Block Q Paeds

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Source: Amboss and Parvez Akbar

Glycogen storage disorders

- hereditary metabolic disorders characterized by defects in the enzymes responsible for glycogenolysis or glycolysis.
- 13 different types have been described
- Almost all these conditions are autosomal recessive, except Type VII which is X-linked
- All types cause abnormal accumulation of glycogen due to impaired glycogen metabolism.
- Liver, heart, and muscle are the most common sites of glycogen storage and are, therefore, predominantly affected.
- Type I (von Gierke disease)
- Type II (Pompe disease) - mainly affects heart muscle. It presents with signs and symptoms of heart failure, cardiomegaly, cyanosis or shock. In CXR heart is grossly enlarged
- Type III (Cori disease)
- Type IV (Andersen disease)
- Type V (McArdle disease) - McArdle affects the Muscles.
- Type VI (Hers disease)
- Muscle involvement - Seen in types II, III, IV, V
    - Easy fatiguability, exercise intolerance
    - Cramps
    - Rhabdomyolysis → myoglobinuria (burgundy-colored urine)
    - progressive weakness of extremities and trunk (proximal myopathy)
    - Cardiac involvement - Seen in several types (e.g., type II, type III)
- Liver involvement - Seen in types I, III, IV
    - Hypoglycemia (typically fasting hypoglycemia) and ketosis
    - Symptoms of hypoglycemia in infancy: seizures, hypotonia, poor feeding, cyanosis, irritability
    - Hepatomegaly → distended abdomen
- Additional clinical manifestations
    - Growth delay/growth retardation/failure to thrive: types I, II, III, IV
    - Anemia: type I
    - Hyperlipidemia: types I, III
    - Macroglossia: type II
    - Lactic acidosis: type I
    - Hyperuricemia: type I

Mucopolysaccharidoses

- Mucopolysaccharidoses are a group of metabolic disorders that result in the impaired breakdown of glycosaminoglycans (previously known as mucopolysaccharides), due to mutations in lysosomal enzymes.

- At least nine different types of mucopolysaccharidosis have been identified.
- The two most common conditions are Hurler syndrome and Hunter syndrome.
- Accumulation of glycosaminoglycans, i.e., heparan sulfate (HS) and dermatan sulfate (DS) in both syndromes
- Clinical features that occur in both conditions (typically milder in Hunter syndrome):
    - Developmental delay
    - Facial dysmorphism: frontal bossing, elongated skull , flattened nasal bridge, broad nasal tip, thickened gingiva, anteverted nostrils, constant nasal discharge, spaced and protruded eyes.
    - Airway obstruction
    - Hepatosplenomegaly
- Hurler syndrome (mucopolysaccharidosis type I)
    - Autosomal recessive
    - Deficiency of α-L-iduronidase (enzyme responsible for the hydrolysis of glycosaminoglycans)
    - Corneal clouding
    - Hypertrichiosis
    - Failure to thrive
    - Dysostosis multiplex (a distinct pattern on radiograph)
    - gingival hyperplasia and thickening of alveolar ridge
    - Dental eruption is delayed
    - persistent rhinorrhea or noisy breathing
    - Inguinal hernia
- Dysostosis multiplex
    - skull is enlarged and elongated (dolichocephaly), calvarium is thick, sella is J wooden shaped or boot shaped
    - vertebral bodies in lower thoracic and upper lumbar areas have a beaking of antero-inferior surface caused by hypoplasia of their antero-superior areas. A dorsal kyphosis, or gibbus deformity develops
    - Ribs are thickened, except where they join the spine. They have oar-shaped appearance
    - Distal humerus and ulna may show an abnormal angulation (Madelung's deformity)
    - Pelvis may have flaring of iliac bones, shallow acetabular areas, and progressive coxavalga
    - Long bones become shortened and thickened. There are signs of expansion of medullary cavity
    - There may be hypoplasia of odontoid process
    - Metacarpals have a proximal narrowing with distal widening (bullet shaped appearance)
- Hunter syndrome (mucopolysaccharidosis type II)
    - X-linked recessive
    - Deficiency of iduronate-2-sulfatase
    - Aggressive behavior

