

GLYCOGEN STORAGE DISEASES

SUMMARY • HEPATIC TYPES • MUSCLE TYPES

KMU FINAL YEAR PAEDS

THE MASTER MNEMONIC TABLE

Type	Name	Mnemonic / Key Feature
Type I	Von Gierke	"Gierke = Glucose Gone". (Liver cannot release Glucose).
Type II	Pompe	"Pompe affects the Pump (Heart)". Cardiomegaly.
Type III	Cori	"Cori = Coral". Coral has branches. Defect in De-branching enzyme.
Type IV	Andersen	"Andersen = Abnormal Branching". Cirrhosis & Death.
Type V	McArdle	"McArdle = Muscle". Muscle cramps after exercise.
Type VI	Hers	"Hers = Hepatic Phosphorylase". Mild Von Gierke.
Type VII	Tarui	"Tarui = Two Issues". Muscle cramps + Hemolysis (RBCs).
Type IX	Kinase	"Type 9 = K-9". Phosphorylase Kinase . (X-Linked).

1. TYPE I: VON GIERKE (THE CLASSIC)

Enzyme: Glucose-6-Phosphatase.

Key Features (The 5 H's):

1. Hypoglycemia (Severe, Seizures).
2. Hepatomegaly (Doll-face, Massive liver).
3. Hyperlipidemia (High TG).
4. Hyperuricemia (Gout).
5. Hyperlacticacidemia (**High Lactate**).

2. TYPE III: CORI (MILDER)

Enzyme: De-branching Enzyme.

Differentiator: Like Von Gierke BUT **Normal Lactate**.

- "Limit Dextrin" accumulates.
- Gluconeogenesis is intact (so hypoglycemia is milder).

3. TYPE IV: ANDERSEN (FATAL)

🚨 **CIRRHOSIS ALERT**

Enzyme: Branching Enzyme.

Pathology: Long, straight glycogen chains (like foreign bodies) -> Immune reaction -> Liver Cirrhosis.

Outcome: Death by age 5.

4. TYPE II: POMPE (CARDIAC)

🚨 **CARDIAC KILLER**

Enzyme: Acid Maltase (Lysosomal).

Key Triad:

1. Cardiomegaly (Massive heart).
 2. Hypotonia ("Floppy Baby").
 3. Macroglossia (Large tongue).
- Death < 2 years.**

5. TYPE V: MCARDLE (MUSCLE)

Enzyme: Muscle Phosphorylase.

Patient: Teenager/Adult with exercise intolerance.

Signs:

- Cramps/Pain after exercise.
- **Myoglobinuria:** Red urine (Rhabdomyolysis).
- **Second Wind:** Symptoms improve after 10 mins.
- **Test:** Lactate does **NOT rise** after exercise.

6. TYPE VII: TARUI (MUSCLE + BLOOD)

Enzyme: Phosphofructokinase (PFK).

Clue: Identical to McArdle (Cramps) **PLUS Hemolysis** (Anemia/Jaundice).

7. CLINICAL SCENARIOS

Q: 6 month infant, doll-face, seizures. Labs: Low Glucose, High Lactate, High Uric Acid.

Von Gierke (Type I). Acidosis is the key.

Q: 4 month old floppy baby with massive heart on X-ray.

Pompe Disease (Type II). "Pump" failure.

Q: 20 year old male, cramps and red urine after gym. Flat Lactate curve.

McArdle Disease (Type V).

MUCOPOLYSACCHARIDOSES (MPS)

HURLER • HUNTER • SANFILIPPO • MORQUIO

KMU FINAL YEAR PAEDS

THE MPS "NAME-GAME" TABLE

Type	Name	Enzyme (The Exam Question)	Key Mnemonic / Feature
I	Hurler	Alpha-L-Iduronidase	"Hurler = Hazy Cornea". Classic severe form.
II	Hunter	Iduronate Sulfatase	"Hunters need Clear Eyes to aim" (No corneal clouding).
III	Sanfilippo	Heparan N-sulfatase	"San-Flip-o" = Brain Flips out. (Severe Neuro/Behavior).
IV	Morquio	Galactosamine-6-sulfatase	"Morquio = Massive Skeletal". (Severe dysplasia, Normal Brain).
VI	Maroteaux	Arylsulfatase B	"Maroteaux = Minds are OK". (Normal Intelligence).
VII	Sly	Beta-glucuronidase	"Sly is Seven". (Very Rare).

1. INHERITANCE RULE (THE EXCEPTION)

General Rule: All MPS types are **Autosomal Recessive**.
The Exception: Hunter Syndrome (Type II).

