, asymptomatic; II (24–72 h): RUQ pain, rising transaminases; III (72–96 h): hepatic failure, coagulopathy, encephalopathy; IV: recovery.
- **Rumack-Matthew nomogram:** Plot serum paracetamol level at **≥4 hours post-ingestion** (levels before 4 h unreliable — still absorbing). Treatment line: **150 mcg/mL at 4 h** (some use 100-line for high-risk). If above line → NAC. Nomogram INVALID for staggered/chronic ingestion, delayed presentation >24 h, or extended-release formulations — treat on clinical grounds.
- **N-acetylcysteine (NAC):** Replenishes glutathione. **IV loading 150 mg/kg** over 1 hour, then 50 mg/kg over 4 h, then 100 mg/kg over 16 h (classic 3-bag regimen; modified 2-bag regimens also used). Oral protocol: 140 mg/kg load then 70 mg/kg q4h × 17 doses. Give NAC if: level above treatment line, unknown ingestion time

with suspected toxicity, evidence of liver injury (rising transaminases/INR), or presentation >24 h with any concern. NAC is most effective within **8 hours** but has benefit even in established liver failure. Anaphylactoid reaction (flushing, urticaria) → slow/stop infusion, give antihistamine, restart slower.

4.2 Organophosphates (and carbamates)

- **Mechanism:** Irreversible (OP) acetylcholinesterase inhibition → cholinergic crisis. Carbamates inhibit reversibly (shorter course, pralidoxime less useful).
- **SLUDGE + extras:** **S**alivation, **L**acrimation, **U**rination, **D**efecation, **G**I cramps, **E**mesis — plus miosis (pinpoint pupils), bronchorrhea/bronchospasm, bradycardia, muscle fasciculations then weakness/paralysis, seizures, altered sensorium. Garlic/petroleum odor may be present.
- **Treatment:**
 - **Atropine:** 0.02–0.05 mg/kg IV (minimum 0.1 mg — smaller doses cause paradoxical bradycardia), double dose q5–15 min until **atropinization:** clear lungs (drying of bronchorrhea is the endpoint — NOT pupil size), HR >80, SBP >80. Then infusion.
 - **Pralidoxime (2-PAM):** 25–50 mg/kg IV over 30 min (max 1–2 g), then infusion 10–20 mg/kg/hr — reactivates cholinesterase; most effective within 24–48 h before "aging". Treats nicotinic effects (muscle weakness) that atropine doesn't.
 - Benzodiazepine for seizures; supportive ventilation (bronchorrhea + weakness = intubation often needed).
 - **Delayed syndromes:** Intermediate syndrome (proximal muscle weakness, cranial nerve palsies, respiratory failure at 24–96 h); OP-induced delayed polyneuropathy (weeks).

4.3 Iron

- **Toxic dose:** >20 mg/kg elemental iron = GI symptoms; >60 mg/kg = potentially lethal. (Ferrous sulfate is ~20% elemental iron.)
- **Phases of toxicity:** I (0–6 h): vomiting, diarrhea, GI bleed; II (6–24 h): apparent recovery — deceptive latent phase; III (12–48 h): shock, metabolic acidosis, hepatic failure, coagulopathy; IV (2–6 weeks): GI strictures/pyloric scarring.
- **Investigations:** Serum iron at 4–6 h (>500 mcg/dL concerning; >1000 severe), ABG, glucose, LFTs, coagulation, AXR (iron tablets are radiopaque — count pills).
- **Deferoxamine:** Indications — serum iron >500 mcg/dL, severe symptoms (shock, acidosis, altered sensorium), or radiopaque pills with symptoms. Dose 15 mg/kg/hr IV infusion (max ~6 g/day; rapid infusion causes hypotension). Chelated ferrioxamine turns urine **vin-rose** color. Continue until urine clears and child asymptomatic. Caution: prolonged use (>24 h) risks ARDS and Yersinia/mucormycosis infection.

4.4 Salicylates

- **Toxic dose:** >150 mg/kg (mild), >300 mg/kg (severe), >500 mg/kg potentially lethal. Uncouples oxidative phosphorylation → hypermetabolism, respiratory alkalosis THEN high-anion-gap metabolic acidosis (children often present directly acidotic).

- **Features:** Tinnitus, hyperventilation, vomiting, hyperthermia, sweating, altered sensorium; **do NOT rely on a single level** — repeat levels q2h (enteric-coated tablets form concretions; levels can rise for 12+ h).
- **Treatment:**
- **Urinary alkalization:** Sodium bicarbonate 1–2 mEq/kg bolus then infusion to keep urine pH 7.5–8.5 — traps ionized salicylate in urine ("ion trapping"). Correct hypokalemia first (alkalinization fails if K⁺ low).
- **Hemodialysis:** Indications — severe acidosis, altered sensorium, pulmonary/cerebral edema, renal failure, salicylate >100 mg/dL (acute) or >60 mg/dL (chronic), clinical deterioration despite therapy.
- Activated charcoal if early; NO emesis; cautious fluids (risk of pulmonary/cerebral edema — avoid fluid overload).
- **Exam pearl:** A child with tinnitus + hyperpnea + combined respiratory alkalosis/metabolic acidosis = salicylate poisoning → alkalinize urine, dialyze if severe.

4.5 Hydrocarbons (kerosene — classic Indian exam vignette)

- **Danger is aspiration, not ingestion:** Low viscosity, high volatility → chemical pneumonitis. CXR shows bilateral infiltrates 6–12 h post-aspiration.
- **NO emesis, NO gastric lavage, NO activated charcoal** (all increase aspiration risk). Management is supportive: O₂, bronchodilators, ventilation if needed; antibiotics only for proven secondary infection; observe asymptomatic children 6–8 h.

4.6 Button battery ingestion

- **Surgical emergency if lodged in esophagus:** Liquefactive necrosis from hydroxide generation at the negative pole — esophageal perforation can occur within **2 hours**, with fistula to trachea/aorta (fatal hemorrhage days later).
- **Management:** X-ray neck/chest/abdomen immediately (battery shows "double-ring/halo sign"; distinguish from coin — coin has single uniform edge). **Esophageal battery = emergent endoscopic removal** (ideally within 2 h). Give honey (1 tsp q10 min, max 6 doses) or sucralfate en route if <12 h and child can swallow — delays tissue injury. Batteries beyond esophagus in asymptomatic child: observe with serial X-rays; intervene for symptoms, large battery (≥20 mm), age <5 years, or failure to progress.

4.7 Lead poisoning

- **Sources:** Paint chips (old housing), surma/kajal, battery recycling, contaminated water/soil.
- **Features:** Abdominal colic/constipation, anemia (basophilic stippling, microcytic), developmental delay, encephalopathy/seizures at high levels (>70–100 mcg/dL), Burton lines on gums, Fanconi syndrome.
- **Chelation:**
- **Encephalopathy or level >70 mcg/dL: Dimercaprol (BAL)** 4 mg/kg IM q4h + **CaNa₂EDTA** 25–50 mg/kg/day IV infusion — BAL first (it redistributes lead to brain if given without EDTA cover... actually BAL mobilizes lead; always start BAL before EDTA to avoid driving lead into CNS).
- **Asymptomatic 45–69 mcg/dL: Succimer (DMSA)** 10 mg/kg/dose PO q8h × 5 days then q12h × 14 days — oral, outpatient-friendly.

- **<45 mcg/dL:** Remove source, nutritional optimization (iron, calcium), repeat monitoring.
- **Exam pearl:** Lead encephalopathy = dimercaprol + EDTA; moderate asymptomatic elevation = oral succimer. Always do abdominal X-ray (lead paint chips are radiopaque) and consider whole-bowel irrigation if ingested paint visible.

4.8 Other high-yield antidotes (one-line each)

- Opioids → **naloxone** 0.1 mg/kg IV (max 2 mg; neonate 0.01 mg/kg).
- Benzodiazepines → flumazenil (avoid in chronic users/mixed TCA overdose — precipitates seizures).
- Organophosphate → atropine + pralidoxime (above).
- Methanol/ethylene glycol → **fomepizole** (preferred) or ethanol; hemodialysis; folate/thiamine/pyridoxine cofactors. Osmolar gap + metabolic acidosis + visual symptoms (methanol) or calcium oxalate crystals (ethylene glycol).
- Carbon monoxide → 100% O₂ (reduces half-life from ~5 h to ~1 h); hyperbaric O₂ for severe (coma, cardiac ischemia, pregnancy). Co-oximetry (NOT standard pulse oximetry — falsely normal SpO₂).
- Digoxin → digoxin-specific Fab fragments (indications: K⁺ >5.5, malignant arrhythmia, massive ingestion).
- Warfarin/superwarfarin → vitamin K + FFP/4-factor PCC for bleeding.
- Cyanide → hydroxocobalamin (preferred) or sodium nitrite + sodium thiosulfate.
- Calcium channel blocker/beta-blocker → high-dose insulin euglycemia therapy, glucagon, calcium, vasopressors.
- Isoniazid → pyridoxine (vitamin B6) gram-for-gram of INH ingested.
- Caustic ingestion → NO emesis/lavage/charcoal; keep NPO, endoscopy within 24 h (not immediately — perforation risk), steroids controversial.

5. Pediatric Trauma

5.1 Primary survey — ABCDE (treat as you find)

- **A — Airway with C-spine protection:** Jaw thrust (no head tilt if C-spine injury suspected), suction, oropharyngeal airway if unconscious without gag. C-collar; clear clinically or by imaging (NEXUS criteria adapted; low threshold in children).
- **B — Breathing:** RR, SpO₂, chest rise, breath sounds, tracheal position. Treat tension pneumothorax (needle decompression 2nd intercostal space midclavicular line → chest drain), open pneumothorax (3-sided occlusive dressing), massive hemothorax, flail chest.
- **C — Circulation:** HR, BP, cap refill, pulses, pelvis stability, external bleeding (direct pressure; tourniquet for exsanguinating limb bleed; pelvic binder). **Two large-bore IVs/IO;** blood samples (cross-match, Hb, gas, lactate).
- **D — Disability:** Pediatric GCS, pupils, limb movement, glucose (hypoglycemia mimics deterioration).
- **E — Exposure:** Fully undress, log-roll, perineal/axillary inspection, temperature control (hypothermia worsens coagulopathy — the lethal triad: hypothermia, acidosis, coagulopathy).

5.2 Pediatric Glasgow Coma Scale (modified verbal/motor for infants)

Component >1 year

Eye (1–4) Spontaneous 4 → None 1

Verbal (1–5) Oriented 5, Confused 4, Inappropriate words 3, Incomprehensible sounds 2, None 1

Motor (1–6) Obeys 6 → None 1

<1 year (infant modification)

Same

Coos/babbles 5, Irritable cry 4, Cries to pain 3, Moans to pain 2, None 1

Spontaneous movements 6 → None 1

- **GCS ≤8** → **intubate** (cannot protect airway). E3V4M5 = 12, etc. A drop of ≥2 points = deteriorating — rescan.

5.3 Hemorrhagic shock in trauma

- **Recognition:** Tachycardia + delayed cap refill + narrow pulse pressure → hypotension (late). Class-based blood loss estimation is less used now; treat physiology.
- **Management:**
 - Stop the bleeding: direct pressure, tourniquet, pelvic binder, splint long-bone fractures (femur fracture alone can hide 1–1.5 L in adolescent thigh).
 - **20 mL/kg isotonic bolus**; reassess; if ongoing bleeding → **blood early** — packed RBCs 10–20 mL/kg; move to balanced resuscitation (PRBC:FFP:platelets ≈ 1:1:1) in massive transfusion; activate massive transfusion protocol if needed.
 - **Tranexamic acid (TXA):** 15 mg/kg IV (max 1 g) within **3 hours** of injury (CRASH-2/CRASH-3 extrapolation; pediatric trauma guidance supports early TXA in significant hemorrhage/TBI).
 - Permissive hypotension is NOT recommended in children with TBI — maintain age-appropriate BP/CPP.
 - Calcium replacement during massive transfusion (citrate toxicity → hypocalcemia); keep warm; correct acidosis.
 - **FAST exam** (hepatorenal, splenorenal, pericardial, pelvic views) for free fluid in unstable blunt trauma; CT abdomen/pelvis with contrast if stable.

5.4 Head injury and raised ICP

- **Signs of raised ICP:** Headache, vomiting, drowsiness, bradycardia, hypertension, irregular respirations (**Cushing triad** — late), unequal pupils, posturing, bulging fontanelle (infants).
- **Management:**
 - Head end elevated 30°, neck midline (no tight collar/ties impeding jugular drainage), adequate analgesia/sedation, treat fever, correct hypotension/hypoxia/hypoglycemia aggressively.
 - **Hypertonic saline 3% 5–10 mL/kg** (preferred in hypotensive/trauma child) or **mannitol 0.25–1 g/kg** for acute herniation signs — both reduce ICP; avoid mannitol if hypotensive or in renal failure.
 - **Hyperventilation ONLY as temporary bridge** to imminent herniation (target pCO₂ 30–35 briefly) — prophylactic hyperventilation worsens cerebral ischemia.
 - CSF drainage via EVD if indicated; decompressive craniectomy for refractory intracranial hypertension.

- Maintain CPP: age-appropriate — MAP – ICP; CPP target ~40–50 mmHg (infants/young) to 50–60 (older children). Avoid hypotension (SBP $<70 + 2 \times \text{age}$ is hypotension in 1–10 yr) and hypoxia ($\text{SpO}_2 < 90\%$) — both double mortality in TBI.
- **Second impact / return to play** and post-concussion guidance are lower-yield for SS but know: no same-day return to play after concussion.

6. Mechanical Ventilation Basics

6.1 Modes

- **Assist-Control (AC/CMV):** Every breath is a full machine breath — patient-triggered or time-triggered. Guarantees minute ventilation; risk of breath-stacking/hyperinflation if tachypneic. Good for initial stabilization.
- **SIMV (Synchronized Intermittent Mandatory Ventilation):** Set mandatory breaths synchronized with patient effort; patient breathes spontaneously between (with pressure support). Weaning mode historically; less used now.
- **Pressure Support (PS):** Patient-triggered, pressure-limited, flow-cycled — entirely patient-driven; used for spontaneous breathing trials and weaning. No backup rate (apnea risk if used alone in unreliable drive).
- **HFOV (High-Frequency Oscillatory Ventilation):** Very small tidal volumes at very high rates (5–15 Hz) around a constant mean airway pressure — lung-protective rescue for severe PARDS/air leak. Requires expertise; not first-line per current evidence.
- **CPAP/PEEP:** Continuous positive airway pressure — splints airways/alveoli open; used in bronchiolitis, post-extubation, cardiogenic pulmonary edema (non-invasive).

6.2 ARDSnet / lung-protective principles (pediatric ARDS — PALICC)

- **Low tidal volume: 6 mL/kg predicted body weight** (5–8 range; use PBW not actual weight in obesity).
- **PEEP titration:** Adequate PEEP to recruit and prevent atelectrauma — titrate to $\text{FiO}_2/\text{SpO}_2$ targets (ARDSnet FiO_2 –PEEP table concept); higher PEEP in moderate-severe PARDS.
- **Plateau pressure <28 – 30 cm H_2O** ; driving pressure as low as possible.
- **Permissive hypercapnia:** Accept pH ≥ 7.15 – 7.20 to allow lung protection (except raised ICP, pulmonary hypertension, severe metabolic acidosis).
- **Prone positioning** for severe PARDS ($\text{PaO}_2/\text{FiO}_2 < 150$) — improves oxygenation and mortality in adults; pediatric data supportive for oxygenation.
- **Conservative fluid strategy** once shock resolved; neuromuscular blockade (cisatracurium) early in severe ARDS with ventilator dyssynchrony.
- **Refractory hypoxemia rescue:** Inhaled nitric oxide (bridge), HFOV, ECMO (consider when OI >25 – 40 or refractory despite optimal care).

6.3 Ventilator-associated pneumonia (VAP) prevention bundle

- Head of bed elevated 30–45°; **daily sedation interruption** and readiness-to-wean assessment; DVT and stress-ulcer prophylaxis (age-appropriate); **oral care with chlorhexidine** (or toothbrushing protocol); subglottic suctioning (ETT with dorsal lumen in older children); avoid nasal intubation; cuff pressure 20–30 cm H₂O; hand hygiene; minimize ventilator circuit breaks.