    - Hyperactivity
    - No corneal clouding
    - Pearly papules (ivory raised papules)
    - Carpal tunnel syndrome
- Diagnosis
    - Increased urinary levels of dermatan sulfate (DS) and heparan sulfate (HS)
    - Enzyme assay to confirm specific enzyme deficiency (definitive test)
    - Hurler syndrome is confirmed by demonstrating deficient α-L-iduronidase in leukocytes or cultured skin fibroblasts
- Treatment
    - Symptomatic and palliative treatment
    - Enzyme replacement therapy
    - Bone marrow transplantation

<u>Galactosemia</u>

- Galactosemia refers to hereditary defects in enzymes that are responsible for the metabolism of galactose (galactose is a component of the disaccharide lactose, which is present in breast milk).
- **Galactokinase deficiency**
    - Mild disease
    - Accumulation of galactitol in tissues
    - Galactose is present in blood and urine
    - Cataracts
    - Infants often do not track objects with their eyes and show no social smile on physical examination
    - Pseudotumor cerebrii
- **Classic galactosemia (Galactose-1-phosphate uridyltransferase deficiency)**
    - Severe manifestations
    - Accumulation of toxic substances in tissues (e.g., galactitol in the lens)
    - Poor feeding
    - Failure to thrive
    - Vomiting, diarrhea
    - Jaundice, hepatomegaly
    - Cataracts
    - Cognitive impairment
    - ↑ Risk of E. coli sepsis (esp. in neonates)
    - Hypoglycemia
- **Galactose-6-phosphate epimerase deficiency**
    - Mostly asymptomatic
    - Possible symptoms:
      Jaundice
      Hypotonia
      Dysmorphic features

Failure to thrive
Splenomegaly
Cataract
Sensorineural hearing loss
Cognitive deficiencies

- Diagnosis
  - Newborn screening test: ↑ galactose/galactose-1-phosphate in blood
  - Urine galactose levels: galactosuria
  - Presence of ketones in urine
  - Total serum bilirubin: hyperbilirubinemia
- Treatment
  - Complete cessation of lactose-containing feeds and lifelong adherence to a galactose-free and lactose-free diet

Phenylketonuria

- Autosomal recessive disorder
- Amino acid metabolism disorder
- Classic PKU - Defective phenylalanine hydroxylase
- Malignant PKU - Deficient tetrahydrobiopterin aka BH4
- impaired conversion of phenylalanine to tyrosine → tyrosine becomes nutritionally essential (classical PKU)
- Excess of phenylalanine is transformed into phenylketone metabolites (e.g., phenylpyruvate, phenylacetate, and phenyllactate) that are excreted in the urine
- Tyrosine deficiency → decreased neurotransmitter, melanin, and thyroxine synthesis
- Phenylalanine accumulation
- Musty odor (due to an increase in aromatic amino acids)
- Light skin and hair, blue eyes
- Growth restriction
- Psychomotor delay
- Seizures
- Eczema
- Diagnosis
  - quantitative measurement of plasma phenylalanine (Normal is 1mg/dL) (In PKU usually greater than 30 mg/dL)
  - Newborn screening: direct measurement of serum phenylalanine levels on 2nd–3rd day after birth (phenylalanine levels are normal at birth because of circulating maternal PAH)
  - If screening test is positive: oral tetrahydrobiopterin loading test
    If phenylalanine levels are decreased: BH4 deficiency
    If phenylalanine levels remain unchanged: PAH deficiency
  - Ferric chloride test: Identification of phenylketones in urine
- Management
  - Low phenylalanine and high tyrosine diet

- BH4 deficiency: supplementation of BH4 and possibly levodopa and 5-hydroxytryptophan