- It is **X-Linked Recessive**.
- **Mnemonic:** "The Hunter is a Man" (affects males).

2. TYPE I: HURLER SYNDROME

Enzyme: Alpha-L-Iduronidase.

Clinical Features:

- **Corneal Clouding** (Key sign).
- Coarse Facies ("Gargoylism").
- Hepatosplenomegaly.
- Intellectual Disability.

3. TYPE II: HUNTER SYNDROME

Enzyme: Iduronate Sulfatase.

The Hunter's Code:

1. **X-Linked** (Males only).
2. **Clear Corneas** (Hunters need clear vision).
3. **Aggressive Behavior**.
4. **Pebbly Skin** (Nodular rash on back).

4. DIAGNOSIS & MANAGEMENT

Screening: Urine GAGs (Glycosaminoglycans).

Confirmatory: **Enzyme Assay** (in WBCs).

Treatment:

- **Enzyme Replacement Therapy (ERT):** Available for Hurler, Hunter, Maroteaux.
- **Bone Marrow Transplant:** Preserves intelligence if done early in Hurler.

5. TYPE III: SANFILIPPO SYNDROME

🧠 **THE BRAIN TYPE**

Focus: Central Nervous System.

Features: Severe Neurodegeneration, hyperactivity, insomnia, and behavioral problems.
Somatic: Mild physical features (child looks normal).
Substrate: Accumulates Heparan Sulfate.

6. TYPE IV: MORQUIO SYNDROME

Focus: Skeleton (Bone).

Features: Severe skeletal dysplasia, short stature, knock knees.

Key Risk: Atlanto-axial instability (Neck) -> Cord compression.

Intellect: Normal.

7. TYPE VI: MAROTEAUX-LAMY

Enzyme: Arylsulfatase B.

Features: Looks like Hurler (Coarse face, cloudy cornea).

BUT: Normal Intelligence.
"Maroteaux's Mind is Okay."

8. CLINICAL SCENARIOS (HIGH YIELD)

Q: 4yo boy, coarse facies, short stature, hepatosplenomegaly. CLEAR corneas. Aggressive.
Hunter Syndrome (Type II). (Male + Clear Cornea).

Q: 2yo girl, developmental delay, CLOUDY corneas, coarse features.

Hurler Syndrome (Type I). (Female + Cloudy).

Q: Child with severe skeletal deformity but tops math class (Normal IQ).

Morquio (Type IV).

PORPHYRIAS

1. THE BASIC CONCEPT

What is it? A defect in the Heme Synthesis Pathway (Hemoglobin).

The Problem: Enzyme block -> Accumulation of toxic precursors (Porphyrins).

Two Main Types:

1. **Acute:** Neuro-visceral symptoms (Pain/Psychosis).
2. **Cutaneous:** Skin blistering/Photosensitivity.

4. PORPHYRIA CUTANEA TARDA (PCT)

"The Vampire Disease"

- Most common porphyria.
- **Photosensitivity:** Blistering/Scarring on sun-exposed areas (hands/face).
- **Hypertrichosis:** Excess hair growth on face.
- **Urine:** Tea-colored (loaded with uroporphyrins).
- **Trigger:** Alcohol, Iron overload, Hepatitis C.

2. ACUTE INTERMITTENT PORPHYRIA (AIP)

"The 5 Ps" (Classic Presentation)

1. **Painful Abdomen** (Severe, Colicky, No surgical cause).
 2. **Port-Wine Urine** (Darkens on standing).
 3. **Polyneuropathy** (Weakness, numbness).
 4. **Psychological Disturbances** (Hallucinations/Anxiety).
 5. **Precipitated by Drugs** (P450 Inducers).
- Enzyme: Porphobilinogen Deaminase Deficiency.*

3. PRECIPITATING DRUGS (AVOID!)

"Sulfonamides & Barbiturates"

- Alcohol
 - Barbiturates (Phenobarbitone)
 - Oral Contraceptives (OCPs)
 - Sulfonamides
 - Anti-epileptics (Carbamazepine, Phenytoin)
- Safe drugs: Paracetamol, Aspirin, Penicillin.*

5. DIAGNOSIS & MANAGEMENT

Type	Diagnostic Test	Treatment
Acute (AIP)	Urine Porphobilinogen (PBG) is HIGH during attack.	IV Heme Arginate (Hematin). High Carbohydrate diet (Glucose loads). Avoid triggers.
Cutaneous (PCT)	Plasma/Urine Porphyrins.	Venesection (Remove blood/iron). Low dose Chloroquine. Sun protection.

