Protein-Calorie Malnutrition

1. **Protein-Calorie Malnutrition (PCM)** results from **inadequate intake of calories and/or protein**, leading to **growth failure, immune dysfunction, and developmental delays**.
2. **Kwashiorkor → Protein deficiency with adequate calories → Edema, fatty liver, flaky-paint dermatitis, flag sign in hair, apathy, and moon face**.
3. **Marasmus → Severe calorie deficiency (both protein & energy) → Muscle wasting, loss of subcutaneous fat, "old man" face, NO edema**.
4. **Kwashiorkor vs. Marasmus → Kwashiorkor has edema due to hypoalbuminemia**, while **marasmus lacks edema and shows severe wasting**.
5. **Marasmic-Kwashiorkor → Combination of both** → Severe wasting **with** edema.
6. **Growth parameters**: PCM primarily affects **weight first**, followed by **height** in chronic cases.
7. **Immune compromise**: **Decreased T-cell function**, leading to **higher infection risk (measles, pneumonia, diarrhea)**.
8. **Biochemical findings**:
    - **Kwashiorkor → Low albumin, fatty liver, elevated AST/ALT**.
    - **Marasmus → Normal albumin, severe fat & muscle loss**.
9. **Management** (WHO guidelines):
    - **Phase 1 (stabilization)** → Treat **hypoglycemia, hypothermia, dehydration, and infections** before refeeding.
    - **Phase 2 (rehabilitation) → Slow refeeding with F-75, then F-100 formula**, micronutrient supplementation, and gradual caloric increase.
10. **Refeeding syndrome risk** → Sudden **increase in insulin**, leading to **hypophosphatemia, hypokalemia, and cardiac complications** if refeeding is too rapid.

Porphyria

1. **Porphyrias** are **disorders of heme biosynthesis**, leading to **accumulation of toxic intermediates**.
2. **Acute Intermittent Porphyria (AIP) → Deficiency of porphobilinogen deaminase (PBG deaminase)** → Accumulation of **porphobilinogen (PBG) and δ-ALA**.
3. **AIP symptoms** (5 P's): **Pain (abdominal), Polyneuropathy, Psychiatric symptoms, Port-wine urine, Precipitated by drugs/alcohol**.
4. **AIP urine changes**: **Darkens on standing (oxidation of PBG)** but is **colorless when fresh**.

5. **Drugs triggering AIP attacks**: **Barbiturates, sulfonamides, phenytoin, alcohol, rifampin** (P450 inducers).
6. **Management of AIP**: **IV glucose and hemin** (downregulates ALA synthase).
7. **Congenital Erythropoietic Porphyria (Gunther's Disease)** → **Deficiency of uroporphyrinogen III synthase** → Accumulation of **uroporphyrin I and coproporphyrin I**.
8. **Gunther's disease symptoms**: **Severe photosensitivity, erythrodontia (red teeth), hemolytic anemia**.
9. **Porphyria Cutanea Tarda (PCT)** → **Most common porphyria**, due to **uroporphyrinogen decarboxylase deficiency**, leading to **blistering photosensitivity and hyperpigmentation**.
10. **PCT triggers**: **Alcohol, Hepatitis C, Estrogens, Iron overload**.
11. **Pediatric presentation**: Porphyrias may present with **neurovisceral symptoms (AIP) or cutaneous photosensitivity (Gunther's/PCT)** in childhood.
12. **Diagnosis**:

- **AIP** → ↑ **PBG and ALA in urine** (reddish/brown color).
- **Cutaneous porphyrias** → ↑ **plasma and urine porphyrins**.

13. **Treatment**:

- **Acute attacks** → **IV glucose, hemin, avoid triggers**.
- **Cutaneous porphyrias** → **Sun protection, phlebotomy (if iron overload), antimalarials (hydroxychloroquine)**.