Kawasaki Disease

- Kawasaki disease is an acute, necrotizing vasculitis of unknown etiology.
- The condition primarily affects children under the age of five and is more common among those of Asian descent.
- The disease is characterized by a high fever, desquamative rash, conjunctivitis, mucositis (e.g., “strawberry tongue”), cervical lymphadenopathy, as well as erythema and edema of the distal extremities.
- However, coronary artery aneurysms are the most concerning possible manifestation as they can lead to myocardial infarction or arrhythmias.
- Clinical diagnosis requires fever for at least 5 days and one of the following:
  ≥ 4 other specific symptoms
  < 4 specific symptoms and involvement of the coronary arteries
- Specific symptoms include:
  - Erythema and edema of hands and feet, including the palms and soles (the first week)
  - Possible desquamation of fingertips and toes after 2–3 weeks
  - Polymorphous rash, originating on the trunk
  - Painless bilateral “injected” conjunctivitis without exudate
  - Oropharyngeal mucositis
    Erythema and swelling of the tongue (strawberry tongue)
    Cracked and red lips
  - Cervical lymphadenopathy (mostly unilateral)
- Diagnosis
  - ↑ ESR and CRP
  - Leukocytosis
  - Thrombocytosis
  - ↑ AST, ALT
  - Echocardiography - For evaluating coronary artery aneurysms
- Treatment
  - IV immunoglobulin (IVIG): High single-dose to reduce the risk of coronary artery aneurysms. Most effective if given within the first 10 days following disease onset
  - High-dose oral aspirin
    Patients receiving long term aspirin therapy are candidates for annual influenza vaccination to reduce the risk of Reye syndrome. Varicella vaccination should be strongly considered.
  - IV glucocorticoids: may be considered in addition to standard treatment, esp. in cases of treatment-refractory disease, as they lower the risk of coronary involvement

Marfan syndrome

- Autosomal dominant disease caused by mutation of fibrillin-1 gene (FBN1) on chromosome 15
- Defective fibrillin → defective elastin → defective connective tissue throughout the body
- Tall stature with disproportionately long extremities; joint hypermobility
- Arachnodactyly (achromachia): abnormally long, slender fingers and toes
- Aortic aneurysm and dissection
- Lens subluxation superiorly and temporally
- Heart valve defects (mitral valve prolapse)
- Skin hyperelasticity
- High-arched palate
- Pectus deformity
    - Pectus carinatum: a sternal deformity where the middle and lower portion of the sternum protrude forward (also known as sternal kyphosis)
    - Pectus excavatum: a sternal deformity where the middle and lower portion of the sternum protrudes inward
- Pes planus (flat foot) or hindfoot valgus
- Spinal deformities (scoliosis, hyperkyphosis)
- Vertical overdevelopment of the head (dolichocephaly)
- Winged scapula
- Habitual dislocations (particularly the patella and shoulder)
- Acetabular protrusion
- Visual impairment: ectopia lentis (lens dislocation) → lens subluxation superiorly and temporally

Collagen Types

- Type I collagen: bone → Osteogenesis imperfecta
- Type II collagen: cartilage
- Type III collagen: vessels → Ehlers-Danlos (vascular type)
- Type IV collagen: basement membrane → Alport, Goodpasture

Ehlers-Danlos syndrome

- Heterogeneous group of six connective tissue disorders with variable inheritance (autosomal recessive or dominant)
- Mutation in genes controlling synthesis of collagen
- Classic type: mutations in COL5A1, COL5A2 → type V collagen defect
- Vascular type: type III procollagen defect
- Defective collagen cross-linking and fibril synthesis
- Joint hypermobility (most common)
- Skin hyperextensibility
- Heart valve defects (particularly mitral valve prolapse)
- Aneurysms/dissections of the iliac, splenic, renal arteries, or the aorta