6.4 Weaning and extubation criteria

- **Readiness:** Underlying cause resolving, hemodynamically stable (minimal/no vasoactives), adequate mentation and cough/gag, SpO₂ ≥94% on FiO₂ ≤0.4–0.5 with PEEP ≤5–8, pH normal, afebrile or controlled infection.
- **Spontaneous breathing trial (SBT):** 30–120 min on CPAP/PS (PS 5–10 + PEEP 5) — pass criteria: RR, SpO₂, HR, BP stable; no increased work of breathing, diaphoresis, agitation.
- **Extubation readiness specifics:** Strong cough, manageable secretions, gag reflex present, leak around ETT cuff (absence of leak suggests airway edema — consider steroids; leak test less reliable in children), RSBI not validated in small children — use clinical SBT.
- **Post-extubation:** Humidified O₂, watch for stridor (nebulized adrenaline + dexamethasone if croup-like stridor), NIV/HFNC for high-risk (prolonged ventilation, cardiac disease, weak cough).

7. PALS Algorithms (AHA Pediatric Advanced Life Support)

7.1 Bradycardia with poor perfusion

- **Definition:** HR <60/min WITH cardiopulmonary compromise (hypotension, altered sensorium, poor perfusion) despite O₂ and ventilation.
- **Steps:** Support ABCs → O₂ → ventilate if needed → if HR remains <60 with poor perfusion: **epinephrine 0.01 mg/kg IV/IO** (0.1 mL/kg of 1:10,000), repeat q3–5 min. If IV/IO unavailable: 0.1 mg/kg ET (1:1000). Consider atropine 0.02 mg/kg (min 0.1 mg, max 0.5 mg child / 1 mg adolescent) for vagally-mediated or primary AV block. Transcutaneous pacing as bridge for symptomatic bradycardia unresponsive to drugs (capture rarely sustained in small children — drugs first).

7.2 Tachycardia with poor perfusion

- **Narrow-complex SVT, unstable (poor perfusion, hypotension, altered sensorium): Synchronized cardioversion 0.5–1 J/kg;** if ineffective, increase to 2 J/kg. Sedate if conscious (do not delay cardioversion for deep sedation in crashing child).
- **Stable SVT:** Vagal maneuvers (ice to face in infants) → adenosine 0.1 mg/kg IV rapid push (max 6 mg), then 0.2 mg/kg (max 12 mg).
- **Wide-complex tachycardia (probable VT) with poor perfusion:** Synchronized cardioversion 0.5–1 J/kg → 2 J/kg. If pulseless VT → unsynchronized defibrillation per VF algorithm.
- **Sinus tachycardia** (fever, pain, hypovolemia, sepsis): NEVER cardiovert — treat the cause.

7.3 Asystole / PEA (non-shockable)

- **No defibrillation — ever — for asystole/PEA.**
- High-quality CPR (100–120/min, depth $\frac{1}{3}$ AP diameter: ~4 cm infant, ~5 cm child), minimize interruptions.
- **Epinephrine 0.01 mg/kg IV/IO q3–5 min** (first dose ASAP).
- Search/treat reversible causes — **Hs and Ts:** Hypoxia, Hypovolemia, Hydrogen ion (acidosis), Hypo/hyperkalemia, Hypothermia, Hypoglycemia; Tension pneumothorax, Tamponade, Toxins, Thrombosis (pulmonary/coronary), Trauma.

7.4 VF / pulseless VT (shockable)

- Defibrillate promptly: **2 J/kg first shock → 4 J/kg subsequent shocks** (adult: 120–200 J biphasic). Resume CPR immediately for 2 min after shock.
- **Epinephrine 0.01 mg/kg IV/IO q3–5 min** (after 2nd shock in PALS sequencing).
- **Amiodarone 5 mg/kg IV/IO** (max 300 mg) for refractory VF/pVT — may repeat twice; OR **lidocaine 1 mg/kg** if amiodarone unavailable.
- Treat Hs and Ts; consider magnesium 25–50 mg/kg (max 2 g) for torsades.

7.5 Post-ROSC (return of spontaneous circulation) care

- **ABCDE reassessment;** maintain normoxia (titrate FiO_2 to SpO_2 94–99% — avoid hyperoxia), normocapnia (avoid hyperventilation AND hypoventilation), normotension (age-appropriate SBP; treat hypotension with fluids/vasoactives).
- **Targeted temperature management:** Prevent/treat fever aggressively; maintain normothermia or mild therapeutic hypothermia per local protocol — **fever after ROSC worsens neurologic injury** (actively avoid hyperthermia).
- 12-lead ECG (rule out STEMI-equivalent/primary cardiac cause in adolescents), bedside echo, correct electrolytes/glucose, identify and treat precipitating cause (Hs and Ts).
- **Prognostication:** Not by a single variable — use clinical exam + EEG + imaging over 72+ hours; pupillary/corneal reflexes, myoclonus status epilepticus, and SSEP guide but never alone within 72 h.

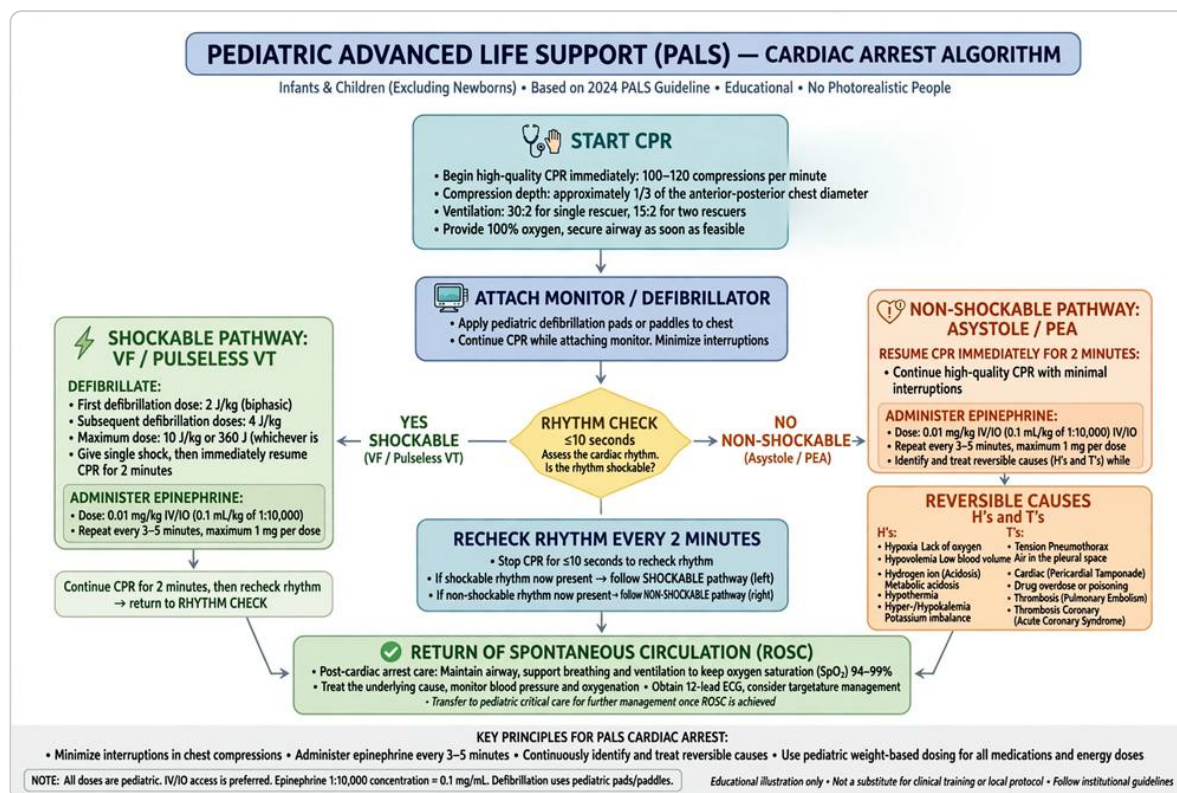


Figure 10.2 — Pediatric cardiac arrest (PALS) algorithm

8. Anaphylaxis

- **Diagnosis (clinical — do not wait for tryptase):** Acute onset with skin/mucosal involvement (urticaria, angioedema) PLUS respiratory compromise (wheeze, stridor) OR cardiovascular collapse/hypotension OR severe GI symptoms; OR hypotension alone after exposure to a known allergen. Biphasic reactions can recur 4–12 h later — observe 4–6 h (longer if severe).
- **First and most important — IM EPINEPHRINE: 0.01 mg/kg IM (max 0.5 mg) of 1:1000 (1 mg/mL)** into the **anterolateral thigh** (vastus lateralis). Repeat q5–15 min as needed. There are NO absolute contraindications to epinephrine in anaphylaxis.
- **Positioning:** Supine with legs elevated (left lateral if vomiting/pregnant); do NOT stand the child up (empty-ventricle deaths reported).
- **Adjuncts — NOT first-line, never before epinephrine:**
 - IV fluids 20 mL/kg for hypotension (large volumes may be needed — vasodilation + capillary leak).
 - H1 antihistamine (cetirizine/diphenhydramine) and H2 blocker for skin symptoms only.
 - **Steroids (methylprednisolone/hydrocortisone) do NOT treat acute anaphylaxis** — onset too slow; may reduce biphasic risk but never substitute for epinephrine.
 - Nebulized salbutamol for persistent bronchospasm; nebulized adrenaline for stridor.
 - Epinephrine infusion (0.05–0.3 mcg/kg/min) for refractory hypotension; consider glucagon if on beta-blockers.

- **Discharge:** Prescribe adrenaline auto-injector, demonstrate use, written action plan, allergist referral, avoidance education.

9. Burns

- **Estimation — Lund and Browder chart** (preferred in children — adjusts for age-related body proportions; head is proportionally larger in infants). Rule of nines is adult-based (head 9%, each arm 9%, each leg 18%, trunk 36%) — inaccurate in small children; use Lund-Browder or palmar method (child's palm $\approx$ 1% TBSA) for scattered burns.
- **Depth:** Superficial (epidermal — erythema, painful, no blisters, heals <7 days); superficial partial-thickness (blisters, pink, painful, blanches); deep partial-thickness (mottled, reduced sensation); full-thickness (white/charred, leathery, insensate, no blanching — needs grafting).
- **Parkland formula:** $4 \text{ mL} \times \text{weight (kg)} \times \% \text{TBSA}$ (second/third-degree burns) = total crystalloid (RL preferred) in first 24 h; **half in first 8 hours** from time of burn, half over next 16 h. Plus maintenance fluids separately (children need maintenance + Parkland; Holliday-Segar). Titrate to urine output 1–2 mL/kg/h. (Some centers use 3 mL/kg/% — know 4 as the exam answer.)
- **Inhalation injury:** Suspect with facial burns, singed nasal hair, carbonaceous sputum, hoarseness/stridor, enclosed-space fire, altered sensorium. **Early elective intubation** — airway edema progresses rapidly; do not wait for obstruction. 100% O₂; check carboxyhemoglobin and lactate (cyanide co-toxicity in enclosed fires — hydroxocobalamin if suspected).
- **Other essentials:** Tetanus prophylaxis; analgesia (IV morphine — burns are intensely painful); wound care — cool running water 20 min if early (not ice), cling film cover; **escharotomy** for circumferential full-thickness burns compromising limb perfusion or chest excursion; silver sulfadiazine/occlusive dressings; early enteral nutrition (hypermetabolic state); watch for compartment syndrome, sepsis, and curling's ulcers (stress ulcer prophylaxis).

10. Near-Drowning and Hypothermia (Brief)

- **Near-drowning (now "non-fatal drowning"):** Primary injury is **hypoxia** — laryngospasm, aspiration, V/Q mismatch. **Do NOT attempt to drain water from lungs** (Heimlich/abdominal thrusts waste time). Management: immediate rescue ventilation/CPR (drowning algorithm starts with 5 rescue breaths in children), O₂, rewarming, observe 6–24 h (delayed pulmonary edema/ARDS possible). Hypothermia is neuroprotective only if cooling preceded hypoxia — **never delay resuscitation to cool**; conversely, **do not declare death until rewarmed** ("no one is dead until warm and dead"). Prognostic factors: submersion time (>10 min poor), time to effective CPR, GCS on arrival, need for ongoing CPR in ED.
- **Hypothermia (<35°C):** Handle gently (myocardium irritable — VF risk with rough handling). **Mild (32–35°C):** passive rewarming (blankets, warm room). **Moderate–severe (<32°C):** active rewarming — warm IV fluids (38–42°C), warm humidified O₂, body cavity lavage, ECMO/CPB if cardiac instability ("gold standard" for severe hypothermia with arrest). Drugs (epinephrine, antiarrhythmics) are poorly effective <30°C — withhold or space doses; **defibrillation often fails <30°C** — rewarm first, though a single shock attempt is

reasonable. Correct hypoglycemia; expect hyperkalemia on rewarming. Frostbite: rapid rewarming in 37–39°C water, no rubbing, ibuprofen, tetanus update.

Practice MCQs

Q1. A 3-year-old with septic shock remains hypotensive with cold extremities, delayed capillary refill, and narrow pulse pressure after 60 mL/kg isotonic fluids. The most appropriate next step is: A) Continue fluid boluses to 100 mL/kg B) Start epinephrine infusion 0.05–0.3 mcg/kg/min C) Start norepinephrine infusion D) Give hydrocortisone bolus **Answer: B** — This is fluid-refractory cold shock (low cardiac output, narrow pulse pressure). Epinephrine 0.05–0.3 mcg/kg/min is first-line for pediatric cold shock. Norepinephrine is for warm (vasodilatory) shock. Further fluids risk overload; steroids are only for catecholamine-resistant shock with suspected adrenal insufficiency.

Q2. A 5-year-old presents with vomiting, Kussmaul breathing, glucose 480 mg/dL, pH 7.18, and strongly positive ketones. The correct insulin strategy is: A) Regular insulin 0.1 U/kg IV bolus then infusion B) Subcutaneous insulin glargine immediately C) Start insulin infusion 0.05–0.1 U/kg/hr after ~1 hour of fluid resuscitation D) Insulin infusion only after pH normalizes **Answer: C** — In pediatric DKA, insulin infusion (0.05–0.1 U/kg/hr, no bolus) starts after ~1 hour of isotonic fluid resuscitation. IV bolus insulin is avoided in children due to hypoglycemia and cerebral edema risk. Transition to subcutaneous insulin only after acidosis resolves with overlap.

Q3. During DKA treatment, an 8-year-old develops severe headache, drowsiness, and bradycardia 6 hours into therapy. Blood glucose has fallen from 520 to 280 mg/dL. The immediate management is: A) Mannitol 0.5–1 g/kg IV or 3% saline, reduce fluids, elevate head B) CT head before any treatment C) Increase fluid rate to correct dehydration faster D) Give sodium bicarbonate for worsening acidosis **Answer: A** — Headache with altered sensorium during DKA treatment is cerebral edema until proven otherwise. Treat immediately with mannitol 0.5–1 g/kg (or 3% saline 5–10 mL/kg), reduce fluid rate, elevate head 30° — do not wait for imaging. Increasing fluids or giving bicarbonate worsens cerebral edema.

Q4. A 4-year-old has had continuous generalized tonic-clonic seizures for 8 minutes. IV access is secured and glucose is normal. The first-line drug and dose is: A) Fosphenytoin 20 mg PE/kg IV B) Levetiracetam 60 mg/kg IV C) Midazolam infusion 0.1 mg/kg/hr D) Lorazepam 0.1 mg/kg IV **Answer: D** — Status epilepticus (≥5 min) first-line therapy is a benzodiazepine: lorazepam 0.1 mg/kg IV (max 4 mg), repeatable once. Fosphenytoin and levetiracetam are second-line agents given after benzodiazepines; midazolam infusion is for refractory status.

Q5. A 2-year-old ingested an unknown amount of paracetamol 6 hours ago. Serum level is 180 mcg/mL. The Rumack-Matthew nomogram treatment line at 4 hours is 150 mcg/mL. The next step is: A) Observe and repeat level in 6 hours B) Gastric lavage C) Start N-acetylcysteine immediately D) Hemodialysis **Answer: C** — A 6-hour level of 180 mcg/mL lies above the treatment line extrapolated from the 150 mcg/mL-at-4h nomogram, so NAC is indicated. NAC (150 mg/kg IV loading) is most effective within 8 hours. Levels before 4 hours are unreliable; lavage is rarely indicated and dialysis is not primary therapy for paracetamol.

Q6. A farmer's child presents with pinpoint pupils, bronchorrhea, fasciculations, and bradycardia after organophosphate exposure. The endpoint for atropine titration is: A) Pupillary dilation B) Heart rate >120/min C) Resolution of fasciculations D) Drying of bronchial secretions with clear lungs **Answer: D** — Atropinization

endpoint is drying of bronchorrhea (clear lungs), HR >80, and SBP >80 — not pupil size, which is unreliable. Atropine treats muscarinic effects; fasciculations (nicotinic) require pralidoxime. Start 0.02–0.05 mg/kg IV (min 0.1 mg), doubling q5–15 min.