Down Syndrome (Trisomy 21)

1. **Down syndrome (Trisomy 21)** is the **most common chromosomal disorder**, caused by **meiotic nondisjunction (95%)**, **Robertsonian translocation (4%)**, or **mosaicism (1%)**.
2. **Facial features**: **Flat facial profile, epicanthal folds, upslanting palpebral fissures, Brushfield spots (white-gray spots on iris), small ears, and protruding tongue**.
3. **Hand signs**: **Single palmar crease (Simian crease), short broad hands, clinodactyly (curved 5th finger), and wide sandal gap between 1st and 2nd toes**.
4. **Neonatal hypotonia**: Poor Moro reflex, weak suck, and floppy baby appearance at birth.
5. **Cardiac defects** (50% cases): **Endocardial cushion defects (atrioventricular septal defect - AVSD is most common), VSD, ASD**.
6. **Gastrointestinal anomalies**: **Duodenal atresia ("double bubble" sign), Hirschsprung disease, imperforate anus, TE fistula, celiac disease**.
7. **Increased risk of**:

- **Acute lymphoblastic leukemia (ALL)**
- **Hypothyroidism**
- **Early-onset Alzheimer's disease (APP gene on chromosome 21)**

8. **Growth and development**: Short stature, delayed milestones, and **mild to moderate intellectual disability**.
9. **Atlantoaxial instability**: Risk of **spinal cord compression**, presenting with **gait abnormalities, bowel/bladder dysfunction, and hyperreflexia**.
10. **Screening during pregnancy**:

- **First trimester → ↑ β-hCG, ↓ PAPP-A, increased nuchal translucency**.
- **Second trimester (Quad screen) → ↑ β-hCG, ↑ Inhibin A, ↓ AFP, ↓ Estriol**.

11. **Definitive prenatal diagnosis**: **Chorionic villus sampling (1st trimester) or amniocentesis (2nd trimester) for karyotyping**.
12. **Lifespan**: **Shortened due to congenital heart defects and Alzheimer's**, but many live into their 50s-60s.

Collagen Disorders

1. **Collagen disorders** are a group of **connective tissue diseases** caused by **mutations affecting collagen synthesis, structure, or processing**.
2. **Osteogenesis Imperfecta (OI) → Defect in Type I collagen** (COL1A1 or COL1A2 mutation) → **Brittle bones, blue sclerae, hearing loss, and dental imperfections**.
3. **Ehlers-Danlos Syndrome (EDS) → Defective collagen synthesis** (mostly Type V and III) → **Hyperextensible skin, joint hypermobility, easy bruising, and poor wound healing**.
4. **Vascular EDS (Type IV) → Defective Type III collagen → Risk of arterial, bowel, and uterine rupture** (most severe form).
5. **Classical EDS (Type I/II) → Defective Type V collagen → Severe skin hyperextensibility and atrophic scarring**.
6. **Marfan Syndrome → Defect in fibrillin-1 (FBN1 gene)**, which supports **Type I collagen → Tall stature, arachnodactyly, lens dislocation (upward), aortic root dilation**.
7. **Loeys-Dietz Syndrome** → Similar to Marfan but with **hypertelorism (wide-set eyes), cleft palate, and arterial tortuosity**.
8. **Alport Syndrome → Type IV collagen defect → Hematuria, progressive renal failure, sensorineural hearing loss, and ocular abnormalities (anterior lenticonus)**.

9. **Stickler Syndrome → Mutation in COL2A1, COL11A1, or COL11A2 → Cleft palate, hearing loss, myopia, joint hypermobility**.
10. **Bethlem Myopathy → Mild collagen VI disorder** → Causes **proximal muscle weakness, joint contractures, and respiratory issues**.

Glycogen Storage Diseases (GSDs)