6. CLINICAL SCENARIO

Q: 20F, severe abdominal pain, confused. Surgeons found nothing. Urine turned dark in the bag. She takes OCPs.
Acute Intermittent Porphyria. (Pain + Psych + Dark Urine + Drug Trigger).

Q: A child screams when taken out in the sun. Hands become red and swollen immediately. No blisters yet.

Erythropoietic Protoporphyrin (EPP). Painful photosensitivity without blisters initially.

COLLAGEN DISORDERS

MARFAN • EHLERS-DANLOS • OSTEOGENESIS IMPERFECTA

KMU FINAL YEAR MULTISYSTEM MODULE

7. OSTEOGENESIS IMPERFECTA (OI)

"Brittle Bone Disease"

• Defect in **Type 1 Collagen**.

• **BITE Mnemonic:**

1. **Bones:** Multiple fractures (often mistaken for child abuse).
2. **I (Eye): Blue Sclera** (choroid shows through thin sclera).
3. **Teeth:** Dentinogenesis Imperfecta (Discolored/weak teeth).
4. **Ear:** Hearing loss (conductive).

Rx: Bisphosphonates (Pamidronate) to strengthen bone.

10. EHLERS-DANLOS SYNDROME (EDS)

Defect: Collagen synthesis (Type V or III).

Classic Signs:

- **Hyper-extensible Skin:** Stretchy like rubber.
- **Hyper-mobile Joints:** "Contortionist", frequent dislocations.
- **Tissue Fragility:** Cigarette paper scars, easy bruising.

Vascular EDS (Type IV): The dangerous one. Risk of rupture of large arteries (Aorta) or hollow organs (Uterus/Bowel).

8. MARFAN SYNDROME

Defect in **Fibrillin-1** (Chromosome 15).

Clinical Triad:

1. **Skeletal:** Tall, long fingers (Arachnodactyly), Arm span > Height, Pectus excavatum.
 2. **Ocular:** Ectopia Lentis (Lens dislocation **Upward & Outward**).
 3. **Cardiac (Killer):** Aortic Root Dilation -> **Aortic Dissection** / Regurgitation. Mitral Valve Prolapse.
- Signs:** Wrist Sign (Thumb overlaps pinky) + Thumb Sign.

11. OTHER COLLAGEN SYNDROMES

Alport Syndrome: Type IV Collagen (BM). "Can't See (Eye), Can't Pee (Kidney), Can't Hear (Ear)".

Stickler Syndrome: Type II/XI Collagen. Flat face (Pierre Robin Sequence), Myopia, Retinal detachment, Joint pain.

Loeys-Dietz Syndrome: TGF-Beta defect. Marfan-like + Hypertelorism (Wide eyes) + Bifid Uvula + Tortuous arteries.

Bethlem Myopathy: Type VI Collagen. Proximal muscle weakness + Finger flexion contractures.

9. MARFAN VS HOMOCYSTINURIA

Both are tall with long limbs. How to tell apart?

- **Marfan:** Normal IQ. Lens goes **UP**. Aortic Dissection risk.
- **Homocystinuria: Intellectual Disability.** Lens goes **DOWN**. Thrombosis (Stroke) risk.

12. CLINICAL SCENARIOS

Q: 6 year old boy brought with 3rd fracture this year. Blue sclera noted. Teeth are brownish.

Osteogenesis Imperfecta. Rule out Non-Accidental Injury (Child Abuse), but Blue Sclera confirms OI.

Q: 14M with hematuria and hearing loss. Uncle had a kidney transplant at age 30.

Alport Syndrome. X-linked dominant. Type IV Collagen defect affects Kidney, Ear, and Eye.

Q: Tall basketball player collapses. Sudden chest pain. Examination shows murmur. Lens dislocation noted.

Marfan Syndrome with Aortic Dissection. Immediate Echo/CT Angio needed.

METABOLIC DISORDERS

GALACTOSEMIA • PHENYLKETONURIA • SCREENING

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1. GALACTOSEMIA (THE ACUTE KILLER)

🚨 MEDICAL EMERGENCY

Definition: Inability to metabolize Galactose (Milk sugar).

Enzyme Defect: GALT (Galactose-1-Phosphate Uridyl Transferase).

Presentation: Newborn starts breast feeding -> Vomiting, Jaundice, Hepatomegaly.

The Killer: E. Coli Sepsis (Accumulated galactose inhibits leukocyte activity).