Osteogenesis imperfecta

- Rare, autosomal dominant inherited bone disorder due to mutation in COL1A1 or COL1A2 genes
- Mutation in type I collagen gene → decreased synthesis of type 1 collagen
- Brittle bones and frequent and/or multiple fractures from minimal trauma
- Growth retardation
- Skeletal deformities
- Blue sclera
- Progressive hearing loss (due to abnormal ossicles)

Alport syndrome

- a genetic disorder that is characterized by glomerulonephritis, often in combination with sensorineural hearing loss and sometimes eye abnormalities (Patients with Alport syndrome can't pee, can't see, can't hear a bee)
- Genetic defect of type IV collagen chains (component of the basement membrane of the kidneys, eye, and cochlea) → kidney damage (glomerulonephritis), sensorineural hearing loss, and ocular abnormalities
- usually inherited in an X-linked dominant pattern
- Initially intermittent gross hematuria (may present in infancy)
- As glomerular damage progresses, symptoms of nephritic syndrome and chronic kidney disease occur (usually leads to ESRD between 16–35 years of age)
- Sensorineural hearing loss
- Ocular findings: retinopathy, anterior lenticonus (a congenital conical elevation at the anterior pole or posterior pole of the crystalline lens in the eye)

Porphyrias

- Porphyrias are a rare group of inherited or (less commonly) acquired metabolic disorders in which defective enzymes impair the biosynthesis of heme in the liver and/or bone marrow.
- All porphyrias are characterized by the accumulation of porphyrin, or intermediates of its biosynthesis, which can cause a variety of symptoms depending on the organs involved (e.g., skin, liver, CNS).
- **Porphyria cutanea tarda (PCT)**
    - Most common porphyria
    - uroporphyrin accumulates in the skin → sunlight-dependent skin damage (chronic photosensitivity)
    - manifests with chronic, blistering cutaneous photosensitivity and tea-colored urine.
    - Susceptibility factors: Iron overload leading to increased hepatic iron stores, Alcohol, smoking, Hepatitis C, HIV, Hepatic steatosis, Estrogen therapy, Sunlight exposure
    - The diagnosis of PCT is confirmed by detecting porphyrins in urine or serum.
    - Management consists of rigorous photoprotective measures, regular phlebotomy or low-dose hydroxychloroquine, and avoiding risk factors.
- **Acute intermittent porphyria (AIP)**

    - second most common form
    - accumulation of heme intermediates porphobilinogen (PBG) and δ-aminolevulinic acid (ALA)
    - characterized by life-threatening attacks of severe abdominal pain, nausea and vomiting, tachycardia, and neuropsychiatric abnormalities.
    - The 5 P's of acute intermittent porphyria: Painful abdomen, Polyneuropathy, Psychologic disturbances, Port wine-colored pee, Precipitated by triggers like drugs
    - The skin is not involved in acute intermittent porphyria.
    - Attacks are generally triggered by certain medications, alcohol, infections, or fasting.
    - The diagnosis of AIP is confirmed by detecting metabolic heme precursors in urine, which often appears reddish.
    - The goal of therapy is to stop the acute attack as quickly as possible while providing supportive and symptomatic care.
    - Hemin therapy: Hemin is an iron-containing porphyrin that decreases the activity of δ-aminolevulinate synthase, thereby decreasing heme biosynthesis and the accumulation of intermediates.
    - Glucose loading: consider only for mild attacks or as temporizing measure
- **Lead poisoning** is an acquired form of porphyria
- **Congenital erythropoietic porphyria (Gunther disease)**
    - Very rare
    - Severe
    - Autosomal recessive
    - Defective uroporphyrinogen-III synthase
    - Begins in childhood
    - Bone marrow heme biosynthesis impairment
    - Severe photosensitivity leads to light-induced damage → burning sensation and redness of the skin with blisters that can develop into ulcers → scarring
    - Hemolytic anemia
    - Bone marrow hypertrophy → pathologic fractures
    - Port-wine colored urine
    - No causal therapy
    - Avoid exposure to sunlight

Down syndrome

- Down syndrome, also called trisomy 21, is the most common autosomal chromosomal irregularity
- The risk of a trisomy 21 pregnancy increases with maternal age
- Most individuals with Down syndrome have full trisomy 21, which occurs due to meiotic nondisjunction and results in a genotype with three complete copies of chromosome 21 and a total of 47 chromosomes.
- Other less common forms of Down syndrome are translocation trisomy 21 and mosaic trisomy 21.

