

Medical Foods for Inborn Errors of Metabolism: Issues in Patient Access

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National Institutes
of Health

Office of Dietary
Supplements

Medical Foods

- Are the only recognized therapy for many IEM identified on newborn screen and clinically
- Reduce morbidity and mortality
- Have a half century history of use

So, why aren't they accessible to all patients of all ages?

Focus of Discussion

- History of medical foods statutes in the U.S.
- Why and how they are used
- What a medical food is and what it is not
- Barriers to access and reimbursement
- Previous activities to rectify the problem
- Thoughts for a plan for moving forward

Disclaimer:

These are my views

I have no disclosures

History of Medical Food Statutes



1958 to 1972, commercial formulas for IEM were regulated as drugs



1972

Foods for Special Dietary Use

- Usefulness widely accepted
- Limited in number
- Less costly to develop

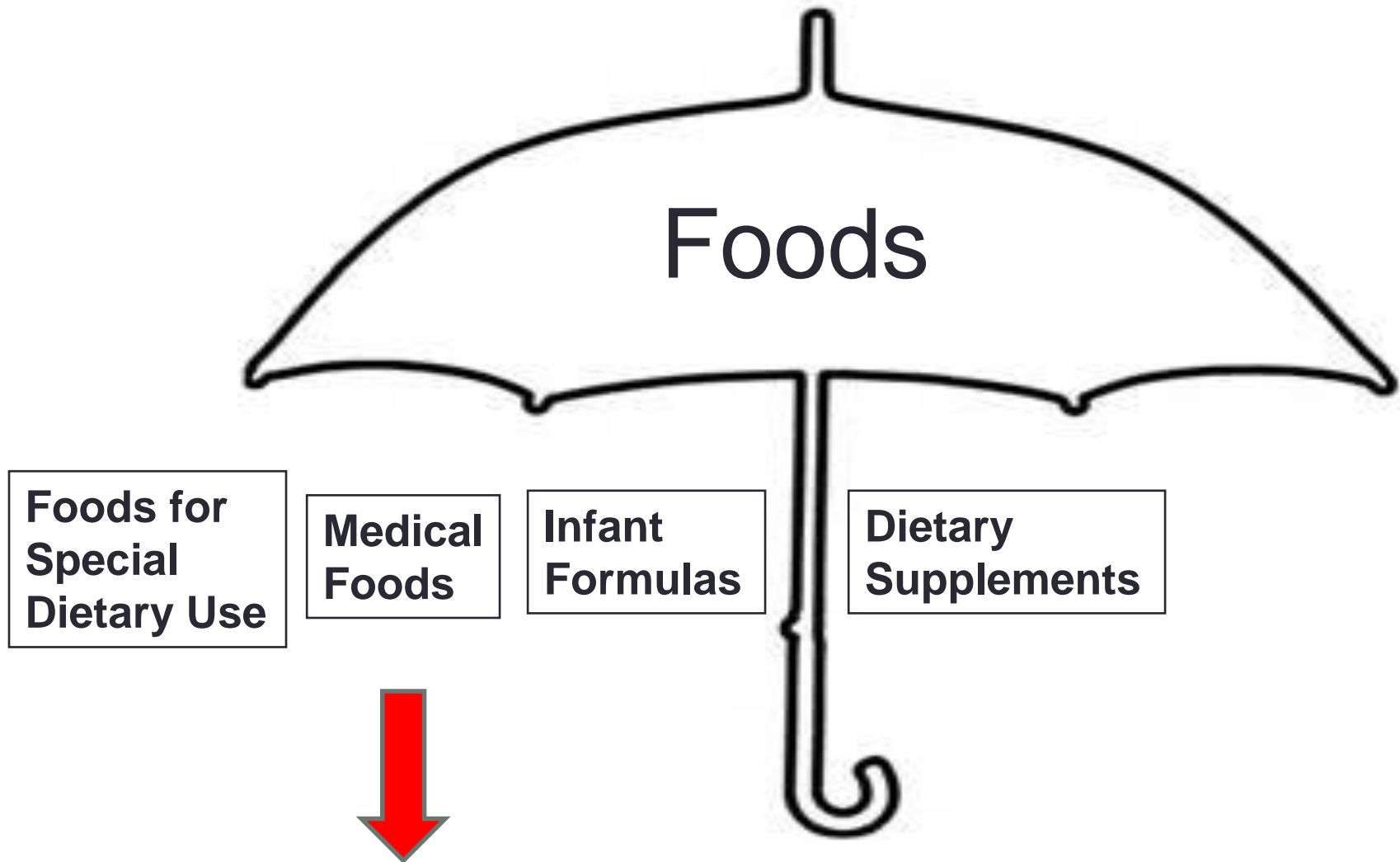


1973

Medical Foods

History, cont:

- 1988, Orphan Drug Amendments created the definition for medical foods as . .
 - “ . . . a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”
- Did not provide FDA with an evaluation mechanism to determine what fits and what does not



Inherent conflict! Foods cannot be used to “diagnose, cure, mitigate, or treat” disease

Medical Food for PAH Deficiency (PKU)—This Was Then



Medical Foods for IEM Today



Medical Food Categories

- Products with a full complement of nutrients EXCEPT the offending nutrient (e.g., for PAHD excludes phenylalanine)

- Power to be reconstituted
- Ready to drink
- Bars



- Modular products
 - Amino acid mixtures
 - Ready to drink, low volume, low calorie
 - Tablets
 - “Sport drinks”



- Foods modified to be low in protein
 - Baked goods, pasta, rice
 - Meat and cheese substitutes
 - Snack foods



Medical Foods Are Management Modalities for Inborn Errors of Metabolism Identified on Newborn Screen

- 19 of the core conditions on the RUSP utilize medical foods and/or amino acids, vitamins, or cofactors
 - **These conditions wouldn't be on the RUSP if it weren't for these treatments**
- Medical foods are required for other IEM diagnosed clinically (e.g., argininemia, OTC deficiency)



Core RUSP Conditions

Metabolic Disorders			Hematology	Others
Organic Acidurias	Fatty Acid Oxidation	Amino Acids		
Propionic acidemia Methylmalonic academia (MUT) Methylmalonic academia (Cbl A,B) Isovaleric acidemia 3-Hydroxy 3 - methylglutaricaciduria 3-Methylcrotonyl-CoA carboxylase Holocarboxylase synthase def β -Ketothiolase deficiency Glutaric acidemia 1	Carnitine uptake defect/carnitine transport Medium-chain acyl-CoA dehydrogenase Very long-chain acyl-CoA dehydrogenase Long-chain L-3-hydroxyacyl-CoA dehydrogenase Trifunctional protein deficiency	Classic Phenylketonuria Maple syrup urine disease Homocystinuria Tyrosinemia 1 Argininosuccinate aciduria Citrullinemia I	Sickle cell anemia S, β -thalassemia Sickle – C disease	Biotinidase deficiency Congenital adrenal hyperplasia Congenital hypothyroid Cystic fibrosis Classic Galactosemia Pompe Hearing loss Severe combined immunodeficiency MPS 1 X-ALD

Conditions in bold are treated with medical foods and/or single amino acids, amino acid mixtures, vitamins, or other cofactors