Q7. A 3-year-old swallowed a button battery 1 hour ago. X-ray shows it lodged in the mid-esophagus. The correct management is: A) Observe with serial X-rays as most pass spontaneously B) Induce vomiting with ipecac C) Activated charcoal and whole-bowel irrigation D) Emergent endoscopic removal, ideally within 2 hours **Answer: D** — An esophageal button battery is a surgical emergency: hydroxide generation causes liquefactive necrosis and perforation within 2 hours. Emergent endoscopic removal is mandatory. Honey/sucralfate may be given en route if the child can swallow. Emesis and charcoal are contraindicated.

Q8. Synchronized cardioversion for an unstable 6-year-old with SVT and poor perfusion should be delivered at: A) 0.5–1 J/kg, increasing to 2 J/kg if ineffective B) 2 J/kg then 4 J/kg C) 50 J fixed dose D) 360 J monophasic **Answer: A** — Unstable tachycardia with a pulse gets synchronized cardioversion at 0.5–1 J/kg, escalating to 2 J/kg. The 2 J/kg → 4 J/kg sequence is for pulseless VF/pVT (unsynchronized defibrillation). Never cardiovert sinus tachycardia.

Q9. A 10-kg infant in asystole has IV access. The correct epinephrine dose and interval is: A) 0.1 mg/kg IV q3–5 min B) 1 mg IV q3–5 min C) 0.01 mg/kg IV q3–5 min D) 0.01 mg/kg IV once only **Answer: C** — PALS cardiac arrest dose is epinephrine 0.01 mg/kg IV/IO (0.1 mL/kg of 1:10,000) every 3–5 minutes = 0.1 mg for this 10-kg infant. The 0.1 mg/kg dose is for endotracheal administration only. Asystole/PEA are never defibrillated.

Q10. A 7-year-old with 25% TBSA burns weighing 20 kg needs fluid resuscitation per the Parkland formula. The total crystalloid for the first 24 hours is: A) 1000 mL B) 2000 mL C) 4000 mL D) 8000 mL **Answer: B** — Parkland: $4 \text{ mL} \times \text{kg} \times \% \text{TBSA} = 4 \times 20 \times 25 = 2000 \text{ mL}$ in 24 h (half in first 8 h from burn time). This is resuscitation fluid in addition to maintenance requirements in children. Lund-Browder chart is preferred over rule of nines for estimating %TBSA in children.

Q11. The most important immediate action in a child with anaphylaxis after a peanut exposure, who has stridor and hypotension, is: A) IM epinephrine 0.01 mg/kg (max 0.5 mg) into the anterolateral thigh B) IV methylprednisolone C) Nebulized salbutamol D) IV antihistamine **Answer: A** — IM epinephrine 0.01 mg/kg (max 0.5 mg) of 1:1000 into the anterolateral thigh is the first and most important treatment; there are no absolute contraindications. Steroids and antihistamines are adjuncts, never substitutes — steroids act too slowly for acute anaphylaxis. Repeat q5–15 min as needed.

Q12. A 6-year-old with septic shock has bounding pulses, flash capillary refill, and wide pulse pressure after fluids. The preferred vasoactive agent is: A) Epinephrine B) Dobutamine C) Dopamine D) Norepinephrine **Answer: D** — Bounding pulses, flash refill, and wide pulse pressure define warm (vasodilatory) shock with low SVR — norepinephrine is first-line. Epinephrine is for cold shock; dobutamine is an inotrope for cardiogenic/low-output states with normal-high SVR.

Q13. In DKA, potassium replacement should be withheld and rechecked when serum K^+ is: A) <3.3 mEq/L — start insulin immediately B) >5.2 mEq/L C) 4.0–5.0 mEq/L D) <5.5 mEq/L **Answer: B** — If K^+ >5.2 mEq/L, hold potassium supplementation and recheck; add 20–30 mEq/L K^+ to fluids once K^+ is 3.3–5.2 with urine output established. Insulin must NOT be started if K^+ <3.3 — replace potassium first, as insulin drives K^+ intracellularly and risks fatal arrhythmia.

Q14. A 5-year-old seizing for 25 minutes has received two doses of lorazepam without response. The next best step is: A) Third dose of lorazepam B) Immediate midazolam infusion without second-line agent C) Oral valproate D) Fosphenytoin 20 mg PE/kg IV or levetiracetam 40–60 mg/kg IV **Answer: D** — After adequate benzodiazepines fail, give a second-line agent: fosphenytoin 20 mg PE/kg IV (max 1500 mg PE) or levetiracetam 40–60 mg/kg IV. Only if this fails (refractory status) is a continuous midazolam infusion started in PICU with EEG monitoring.

Q15. The classic toxidrome of salivation, lacrimation, urination, defecation, GI cramps, and emesis (SLUDGE) with miosis and bronchorrhea indicates poisoning with: A) Organophosphates B) Tricyclic antidepressants C) Salicylates D) Carbon monoxide **Answer: A** — SLUDGE plus miosis, bronchorrhea/bronchospasm, bradycardia, and fasciculations is the cholinergic toxidrome of organophosphate (acetylcholinesterase inhibitor) poisoning. Treat with atropine (drying secretions as endpoint) plus pralidoxime for nicotinic weakness.

Q16. A 2-year-old with iron poisoning is now 10 hours post-ingestion, lethargic with metabolic acidosis after a period of apparent improvement. Serum iron is 650 mcg/dL. The indicated chelator and regimen is: A) Succimer orally B) Calcium EDTA C) Penicillamine D) Deferoxamine 15 mg/kg/hr IV infusion **Answer: D** — This is phase III iron toxicity (shock, acidosis after the deceptive latent phase II) with serum iron >500 mcg/dL — deferoxamine 15 mg/kg/hr IV is indicated. Succimer is for lead; EDTA is for lead encephalopathy (with dimercaprol). Vin-rose urine confirms chelation; prolonged infusion risks ARDS.

Q17. During the primary survey of a polytrauma child, the "D" in ABCDE stands for: A) Deformity assessment B) Definitive airway C) Disability — pediatric GCS, pupils, limb movement, glucose D) Donor blood cross-match **Answer: C** — D = Disability: rapid neurologic assessment using the pediatric GCS, pupillary response, lateralizing signs, and blood glucose (hypoglycemia mimics deterioration). GCS ≤8 mandates intubation. E = Exposure with temperature control to prevent the lethal triad.

Q18. The earliest clinical sign of shock in children, before hypotension develops, is: A) Tachycardia B) Hypotension C) Oliguria D) Altered sensorium **Answer: A** — Tachycardia is the earliest sign of compensated shock in children; hypotension is a late, pre-arrest sign. Other early markers include delayed capillary refill >2 sec, weak pulses, and mottled extremities. Management must begin on these clinical signs, not blood pressure.

Q19. A ventilated 4-year-old with PARDS should receive a tidal volume of: A) 10–12 mL/kg B) 6 mL/kg predicted body weight C) 15 mL/kg D) 4 mL/kg actual weight in all cases **Answer: B** — Lung-protective ventilation per ARDSnet/PALICC uses 6 mL/kg of predicted body weight, with PEEP titration, plateau pressure <28–30 cm H₂O, and permissive hypercapnia (pH ≥7.15–7.20). Higher tidal volumes cause volutrauma and worsen outcomes.

Q20. A child pulled from a swimming pool is apneic and pulseless. The correct first resuscitation action is: A) Abdominal thrusts to expel water B) Chest compressions only C) Attempt to drain water by hanging the child upside down D) Begin CPR starting with 5 rescue breaths **Answer: D** — Drowning resuscitation prioritizes ventilation: start with 5 rescue breaths (pediatric drowning algorithm), then standard CPR. Never waste time trying to expel water — abdominal thrusts and drainage maneuvers are ineffective and delay oxygenation. Hypoxia is the primary insult.

Q21. A 12-year-old in VF arrest receives a first unsynchronized shock. The correct energy sequence is: A) 2 J/kg then 4 J/kg B) 0.5–1 J/kg synchronized C) 50 J then 100 J D) 360 J monophasic **Answer: A** — Pediatric VF/

pulseless VT: unsynchronized defibrillation at 2 J/kg first shock, then 4 J/kg for subsequent shocks, with 2 minutes of CPR between and epinephrine 0.01 mg/kg q3–5 min. Synchronized 0.5–1 J/kg is for unstable tachycardia with a pulse.

Q22. Kerosene ingestion in a toddler: the correct advice is: A) Induce vomiting immediately B) Gastric lavage within 1 hour C) No emesis or lavage; supportive care and 6–8 hour observation D) Activated charcoal 1 g/kg

Answer: C — Hydrocarbon danger is aspiration causing chemical pneumonitis, not systemic absorption. Emesis, lavage, and charcoal all increase aspiration risk and are contraindicated. Manage supportively with oxygen and observe 6–8 hours; CXR changes appear at 6–12 hours.

Q23. Post-ROSC targeted temperature management in children primarily aims to: A) Cool to 32°C for all patients B) Induce hyperthermia to improve perfusion C) Actively prevent and treat fever, maintaining normothermia D)

Allow permissive hypothermia to 30°C **Answer: C** — The key proven principle is aggressive fever prevention/treatment after ROSC, as hyperthermia worsens neurologic injury. Maintain normothermia (or mild therapeutic hypothermia per protocol); never allow fever. Hyperoxia and hyperventilation should also be avoided.

Q24. A 3-year-old with lead encephalopathy and blood lead 95 mcg/dL requires: A) Oral succimer alone B) Dimercaprol + CaNa₂EDTA C) Observation and source removal only D) Hemodialysis

Answer: B — Lead encephalopathy or level >70 mcg/dL requires dimercaprol (BAL) plus CaNa₂EDTA — BAL is started first to avoid redistributing lead into the CNS. Succimer is for asymptomatic levels 45–69 mcg/dL; below 45, remove the source and monitor.

Q25. Before extubating a 5-year-old ventilated for pneumonia, the essential readiness criteria include: A) FiO₂ 0.8 with PEEP 12 and ongoing vasoactive support B) Successful spontaneous breathing trial, strong cough, manageable secretions, SpO₂ ≥94% on FiO₂ ≤0.4–0.5 C) Negative cuff leak test alone D) Extubation directly from full SIMV support **Answer: B** — Extubation readiness requires: resolving underlying disease, hemodynamic stability on minimal vasoactives, a passed spontaneous breathing trial (30–120 min on CPAP/PS), strong cough and gag with manageable secretions, and SpO₂ ≥94% on FiO₂ ≤0.4–0.5 with PEEP ≤5–8. High FiO₂/PEEP or vasoactive dependence (option A) means the child is not ready.

Genetics & Metabolic Disorders

Chapter 11: Genetics & Inborn Errors of Metabolism

Genetics and inborn errors of metabolism (IEM) are among the highest-yield chapters for NEET SS Pediatrics because they are pure pattern recognition — a urine odor, a lab triad, or an enzyme name is often enough to clinch the answer. Examiners love asking the deficient enzyme, the mutated gene, the discriminating metabolite (orotic acid, succinylacetone, very-long-chain fatty acids), and pedigree-based recurrence risks. Master the lab patterns first; the names follow.

Approach to a Suspected Inborn Error of Metabolism

- **Red flags:** parental consanguinity, unexplained sibling deaths or SIDS, recurrent vomiting/dehydration episodes, protein or food aversion, developmental regression after a normal interval, coarse facies/hepatosplenomegaly, unusual urine or body odor, cardiomyopathy, or cytopenias without obvious cause.
- **Catabolic triggers that unmask IEMs:** intercurrent infection, fasting, high-protein load, surgery, dehydration, and drugs such as valproate (inhibits urea cycle → hyperammonemia), steroids, and proline.
- **First-line labs in a metabolic crisis (draw before treatment):** blood ammonia (free-flowing sample, transported on ice, analyzed immediately), arterial blood gas, blood glucose, serum lactate, urine and blood ketones, plasma amino acids, urine organic acids, and acylcarnitine profile by tandem mass spectrometry.
- **Pattern reading is the exam skill:** hyperammonemia + normal anion gap + normal glucose = urea cycle disorder; hyperammonemia + high anion gap + ketosis = organic acidemia; hypoglycemia + absent ketones = fatty acid oxidation defect; hypoglycemia + lactic acidosis = glycogen storage disease type I.
- **Do not delay:** stop protein intake, give IV dextrose to halt catabolism, and arrange urgent hemodialysis access while labs are pending in a comatose hyperammonemic child.

Urea Cycle Disorders

- The urea cycle converts waste nitrogen to urea in periportal hepatocytes. Defects cause hyperammonemia with **normal anion gap, normal blood glucose, and low BUN** (urea is not being made). Respiratory alkalosis is classic (ammonia stimulates the medullary respiratory center).
- **OTC deficiency is the most common UCD** and the only X-linked one (Xp21.1, ornithine transcarbamylase). Females can be symptomatic because of skewed X-inactivation (lyonization). Presents in neonatal males with catastrophic hyperammonemia, or later in heterozygous females with protein aversion, cyclical vomiting, and confusion after protein loads.

- **Orotic acid discriminates the block:** elevated urinary orotic acid in OTC deficiency, citrullinemia (ASS1), and argininosuccinic aciduria (ASL) — because accumulated carbamoyl phosphate spills into pyrimidine synthesis. Orotic acid is **normal in CPS1 and NAGS deficiency** (carbamoyl phosphate is never formed).
- **CPS1 deficiency** (carbamoyl phosphate synthetase I): autosomal recessive, neonatal catastrophic course identical to OTC but no orotic aciduria.
- **Citrullinemia type I** (argininosuccinate synthetase, ASS1): markedly elevated plasma citrulline.
- **Argininosuccinic aciduria** (argininosuccinate lyase, ASL): elevated argininosuccinic acid; trichorrhexis nodosa (fragile hair) is a clue.
- **Arginase deficiency** (ARG1): the mildest and latest-presenting UCD — progressive spastic diplegia and developmental delay rather than neonatal coma; hyperargininemia.
- **NAGS deficiency** (N-acetylglutamate synthase): the only UCD treatable with a specific drug — **carglumic acid** (Carbaglu), a synthetic analogue of N-acetylglutamate, at 100–250 mg/kg/day in divided doses.

Acute hyperammonemia management (numbered steps)

1. **Stop all protein intake** immediately and stop catabolic triggers; do not wait for confirmatory labs.
2. **Reverse catabolism:** IV 10% dextrose at 8–10 mg/kg/min glucose infusion rate, plus IV lipids; correct dehydration and treat infection. Avoid prolonged fasting.
3. **Nitrogen scavenger drugs:** sodium benzoate **250 mg/kg/day** IV or oral in divided doses (conjugates glycine → hippurate); sodium phenylbutyrate/phenylacetate (conjugates glutamine); L-arginine supplementation (becomes essential; contraindicated in arginase deficiency).
4. **Hemodialysis (continuous venovenous hemodialysis/hemodialysis) is the treatment of choice for ammonia removal** — indicated for ammonia >400–500 $\mu\text{mol/L}$, encephalopathy, coma, or failure to respond to medical therapy. Peritoneal dialysis and exchange transfusion are ineffective.
5. **Carglumic acid** 100–250 mg/kg/day for suspected NAGS deficiency or hyperammonemia secondary to organic acidemias.
6. **Avoid** valproate, high-dose steroids, and proline; monitor ammonia, ABG, and electrolytes continuously. Long-term: protein-restricted diet with essential amino acid supplements and liver transplantation as definitive therapy for severe OTC/CPS1.

Organic Acidemias

- Organic acidemias present with **high anion gap metabolic acidosis, ketosis, hyperammonemia, neutropenia/thrombocytopenia, and developmental delay**. The combination of hyperammonemia with a high anion gap points here, not to a UCD.
- **Methylmalonic acidemia (MMA):** defective methylmalonyl-CoA mutase (MUT) or cobalamin cofactor synthesis (cblA, cblB, cblC, cblD). **B12-responsive forms** are treated with hydroxocobalamin; mutase-deficient (mut^0) forms are not. Presents with ketoacidosis, hyperammonemia, megaloblastic changes, and later chronic kidney disease and optic atrophy.