1. **Glycogen Storage Diseases (GSDs)** are a group of **inherited enzyme deficiencies affecting glycogen metabolism**, leading to **hypoglycemia, hepatomegaly, and muscle weakness**.
2. **GSD Type I (Von Gierke Disease) → Glucose-6-phosphatase deficiency → Severe fasting hypoglycemia, hepatomegaly, lactic acidosis, hyperuricemia, hyperlipidemia, doll-like face**. **Management:** Frequent feeding with cornstarch, avoid galactose/fructose.
3. **GSD Type II (Pompe Disease) → Acid α-glucosidase (lysosomal enzyme) deficiency → Cardiomegaly, hypotonia, respiratory failure, macroglossia**. **Infantile form is fatal**; enzyme replacement therapy available.
4. **GSD Type III (Cori Disease) → Debranching enzyme deficiency → Milder hypoglycemia and hepatomegaly compared to Von Gierke, with muscle involvement**. **Normal lactate levels.**
5. **GSD Type IV (Andersen Disease) → Branching enzyme deficiency → Progressive cirrhosis and hepatosplenomegaly**, leading to **liver failure in early childhood**.
6. **GSD Type V (McArdle Disease) → Muscle phosphorylase deficiency → Exercise intolerance, muscle cramps, myoglobinuria (red urine) after exertion, "second-wind" phenomenon**.
7. **GSD Type VI (Hers Disease) → Liver phosphorylase deficiency → Mild fasting hypoglycemia, hepatomegaly, growth retardation, but milder than Von Gierke.**
8. **GSD Type VII (Tarui Disease) → Phosphofructokinase deficiency** → Similar to **McArdle**, but also affects **RBCs**, leading to **hemolysis**.
9. **GSD Type IX → Phosphorylase kinase deficiency → X-linked, hepatomegaly, mild hypoglycemia, variable severity**.
10. **Diagnosis of GSDs**:

- **Von Gierke (GSD I): ↑ Lactate, uric acid, triglycerides, severe fasting hypoglycemia**.
- **Pompe (GSD II): Hypertrophic cardiomyopathy, hypotonia** (biopsy shows lysosomal glycogen).
- **McArdle (GSD V): ↑ CK, myoglobinuria, no lactate rise after exercise**.

11. **General management**:

- **Frequent feeding, uncooked cornstarch, high-protein diet** for liver GSDs.
- **Avoid strenuous exercise in McArdle's disease**.

- **Enzyme replacement therapy for Pompe's disease**.

Mucopolysaccharidoses (MPS)

1. **Mucopolysaccharidoses (MPS)** are **lysosomal storage disorders** caused by **deficient enzymes that degrade glycosaminoglycans (GAGs)** → Progressive **multisystem involvement**.
2. **MPS Type I (Hurler Syndrome) → α-L-iduronidase deficiency → Coarse facial features, corneal clouding, hepatosplenomegaly, developmental delay, skeletal abnormalities (dysostosis multiplex), airway obstruction**. **Most severe form**.
3. **MPS Type II (Hunter Syndrome) → Iduronate-2-sulfatase deficiency** → Similar to Hurler **but no corneal clouding**, and **more aggressive behavior (X-linked inheritance)**.
4. **MPS Type III (Sanfilippo Syndrome) → Deficiency in enzymes degrading heparan sulfate → Severe neurological deterioration with behavioral problems, hyperactivity, and progressive intellectual disability**.
5. **MPS Type IV (Morquio Syndrome) → Galactosamine-6-sulfatase or β-galactosidase deficiency → Short stature, severe skeletal dysplasia, joint laxity, normal intelligence**. **Corneal clouding present**.
6. **MPS Type VI (Maroteaux-Lamy Syndrome) → Arylsulfatase B deficiency** → Similar to Hurler but with **normal intelligence**.
7. **MPS Type VII (Sly Syndrome) → β-glucuronidase deficiency → Hepatosplenomegaly, skeletal deformities, hydrops fetalis**.
8. **Inheritance pattern**:
    - **All MPS are autosomal recessive** except **Hunter syndrome (X-linked recessive)**.
9. **Common features in all MPS**:
    - **Coarse facial features ("gargoyle-like")**
    - **Hepatosplenomegaly**
    - **Skeletal abnormalities (dysostosis multiplex)**
    - **Progressive developmental delay (except Morquio syndrome, which has normal intelligence)**
10. **Diagnosis**:

- **Urinary GAGs (dermatan sulfate, heparan sulfate, keratan sulfate)**
- **Enzyme assay in leukocytes or fibroblasts**
- **Genetic testing for confirmation**

11. **Management**:

- **Enzyme replacement therapy (ERT)** available for **Hurler, Hunter, and Morquio syndromes**.
- **Bone marrow transplant (BMT)** can be beneficial in **Hurler syndrome**.
- **Supportive care for airway obstruction, joint stiffness, and cardiac complications**.