- Full trisomy 21 (~ 95% of cases) - meiotic nondisjunction (Karyotype: ♀: 47,XX,+21 or ♂: 47,XY,+21)
- Translocation trisomy 21 (3–4% of cases) - Karyogram shows a total number of 45 chromosomes and may be expressed as either ♀: 45,XX,t(14;21) or ♂: 45,XY,t(14;21)
- Mosaic trisomy 21 (1–2% of cases) - two cell lines are present, the trisomy 21 cell line and the normal cell line
- Although symptoms may be less severe in mosaic trisomies, the clinical manifestation generally provides no indication of the underlying genetic mutation.
- Clinically, trisomy 21 manifests as a syndrome involving a characteristic appearance (e.g., upward-slanting palpebral fissures, epicanthal folds, protruding tongue, short stature, transverse palmar crease, sandal gap), organ malformations (e.g., heart defects, duodenal atresia, Hirschsprung disease), and endocrine disorders (e.g., obesity, diabetes mellitus, hypothyroidism).
- Facial and cranial features (craniofacial dysmorphia)
    - Upward-slanting palpebral fissures
    - Epicanthal folds
    - Ocular hypertelorism: a distance between the eyes greater than the 95th percentile
    - Brushfield spots: an aggregation of connective tissue in the periphery of the iris, visible as white or grayish-brown spots.
    - Refractive errors (e.g., myopia, astigmatism)
    - Strabismus
    - Cataracts (congenital, infantile, or juvenile)
    - A small oral cavity together with a large and furrowed tongue results in the appearance of a protruding tongue.
    - High arched and narrow palate
    - Teeth: late development, small size with short roots, large gaps between teeth
    - Brachycephaly
    - Hypoplastic nasal bones, broad and flat nasal bridge
    - Ear anomalies (small, round, low-set ears, adherent earlobes)
    - Short neck, excess skin at the nape of the neck (may be seen on prenatal ultrasound)
- Extremities, soft tissue, and skeletal features
    - Transverse palmar crease: single crease that runs across the palm, along the metacarpophalangeal joints perpendicular to the fingers
    - Sandal gap: a medial displacement of the first toe leading to a large space between the first and second toes [10]
    - Clinodactyly: abnormal curvature of a finger (typically refers to inward curvature of the 5th finger)
    - Camptodactyly - A congenital, fixed digital flexion deformity most often seen in the 5th digit
    - Brachydactyly
    - Connective tissue deficiency → ↑ risk of umbilical and inguinal hernias
    - Marked hyperextension of joints

    - Obesity: prevalence is approx. 50%
    - Atlantoaxial instability
    - Short stature
- Organ malformations and associated conditions
    - Heart: congenital heart defects in ~ 50% of cases (Atrioventricular septal defect, Ventricular septal defect, Tetralogy of Fallot, Patent ductus arteriosus)
    - Gastrointestinal tract: Duodenal atresia/stenosis, Annular pancreas, Anal atresia, Megacolon, Rectal prolapse, Hirschsprung disease)
    - Urogenital system: Hypogonadism, Cryptorchidism, Decreased fertility in men
    - Hypothyroidism
    - Type 1 diabetes
    - Celiac disease
    - Obstructive sleep apnea
    - Hearing loss due to recurrent otitis media
    - Increased risk of leukemia (acute lymphoblastic leukemia, acute myeloid leukemia)
    - Early-onset Alzheimer disease (The amyloid precursor protein, which generates amyloid beta, is located on chromosome 21.)
    - Increased risk of developing epilepsy
    - Delayed motor development
    - Muscle hypotonia
    - Varying levels of intellectual disability (average IQ: 50)
    - Apparent within the first 12 months: Developmental milestones (e.g., sitting, walking, talking) are achieved at approximately twice the age of children without Down syndrome
    - Behavioral disorders
    - Autism spectrum disorder
- Trisomy 21 is associated with an increased risk of malignancy (e.g., high risk of leukemia) and intellectual disability.
- Down syndrome is primarily detected in prenatal tests, including ultrasound measurement of nuchal translucency and maternal blood tests for certain hormones (e.g., increased inhibin A and β-hCG; decreased estriol, alpha-fetoprotein, and pregnancy-associated protein A). Fetal karyotyping via chorionic villus sampling or amniocentesis confirm the diagnosis, but these procedures are associated with an increased risk of fetal injury or loss.

