PEDIATRICS · GENETIC & METABOLIC · VOL. PKU

# Phenylketonuria *(PKU)*

Inborn Error of Metabolism · Autosomal Recessive · NGN NCLEX 2026 High-Yield Review

NGN-READY · NEWBORN SCREEN · DIET FOR LIFE

| 01 | 02 | 03 | 04 | 05 | 06 |
|---|---|---|---|---|---|
| RECOGNIZE CUES | ANALYZE CUES | PRIORITIZE | GENERATE SOLUTIONS | TAKE ACTION | EVALUATE |

WHAT IS PKU?

## A missing enzyme. *A lifelong diet.*

PKU is an **autosomal recessive** deficiency of **phenylalanine hydroxylase (PAH)**, the liver enzyme that converts the amino acid **phenylalanine (Phe) → tyrosine**. Without PAH, dietary Phe accumulates in blood and brain — **neurotoxic**, causing irreversible intellectual disability if untreated. Tyrosine becomes *conditionally essential*, and reduced melanin synthesis explains the classic **fair skin, blonde hair, blue eyes**.

| 1 : 10–25k | 25% | < 6 wks | Life |
|---|---|---|---|
| U.S. INCIDENCE | RISK IF BOTH ♀♂ CARRIERS | TREAT BEFORE TO AVOID ID | DIET DURATION |

CARRIER × CARRIER — AUTOSOMAL RECESSIVE

| | A | a |
|---|---|---|
| A | AA Unaffected | Aa Carrier |
| a | Aa Carrier | aa PKU |

25% Affected · 50% Carrier · 25% Normal

## The Metabolic Block — PAH Enzyme Pathway

WHY PHE RISES · WHY TYROSINE FALLS · WHY MELANIN DROPS

↑↑ PHENYLALANINE BUILDS UP IN BLOOD & BRAIN — NEUROTOXIC

DIETARY PROTEIN → **Phenylalanine** (Phe) — essential AA

BUILDUP

DEFICIENT ENZYME: ~~PAH~~ Phenylalanine Hydroxylase

BLOCKED

↓ TYROSINE (LOW) → **Tyrosine** → ↓ melanin, dopamine

CLINICAL OUTCOMES
- Intellectual disability
- Microcephaly · seizures
- Musty / mousy odor
- Fair skin · blonde hair
- Eczema · vomiting
- Hyperactivity · FTT
- Seizures (≈ 50%)

⚑ NEWBORN SCREENING · THE SINGLE MOST IMPORTANT TEST

## Heel Stick Timing & Pitfalls

- **When:** 24–72 hr after birth, *AFTER* the infant has received **≥ 24 hr of protein feeding** (breast milk or formula).
- **Method:** Lateral heel stick, capillary blood on Guthrie card → tandem mass spectrometry.
- **If discharged < 24 hr:** Repeat screen within **1–2 weeks**.
- **Confirm dx:** Quantitative serum Phe **> 20 mg/dL** (normal < 2 mg/dL).

⚠ CLICK-TRAP CAUSES OF FALSE NEGATIVES
- Screened **before** first protein feed
- Screened < 24 hr of life
- Vomiting / NPO at time of screen
- On TPN without enteral protein

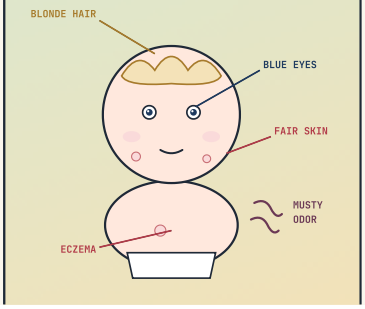
**NCLEX rule:** The screen requires *protein exposure* — without it, there's no Phe to detect.

★ HALLMARK SIGN

## Musty / Mousy Odor

Phenylketones (phenylacetate, phenyllactate) excreted in **urine, sweat & breath** produce a distinctive **musty, mousy, or barnyard** smell. Frequently the *first* clue in untreated infants — and the most testable buzzword for PKU.