Galactosemia & Phenylketonuria (PKU)

Galactosemia

1. **Galactosemia** is caused by **deficiency of galactose-1-phosphate uridyltransferase (GALT)** → **Autosomal recessive** disorder.
2. **Classic galactosemia (GALT deficiency)** → **Accumulation of galactose-1-phosphate** leads to **liver dysfunction, jaundice, vomiting, cataracts, failure to thrive, hypoglycemia, and E. coli sepsis (high risk in neonates).**
3. **Cataracts in neonates** are a classic finding due to **accumulation of galactitol in the lens**.
4. **Diagnosis**:
    - **Newborn screening (enzyme assay for GALT activity)**.
    - **Reducing substances in urine (positive Clinitest, negative glucose oxidase test)**.
5. **Management**: **Eliminate galactose & lactose from the diet** (no dairy products, switch to soy-based formula).
6. **Complications**: **Liver failure, intellectual disability, ovarian failure in females (even with treatment).**

Phenylketonuria (PKU)

7. **PKU is caused by deficiency of phenylalanine hydroxylase (PAH)** → **Autosomal recessive** disorder → **Phenylalanine accumulates and converts to toxic metabolites**.
8. **Symptoms appear after birth when phenylalanine builds up** due to breastfeeding/formula → **Musty body odor, intellectual disability, seizures, fair complexion, eczema, hyperactivity**.
9. **Diagnosis**:
    - **Newborn screening (elevated phenylalanine levels, low tyrosine)**.
    - **Guthrie test (bacterial inhibition assay for phenylalanine)**.
10. **Management**: **Phenylalanine-restricted diet for life (avoid high-protein foods like meat, dairy, nuts, eggs)** + **Tyrosine supplementation**.
11. **Maternal PKU syndrome**: **High phenylalanine in pregnancy causes microcephaly, congenital heart defects, and growth restriction in the fetus**.
12. **Complications if untreated**: **Severe intellectual disability, behavioral issues, epilepsy**.

Kawasaki Disease (KD)

1. **Kawasaki disease (KD)** is an **acute, self-limited vasculitis** of **medium-sized arteries**, primarily affecting children <5 years.
2. **Most serious complication**: **Coronary artery aneurysms**, which can lead to **myocardial infarction**.
3. **Diagnostic criteria ("Warm + CREAM")**:
    - **Fever for ≥5 days** (mandatory) **PLUS 4/5 of the following**:
        - **C**onjunctivitis (bilateral, non-exudative)
        - **R**ash (polymorphous, non-vesicular)
        - **E**rythema/edema of hands & feet (later desquamation)
        - **A**denopathy (cervical, unilateral, >1.5 cm)
        - **M**ucosal changes (strawberry tongue, cracked lips, erythematous oropharynx)
4. **Atypical (incomplete) Kawasaki disease**: Seen in **infants <6 months**, may have fever with **only 2-3 criteria** → Requires echocardiogram for diagnosis.
5. **Laboratory findings**:
    - **↑ CRP & ESR**
    - **Leukocytosis with neutrophilia**
    - **Thrombocytosis (after 2nd week)**
    - **Sterile pyuria**
6. **Cardiac involvement**:
    - **Coronary artery aneurysms** (most feared complication).
    - **Myocarditis, pericarditis, valvular dysfunction**.
    - **Baseline & follow-up echocardiography (at diagnosis and at 6-8 weeks).**
7. **Treatment** (should be started ASAP to prevent aneurysms):
    - **IV immunoglobulin (IVIG) + high-dose aspirin**.
    - **IVIG reduces coronary artery aneurysm risk significantly**.
    - **Aspirin continued at low dose until platelet count normalizes**.
8. **Differential diagnoses**:

- **Scarlet fever** (rash + strawberry tongue, but NO conjunctivitis & no coronary aneurysms).
- **Measles** (cough, coryza, conjunctivitis, Koplik spots).

9. **Complications**:
    - **Giant coronary aneurysms → Myocardial infarction (even in children)**.
    - **Thrombosis or rupture of coronary aneurysms**.
10. **Long-term management**:

- **Aspirin for 6-8 weeks (longer if aneurysms present)**.
- **Yearly cardiovascular follow-up for aneurysms**.

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