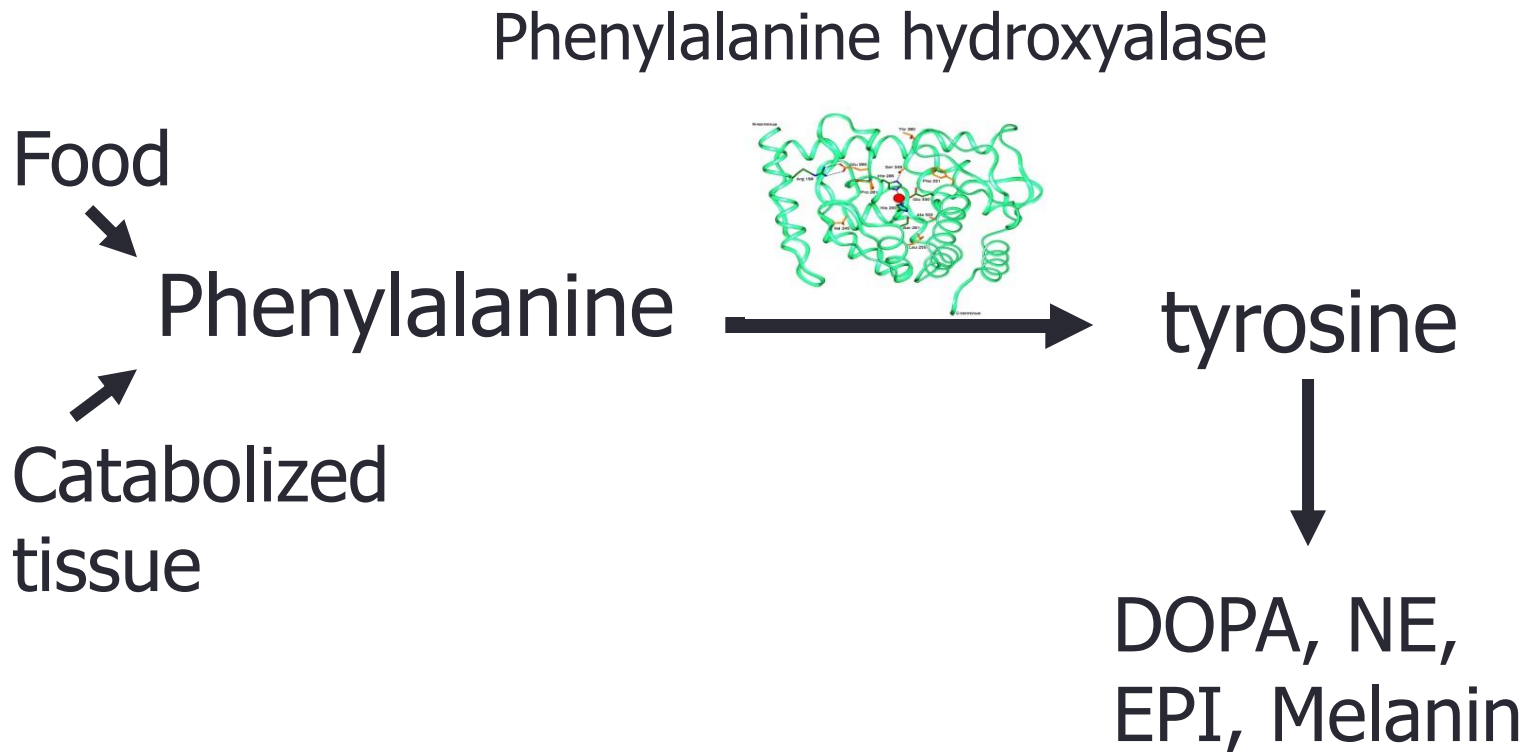
Failure to Treat--Examples

Depends on the condition

- Classic phenylketonuria (PKU)
 - Severe cognitive impairment, autistic-like features
 - Maternal PKU syndrome
- Homocystinuria
 - Cognitive impairment, ectopia lentis, osteoporosis, skeletal deformities
- MSUD
 - Cognitive impairment, growth failure, seizures, coma, cerebral edema, possibly death
- VLCADD
 - Hepatomegaly, cardiomyopathy, hypoketotic hypoglycemia, growth failure

Basic Principles of Dietary Management for IEM Using Phenylalanine Hydroxylase Deficiency (PKU) as an Example