- **Propionic acidemia (PCC):** propionyl-CoA carboxylase deficiency. Same acidotic-hyperammonemic picture plus **pancytopenia and dilated cardiomyopathy/QT prolongation** — cardiomyopathy is the exam's favorite discriminator for propionic acidemia.
- **Isovaleric acidemia:** isovaleryl-CoA dehydrogenase deficiency; the hallmark is a "**sweaty feet**" odor from isovaleric acid. Acute neonatal ketoacidosis or chronic intermittent vomiting and developmental delay.
- **Maple syrup urine disease (MSUD):** branched-chain ketoacid dehydrogenase (BCKD) complex deficiency (BCKDHA, BCKDHB, DBT). **Burnt sugar / maple syrup odor** of urine and cerumen; **leucine is the neurotoxic amino acid** causing cerebral edema. Classic form presents day 4–7 with poor feeding, ketosis without acidosis, and opisthotonos. The **thiamine-responsive variant** is treated with high-dose thiamine (10–20 mg/kg/day); acute crises need dialysis and BCAA-free formulas.
- **Odor board (frequent one-liners):** sweaty feet = isovaleric acidemia; burnt sugar/maple syrup = MSUD; musty/mousy = PKU; boiled cabbage = tyrosinemia type 1; cat urine = 3-methylcrotonylglycinuria / multiple carboxylase deficiency.

Lysosomal Storage Disorders

- Lysosomal disorders are **progressive, with coarse facies, hepatosplenomegaly, skeletal dysplasia (dysostosis multiplex), and developmental regression** — but each has a discriminator. Enzyme replacement therapy (ERT) is available for several.

Sphingolipidoses and related disorders

- **Gaucher disease:** **GBA1** gene, deficient **glucocerebrosidase** (β -glucosidase) → glucosylceramide accumulation in macrophages ("Gaucher cells" — crumpled tissue-paper cytoplasm). **Type 1 (non-neuronopathic, most common):** massive splenomegaly, cytopenias, **Erlenmeyer flask deformity** of the distal femur, bone crises, and avascular necrosis. Types 2 and 3 are neuronopathic. **ERT: imiglucerase** (60 U/kg IV every 2 weeks); substrate reduction with miglustat/eliglustat for type 1.
- **Tay-Sachs disease:** **HEXA** gene, deficient **β -hexosaminidase A** → GM2 ganglioside accumulation. Ashkenazi Jewish ancestry; **cherry-red spot, exaggerated startle (hyperacusis)**, developmental regression, no hepatosplenomegaly (key contrast with Niemann-Pick and Gaucher).
- **Niemann-Pick A/B:** **SMPD1** gene, deficient **acid sphingomyelinase**; cherry-red spot plus hepatosplenomegaly; type A is neurodegenerative and fatal in early childhood, type B spares the brain.
- **Niemann-Pick type C:** **NPC1/NPC2** genes — a cholesterol trafficking defect, not an enzyme deficiency. Hallmark: **vertical supranuclear gaze palsy**, gelastic cataplexy, and ataxia. Treated with **miglustat** (substrate reduction).
- **Fabry disease:** **GLA** gene, deficient **α -galactosidase A, X-linked**. Childhood **acroparesthesia** (burning pain in hands/feet), **angiokeratomas, cornea verticillata**, GI cramping, then adult renal failure, LVH, and stroke. ERT: agalsidase alfa/beta.
- **Pompe disease (GSD II):** **GAA** gene, deficient **acid α -glucosidase** (acid maltase). Infantile form: **massive cardiomegaly, hypotonia ("floppy infant"), macroglossia, and short PR interval**; death by 1–2 years without treatment. Late-onset: limb-girdle weakness and respiratory failure. **ERT: alglucosidase alfa** 20 mg/kg IV every 2 weeks — the classic "enzyme replacement saves the heart" vignette.

Mucopolysaccharidoses (MPS)

- All MPS are autosomal recessive **except Hunter (MPS II), which is X-linked**. Defective glycosaminoglycan (GAG) degradation → dysostosis multiplex, coarse facies, joint stiffness (except Morquio — joint laxity), and corneal clouding (except Hunter and Sanfilippo).
- **MPS I Hurler: IDUA** (α -L-iduronidase); dermatan + heparan sulfate. Severe: coarse facies, corneal clouding, developmental delay, airway disease. **HSCT before age 2** is definitive; ERT laronidase is a bridge.
- **MPS II Hunter: IDS** (iduronate sulfatase), **X-linked**; like Hurler but **no corneal clouding**, with aggressive behavior.
- **MPS III Sanfilippo**: heparan sulfate only; severe neurodegeneration with mild somatic features — the "bad brain, mild body" MPS.
- **MPS IVA Morquio: GALNS**, keratan sulfate; **normal intelligence**, severe skeletal dysplasia with **atlantoaxial instability and odontoid hypoplasia** (anesthesia risk), joint laxity, corneal clouding.
- **MPS VI Maroteaux-Lamy: ARSB** (arylsulfatase B), dermatan sulfate; severe somatic disease with normal intelligence.

Galactosemia, PKU, and Tyrosinemia

- **Classic galactosemia: GALT** (galactose-1-phosphate uridylyltransferase) deficiency. After milk feeds: jaundice, hepatomegaly, vomiting, **cataract** (galactitol accumulation via aldose reductase), and **E. coli sepsis** — the neonatal sepsis-plus-cataract vignette. Urine shows **reducing substances positive with glucose oxidase negative**. Treatment: **lactose-free, soy-based formula** for life; despite diet, long-term risks include ovarian failure and developmental delay. The Duarte variant is benign.
- **Phenylketonuria (PKU): PAH** (phenylalanine hydroxylase) deficiency; phenylalanine cannot convert to tyrosine. **Musty/mousy odor, light pigmentation** (decreased melanin — tyrosine is a melanin precursor), eczema, and severe intellectual disability if untreated. Treatment: **low-phenylalanine diet** started in the first weeks of life; **sapropterin** (synthetic BH4 cofactor, 10–20 mg/kg/day) for BH4-responsive cases. **Maternal PKU**: high maternal phenylalanine is teratogenic (microcephaly, congenital heart disease, growth restriction) — target Phe <360 μ mol/L before conception.
- **Tyrosinemia type 1: FAH** (fumarylacetoacetase) deficiency; toxic metabolites (fumarylacetoacetate, **succinylacetone** — the diagnostic marker) cause liver failure, renal Fanconi syndrome, porphyria-like crises, and hepatocellular carcinoma. **Boiled-cabbage odor**. Treatment: **nitisnone (NTBC) 1 mg/kg/day** once daily plus low-tyrosine/low-phenylalanine diet; liver transplantation if unresponsive or with HCC. Type 2 (TAT deficiency) causes corneal ulcers and palmoplantar keratosis with normal liver.

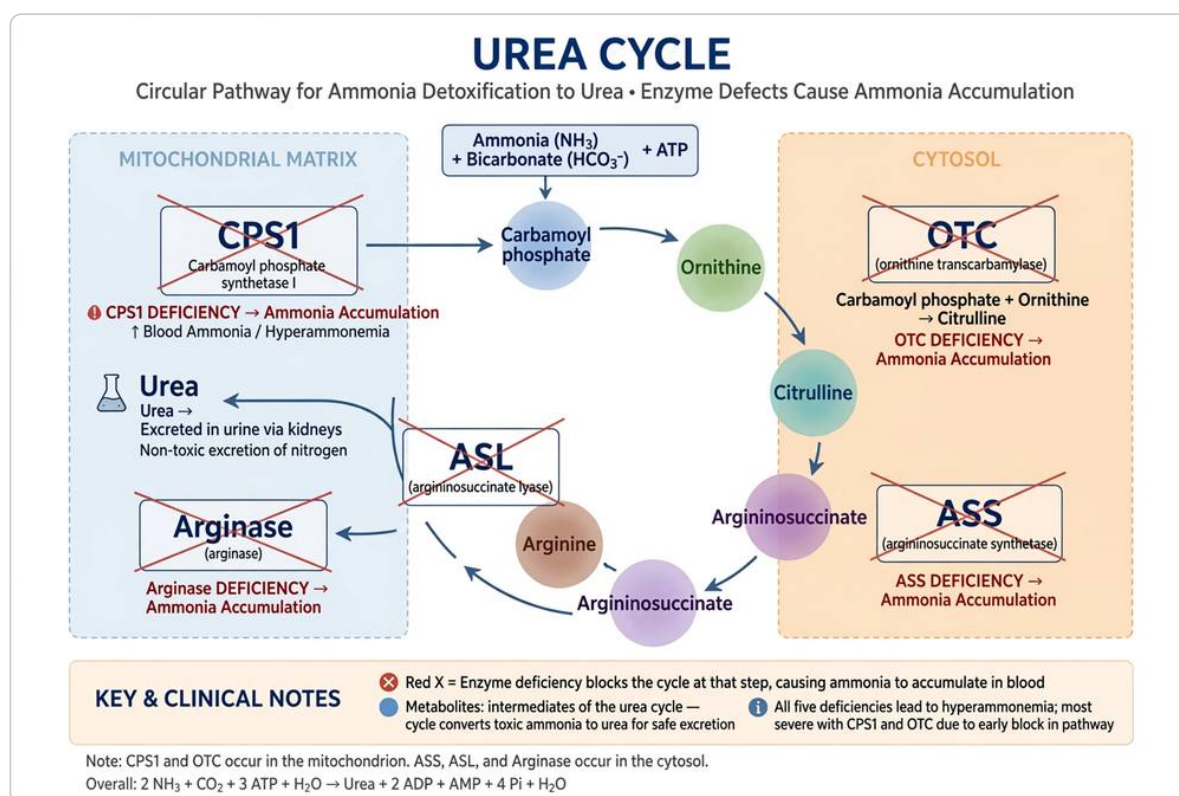


Figure 11.1 — Urea cycle and enzyme defect sites

Glycogen Storage Disorders

- **Type I von Gierke: G6PC** (glucose-6-phosphatase) deficiency — the final common step of glycogenolysis and gluconeogenesis. **Doll-like facies, massive hepatomegaly, severe fasting hypoglycemia with lactic acidosis, hyperuricemia (gout), and hypertriglyceridemia** (xanthomas, pancreatitis). Treatment: continuous glucose — **uncooked cornstarch** therapy; avoid fructose and galactose. Type Ib (SLC37A4, glucose-6-phosphate translocase) adds neutropenia and infections.
- **Type II Pompe:** covered above (GAA; cardiac + muscle).
- **Type III Cori/Forbes: AGL** (debrancher enzyme) deficiency; hepatomegaly and hypoglycemia like type I but milder, with progressive myopathy — the "liver plus muscle" GSD.
- **Type V McArdle: PYGM** (muscle phosphorylase/myophosphorylase) deficiency; exercise intolerance with cramps, **"second wind" phenomenon** (symptoms ease after brief rest as fatty acids take over), myoglobinuria, and markedly elevated CK. Forearm ischemic exercise test shows no lactate rise.
- **Exam shortcut:** hypoglycemia + lactic acidosis + hepatomegaly = GSD I; cardiomegaly + hypotonia = Pompe; second wind = McArdle.

Fatty Acid Oxidation Defects

- The signature is **hypoketotic hypoglycemia** — low glucose with inappropriately absent ketones — plus hepatomegaly, hyperammonemia, and Reye-like episodes during fasting or illness. **Fasting must be avoided;** illness needs emergency glucose polymer regimens.

- **MCAD deficiency (ACADM):** the **most common fatty acid oxidation defect**, picked up on newborn screening. Presents at 3–24 months with hypoketotic hypoglycemia, vomiting, and lethargy after a fast; sudden death is reported. Management is avoidance of fasting and carnitine during crises.
- **VLCAD deficiency (ACADVL):** neonatal cardiomyopathy and arrhythmias, or later exercise-induced rhabdomyolysis and myoglobinuria. Long-chain defects (VLCAD, CPT II, TFP) need low-long-chain-fat diets with medium-chain triglyceride supplementation.

Dysmorphology: High-Yield Syndromes

- **Down syndrome (trisomy 21): atrioventricular septal defect (AV canal)** — the most characteristic cardiac lesion; **duodenal atresia** (double bubble), Hirschsprung disease, atlantoaxial instability, and markedly increased risk of **transient myeloproliferative disorder (TMD)** and AML/ALL. Maternal age is the risk factor; first-trimester screening uses nuchal translucency + PAPP-A + free β -hCG.
- **Turner syndrome (45,X0):** short stature (SHOX haploinsufficiency), webbed neck, shield chest, **coarctation of the aorta**, streak gonads with primary amenorrhea, and normal intelligence. Give growth hormone; estrogen replacement at puberty.
- **Noonan syndrome: PTPN11** (RASopathy), autosomal dominant. **Pulmonary valve stenosis** (most common cardiac lesion), hypertrophic cardiomyopathy, webbed neck, short stature, and bleeding diathesis — a Turner-like phenotype with a normal karyotype.
- **Williams syndrome: 7q11.23 microdeletion** involving **ELN** (elastin). **Supravalvular aortic stenosis**, elfin facies, infantile hypercalcemia, and the classic "**cocktail-party**" **speech** — overly friendly, loquacious personality.
- **Marfan syndrome: FBN1** (fibrillin-1), autosomal dominant. **Aortic root dilatation/dissection**, **ectopia lentis displaced upward (superotemporal)**, arachnodactyly, pectus deformity. Contrast **homocystinuria**: lens displaced **downward**, intellectual disability, marfanoid habitus, thromboembolism.
- **Achondroplasia: FGFR3** (G380R), autosomal dominant, ~80% de novo. Rhizomelic dwarfism, frontal bossing, **trident hand**, normal intelligence; monitor for foramen magnum stenosis. The lethal counterpart is thanatophoric dysplasia (also FGFR3).

Inheritance Patterns, Pedigrees, and Recurrence Risks

- **Autosomal dominant:** 50% recurrence risk; vertical transmission, both sexes affected. Examples: achondroplasia, Marfan, Noonan, neurofibromatosis.
- **Autosomal recessive:** 25% recurrence risk for each pregnancy regardless of prior children; consanguinity raises risk. Most IEMs (all UCDs except OTC, all organic acidemias, PKU, galactosemia, Tay-Sachs, Gaucher, all MPS except Hunter).
- **X-linked recessive:** affected father → all daughters are carriers, no sons affected; carrier mother → 50% of sons affected, 50% of daughters carriers. Examples: OTC deficiency (functionally X-linked dominant — heterozygous females can be symptomatic), Hunter syndrome, Fabry, Duchenne muscular dystrophy.
- **X-linked dominant:** affected father → all daughters affected, no sons affected. Example: incontinentia pigmenti (lethal in males).

- **Mitochondrial:** strictly **maternal inheritance** — all children of an affected mother inherit the mutation, none of an affected father's. **Heteroplasmy** (mix of mutant and normal mtDNA) and the **threshold effect** explain variable severity. Examples: MELAS (m.3243A>G), MERFF, LHON.
- **Imprinting:** the same deletion has different phenotypes by parent of origin — 15q11-13 paternal deletion = Prader-Willi, maternal deletion = Angelman.
- **Hardy–Weinberg one-liner:** carrier frequency $\approx 2q$ when q^2 is the disease incidence (used for Tay-Sachs and cystic fibrosis risk questions).

Newborn Screening

- **Tandem mass spectrometry (MS/MS)** on a dried blood spot (day 2–5 of life) screens amino acid disorders (PKU, MSUD), organic acidemias (MMA, propionic, isovaleric), fatty acid oxidation defects (MCAD, VLCAD), and some UCDs (citrullinemia, argininosuccinic aciduria) in a single run via acylcarnitine and amino acid profiles.
- Disorders needing separate assays: **galactosemia** (GALT enzyme activity), congenital hypothyroidism (TSH), congenital adrenal hyperplasia (17-OHP), G6PD, and cystic fibrosis (IRT).
- A positive screen is never diagnostic — confirm with plasma amino acids, urine organic acids, enzyme assay, or molecular testing before counseling the family.

Leukodystrophies (lysosomal white-matter disorders — frequent distractors)

- **Krabbe disease:** **GALC** (galactocerebrosidase) deficiency → psychosine accumulation; **globoid cells** on biopsy. Irritable infant with hypertonia, optic atrophy, and peripheral neuropathy; HSCT helps only if done presymptomatically.
- **Metachromatic leukodystrophy (MLD):** **ARSA** (arylsulfatase A) deficiency → sulfatide accumulation; developmental regression with peripheral neuropathy; **metachromatic granules** in urine. Late-infantile form is most common.
- **X-linked adrenoleukodystrophy (X-ALD):** **ABCD1** gene — defective very-long-chain fatty acid (VLCFA) transport into peroxisomes → **elevated plasma VLCFA (C26:0)**. Boys develop adrenal insufficiency plus progressive demyelination; **Lorenzo's oil** and HSCT are options early. This is a peroxisomal, not lysosomal, disorder — a favorite exam trap.