Protein-energy malnutrition (PEM)

- Protein-energy malnutrition (PEM) describes pathological conditions resulting from a deficiency of dietary protein and/or total calories.
- Primary PEM: due to inadequate macronutrient intake
    - Marasmus: due to deficiency of all macronutrients and total calories
    - Kwashiorkor: due to protein deficiency
    - Marasmic kwashiorkor: a severe form with features of both marasmus and kwashiorkor

- Secondary PEM: due to chronic illnesses or drugs disrupting appetite, digestion, absorption, metabolism, and/or increased energy/protein demand

Primary PEM

- Susceptibility to infections
- Growth stunting as a sign of chronic malnutrition
- In severe cases: bradycardia, hypotension, pancreatic insufficiency, and hypothermia

Clinical diagnosis of Primary PEM

- H&P: Take a thorough history and physical exam, focusing on nutrition/potential child maltreatment and typical clinical features.
- Anthropometrics: to assess the degree of malnutrition
    - Height/length
    - Weight
    - Weight-for-length/height (WFL/H) represented as a Z-score or a percentile
    - Height/length-for-age (HFA) represented as a Z-score or a percentile
    - Mid-upper arm circumference (MUAC)
    - BMI
- WHO diagnostic criteria: for primary PEM in children aged 6–60 months
- Marasmus
    - WFL/H z-score < -3 OR
    - MUAC < 11.5 cm
- Kwashiorkor
    - WFL/H z-score < -2 OR
    - MUAC < 12.5 cm WITH
    - Bilateral pitting edema

<u>Kwashiorkor</u>

- Deficiency: Primarily protein, e.g., due to Premature cessation of breastfeeding, Chronic GI infection, inadequate intake of staple foods without the necessary amounts of proteins (e.g., sweet potatoes, cassava)
- Calorie intake: Variable (can be normal or even high)
- Bilateral pitting edema, anasarca in severe cases
- Distended abdomen (due to hepatomegaly, intestinal distention, and weakened abdominal muscles)
- Hepatomegaly
- Skin changes: thin, dry, peeling skin with areas of hyperpigmentation and hyperkeratosis (flaky skin)
- Hair changes: dry, hypopigmented hair that falls out easily
- Rounded cheeks (moon face)
- Muscle atrophy
- Variable weight for height
- Apathetic affect

Marasmus

- Deficiency: All major nutrients
- Calorie intake: Deficient
- Severe energy deficiency leads to a catabolic state → breakdown of adipose tissue, muscle, and, ultimately, organ tissue for energy
- Profound muscle wasting (broomstick extremities)
- Loss of subcutaneous fat
- Pronounced chest bone, ribs, and facial bones
- Failure to thrive: Low weight for height
- Thin, dry skin
- Thin, sparse hair
- Irritable affect
- No edema

