FND 431 - Metabolic Lab: PKU and Galactosemia

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PKU:

1. What is phenylketonuria?
    - Phenylketonuria (PKU) - which literally means phenylalanine ketones in the urine - is an inborn error of metabolism due to the lack of, or deficiency of, the phenylalanine hydroxylase (PAH) enzyme. Lack of the enzyme causes the amino acid phenylalanine to not convert ("break down") into tyrosine. The phenylalanine builds up in the blood impacting neurological function. Left untreated, results are permanent cognitive impairment which includes brain damage, paralysis, epilepsy, cognitive function, and IQ (Hood et al., 2014).

2. What is the newborn screening process for PKU?
    - The newborn screening (NBS) process is a blood test to determine PHE levels in the blood. It is conducted within the first week of birth (usually the first 2 days) using blood spots that are collected on a special type of filter paper. The paper is sent to the state public health laboratory, or approved contracted labs, to be evaluated. In Colorado, the test screens for 45 conditions, including PKU. (U.S. Department of Health and Human Services, 2020).
    - If the test is positive, meaning blood PHE level > 1.7 mg/dL (Academy of Nutrition and Dietetics, n.d.), then the originating hospital is notified and subsequently the family is notified. In the US, the process of state lab results can take up to 10 days and

once received by the hospital, another 3-5 days can go by before the hospital contacts the primary care pediatrician who would then contact the family. Most positive PKU diagnosis are not relayed to the family until at least 10-12 days after birth, meaning that some unavoidable impact has occurred, due to normal intake of protein containing nutrition and subsequent PHE build up.

- The exact same process and filter paper are used in many clinics as a way to conduct regular blood testing – i.e. monthly evaluation of PHE levels to perform a dietary assessment based on growth and dietary intake.

3. Why is it important to accomplish screening as soon after birth as possible?
    - Once the newborn with PKU begins to intake any type of protein containing nutrition (breast milk or formula) they begin to build up PHE in their blood stream. Because they lack an enzyme to break down the PHE, it builds up and crosses the blood brain barrier, primarily effecting the prefrontal cortex. The earlier the diagnosis, the sooner blood levels can be corrected and the lower the impact to brain function.
    - In Classic PKU, untreated phenylketonuria results in the loss of approximately 4 IQ points per month, starting at birth through the first 5 years of life. A patient treated as close to birth as possible, and who maintains proper, stable, blood levels can be expected to achieve relatively comparable IQ to their siblings (Romani et al., 2019).

4. Why does a baby with a confirmed diagnosis of PKU have elevated blood PHE levels?
    - An infant with PKU does not have PAH enzyme. That enzyme is used in the metabolic chain to complete the conversion of PHE to TYR. No other natural metabolic path exists to break down the PHE, therefore it builds up.

5. What is the goal of the PKU diet?
    - The primary goal is to maintain blood levels within treatment range (detailed in the question below). A 24- hour diet prescription is created to ensure total PHE intake from all sources (formula, food, supplements, other beverages) is no more or less than the individual can metabolize. That is accomplished by providing approximately 85% of nutritional protein intake through MNT (Academy of Nutrition and Dietetics, n.d.b)– oral formula that consists of a synthetic PHE free protein source. The PHE free formula is supplemented via oral nutrition sources or natural food to establish the maximum tolerable intake of PHE. Each individual is different, however most classic PKU individuals (nearly absent PAH function) can tolerate 300-450 mg PHE per day in supplements or food. Non-formula food intake is allowed in very small amounts – each food item is weighed, measured to calculate PHE intake. Specialty Low Protein food items are available to mimic typical foods: breads, pasta, cakes, cookies. These items can provide calories to the diet and help the individual fit within social norms of eating without adding protein or PHE.

6. What are acceptable treatment blood phe levels? What are acceptable tyrosine levels?
    - PHE treatment range: 2-6 mg/dL. (NCM states <10 mg/dL which is contrary to the US national guidelines) (Academy of Nutrition and Dietetics, n.d.b; National PKU Alliance, n.d.)
    - TYR treatment range: 1 mg/dL
7. How long will infants have to remain on the PKU diet?
    - Their entire life. In the past, children were taken off the diet at age 5 since it was assumed brain development was complete. However subsequent studies showed

increased neurological effects in untreated children, adolescents and adults. Effect range from mild attention deficit disorder, to mood disorders, to paralysis. There is established correlation between untreated PKU and increased incidence of anxiety, depression and suicide. (National PKU Alliance, n.d.)