Two more organic acidemias examiners love

- **Glutaric aciduria type 1:** **GCDH** (glutaryl-CoA dehydrogenase) deficiency. **Macrocephaly** at birth, then acute striatal injury during febrile illness → dystonia/dyskinesia. Treated with lysine-restricted diet and carnitine; encephalopathic crises need aggressive anti-catabolic therapy.
- **Multiple carboxylase deficiency (biotinidase/holocarboxylase synthetase):** presents with **seborrheic dermatitis/alopecia, ataxia, ketolactic acidosis, and organic aciduria** — dramatically responsive to **biotin** supplementation. The "rash + acidosis = try biotin" vignette.

MENDELIAN INHERITANCE — PEDIGREE CHARTS

Four common inheritance patterns shown with standard pedigree notation

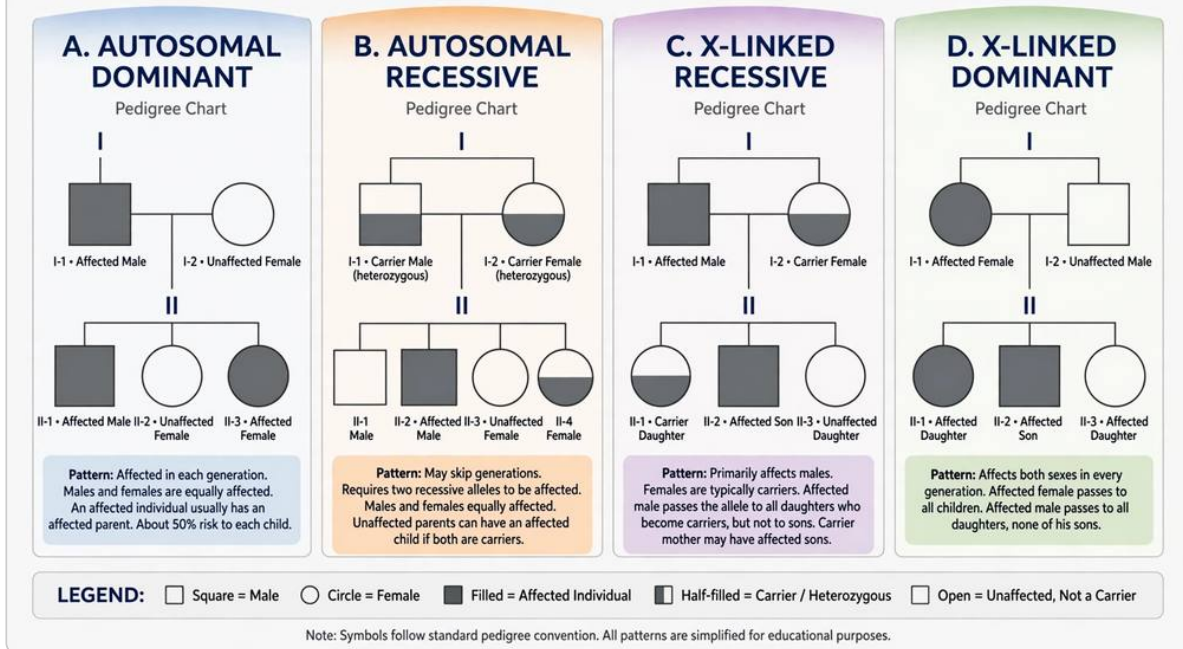


Figure 11.2 — Mendelian inheritance patterns

Mitochondrial Disorders and Imprinting

- **Mitochondrial inheritance is strictly maternal**; all children of an affected mother inherit the mutation. **Heteroplasmy** (variable mutant load across tissues) and the **threshold effect** explain why severity differs between siblings.
- **MELAS: m.3243A>G** — mitochondrial encephalomyopathy, **lactic acidosis, and stroke-like episodes** (that do not respect vascular territories); treated acutely with arginine.
- **MERRF**: myoclonic epilepsy with **ragged-red fibers** on muscle biopsy.
- **LHON**: painless bilateral optic atrophy in young males (maternal inheritance despite male predominance).
- Muscle biopsy showing **ragged-red fibers** (Gomori trichrome) and elevated lactate/pyruvate ratio point to mitochondrial disease; coenzyme Q10, riboflavin, and carnitine are supportive.
- **Imprinting (parent-of-origin effect)**: 15q11-13 **paternal deletion** → **Prader-Willi** (neonatal hypotonia, hyperphagia/obesity, short stature); **maternal deletion** → **Angelman** (severe intellectual disability, ataxic "happy puppet" gait, inappropriate laughter, seizures). **Beckwith-Wiedemann** (11p15, paternal uniparental disomy) causes macrosomia, macroglossia, omphalocele, and Wilms tumor risk.

Purine and Pyrimidine Disorders (short but testable)

- **Lesch-Nyhan syndrome: HPRT1** (hypoxanthine-guanine phosphoribosyltransferase), **X-linked recessive**. Purine salvage failure → uric acid overproduction with **self-mutilation (lip/finger biting)**, **dystonia**,

choreoathetosis, and intellectual disability; gouty tophi and urate nephrolithiasis. Allopurinol controls hyperuricemia but not the neurobehavioral features.

- **Adenosine deaminase (ADA) deficiency**: autosomal recessive; the most common cause of **SCID** in some series — lymphopenia with absent tonsils and thymic shadow. Treated with PEG-ADA enzyme replacement, HSCT, or gene therapy.
- **Orotic aciduria (UMP synthase deficiency)**: megaloblastic anemia unresponsive to B12/folate with orotic acid crystalluria; treated with uridine.

Pedigree Worked Examples

- **Worked example 1 (X-linked)**: A woman whose brother died of OTC deficiency in the neonatal period is a obligate or possible carrier. With a normal partner, each son has a 50% risk of being affected and each daughter a 50% risk of being a carrier. If she has 4 sons and all are healthy, her posterior carrier probability falls — but molecular testing of OTC is definitive and preferred over pedigree math in the exam.
- **Worked example 2 (autosomal recessive with consanguinity)**: First-cousin parents with one child with Tay-Sachs ask about prenatal diagnosis for the next pregnancy. Recurrence risk is 25%; offer chorionic villus sampling with HEXA enzyme assay or targeted mutation analysis (the 4-bp insertion in exon 11 is common in Ashkenazi Jews).
- **Worked example 3 (mitochondrial)**: A mother with MELAS (m.3243A>G) asks about risk to children: essentially 100% will inherit the mutation, but clinical severity is unpredictable because of heteroplasmy — counsel on variable expressivity, not on a fixed percentage.
- **Exam traps**: a "dominant" pedigree with male-to-male transmission rules out X-linkage; pseudodominance (affected child of an affected parent in AR disease) occurs with consanguinity or high carrier frequency; new mutations explain sporadic achondroplasia and Marfan with unaffected parents.

Rapid-Fire Lab Patterns (revise the night before)

- Hyperammonemia + normal anion gap + normal glucose + low BUN → **urea cycle disorder**; add elevated orotic acid → OTC/citrullinemia/ASA; normal orotic acid → CPS1/NAGS.
- Hyperammonemia + high anion gap + ketosis + cytopenias → **organic acidemia** (MMA/propionic/isovaleric).
- Hypoglycemia + absent ketones → **fatty acid oxidation defect** (MCAD); hypoglycemia + lactic acidosis → **GSD I**.
- Cherry-red spot + no organomegaly + hyperacusis → **Tay-Sachs**; cherry-red spot + hepatosplenomegaly → **Niemann-Pick A/B**.
- Corneal clouding + dysostosis multiplex → **MPS** (all except Hunter have clouding; Hunter is X-linked).
- Vertical gaze palsy → **Niemann-Pick C**; angiokeratomas + acroparesthesia → **Fabry**; Erlenmeyer flask femur → **Gaucher**; massive cardiomegaly in a floppy infant → **Pompe**.
- Reducing substances positive / glucose oxidase negative → **galactosemia**; musty odor → **PKU**; sweaty feet → **isovaleric acidemia**; burnt sugar → **MSUD**; boiled cabbage + succinylacetone → **tyrosinemia type 1**.

- Elevated VLCFA → **X-ALD**; elevated C8 acylcarnitine → **MCAD**; elevated C5 → **isovaleric acidemia**; elevated C3 → **propionic/MMA**.

Practice MCQs

Q1. A 3-day-old term male neonate becomes lethargic and refuses feeds 24 hours after birth, progressing to coma. Labs: ammonia 1200 $\mu\text{mol/L}$, normal anion gap, normal glucose, BUN low, urinary orotic acid markedly elevated. Which enzyme is most likely deficient? A) Carbamoyl phosphate synthetase I B) Ornithine transcarbamylase C) Argininosuccinate synthetase D) N-acetylglutamate synthase **Answer: B** — Catastrophic neonatal hyperammonemia with normal anion gap/glucose and elevated orotic acid is classic OTC deficiency, the most common and only X-linked UCD. CPS1 and NAGS deficiency have normal orotic acid; citrullinemia would show markedly elevated plasma citrulline.

Q2. A 6-month-old with developmental regression, exaggerated startle response to sound, and a cherry-red spot on funduscopy is brought for evaluation. There is no hepatosplenomegaly. The deficient enzyme is: A) Acid sphingomyelinase B) Glucocerebrosidase C) β -hexosaminidase A D) α -galactosidase A **Answer: C** — Tay-Sachs disease (HEXA, β -hexosaminidase A) presents with regression, hyperacusis/exaggerated startle, and cherry-red spot without organomegaly. Niemann-Pick A/B also has cherry-red spot but with hepatosplenomegaly.

Q3. A 10-day-old infant on breastfeeds develops jaundice, hepatomegaly, vomiting, and bilateral cataracts, and blood culture grows *E. coli*. Urine is positive for reducing substances but negative on glucose oxidase testing. The treatment of choice is: A) Low-phenylalanine diet B) Nitisone and low-tyrosine diet C) Uncooked cornstarch therapy D) Lactose-free soy-based formula **Answer: D** — Classic galactosemia (GALT deficiency): cataract from galactitol, *E. coli* sepsis, and reducing substances with negative glucose oxidase. Management is lifelong lactose-free, soy-based formula.

Q4. A 2-year-old boy has coarse facies, corneal clouding, dysostosis multiplex, hepatosplenomegaly, and developmental delay. His maternal uncle had similar features. The most likely diagnosis is: A) Hurler syndrome B) Sanfilippo syndrome C) Morquio syndrome D) Hunter syndrome **Answer: D** — Hunter syndrome (MPS II, IDS deficiency) is the only X-linked MPS — hence the affected maternal uncle. It resembles Hurler but characteristically lacks corneal clouding; here the vignette's X-linked pedigree is the discriminator.

Q5. A neonate with hyperammonemia (900 $\mu\text{mol/L}$), high anion gap metabolic acidosis, ketosis, and neutropenia is most likely to have: A) OTC deficiency B) Propionic acidemia C) CPS1 deficiency D) MCAD deficiency **Answer: B** — Hyperammonemia combined with high anion gap acidosis, ketosis, and cytopenias defines the organic acidemias; propionic acidemia is the prototype. UCDs have normal anion gap and normal glucose, while MCAD causes hypoketotic hypoglycemia without acidosis.

Q6. Which of the following statements about urea cycle disorders is FALSE? A) OTC deficiency is the most common UCD B) Orotic acid is elevated in OTC deficiency C) Hemodialysis is the treatment of choice for ammonia removal D) CPS1 deficiency presents with elevated urinary orotic acid **Answer: D** — Orotic acid is normal in CPS1 (and NAGS) deficiency because carbamoyl phosphate is never formed; it is elevated in OTC, citrullinemia, and argininosuccinic aciduria where carbamoyl phosphate accumulates.

Q7. A 4-year-old boy presents with burning pain in his hands and feet, clusters of dark red skin papules over his trunk, and cornea verticillata on slit-lamp examination. The deficient enzyme is: A) α -galactosidase A B) Acid α -glucosidase C) Arylsulfatase B D) α -L-iduronidase **Answer: A** — Fabry disease (GLA, X-linked): childhood acroparesthesia, angiokeratomas, and cornea verticillata, progressing to renal failure and LVH in adulthood.

Q8. A 5-day-old neonate has poor feeding, a burnt-sugar odor to the urine, ketosis without significant acidosis, and increasing opisthotonos. The neurotoxic amino acid in this disorder is: A) Phenylalanine B) Tyrosine C) Leucine D) Methionine **Answer: C** — Maple syrup urine disease (BCKD deficiency): burnt-sugar/maple-syrup odor, and leucine is the neurotoxic branched-chain amino acid causing cerebral edema.

Q9. A child with massive splenomegaly, pancytopenia, bone pain, and an Erlenmeyer flask deformity of the distal femur is diagnosed with Gaucher disease. The specific treatment is: A) Imiglucerase enzyme replacement B) Miglustat only C) Hematopoietic stem cell transplantation D) Sodium benzoate **Answer: A** — Gaucher type 1 (glucocerebrosidase deficiency) is treated with enzyme replacement therapy, imiglucerase 60 U/kg IV every 2 weeks. HSCT is the definitive therapy for Hurler, not Gaucher.

Q10. A 3-month-old "floppy infant" has marked cardiomegaly on chest X-ray, macroglossia, hypotonia, and a short PR interval on ECG. The definitive treatment is: A) Liver transplantation B) Alglucosidase alfa C) Carglumic acid D) High-dose thiamine **Answer: B** — Infantile Pompe disease (GAA, acid α -glucosidase deficiency): cardiomegaly, hypotonia, macroglossia. ERT with alglucosidase alfa 20 mg/kg every 2 weeks dramatically improves cardiac outcomes.

Q11. A newborn screening report shows elevated phenylalanine with normal tyrosine. The infant has a musty body odor and lighter pigmentation than siblings. The teratogenic risk if this condition is uncontrolled in a future pregnancy includes: A) Neural tube defects B) Limb reduction defects C) Renal agenesis D) Microcephaly and congenital heart disease **Answer: D** — PKU (PAH deficiency): musty odor, hypopigmentation. Maternal PKU syndrome causes microcephaly, congenital heart disease, and growth restriction; maternal Phe must be kept <360 μ mol/L preconception.

Q12. A 2-year-old with doll-like facies, massive hepatomegaly, fasting hypoglycemia, lactic acidosis, hyperuricemia, and hypertriglyceridemia most likely has deficiency of: A) Debrancher enzyme B) Muscle phosphorylase C) Glucose-6-phosphatase D) Acid maltase **Answer: C** — Glycogen storage disease type I von Gierke (G6PC): doll-like facies, hepatomegaly, hypoglycemia with lactic acidosis, hyperuricemia, hypertriglyceridemia. Treated with uncooked cornstarch.

Q13. A 14-year-old complains of exercise-induced muscle cramps and dark urine after football; symptoms ease if he rests briefly and resumes ("second wind"). CK is markedly elevated. The deficient enzyme is: A) Myophosphorylase B) Phosphofructokinase C) Carnitine palmitoyltransferase II D) Acid α -glucosidase **Answer: A** — McArdle disease (GSD V, PYGM myophosphorylase deficiency): exercise intolerance, second-wind phenomenon, myoglobinuria, high CK; forearm ischemic test shows no lactate rise.

Q14. An 18-month-old develops vomiting, lethargy, and hypoglycemia (28 mg/dL) with absent urinary ketones after a 12-hour fast during gastroenteritis. Ammonia is mildly elevated. The most likely diagnosis is: A) GSD type I B) MCAD deficiency C) MSUD D) Propionic acidemia **Answer: B** — Hypoketotic hypoglycemia after fasting is the hallmark of fatty acid oxidation defects; MCAD (ACADM) is the most common, presenting at 3–24 months. GSD I would show lactic acidosis; organic acidemias show ketoacidosis.

Q15. A 6-year-old girl has short stature, normal intelligence, severe kyphoscoliosis, odontoid hypoplasia with atlantoaxial instability, corneal clouding, and joint laxity. Urinary keratan sulfate is elevated. The diagnosis is: A) Hurler syndrome B) Maroteaux-Lamy syndrome C) Hunter syndrome D) Morquio syndrome **Answer: D** — MPS IVA Morquio (GALNS deficiency): keratan sulfate excretion, normal intelligence, severe skeletal dysplasia with atlantoaxial instability, joint laxity (unlike other MPS with stiff joints).

Q16. A neonate in hyperammonemic coma has ammonia 1100 $\mu\text{mol/L}$ refractory to dextrose and sodium benzoate. The most effective method of ammonia removal is: A) Exchange transfusion B) Peritoneal dialysis C) Hemodialysis D) Forced alkaline diuresis **Answer: C** — Hemodialysis (continuous venovenous hemodialysis/hemodialysis) is the treatment of choice for ammonia removal in severe or refractory hyperammonemia; peritoneal dialysis and exchange transfusion are ineffective.