2. CLINICAL FEATURES & DIAGNOSIS

Classic Triad:

1. Liver Failure (Jaundice, Coagulopathy).
2. **Cataracts:** "Oil Drop" cataract (visible in first few weeks).
3. Brain Damage (Intellectual disability if untreated).

Diagnosis:

- Screening: **Reducing Substances** in urine (Positive for Galactose, Negative for Glucose).
- Confirmatory: GALT enzyme assay in RBCs.

3. TREATMENT

STOP MILK IMMEDIATELY!

- Switch to **Soy-Based Formula** (Galactose-free).
- Life-long avoidance of milk/dairy.
- *Breastfeeding is Contraindicated.*

4. PHENYLKETONURIA (PKU)

Definition: Inability to convert Phenylalanine (Phe) to Tyrosine.

Enzyme Defect: Phenylalanine Hydroxylase.

Result: Phe accumulates (toxic to brain) -> Tyrosine becomes deficient (needed for melanin/dopamine).

5. CLINICAL FEATURES (THE BLONDE CHILD)

Appearance: Fair skin, Blue eyes, Blonde hair (Lack of Melanin from Tyrosine deficiency).

Odor: **Musty / Mousy Body Odor** (due to phenyl-ketones in sweat/urine).

Neurology: Severe Intellectual Disability, Microcephaly, Seizures, Eczema.

6. MANAGEMENT OF PKU

Diet is Key:

- Restrict Phenylalanine (Low protein diet - no meat, eggs, dairy).
- **Supplement Tyrosine** (It becomes an essential amino acid).
- **Maternal PKU:** Pregnant women with PKU must control diet rigidly, or the baby will have microcephaly/heart defects (even if baby doesn't have PKU).

7. SCENARIOS

Q: 1 week old baby, jaundice, vomiting, hepatomegaly. Urine positive for reducing substances. Blood culture grows E. Coli.

Classic Galactosemia. Stop breast feed. Start Soy formula.

Q: 2 year old child, fair hair, blue eyes, developmental delay. Mother says his sweat smells "musty".

Phenylketonuria (PKU). Check Phenylalanine levels.

KAWASAKI DISEASE

CRASH & BURN • CORONARY ANEURYSM • ASPIRIN

KMU FINAL YEAR PAEDS

8. DIAGNOSTIC CRITERIA

"CRASH and Burn" (Fever > 5 Days + 4 of 5 features)

1. **Conjunctivitis:** Bilateral, non-purulent (Red eyes, no discharge).
2. **Rash:** Polymorphous (Any shape, primarily trunk).
3. **Adenopathy:** Cervical LN > 1.5cm (Usually unilateral).
4. **Strawberry Tongue:** Red cracked lips, oral erythema.
5. **Hands & Feet:** Edema/Erythema (Acute), Desquamation/Peeling (Subacute).

Burn: High grade fever > 5 days (Unresponsive to antibiotics).

9. THE 3 PHASES

1. **Acute (Day 1-11):** Fever + CRASH signs. Myocarditis risk.
2. **Subacute (Day 11-21):** Fever resolves. **Peeling of skin** (fingers/toes). Highest risk of **Coronary Aneurysms**. Thrombocytosis (High Platelets).
3. **Convalescent (Day 21+):** Recovery. Beau's lines on nails.

10. COMPLICATIONS (THE BIG DANGER)

🚨 CORONARY ARTERY ANEURYSMS

- Occur in 25% of untreated children.
- Can lead to Myocardial Infarction (MI) in a child.
- Investigation: Echocardiography (Baseline and repeat at 6 weeks).

11. MANAGEMENT (THE EXCEPTION)

1. IVIG (Intravenous Immunoglobulin):

- High dose (2g/kg) single infusion.
- Prevents coronary aneurysms if given in first 10 days.

2. Aspirin (The Rule Breaker):

- Normally contraindicated in kids (Reye Syndrome).
- **Kawasaki is the ONLY exception.**
- High dose (Anti-inflammatory) initially.
- Low dose (Anti-platelet) later for 6 weeks.

12. CLINICAL SCENARIOS

Q: 3 year old boy with fever for 6 days. Eyes are red without pus. Lips are cracked and bleeding. Swollen hands. Rash on trunk.

Kawasaki Disease. Classic presentation. Admit immediately for IVIG + Aspirin.

Q: Child treated for Kawasaki disease 2 weeks ago now presents with sudden chest pain and collapse.

Myocardial Infarction secondary to Coronary Artery Aneurysm thrombosis.

Q: Why do we delay measles vaccine in a child treated for Kawasaki?

IVIG contains antibodies that will neutralize the live vaccine. Delay for 11 months.