8. Download and attach PKU diet information from the NCM with submission.

Galactosemia:

1. What is galactosemia?
    - Galactosemia is a disorder of carbohydrate metabolism. It results from the dysfunctional conversion of galactose to glucose via deficient enzymes (galactokinase, galactose-1-phosphate uridyl transferase or uridine diphosphate (UDP)-galactose-4′-epimerase) (Pasquali et al., 2018). This causes a buildup of galactose and/or galactose-1-phosphate and other galactose metabolites, which can cause intellectual disability.
    - Duarte galactosemia results from a combination of alleles that are heterozygous (one allele for galactosemia and one Duarte allele for Duarte galactosemia). This combination is referred to as “D/G galactosemia” and accounts for approximately 5-20% of the GALT enzyme: children affected by this genetic anomaly can develop without medical complications or adverse complications (Mahan & Raymond, 2017).
2. What is the newborn screening process for classic galactosemia?
    - In their Nature article, Pasquali et al. describe “newborn screening for classic galactosemia has been implemented in all of the United States, while screening for galactokinase deficiency and UDP-galactose-4′-epimerase deficiency is not universal.” They also state that “For each of these conditions, the diagnosis is based

on the demonstration of severely reduced or absent enzyme activity in red blood cells (RBCs). DNA analysis of the *GALT*, *GALK1*, or *GALE* genes is often performed as part of the diagnostic evaluation" (Pasquali et al., 2018).

> "...Newborn screening for classic galactosemia identifies patients with decreased GALT activity in dried blood spots (DBS) and, for some states, elevated galactose sugars. States including galactose sugars as part of their screening also identify cases of GALK and GALE deficiencies, while those relying only on galactose sugars alone may miss cases of GALT deficiency in patients on a galactose-limited diet. Galactosemia testing may also be initiated by a positive family history, or by nonspecific features of the disease in an older patient" (Pasquali et al., 2018).

3. Describe the MNT for galactosemia.
    - The goal of MNT for galactosemia is to completely eliminate galactose from the diet for the life of the patient (Mahan & Raymond, 2017). All foods containing milk, milk products and lactose are to be avoided. Lactose is included because it is a disaccharide containing galactose and glucose. Infant formula is soy based and careful food label reading is paramount to compliance. Fillers and bulking agents can hide milk products such as casein and caseinate, which patients should be aware of.

Metabolic Nutrition Labs/Centers

1. Each group member is to find a metabolic nutrition center in your area (for every student in the group). Include their address and phone numbers as well as website address if applicable.

- Karen Casey- the largest Metabolic Clinic in the Regional West is at Children's Hospital in Aurora Colorado. They treat patients of all ages with nutrition related metabolic conditions who live in CO, NM, Wyoming. The lead Metabolic Registered Dietitian is Casey Burns.

  Casey Burns Metabolic Dietitian
  Inherited Metabolic Disease Clinic
  Children's Hospital Colorado
  13123 East 16th Avenue, Box 153
  Aurora, CO 80045
  Phone: (303) 724-2366
  Website: https://www.childrenscolorado.org/doctors-and-departments/departments/genetics/

- Jenny McKee Alderman- UNC-Chapel Hill Children's Hospital has a department devoted solely to Pediatric Genetics and Metabolism.

  UNC Hospitals Children's Specialty Clinic
  101 Manning Drive
  N.C. Children's Hospital
  Ground Floor
  Chapel Hill, NC 27514
  Phone: (984) 974-1401
  Website: https://www.uncchildrens.org/uncmc/unc-childrens/care-treatment/genetic-disorders/

- Keith Wectawski

  Shodair Children's Hospital

  2755 Colonial Drive PO Box 5539

  Helena, Montana 59604

  406.444.7500

  Website: https://shodair.org/genetics/

- Nadia Lopez

  UVA Children's Hospital

  1215 Lee Street

  Charlottesville, VA 22903

  434-924-0123

  Website: https://childrens.uvahealth.com/services/pediatric-genetics

- Sharon Dennison

  The Children's Hospital at OU Medical Center

  1200 Children's Avenue

  Oklahoma City, OK 73104

  Phone: 405-271-4211

  Website: https://www.oumedicine.com/oumedicine/pediatric-services/genetics#

2. As a group, list the <u>foods and formulas</u> available for 2 different metabolic disorders that have a restricted amino acid (Use the NCM to find and compare formulas), their functions. Once formulas have been identified, each group member is to research the price, and where they are available. For those of you who live in rural areas, what is the availability of special foods and formulas?