**If you see "musty / mousy odor" in a stem → think PKU.**




▣ CLINICAL MANIFESTATIONS (UNTREATED)

## Recognize the Cues

▸ EARLY (INFANT)
- **Musty / mousy odor** (urine, breath, sweat)
- Vomiting · poor feeding · FTT
- Irritability · lethargy alternating
- Eczema, dry skin
- Fair skin · blonde hair · blue eyes

▸ LATE (IF UNTREATED)
- **Severe intellectual disability** (irreversible)
- Microcephaly
- Seizures (≈ 50%)
- Hyperactivity · aggression
- Tremor · spasticity · ataxia
- Decreased melanin → photosensitive

**The Window:** Brain damage begins within the **first weeks of life**. Initiating low-Phe diet **before 3–6 weeks** of age prevents intellectual disability. After ~ 1 year, damage is largely irreversible.

CLASSIC UNTREATED PKU INFANT

DIETARY MANAGEMENT · THE ONLY TREATMENT

## Low-Phenylalanine Diet — For Life

| CATEGORY | FOODS / ITEMS | WHY |
|---|---|---|
| ✕ AVOID | **HIGH-PROTEIN:** meat, fish, poultry, eggs, dairy (milk, cheese, yogurt), legumes (beans, lentils, peas), nuts, soy, peanut butter. **ASPARTAME** — diet sodas, sugar-free gum, NutraSweet®, Equal®, many sugar-free meds. | Highest Phe content. Aspartame = Phe + aspartate; even small amounts spike levels. |
| ⚠ LIMIT | Breads, pasta, cereals, rice, potatoes, corn — counted in **Phe milligrams/day** per the metabolic dietitian's plan. | Moderate Phe; must be measured, not free-feed. |
| ✓ SAFE | Most **fruits**, most **non-starchy vegetables**, sugars, fats, oils, jellies — low or no Phe. | Negligible Phe. Use freely within calorie needs. |
| ⊕ FORMULA | **Phe-free / low-Phe medical formula:** Lofenalac®, Phenex-1® / Phenex-2®, Phenyl-Free®, PKU Anamix®. Provides protein, tyrosine, vitamins, minerals. | Lifelong source of protein WITHOUT Phe; tyrosine supplementation. |

**Breastfeeding? YES** — possible with strict monitoring. Phe-free formula is given *first*, then limited breastfeeding to control Phe intake. Never the sole source.

**Adjunct Rx (older child/adult): Sapropterin (Kuvan®)** — BH4 cofactor; helps a subset of responders. **Pegvaliase** (adults ≥ 18). Diet still required.

NCLEX CLICK-TRAP

## ASPARTAME = PHENYLALANINE

Aspartame is a synthetic sweetener that **breaks down into phenylalanine** in the gut. Every product containing it carries a warning: *"PHENYLKETONURICS: Contains Phenylalanine."*

FOUND IN

Diet sodas · Crystal Light® · sugar-free gum · sugar-free yogurts · chewable vitamins · many **OTC and Rx liquids/chewables** (always read the label).

**Teach parents to read every label — including medications, vitamins, mouthwash, toothpaste.**

PHE LAB TARGETS

## Monitor for Life

| | |
|---|---|
| Normal Phe | < 2 mg/dL |
| Diagnostic | > 20 mg/dL |
| Goal — child | 2 – 6 mg/dL |
| Goal — adult | 2 – 10 mg/dL |
| Goal — pregnancy | 2 – 6 mg/dL |

Check Phe **weekly** in infancy, monthly in childhood, q3 mo as adults; **pre-conception & weekly** in pregnancy.

MATERNAL PKU SYNDROME

## Diet BEFORE Conception

Even if the fetus does *not* inherit PKU, elevated maternal Phe crosses the placenta and is **teratogenic**.