Secondary protein-energy malnutrition

- A form of PEM caused by illnesses affecting appetite, digestion, absorption, metabolism, and/or increased energy/protein demand rather than a lack of calorie intake.
- usually observed in Chronically ill, hospitalized patients, Elderly, Chronic alcoholics
- Cachexia/wasting syndrome: a form of secondary PEM caused by an underlying illness that causes chronic muscle breakdown despite nutritional supplementation
  Cachexia can be seen in Neoplasm, AIDS, Chronic renal failure, Congestive heart failure, COPD
- Depleted subcutaneous fat and skeletal muscle (as seen in marasmus)
- Lower extremity edema
- Bradycardia, hypotension, and hypothermia
- Delayed wound healing, increased risk of decubitus
- Susceptibility to infections

Treatment of Protein Energy Malnutrition

- Hydration (typically oral)
- Nutritional rehabilitation: must occur slowly to prevent refeeding syndrome
  - Should be initiated slowly at ~ 20% above the child's recent intake.
  - Slowly increase calorie intake while monitoring lab values daily.
  - For kwashiorkor, protein should slowly be introduced into the diet to avoid acute liver injury.
- Treat complications (e.g., infection)
- For secondary PEM
  - Treat the underlying condition
  - Nutritional counseling
  - In anorexia-cachexia syndrome: consider corticosteroids (e.g., prednisolone) and cannabinoids (e.g., dronabinol)

- Refeeding syndrome is a frequent complication if nutritional rehabilitation occurs too rapidly (sudden shift from a catabolic to an anabolic state): It is characterized by fluid retention, hypophosphatemia, hypomagnesemia, and hypokalemia.

10 steps of recovery for severely undernourished children

- The first 9 steps usually take at least 1–3 weeks depending on the child's general status and recovery

1. Hypoglycemia
2. Hypothermia
3. Dehydration
4. Electrolyte imbalance
5. Infections
6. Micronutrient deficiencies
7. Cautious feeding
8. Catch-up growth
9. Sensory stimulation and emotional support
10. Prepare for follow-up after recovery

Step 1 and 2: Treat Hypoglycemia and Hypothermia

- Stabilization: initiate immediately and continue for up to 2 days
- Blood glucose and body temperature should be managed simultaneously
- Administer glucose (oral liquid glucose if child is conscious; IV glucose infusion if child is unconscious).
- Feed every 2 hours, also during the night
- Take axillary (hypothermia: < 35.0 °C) or rectal (hypothermia: < 35.5 °C) temperature
- Rewarm the child, especially the head (with e.g., clothes, blankets, heating lamp, skin to skin with the mother).

Step 3: Treat Dehydration

- Rehydrate orally (intravenous rehydration might lead to circulatory overload and thus to heart failure).
- Use the WHO standard oral rehydration solution as it contains less sodium and more potassium than normal saline or lactated Ringer's solution
- ReSoMal can be used orally or by NG tube. ReSoMal is a rehydration solution for children with severe acute malnutrition. It is modification of standard ORS recommended by WHO. ReSoMal contains less sodium, and more potassium than standard ORS and is intended for severely malnourished child with diarrhea.
- Monitor heart rate, respiratory rate, and frequency of urine, stool, and vomit.
- Monitor skin turgor, lacrimation, and fontanelle depth
- Continue breastfeeding if child is breastfed.

Step 4: Treat Electrolyte imbalance

- Stabilization and rehabilitation: initiate immediately and continue for up to 6 weeks
- Test serum electrolyte levels.

- Rehydrate with low sodium fluid.
- Give low sodium food.
- Administer potassium and magnesium.
- Monitor serum electrolyte levels.

Step 5: Treat Infections
- Stabilization: initiate immediately and continue for up to 7 days
- Identify the source of infection if possible.
- Administer prophylactic broad-spectrum antibiotics (e.g., cotrimoxazole, ampicillin).
- Administer measles vaccine in unimmunized children > 6 months of age.

Step 6: Treat Micronutrient deficiencies
- Stabilization and rehabilitation: initiate immediately and continue for up to 6 weeks
- Administer multivitamin supplements first (especially vitamin A, unless it has been given within the past 4 weeks).
- Administer folic acid.
- Administer trace elements: zinc, copper, iron.