Q17. A child with developmental regression, vertical supranuclear gaze palsy, gelastic cataplexy, and mild hepatosplenomegaly is most likely to have a defect in: A) SMPD1 B) GBA1 C) NPC1 D) HEXA **Answer: C** — Niemann-Pick type C (NPC1/NPC2 cholesterol trafficking defect): vertical gaze palsy is pathognomonic, with gelastic cataplexy and ataxia. Treated with miglustat.

Q18. Parents who are both carriers of an autosomal recessive IEM ask about the risk in their next pregnancy after having one affected child. The correct recurrence risk is: A) 10% B) 25% C) 50% D) 100% **Answer: B** — Autosomal recessive recurrence risk is 25% for each pregnancy, independent of previous outcomes. Consanguinity increases the prior probability of carrier status but not the 25% figure once both are known carriers.

Q19. A woman with OTC deficiency (heterozygous, symptomatic) and a normal husband ask about their children. Which statement is correct? A) All sons will be affected B) No daughters can be affected C) All daughters will be symptomatic D) 50% of sons affected, 50% of daughters are carriers **Answer: D** — X-linked inheritance: a carrier mother transmits the mutation to 50% of sons (affected) and 50% of daughters (carriers, who may be symptomatic due to lyonization). An affected father would give the mutation to all daughters.

Q20. A 3-year-old boy has developmental delay, self-mutilation, dystonia, and hyperuricemia with gouty tophi. The enzyme defect and inheritance are: A) HGPRT deficiency, X-linked recessive B) Adenosine deaminase deficiency, autosomal recessive C) Glucose-6-phosphatase deficiency, autosomal recessive D) Fumarylacetoacetase deficiency, autosomal recessive **Answer: A** — Lesch-Nyhan syndrome (HGPRT1, hypoxanthine-guanine phosphoribosyltransferase, X-linked recessive): self-mutilation, dystonia, hyperuricemia from purine overproduction.

Q21. A neonate presents with liver failure, renal Fanconi syndrome, and a boiled-cabbage odor; succinylacetone is detected in urine. The specific drug treatment (dose) is: A) Nitisinone 1 mg/kg/day B) Carglumic acid 100 mg/kg/day C) Sapropterin 20 mg/kg/day D) Sodium benzoate 250 mg/kg/day **Answer: A** — Tyrosinemia type 1 (FAH deficiency): succinylacetone is diagnostic; nitisinone (NTBC) 1 mg/kg/day once daily plus low-tyrosine/phenylalanine diet prevents liver failure and HCC.

Q22. A 1-week-old with poor feeding has a "sweaty feet" odor, severe ketoacidosis, and hyperammonemia. Tandem MS shows elevated C5 acylcarnitine. The deficient enzyme is: A) Propionyl-CoA carboxylase B) Methylmalonyl-CoA mutase C) Branched-chain ketoacid dehydrogenase D) Isovaleryl-CoA dehydrogenase

Answer: D — Isovaleric acidemia: sweaty-feet odor, C5 (isovalerylcarnitine) elevation on acylcarnitine profile. Propionic acidemia shows C3 elevation; MSUD shows elevated leucine/isoleucine.

Q23. A 16-year-old tall boy with arachnodactyly, pectus excavatum, aortic root dilatation (45 mm), and upward lens dislocation is counseled. The mutated gene and most feared complication are: A) FBN1; aortic dissection B) COL3A1; arterial rupture C) TGFBR1; hypertrophic cardiomyopathy D) ELN; supraaortic stenosis

Answer: A — Marfan syndrome (FBN1, fibrillin-1, AD): upward (superotemporal) lens dislocation, aortic root aneurysm with risk of dissection — the leading cause of death.

Q24. A child of consanguineous parents has coarse facies, hepatosplenomegaly, and developmental regression. Urinary glycosaminoglycans show excess dermatan and heparan sulfate; enzyme assay confirms α -L-iduronidase deficiency. Definitive therapy if diagnosed before age 2 is: A) Imiglucerase B) Hematopoietic stem cell transplantation C) Miglustat D) Laronidase alone **Answer: B** — Hurler syndrome (MPS I, IDUA): HSCT before age 2 halts neurocognitive decline and is definitive; laronidase ERT does not cross the blood–brain barrier adequately and serves as a bridge.

Q25. A newborn screen by tandem mass spectrometry is reported as "increased C8 acylcarnitine." Parents are advised that during any intercurrent illness the child must: A) Fast for 12 hours to clear metabolites B) Avoid all fats permanently C) Receive emergency glucose polymer feeds and avoid fasting D) Start a low-phenylalanine diet **Answer: C** — Elevated C8 (octanoylcarnitine) indicates MCAD deficiency; the cornerstone of management is avoidance of fasting with emergency glucose polymer regimens during illness to prevent hypoketotic hypoglycemia.

Developmental & Behavioral Pediatrics

Chapter 12: Developmental & Behavioral Pediatrics

Developmental-behavioral pediatrics is disproportionately high-yield for NEET SS: every paper carries questions on milestone red flags, DSM-5 diagnostic criteria (autism, ADHD), screening tools (M-CHAT, Denver-II, Vanderbilt), and first-line pharmacology (stimulants, desmopressin, risperidone). The questions test precision — exact ages, exact criterion counts, exact drug indications — so this chapter is built around numbers, criteria, and differentials rather than narrative prose. Memorize the red-flag ages first; everything else hangs on them.

Autism Spectrum Disorder

- **DSM-5 (single unified diagnosis):** persistent deficits in **social communication and social interaction** across contexts (criterion A — all three subdomains: social-emotional reciprocity, nonverbal communicative behaviors used for interaction, developing/maintaining/understanding relationships) **PLUS restricted, repetitive patterns of behavior, interests, or activities** (criterion B — at least 2 of 4: stereotyped/repetitive speech or motor movements, insistence on sameness/ritualized behavior, highly restricted fixated interests, hyper-/hyporeactivity to sensory input). Symptoms present in early developmental period and cause clinically significant impairment; not better explained by intellectual disability or global developmental delay.
- **Severity levels (the specifiers asked in exams):** **Level 1** — requiring support; **Level 2** — requiring substantial support; **Level 3** — requiring very substantial support. Severity is rated separately for social communication and for restricted repetitive behaviors. Note: specifiers also include "with/without accompanying intellectual impairment" and "with/without accompanying language impairment" — a favorite trap.
- **Early red flags (memorize as 12-14-16-loss):** no babbling by **12 months**; no pointing (or other gestures) by **14 months**; no meaningful single words by **16 months**; **any loss of language or social skills at any age** = referral-worthy regression. Additional flags: no response to name, poor eye contact, lack of joint attention/protodeclarative pointing, echolalia, toe-walking, hand-flapping.
- **Screening: M-CHAT** (Modified Checklist for Autism in Toddlers) at **18 and 24 months** in well-child surveillance; positive M-CHAT requires the **M-CHAT-R/F follow-up interview** before referral — a classic screening-logic question. Definitive diagnosis uses structured tools (**ADOS-2**, **ADI-R**) by a multidisciplinary team; there is no laboratory "autism test."
- **Management — numbered principles:**
- **Early intensive behavioral intervention (EIBI)** is the cornerstone — **Applied Behavior Analysis (ABA)** and related models (ESDM — Early Start Denver Model). Earlier and more intensive (20–40 hours/week) = better language and adaptive outcomes.

- Speech-language therapy and occupational therapy for communication and sensory issues; special education supports.
- **Pharmacotherapy treats associated symptoms, not the core disorder: risperidone and aripiprazole** are the two FDA-approved agents in autism — approved **only for irritability, aggression, and self-injury**, not for social deficits or repetitive behaviors. Monitor weight, metabolic parameters, prolactin, and EPS with antipsychotics.
- Treat comorbidities: ADHD symptoms (stimulants/atomoxetine with caution), anxiety, sleep disturbance (melatonin), epilepsy (screening EEG only if indicated, not routine).
- **Genetics to know:** recurrence risk in siblings ~10–20%; higher concordance in monozygotic twins. Fragile X is the single most common identified monogenic cause — test when autism coexists with intellectual disability.
- **Differential:**
 - **Rett syndrome** — X-linked dominant, **MECP2** mutation; classically girls with apparently normal early development, then **regression at 6–18 months**, loss of purposeful hand use, **hand-wringing/washing stereotypies**, acquired microcephaly, breathing abnormalities. Regression + hand stereotypies + female = Rett.
 - **Heller syndrome (Childhood Disintegrative Disorder, CDD)** — older DSM-IV entity: **profound regression after at least 2 years of completely normal development**, affecting multiple domains (language, social, bowel/bladder, play, motor). Normal-then-regression AFTER age 2 across many domains distinguishes CDD from autism (earlier onset) and Rett (girls, hand-wringing).
 - Social communication disorder (no restricted repetitive behaviors), selective mutism, hearing loss, severe neglect/deprivation.
 - **Prognosis predictors:** early language acquisition and IQ are the strongest predictors of adult independence; ~15% achieve independent living.

Attention-Deficit/Hyperactivity Disorder

- **DSM-5 criteria (counted, not guessed): ≥6 symptoms** from the inattentive list and/or **≥6 symptoms** from the hyperactive-impulsive list (≥5 for age ≥17). Symptoms present for **≥6 months, onset before 12 years**, present in **≥2 settings** (home + school — hence collateral from teachers), and cause functional impairment not better explained by another disorder. Exam trap: parent report alone is insufficient without a second setting.
- **Presentations (DSM-5 term; "subtypes" is the older DSM-IV word): predominantly inattentive, predominantly hyperactive-impulsive, combined.** Girls more often present as inattentive ("daydreamy") and are underdiagnosed.
- **Rating scales: Vanderbilt** (covers DSM symptoms + screens comorbid ODD, conduct disorder, anxiety/depression — the exam favorite because it captures comorbidities), **Conners** (widely validated, shorter forms). Scales support, not replace, clinical diagnosis.
- **Treatment — numbered steps:**
 - **Stimulants are first-line** for school-age children: **methylphenidate** (most exam-tested), mixed amphetamine salts. Dosing principles: start low, titrate weekly to effect; monitor weight, height, blood pressure, heart rate;

document baseline tics and cardiac history (sudden cardiac death risk is population-level, but a cardiac review of systems/family history is required — routine ECG only if indicated).

- **Atomoxetine** (selective norepinephrine reuptake inhibitor): non-stimulant, first-line when there is **active substance-use risk, severe anxiety, or tics worsened by stimulants**; takes weeks for full effect; warn about hepatotoxicity and suicidal ideation (black-box style warning).
- **Alpha-2 agonists — extended-release guanfacine and clonidine**: useful as monotherapy or **adjuncts to stimulants**, particularly with **tics/Tourette or severe hyperactivity/impulsivity**; monitor for sedation, hypotension, bradycardia; never stop abruptly (rebound hypertension).
- Behavioral parent training is first-line for preschoolers (4–5 years); stimulants (methylphenidate) only if behavior therapy fails.
- **Stimulant side effects (the exam list)**: **decreased appetite/weight loss**, insomnia, headache, abdominal pain; **worsening or unmasking of tics**; **growth deceleration** (~1–2 cm over 2 years, usually recovers with drug holidays — monitored on growth charts); mood lability/rebound; rare psychosis; misuse/diversion risk with short-acting preparations (long-acting formulations preferred).
- **Comorbidities to screen**: oppositional defiant disorder, conduct disorder, learning disabilities (~30–50% overlap — always evaluate academics), anxiety, depression, sleep-disordered breathing.
- **Natural history**: hyperactivity wanes with age; inattention persists into adulthood in ~50–60%.

Cerebral Palsy

- **Definition**: a group of **nonprogressive** disorders of movement and posture due to a lesion in the developing brain (injury before, during, or shortly after birth). The lesion is static; the **clinical picture changes** as the child grows (spasticity patterns evolve, contractures develop). Any "progressive" course = not CP — investigate metabolic/genetic disease.
- **Types (etiology-linked — the exam maps type to cause)**:
 - **Spastic diplegia** (legs >> arms): classic of **prematurity**; lesion = **periventricular leukomalacia (PVL)** injuring descending corticospinal fibers to the legs. Scissoring gait; often walks with aids; cognition frequently normal.
 - **Spastic hemiplegia** (one side, arm > leg): **focal perinatal stroke** (middle cerebral artery territory); may have early hand preference (a red flag before 12 months — handedness should not appear before ~18 months), seizures, and later epilepsy.
 - **Dyskinetic (athetoid/dystonic) CP**: **basal ganglia/thalamus injury** — classic cause **kernicterus** (severe neonatal hyperbilirubinemia) and severe hypoxic-ischemic encephalopathy; involuntary writhing movements, abnormal postures; speech often impaired but cognition may be relatively spared.
 - **Ataxic CP**: cerebellar injury; uncommon; wide-based gait, intention tremor, hypotonia.
- Mixed forms exist (spastic-dyskinetic is common in severe HIE).
- **GMFCS (Gross Motor Function Classification System) — levels I–V (memorize functional anchors)**:
 - **I**: walks without limitations (may have minor deficits in speed/balance).
 - **II**: walks with limitations (difficulty on uneven surfaces, stairs; no device needed indoors).
 - **III**: walks using a hand-held mobility device (crutches/cane/walker).

- **IV:** self-mobility with limitations — uses wheelchair, may walk short distances with physical assistance.
- **V:** transported in a manual wheelchair; severe head/trunk control limitations.
- Higher number = greater limitation. GMFCS is stable over time and predicts prognosis — asked directly.
- **Management — numbered approach:**
- **Physiotherapy/occupational therapy** is lifelong and the foundation; early intervention, stretching, strengthening, orthotics (AFOs for ankle stability in diplegia).
- **Botulinum toxin injections** for focal spasticity (gastrocnemius, hamstrings) — improves gait and delays contractures; effects last 3–6 months; repeat injections planned.
- **Oral agents for generalized spasticity:** baclofen (sedation, must taper — abrupt withdrawal can cause seizures/rebound spasticity); **intrathecal baclofen pump** for severe generalized spasticity/dystonia unresponsive to oral therapy.
- **Orthopedic surveillance: hip surveillance with serial radiographs** (migration percentage) — hip subluxation/dislocation is common and painless until late; spinal surveillance for scoliosis in non-ambulant children; soft-tissue releases, osteotomies, selective dorsal rhizotomy in selected spastic diplegia.
- Multidisciplinary comorbidity care: epilepsy (~30–40%), intellectual disability, vision (strabismus, refractive errors), hearing, feeding/nutrition (aspiration risk), drooling (anticholinergics/botulinum to salivary glands), constipation.
- **Differential of motor delay (when it is NOT CP):** progressive neuromuscular disease (Duchenne — Gowers sign, calf pseudohypertrophy, raised CK; spinal muscular atrophy — fasciculations, absent reflexes vs CP's hyperreflexia); metabolic disorders (regression, not static); benign congenital hypotonia; neuromuscular junction disorders. Key discriminators: **CP = nonprogressive + upper-motor-neuron signs (hyperreflexia, clonus, Babinski, scissoring)**. Hypotonia with absent reflexes points to lower-motor-neuron/peripheral disease.
- **Neuroimaging:** MRI brain is the investigation of choice once CP is suspected — PVL in diplegia, porencephaly/focal infarct in hemiplegia, basal ganglia signal change in dyskinetic CP.