FETAL EFFECTS

- Microcephaly
- Congenital heart defects
- Intellectual disability
- IUGR · facial dysmorphism
- Miscarriage

**Phe must be < 6 mg/dL ≥ 3 months before pregnancy and maintained throughout.**

PRIORITY NURSING ACTIONS

## Take Action

- **Ensure protein feeding** ≥ 24 hr *before* heel-stick screen
- Teach Phe-free / low-Phe formula preparation & storage
- **Label reading** — every food, drink, OTC, Rx
- Refer to metabolic dietitian & PKU clinic
- Genetic counseling for parents & siblings
- Routine Phe levels — adjust diet per dietitian
- Monitor growth, development, school performance
- Pre-conception counseling for girls / women

HIGH-YIELD MNEMONIC

## "PKU *BABY*" — Remember the Profile

| B | A | B | Y | P | K | U |
|---|---|---|---|---|---|---|
| BLONDE & BLUE | AVOID ASPARTAME | BRAIN DAMAGE | YUCKY ODOR | PROTEIN RESTRICT | KEEP TYROSINE | UNENDING DIET |
| Hair · eyes · fair skin (↓ melanin) | NutraSweet® = phenylalanine | Irreversible if untreated by ≈ 6 wk | Musty / mousy urine, breath, sweat | No meat, dairy, eggs, nuts, soy | Special Phe-free formula | Lifelong — esp. before pregnancy |

## NGN Bow-Tie • *Clinical Judgment in Action*

RECOGNIZE → PRIORITIZE → EVALUATE

① CUES TO RECOGNIZE

2-week-old infant: **vomiting, poor feeding, musty urine odor**, mild eczema, blonde hair, FTT (–1 SD weight). Mother reports newborn screen was drawn at **14 hours** of life before discharge — never repeated.

② TOP PRIORITY CONDITION

**Phenylketonuria (PKU)** — likely missed on early-drawn newborn screen. Risk for **irreversible neurologic injury** if Phe not lowered immediately.

③ TAKE ACTION × 4

① Draw **quantitative serum Phe** & tyrosine STAT.
② Initiate **Phe-free formula** per dietitian.
③ **Stop all aspartame & high-protein** intake.
④ Refer to **metabolic specialist / PKU clinic**.

× TOP CLICK-TRAPS

## Wrong-Answer Traps

- "PKU is *cured* by infancy" — **NO**, lifelong diet.
- "Stop diet at age 18" — **NO**, lifelong, esp. for pregnancy.
- "Aspartame in moderation is fine" — **NO**.
- "Breastfeeding contraindicated" — **NO**, can mix with Phe-free formula.
- "Screen at birth before first feed" — **NO**, must follow protein feeding.
- "High-protein diet to support growth" — **NO**, opposite of treatment.
- "Tyrosine supplement is unnecessary" — **NO**, it's now conditionally essential.

⚑ RED FLAGS · ESCALATE

## Call the Provider

- Phe levels **> 10 mg/dL** despite reported adherence
- New **seizure** activity or developmental regression
- **Microcephaly** noted on growth chart
- Pregnant patient with Phe not yet at target
- Persistent vomiting / dehydration in infant on formula
- Severe weight loss → over-restriction of protein
- Caregiver knowledge gaps (label reading, formula prep)

★ NGN TEST-TAKING PEARLS

## Pattern Recognition

- "Musty/mousy odor" stem → **PKU**, every time.
- Blonde + blue + fair + delayed → think **↓ melanin from ↓ tyrosine**.
- Best answers always contain **"low-Phe diet"** & **"lifelong"**.
- Reject any option mentioning **aspartame, NutraSweet, Equal**.
- Heel-stick timing: **after 24 hr of feedings**.
- Pregnancy + PKU → **pre-conception** Phe control is the right answer.
- Tyrosine is now **essential**; supplement via formula.

NGN NCLEX · 2026 TEST PLAN

*"No PAH → Phe builds up → brain pays the price. Diet for life."*

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