Step 7: Cautious feeding
- Stabilization: initiate immediately and continue for up to 7 days
- Feed orally (if oral feeding is not possible, feed enterally via nasogastric tube).
- Feed low-osmolarity and low-lactose foods as soon as possible (e.g., milk-based formulas).
- Feed small portions every 2–4 hours.
- Gradually increase feeding volume and decrease frequency (over the course of 1 week depending on the child's general status).
- Monitor vomiting frequency and the child's weight.
- Compensate food loss after vomiting; if oral feeding is refused, administer via nasogastric tube.

Step 8: Catch-up growth
- Rehabilitation: initiate after day 7 and continue for up to 6 weeks
- Replace milk-based formula with higher caloric food (e.g., porridge).
- Increase portion size slowly to prevent heart failure.
- Monitor heart rate and respiratory rate.
- Monitor the child's weight gain daily.
- If child fails to respond to treatment, reassess 1 to 7 and adjust management if necessary.
- If child is breastfed, continue feeding higher caloric food AND breastfeeding (breastmilk does not contain enough sufficient calories and/or protein for rapid rehabilitation).

Step 9: Sensory stimulation and emotional support
- Stabilization and rehabilitation: initiate immediately and continue throughout childhood
- Create an emotionally stable environment.

- Provide stimulation through playtime.
- Restart physical activity once the child is well enough.
- Involve parents as much as possible.

Step 10: Prepare for follow-up after recovery

- Rehabilitation: initiate after day 7 and continue for up to 6 weeks
- Educate parents about correct feeding practices and playtime for the child at home.
- Recommend regular follow-up checks to parents.

Hirschsprung disease

- Hirschsprung disease (congenital aganglionic megacolon) is an inherited disorder primarily affecting newborns.
- The condition is characterized by an aganglionic colon segment, usually the rectosigmoid region, which fails to relax leading to functional intestinal obstruction.
- The first sign of the disease is often when a newborn fails to pass meconium within 48 hours after birth and/or shows symptoms of gastrointestinal obstruction (e.g., bilious vomiting and abdominal distention).
- Digital rectal examination
    - Tight anal sphincter
    - Empty rectum
    - Squirt sign: explosive release of stool and air upon removal of the finger
- Hirschsprung disease always involves the REcTum and is often associated with RET mutations.
- Ultrashort-segment Hirschsprung disease - very short segment of aganglionosis, limited to the distal rectum. usually treated with diet and stool softeners
- Total colonic aganglionosis - significant long-term morbidity and mortality (e.g., enterocolitis, post-operative bowel incontinence)
- Diagnosis usually involves three different modalities: contrast enema, anorectal manometry, and stepwise biopsy for histological detection of aganglionosis.
- Treatment of choice is surgical resection of the aganglionic segment, although it is important to maintain anal sphincter function.
- Surgical correction - definitive treatment to remove the affected segment of the colon and bring the normal ganglionic intestinal ends together
    - Total transanal endorectal pull-through: preferred method that can be done in one stage
    - Abdominoperineal pull-through (Soave procedure): traditionally performed in two stages.
      First stage: diverting colostomy to relieve the dilated bowel .
      Second stage: Resection of the aganglionic segment__ Anastomoses of the normal ganglionic colon segment to either the distal modified rectum or normal (unmodified) distal rectum. ___Preservation of internal anal sphincter function is of the utmost importance.

Other Points

- Most common pediatric seizure: Febrile seizures (2-5% of children)
- First-line status epilepticus: IV Lorazepam 0.1 mg/kg (IM Midazolam if no IV)
- Infantile spasms drug: ACTH or Vigabatrin (TSC-associated)
- Valproate contraindication: Hepatotoxicity in <2 yrs with metabolic disorders
- Wrong temptation: Carbamazepine for absence seizures - worsens them