PKU Formulas listed in the NCM (Academy of Nutrition and Dietetics, n.d.a)

Name	Manufacturer	Type	View
Milupa® PKU 2	Nutricia North America	Amino Acid/Metaboli...	View
Milupa® PKU 3	Nutricia North America	Amino Acid/Metaboli...	View
PKU cooler 10 (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 10 (purple flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 10 (red flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 10 (white flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 15 (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 15 (purple flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 15 (red flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 15 (white flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 20 (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 20 (purple flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 20 (red flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU cooler 20 (white flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU express 15 (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU express15 (lemon flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU express15 (tropical flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU express15 (unflavored)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU express20 (unflavored)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU gel (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU gel (raspberry flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU gel (unflavored)	Vitaflo USA	Amino Acid/Metaboli...	View
PKU Lophlex® LQ (Berry)	Nutricia North America	Amino Acid/Metaboli...	View
PKU Lophlex® LQ (Juicy Orange)	Nutricia North America	Amino Acid/Metaboli...	View
PKU Lophlex® LQ (Juicy Orange, Mixed Berry Bl...	Nutricia North America	Amino Acid/Metaboli...	View
PKU Lophlex® LQ (Mixed Berry Blast)	Nutricia North America	Amino Acid/Metaboli...	View
PKU Lophlex® LQ (Tropical)	Nutricia North America	Amino Acid/Metaboli...	View
PKU Periflex® Junior Plus (Plain, Vanilla, Berry, ...	Nutricia North America	Amino Acid/Metaboli...	View

A patient with insurance, will obtain their formula through third party Enteral Nutrition Distributors: Apria, Epic Home Care or through a specialty pharmacy such as Coram CVS. In some states, coverage for metabolic formula is required by law. If the patient does not have insurance, they will work directly with the manufacture or the hospital clinic. In some extreme cases, the hospital or manufacturer will provide formula, and the patient pays via a sliding scale or an indemnity process. There are also unique commercial companies like Cambrooke that manufacture their own formula and low protein food products. In all cases, a referral from a hospital or RD is required. There is also a grant process through the National Organization for Rare Disorders (rarediseases.org) to help cover cost of formula. ((National PKU Alliance, n.d.).

Most formulas and foods are shipped either directly from the manufacturer or specialty pharmacy. At least for patients who work with Children's hospital (several who live in rural areas) the barrier to obtaining formula is prescription, supply chain, cost not geographic location.

PKU Formulas – Restricted PHE

Formula Brand	Provider or Distributor	Website	
Vitaflo USA Nutricia f Products	Metabolic Clinic Children's Hospital, Aurora, Colorado	www.childrenscolorado.org	Sliding Scale
Vitaflo PKU Cooler	Coram CVS	www.coramhc.com	Insurance Determined
Restore	Epic Home Care	www.epichealthservices.com	Insurance Determined
Vitaflo PKU Cooler 20oz pouch	Amazon	https://www.amazon.com/VF054814-Vitaflo-Cooler20-Liquid-Protein/dp/B00UNZ4NDW	$519.63 This is less than one day of formula
Formula and Food	Commercial Company Cambrooke	www.cambrooke.com	Various Products
LP Food	Dietary Specialties	www.dietspec.com	
LP Food	Ener-g Foods	www.ener-g.com	
LP Food	Schar	www.shop.schaer.com	

Maple Syrup Urine Disease is a genetic disorder the requires the amino acids Leucine, Isoleucine and Valine be restricted in the diet. List of specialty formulas from the NCM

MSUD Formulas Listed in the NCM (Academy of Nutrition and Dietetics, n.d.a)

All Solutions - 15 Items

Name	Manufacturer	Type	View
MSUD Aid	Nutricia North America	Amino Acid/Metaboli...	View
MSUD Analog™	Nutricia North America	Amino Acid/Metaboli...	View
MSUD Analog™	Nutricia North America	Infant Formula	View
MSUD Anamix® Early Years	Nutricia North America	Amino Acid/Metaboli...	View
MSUD cooler (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD cooler (red flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD cooler15 (orange flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD cooler15 (red flavor)	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD express	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD gel	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD Lophlex® LQ	Nutricia North America	Amino Acid/Metaboli...	View
MSUD Maxamaid®	Nutricia North America	Amino Acid/Metaboli...	View
MSUD Maxamum®	Nutricia North America	Amino Acid/Metaboli...	View
MSUD15 express	Vitaflo USA	Amino Acid/Metaboli...	View
MSUD20 express	Vitaflo USA	Amino Acid/Metaboli...	View

Formula Brand	Provider or Distributor	Website	
Vitaflo USA Nutricia f Products	Metabolic Clinic Children's Hospital, Aurora, Colorado	www.childrenscolorado.org	Sliding Scale
Vitaflo MSUD Gel	Nestle Health	https://www.nestlehealthscience.us/vitaflo-usa/inborn-errors-of-metabolism/protein-metabolism/msud	Insurance Determined

References

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Academy of Nutrition and Dietetics. (n.d.b). Nutrition Care Manual: Phenylketonuria (PKU) > Nutrition Intervention. Retrieved from https://www.nutritioncaremanual.org/topic.cfm?ncm_category_id=1&lv1=273102&lv2=24131&lv3=270876&ncm_toc_id=270876&ncm_heading=Nutrition%20Care

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