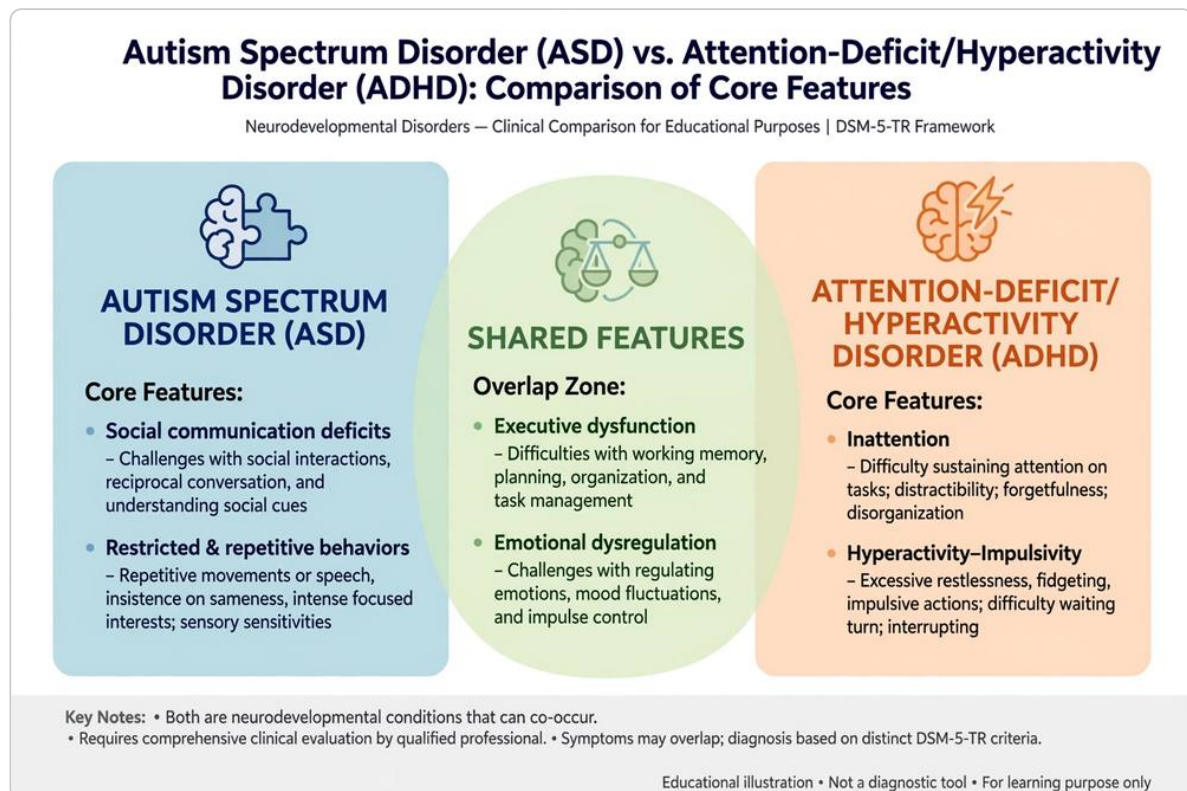


Figure 12.1 — Autism spectrum disorder vs ADHD

Developmental Milestones, Red Flags, and Screening

- **Gross motor:** head control **3–4 months**; rolls over ~4–5 months; sits without support **6–8 months**; crawls ~9 months; pulls to stand ~9–10 months; walks independently **12–15 months** (upper limit 18 months — cannot walk by 18 months = definite referral).
- **Fine motor:** palmar grasp ~4–5 months; transfers objects ~6 months; **pincer grasp (neat, thumb-index) 9–12 months**; scribbles ~15 months; builds tower of 2 cubes ~15 months, 6 cubes by 2 years; copies circle ~3 years.
- **Language:** **cooing 2–3 months**; **babbling (canonical "ba-ba") ~6 months**; first meaningful word **~12 months**; vocabulary explosion ~18 months; **2-word phrases by 24 months**; 50+ words by 24 months; speaks in sentences ~3 years.
- **Social/cognitive:** **social smile 6–8 weeks**; laughs ~4 months; **stranger anxiety 6–9 months**; separation anxiety ~9–12 months; waves bye-bye ~10 months; pretend play ~18 months–2 years; parallel play ~2 years, cooperative play ~3–4 years.
- **Red flags (any one = evaluate, do not "wait and see"):**
 - No social smile by 3 months; persistent fistling beyond 3 months.
 - No head control by 4 months; not sitting by 9 months; not walking by 18 months; **early hand preference (<12–18 months)** — suggests contralateral hemiparesis.
 - No babbling by 9 months (language concern), no pointing by 14 months, no single words by 16 months, no 2-word phrases by 24 months, **any loss of milestones**.
 - Persistent toe-walking beyond ~2–3 years; regression in any domain.

- **Screening tools: Denver-II (Denver Developmental Screening Test II)** — the classic 125-item screen covering personal-social, fine motor-adaptive, language, gross motor; yields normal/suspect/untestable (a screen, not diagnostic). **ASQ (Ages and Stages Questionnaire)** — parent-completed, widely used in primary care. **M-CHAT** at 18/24 months for autism. Remember the hierarchy: **screening ≠ diagnosis** — a failed screen triggers formal developmental assessment.
- **Global developmental delay (GDD) workup — ordered by yield:**
- **Chromosomal microarray is first-line** for unexplained GDD/intellectual disability (detects copy-number variants; higher yield than karyotype).
- **Fragile X testing (FMR1)** in boys (and girls with suggestive features/family history).
- **MRI brain** — especially with abnormal head size, focal neurology, seizures, or motor signs suggesting CP.
- **TSH/free T4** (congenital hypothyroidism is treatable — never miss), plus newborn-screen review.
- Metabolic workup (lactate, ammonia, plasma amino acids, urine organic acids) when there is regression, episodic decompensation, consanguinity, or multisystem disease. EEG if seizures or regression (Landau-Kleffner consideration).
- Also: formal vision and **hearing assessment** in every delayed child; dysmorphism examination with genetics referral.

Intellectual Disability

- **Definition (DSM-5):** deficits in **intellectual functioning** (reasoning, problem-solving, abstract thinking — confirmed by standardized IQ testing) **and** in **adaptive functioning** (conceptual, social, practical domains) with **onset during the developmental period**. Both prongs are required.
- **Classification by IQ with adaptive-function anchors:**
- **Mild (IQ 50–55 to ~70):** largest group; educable — basic literacy/numeracy; with supports can live and work semi-independently.
- **Moderate (IQ 35–40 to 50–55):** trainable — basic self-care, simple supervised work.
- **Severe (IQ 20–25 to 35–40):** limited communication, needs daily supervision for self-care.
- **Profound (IQ <20–25):** minimal communication, total care, often with severe motor/sensory impairments.
- DSM-5 severity is now graded by **adaptive functioning**, not IQ alone — but IQ bands remain the exam's numeric anchor.
- **Fragile X syndrome: FMR1 gene, Xq27.3, CGG trinucleotide repeat expansion** — full mutation >200 repeats (premutation 55–200; normal <45). Most common inherited cause of intellectual disability; second most common genetic cause after Down syndrome. Features: **long narrow face, large ears, macroorchidism (postpubertal)**, mitral valve prolapse, hyperextensible joints; autism-like behaviors (gaze aversion, hand-flapping). **Anticipation** through maternal transmission (premutation expands to full mutation). Premutation carriers: females at risk of premature ovarian insufficiency; older males at risk of FXTAS (fragile X-associated tremor/ataxia syndrome).
- **Down syndrome (trisomy 21) developmental profile:** mild-to-moderate intellectual disability (IQ typically 30–70) with **relative strength in social/visual learning** and **relative weakness in expressive language and verbal short-term memory** — a frequently tested profile. Developmental milestones delayed but follow

normal sequence. Early intervention, and screen for associated conditions (congenital heart disease, hypothyroidism, hearing loss, atlantoaxial instability) that compound developmental delay.

- **Other high-yield syndromic causes:** Williams syndrome (7q11.23 deletion — "cocktail party" hypersociability, supraaortic stenosis); Angelman (15q11–13 maternal — happy puppet, severe ID, ataxic gait, seizures); Prader-Willi (paternal 15q11–13 — neonatal hypotonia then hyperphagia/obesity); Rett (MECP2, discussed above).

Learning Disabilities

- **Core concept:** specific learning disorder = persistent difficulty in an academic skill **despite normal intelligence, adequate instruction, and intact vision/hearing** — an IQ–achievement discrepancy in the older framing; DSM-5 requires academic skills **substantially below age expectation** interfering with function, present ≥6 months despite intervention. Diagnosis is psychoeducational testing, not a single lab test.
- **Dyslexia (reading disorder):** the most common learning disability. Core deficit is **phonologic processing** — difficulty mapping sounds to letters (decoding), slow nonfluent reading, poor spelling. Signs: late talking, rhyming difficulty, letter reversals beyond early grades, avoidance of reading. **Intervention is multisensory, structured phonics-based reading instruction** (Orton-Gillingham-type programs) — intensive and early; accommodations (extra time, audiobooks) help but do not replace remediation. Dyslexia is lifelong but manageable.
- **Dyscalculia:** impaired number sense — difficulty with magnitude comparison, arithmetic facts, mathematical reasoning; may coexist with dyslexia.
- **Dysgraphia:** impaired written expression — illegible handwriting, poor spelling/grammar organization despite intact ideas; keyboarding accommodations and occupational therapy.
- **DCD — Developmental Coordination Disorder:** motor coordination **substantially below age level** (clumsy, drops things, poor handwriting, difficulty with sports/dressing), interfering with daily life, **not explained by** CP, muscular dystrophy, or visual impairment; onset early; often co-occurs with ADHD and dyslexia. Managed with task-oriented occupational/physical therapy, not drugs.
- **Exam logic:** rule out the reversible/acquired causes first — **hearing/vision screening, ADHD, anxiety/depression, inadequate schooling, intellectual disability** — before labeling a specific learning disorder.

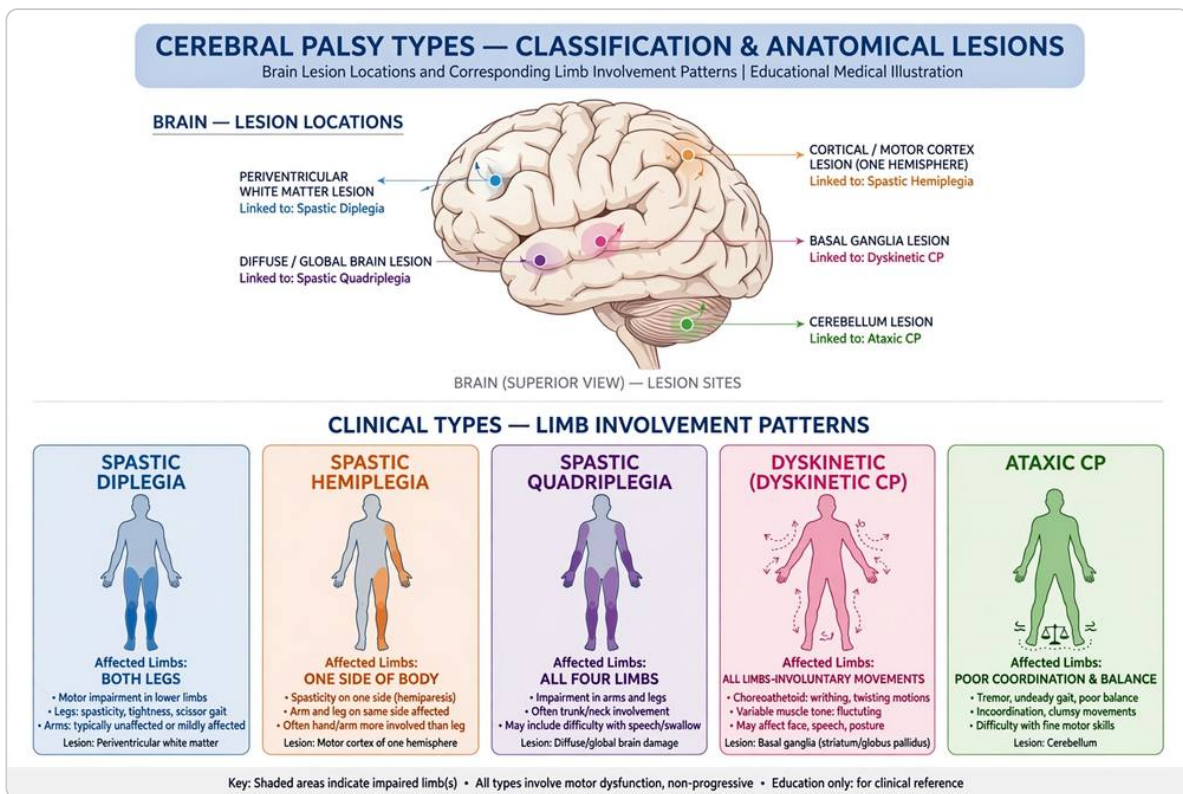


Figure 12.2 — Cerebral palsy: lesion sites and motor patterns

Speech and Language Disorders

- **Developmental stuttering:** onset typically **2–5 years**; repetitions/prolongations/blocks with relatively **fluent onset of speech between episodes**; often familial; majority of preschool stuttering **resolves spontaneously** — refer if it persists >6–12 months, there is family history of persistent stuttering, or there is tension/struggle behavior. Speech therapy (fluency shaping) is the treatment; reassurance and slow parental speech models for young children.
- **Cluttering:** distinct from stuttering — **rapid, irregular speech rate with excessive co-articulation, collapsing syllables, and poor intelligibility**, often with disorganized language formulation; the speaker is typically unaware. Test contrast: stuttering = repetitions/blocks with awareness; cluttering = rapid telescoped speech without awareness.
- **Any language delay** → **hearing assessment first. BERA (brainstem-evoked response audiometry/ABR)** and **OAE (otoacoustic emissions)** are the objective newborn/infant tests; behavioral audiometry in older children. Congenital sensorineural hearing loss must be identified by newborn screening — late-identified loss devastates language. Red flags: no startle to loud sound in infancy, inattentive "as if deaf," recurrent otitis media with effusion (conductive loss → fluctuating language delay).
- **Social (pragmatic) communication disorder:** persistent difficulty using language for social purposes (greetings, conversational turn-taking, adjusting speech to context, understanding nonliteral language) **without restricted repetitive behaviors** — that absence is what separates it from autism.
- **Childhood apraxia of speech:** inconsistent errors, groping oral movements, impaired prosody — intensive speech therapy; versus dysarthria (weakness-based, seen in CP).

Tic Disorders and Tourette Syndrome

- **Definitions:** tics are sudden, rapid, recurrent, nonrhythmic motor movements or vocalizations. **Tourette syndrome** = **multiple motor tics AND ≥ 1 vocal tic** (not necessarily simultaneous), persisting **>1 year**, **onset before 18 years**, not attributable to substances or another medical condition. **Persistent (chronic) tic disorder** = single or multiple motor OR vocal tics (not both) >1 year. **Provisional tic disorder** = tics <1 year.
- **Clinical features:** waxing-waning course; **suppressibility** (briefly) and **premonitory urge** distinguish tics from other movements; worsen with stress, excitement, fatigue; improve with focused activity/sleep. Coprolalia is dramatic but uncommon (~10%). High comorbidity: **ADHD and OCD** — screen every Tourette patient for both.
- **Stereotypies vs tics (classic bedside distinction):** stereotypies (hand-flapping, rocking, seen in autism/ID) are **rhythmic, prolonged, bilateral, start before age 3**, occur when excited/bored, and **lack a premonitory urge**; tics are brief, nonrhythmic, suppressible, with urge, onset typically 4–6 years.
- **Treatment — numbered steps:**
 - **Education and reassurance** — most tics are mild and do not require drugs; treat only if tics cause impairment, pain, or social dysfunction.
 - **Alpha-2 agonists (guanfacine, clonidine)** are preferred first-line pharmacologic agents, especially with coexisting ADHD.
 - **Antipsychotics for severe/disabling tics:** haloperidol, pimozide (ECG monitoring — QT prolongation), risperidone, aripiprazole. Monitor metabolic and EPS effects.
 - **CBIT (Comprehensive Behavioral Intervention for Tics)** — habit-reversal training; first-line behavioral therapy, effective and side-effect free.
 - **Differential of abnormal movements:** Sydenham chorea (rheumatic fever — "piano-playing" movements, emotional lability), Wilson disease (adolescent movement disorder + Kayser-Fleischer rings + low ceruloplasmin), PANDAS/PANS (abrupt tic/OCD onset after streptococcal infection — controversial but exam-tested), myoclonus, dystonia, seizures.

Elimination Disorders and Breath-Holding Spells

- **Enuresis:** involuntary voiding **≥ 2 times/week for ≥ 3 months** in a child **≥ 5 years**; **primary nocturnal enuresis** (never dry ≥ 6 months — 80–90% of cases) vs secondary (relapse after ≥ 6 months dry — look for UTI, constipation, diabetes, stress). Evaluate: daytime symptoms, constipation, UTI, family history, sleep apnea/snoring.
- **Enuresis treatment — ranked by long-term effectiveness:**
 - **Enuresis alarm (conditioning therapy)** — **most effective long-term** with lowest relapse rate; requires motivated family and 2–3 months of consistent use.
 - **Desmopressin (oral)** — reduces nocturnal urine production; effective short-term (camps, sleepovers); counsel on **fluid restriction in the evening to avoid hyponatremia/water intoxication**; nasal formulation withdrawn for enuresis due to safety concerns.

- Treat constipation and any daytime voiding dysfunction; limit evening fluids/caffeine; void before bed. Imipramine is obsolete for routine use (cardiotoxicity).
- **Encopresis:** repeated passage of feces in inappropriate places in a child ≥ 4 years; **retentive (constipation-associated) in ~90%** — fecal impaction with overflow incontinence; nonretentive is rarer (behavioral/developmental). Management: **disimpaction first** (oral polyethylene glycol $\pm$ enemas), then **maintenance laxative therapy (PEG) for months** with toilet sitting routine and behavioral reinforcement; address withholding behavior. Never punish.
- **Breath-holding spells:** onset **6–18 months**, peak ~ 2 years, resolve by ~ 5 years; precipitated by crying/pain/fright/anger; benign but frightening.
- **Cyanotic spells (most common):** prolonged crying $\rightarrow$ forced expiration $\rightarrow$ apnea $\rightarrow$ cyanosis $\rightarrow$ brief loss of consciousness/posturing; resumes breathing spontaneously.
- **Pallid spells:** sudden fright/pain $\rightarrow$ vagal response $\rightarrow$ bradycardia/asystole $\rightarrow$ pallor $\rightarrow$ limp syncope; may have brief jerks mimicking seizures.
- **Management:** reassurance — no antiepileptics; keep the child safe during the spell (lay flat, nothing in the mouth). **Iron therapy (ferrous sulfate) reduces frequency of frequent spells** even in non-anemic children — the exam's therapeutic pearl. Evaluate for iron deficiency anemia. Differentiate from epilepsy: spells are always provoked by an emotional trigger, with no postictal phase.

Practice MCQs

Q1. A 22-month-old boy is brought for speech delay. He has no babbling documented at 12 months, no pointing by 14 months, and no meaningful words even now. He avoids eye contact, flaps his hands when excited, and lines up his toys for hours. His parents report he said "mama" at 14 months but stopped using it by 18 months. Which of the following features in this child is an absolute red flag warranting urgent developmental referral? A) Loss of the word "mama" at 18 months B) Hand flapping when excited C) Lining up toys for hours D) Absence of meaningful words at 22 months **Answer: A** — Any loss of previously acquired language or social skills at any age is a red flag mandating urgent evaluation; regression is the single most alarming feature. The other options are characteristic autistic features but the loss of skills is the referral trigger.

Q2. A 4-year-old girl meets DSM-5 criteria for autism spectrum disorder. She has fluent speech but cannot hold a reciprocal conversation, misreads social cues, and insists on taking the same route to school daily with severe distress at any detour. She needs help organizing her day but manages classroom routines with support. What is her severity level? A) Level 3 — requiring very substantial support B) Level 2 — requiring substantial support C) Cannot be graded without IQ testing D) Level 1 — requiring support **Answer: D** — She functions with support but needs organizational help and has marked inflexibility — Level 1 (requiring support). Level 2 needs substantial support across settings; Level 3 needs very substantial support. IQ testing is not required to assign severity levels.

Q3. Parents of a 20-month-old with suspected autism ask about screening. The pediatrician performs the M-CHAT, which is positive. What is the correct next step? A) Diagnose autism spectrum disorder B) Administer the M-CHAT-R/F follow-up interview C) Order chromosomal microarray D) Start risperidone for irritability **Answer: B** — A positive M-CHAT must be followed by the structured follow-up interview (M-CHAT-R/F) before referral;

the M-CHAT is a screen, not a diagnostic instrument. Definitive diagnosis uses ADOS-2/ADI-R by a multidisciplinary team.

Q4. A 7-year-old boy with autism and severe intellectual disability has frequent episodes of head-banging and aggression toward his sibling, unresponsive to behavioral intervention. His parents ask about medication. Which drug has FDA approval for this indication in autism? A) Methylphenidate B) Fluoxetine C) Melatonin D) Risperidone **Answer: D** — Risperidone (and aripiprazole) are FDA-approved in autism specifically for irritability, aggression, and self-injurious behavior — not for core social or repetitive symptoms. Monitor weight, metabolic parameters, prolactin, and EPS.

Q5. A 30-month-old girl presented with normal development until 14 months, then lost purposeful hand use and spoken words. She now wrings her hands continuously, has acquired microcephaly, and shows irregular breathing while awake. MECP2 testing is ordered. The most likely diagnosis is: A) Rett syndrome B) Childhood disintegrative disorder C) Autism spectrum disorder, Level 3 D) Landau-Kleffner syndrome **Answer: A** — Regression at 6–18 months after normal early development, loss of purposeful hand use, hand-wringing stereotypies, acquired microcephaly, and breathing dysregulation in a girl with MECP2 mutation = Rett syndrome. CDD requires ≥ 2 years of normal development; Landau-Kleffner is acquired epileptic aphasia.

Q6. An 8-year-old boy is referred for poor school performance. His teacher reports he cannot sustain attention, loses things daily, and is easily distracted; his mother reports identical behaviors at home for the past year. He had similar difficulties since age 5. Which DSM-5 requirement for ADHD is already satisfied by this history? A) Six-month duration only B) Exclusion of learning disability C) Onset before 12 years and presence in 2+ settings D) Documented IQ below 70 **Answer: C** — Symptoms are present at home and school (2+ settings), have lasted a year (≥ 6 months), and began at age 5 (before 12 years). ADHD requires ≥ 6 inattentive and/or hyperactive-impulsive symptoms meeting these thresholds; low IQ is not a criterion and learning disability must be assessed but is a comorbidity, not an exclusion.

Q7. A 9-year-old girl with combined-presentation ADHD is started on methylphenidate. At follow-up, her parents report reduced appetite with 1.5 kg weight loss and new eye-blinking tics. Her growth chart shows height velocity slowing. Which side effect of stimulants is the parents' most appropriate concern for long-term monitoring? A) Growth deceleration requiring height/weight monitoring B) Permanent growth failure C) Inevitable progression to Tourette syndrome D) Hepatotoxicity **Answer: A** — Stimulants cause appetite suppression and modest growth deceleration ($\sim 1\text{--}2$ cm over 2 years), usually recovering with drug holidays; monitor growth charts. Tics may be unmasked but do not inevitably become Tourette; hepatotoxicity is an atomoxetine concern.

Q8. A 10-year-old boy with ADHD and a history of motor tics worsened by methylphenidate, plus significant anxiety, needs pharmacotherapy. Which is the most appropriate choice? A) Mixed amphetamine salts B) Short-acting methylphenidate at higher dose C) Imipramine D) Atomoxetine **Answer: D** — Atomoxetine (SNRI) is preferred when stimulants worsen tics, with comorbid anxiety, or substance-misuse risk. It takes weeks for full effect; counsel about hepatotoxicity and suicidal-ideation warnings. Guanfacine is another option, but atomoxetine is the listed best fit here.

Q9. A 6-year-old born at 28 weeks gestation walks with a scissoring gait, has increased tone in both lower limbs with brisk reflexes, and normal upper-limb function and cognition. MRI shows periventricular white-matter injury. The most likely diagnosis and lesion are: A) Spastic hemiplegia — middle cerebral artery infarct B) Spastic diplegia — periventricular leukomalacia C) Dyskinetic CP — basal ganglia injury from kernicterus D)

Ataxic CP — cerebellar hemorrhage **Answer: B** — Prematurity + legs >> arms spasticity + scissoring + PVL on MRI = spastic diplegic CP, the classic preterm phenotype. Hemiplegia follows focal stroke; dyskinetic CP follows kernicterus/basal ganglia injury.

Q10. A 5-year-old with spastic diplegic CP walks indoors without a device but struggles on stairs and uneven ground. According to GMFCS, his level is: A) Level I B) Level III C) Level II D) Level IV **Answer: C** — GMFCS II: walks with limitations (stairs, uneven surfaces) but without a hand-held device. Level I walks without limitations; Level III needs a hand-held mobility device; Level IV uses a wheelchair.

Q11. Parents of a 4-year-old with spastic diplegia ask about botulinum toxin injections for calf tightness. The correct counseling is: A) It reduces focal spasticity for 3–6 months and can delay contractures B) It permanently cures spasticity C) It is contraindicated in children under 10 years D) It replaces the need for physiotherapy **Answer: A** — Botulinum toxin provides temporary (3–6 month) focal spasticity reduction, improving gait and delaying contractures; repeat injections are planned and physiotherapy continues. For severe generalized spasticity, intrathecal baclofen pump is considered.

Q12. A 14-month-old is not walking independently but cruises along furniture. His parents are anxious. Examination is normal with no dysmorphic features. What is the most appropriate advice? A) Order MRI brain immediately B) Start physiotherapy for motor delay C) Test for Duchenne muscular dystrophy D) Reassure — walking by 12–15 months (upper limit 18 months) is normal **Answer: D** — Independent walking is expected by 12–15 months with 18 months as the definite referral threshold; cruising at 14 months with a normal exam warrants reassurance and surveillance, not workup.

Q13. A 16-month-old girl has no pincer grasp, cannot sit without support, and has no words. She was a term infant with an uneventful perinatal history. After confirming vision and hearing are normal, what is the first-line investigation for her global developmental delay? A) Karyotype B) Chromosomal microarray C) Urine organic acids D) EEG **Answer: B** — Chromosomal microarray is the first-line test for unexplained GDD/ID (highest yield, detects copy-number variants). Fragile X testing, MRI brain, and TSH follow; metabolic workup is reserved for regression, episodic decompensation, or multisystem clues.

Q14. A 5-year-old boy with moderate intellectual disability has a long narrow face, large ears, and macroorchidism. His maternal uncle had similar features. The underlying genetic mechanism is: A) Trinucleotide CGG repeat expansion >200 in FMR1 B) Maternal deletion of 15q11–13 C) Trisomy 21 nondisjunction D) MECP2 loss-of-function mutation **Answer: A** — Long face, large ears, postpubertal macroorchidism, X-linked family pattern = fragile X syndrome: FMR1 CGG full mutation (>200 repeats). Premutation is 55–200; anticipation occurs through maternal transmission.

Q15. A 7-year-old with Down syndrome is being assessed for school placement. Which developmental profile best describes the typical cognitive pattern in Down syndrome? A) Uniform severe impairment in all domains B) Relative strength in expressive language, weakness in visual learning C) Relative strength in social and visual learning, weakness in expressive language and verbal short-term memory D) Normal cognition with isolated motor delay **Answer: C** — Down syndrome typically shows mild-to-moderate ID with relative strengths in social/visual learning and relative weaknesses in expressive language and verbal short-term memory — the classic tested profile.

Q16. An 8-year-old boy reads slowly, guesses words from first letters, and cannot segment sounds in spoken words despite normal intelligence, intact hearing/vision, and good schooling. The core deficit and evidence-based intervention are: A) Visual processing deficit — tinted lenses B) Attention deficit — stimulant medication C) Low motivation — grade retention D) Phonologic processing deficit — structured multisensory phonics instruction

Answer: D — Dyslexia's core deficit is phonologic processing (sound-to-letter mapping); the evidence-based intervention is intensive, structured, multisensory phonics-based reading instruction (Orton-Gillingham type). It is a specific learning disorder, not a vision problem or ADHD.

Q17. A 6-year-old is described as extremely clumsy — frequently drops objects, cannot tie shoelaces or catch a ball, and avoids playground games. Neurologic examination, muscle strength, reflexes, and vision are normal. He has no spasticity or weakness. The most likely diagnosis is: A) Spastic diplegic cerebral palsy B) Developmental coordination disorder C) Duchenne muscular dystrophy D) Ataxic cerebral palsy **Answer: B** — Motor coordination substantially below age level interfering with daily life, with a normal neurologic exam excluding CP, muscular dystrophy, and visual impairment = developmental coordination disorder (DCD). DCD commonly co-occurs with ADHD and dyslexia and is managed with task-oriented OT/PT.

Q18. A 3-year-old boy began repeating initial sounds of words ("b-b-ball") 4 months ago without struggle or embarrassment, and his speech is otherwise fluent. Family history is negative. The best management is: A) Immediate intensive fluency therapy B) Trial of risperidone C) Reassurance with monitoring — most preschool stuttering resolves spontaneously D) BERA testing **Answer: C** — Early developmental stuttering at 2–5 years without tension/struggle behavior and of short duration usually resolves spontaneously; refer if it persists >6–12 months, shows struggle, or has a family history of persistent stuttering. BERA is for language delay with suspected hearing loss.

Q19. A 4-year-old speaks so rapidly that syllables collapse together ("Iwenttothestore"), is hard to understand, and seems unaware of the problem. His language comprehension is normal. This best describes: A) Cluttering B) Developmental stuttering C) Social communication disorder D) Childhood apraxia of speech **Answer: A** — Rapid, irregular rate with excessive co-articulation, telescoped syllables, poor intelligibility, and lack of awareness = cluttering. Stuttering involves repetitions/prolongations/blocks with awareness; apraxia shows inconsistent errors with groping.

Q20. A 2-year-old with no spoken words startles poorly to loud sounds and seems inattentive. Otoscopy is normal. What is the most appropriate next investigation? A) MRI brain B) Chromosomal microarray C) Trial of hearing aids D) BERA/ABR hearing assessment **Answer: D** — Any language delay mandates objective hearing assessment first; BERA/ABR (with OAE) is the objective test for infants/toddlers. Hearing aids are fitted only after audiologic diagnosis; microarray and MRI come later in the GDD workup.

Q21. A 9-year-old boy has had multiple motor tics (eye blinking, shoulder shrugging) and vocal tics (throat clearing, grunting) for 2 years, onset at age 7. He can briefly suppress them and describes an urge before they occur. Tics interfere with classroom participation. The diagnosis and preferred first-line drug are: A) Provisional tic disorder — haloperidol B) Tourette syndrome — guanfacine C) Sydenham chorea — penicillin D) Stereotypic movement disorder — risperidone **Answer: B** — Multiple motor + ≥ 1 vocal tic, >1 year, onset before 18 = Tourette syndrome. Alpha-2 agonists (guanfacine/clonidine) are preferred first-line pharmacologic agents, especially with ADHD; antipsychotics are reserved for severe tics. CBIT is first-line behavioral therapy.

Q22. A 5-year-old with autism rocks back and forth and flaps his hands when excited. His 8-year-old cousin blinks hard and jerks his neck briefly, describing a "need to do it." Which statement correctly distinguishes these movements? A) Both are tics B) The 5-year-old has tics and the cousin has stereotypies C) The 5-year-old has stereotypies — rhythmic, prolonged, without premonitory urge; the cousin has tics — brief, suppressible, with urge D) Neither requires any evaluation **Answer: C** — Stereotypies (autism/ID): rhythmic, prolonged, bilateral, onset <3 years, no premonitory urge. Tics: brief, nonrhythmic, suppressible, preceded by urge, typical onset 4–6 years. The distinction is a favorite bedside question.

Q23. A 7-year-old boy wets the bed 4–5 nights per week, has never been dry for more than a few weeks, and has no daytime symptoms, constipation, or UTI. Examination and urinalysis are normal. Which treatment has the best long-term cure rate? A) Enuresis alarm B) Desmopressin C) Imipramine D) Fluid restriction alone **Answer: A** — Primary nocturnal enuresis: the enuresis alarm (conditioning therapy) has the best long-term effectiveness and lowest relapse rate. Desmopressin works short-term (camps/sleepovers) but relapses on stopping; counsel evening fluid restriction to avoid hyponatremia. Imipramine is obsolete (cardiotoxicity).

Q24. A 5-year-old passes stool in his underwear 3–4 times per week. He has a history of painful defecation, avoids the toilet, and abdominal examination reveals a palpable fecal mass. Rectal examination is deferred. The first step in management is: A) Behavioral punishment for soiling B) Immediate anorectal manometry C) High-dose loperamide D) Disimpaction with polyethylene glycol ± enemas, then maintenance laxative therapy **Answer: D** — Retentive encopresis (~90% of cases): fecal impaction with overflow incontinence. Management is disimpaction first, then months of maintenance PEG with scheduled toilet sitting and positive reinforcement. Punishment worsens withholding; loperamide is contraindicated.

Q25. An 18-month-old has episodes in which prolonged crying after a minor fall leads to forced expiration, apnea, deep cyanosis, and brief loss of consciousness, after which she recovers spontaneously. Episodes occur 3–4 times weekly. Neurologic examination and EEG are normal. The most appropriate management is: A) Start sodium valproate B) Reassurance plus iron therapy to reduce spell frequency C) Urgent MRI brain D) Vagal nerve stimulation **Answer: B** — Classic cyanotic breath-holding spells: always provoked by an emotional trigger, self-resolving, no postictal phase, normal EEG — no antiepileptics. Reassurance is the mainstay; iron therapy reduces frequency of frequent spells even without anemia. Pallid spells involve vagal bradycardia after fright/pain.