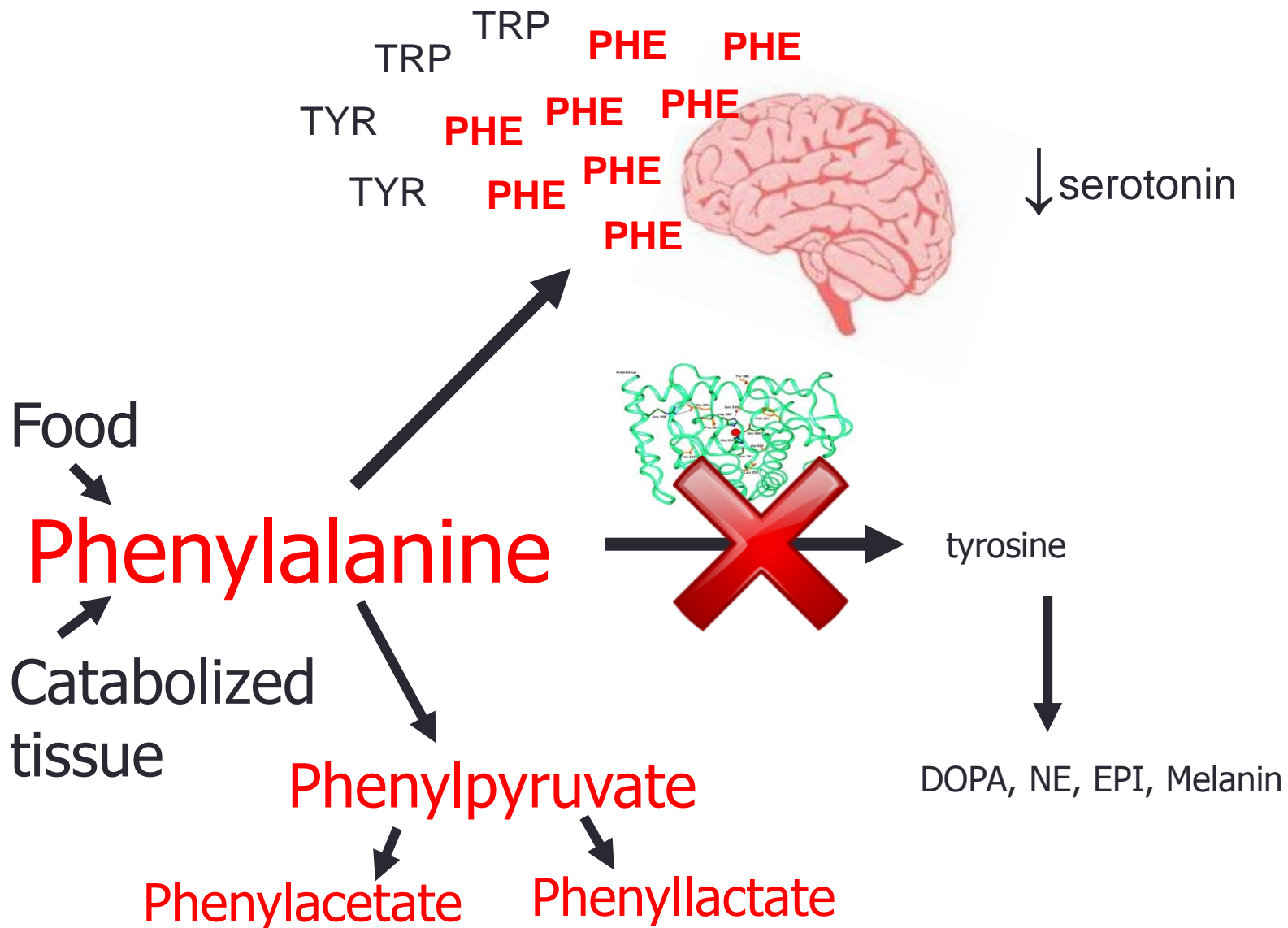
Normal Phenylalanine Metabolism



Phenylalanine Hydroxylase Deficiency



Phenylalanine Hydroxylase Deficiency



Phenylalanine Hydroxylase Deficiency

Solution:

Restrict the precursor

Food

Phenylalanine

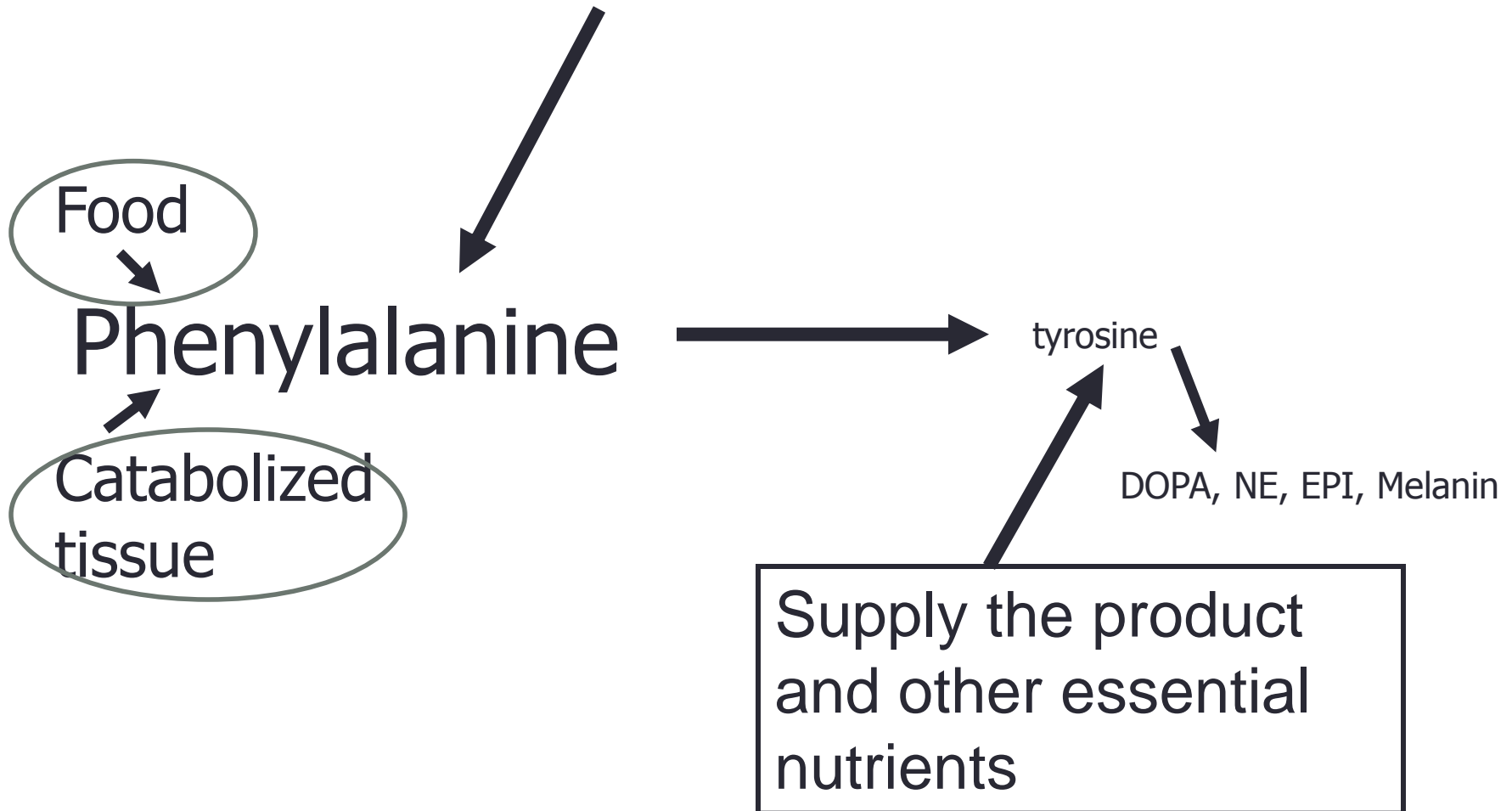
Catabolized
tissue



tyrosine

DOPA, NE, EPI, Melanin

Supply the product
and other essential
nutrients



That Is Done with Medical Foods

- Supply a source of protein for body growth and development
- Devoid of the offending nutrient
- Also contains essential nutrients, carbohydrate, and fat
- Along with the small amount of natural protein in a carefully planned diet
- Is the primary intervention
- Prevent or reduce adverse medical and developmental outcomes
- When used early at or near birth and continued throughout life can lead to normal or near-normal health outcomes

Medical Foods Work!



Sample daily intake for a 8 yr old with PAH deficiency

Phe tolerance of 350 mg (~ 6 g natural protein)

		g pro	kcal
Breakfast:	1 slice low pro bread	0.2	60
	1 slice low pro bread	0.4	190
Luncheon:	1 oz chicken	0.8	70
	1 oz chicken	0.2	19
	1 oz cheese	0.4	65
	1 oz chicken	0.4	190
Snack:	1 oz chicken	0.8	164
Dinner:	50 g low protein rice	0.3	176
	3 T tomato sauce	0.6	14
	8 oz medical formula	14	190
Snack:	3/4 oz potato chips	1.3	110
	12 oz fruit drink	0	160
		<hr/>	<hr/>
		49 g	1400

Reality Check:

1 oz cheese= 355 mg Phe

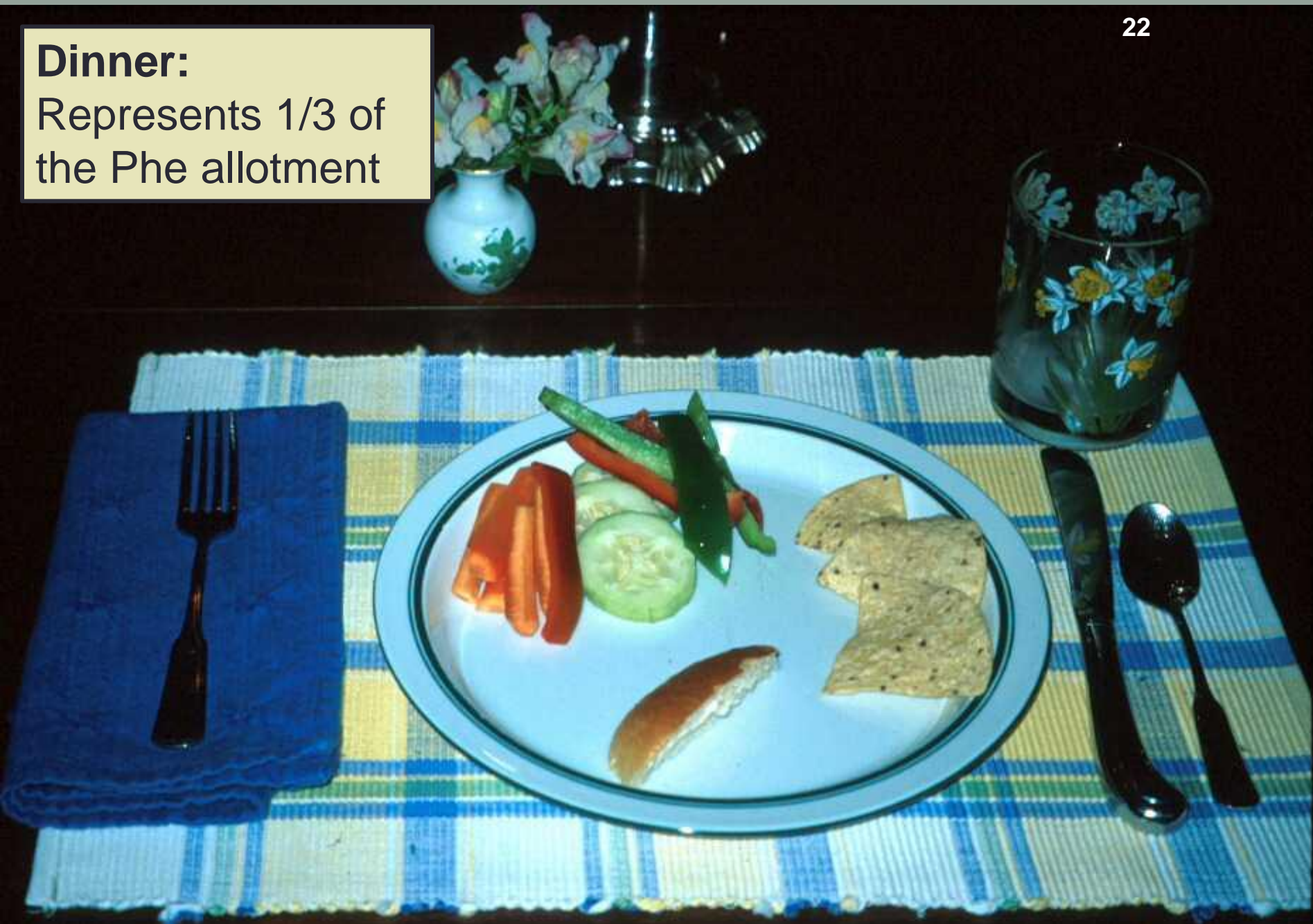
1 oz chicken= 345 mg Phe

6 g protein
and 583 kcal
from natural
foods

43 g protein
and 825 kcal
from medical
foods

Dinner:

Represents 1/3 of
the Phe allotment



Slide courtesy of Helen McCune

Dinner: Add
medical foods and
you get a meal



Slide courtesy of Helen McCune

The gear needed to feed a child with maple syrup urine disease

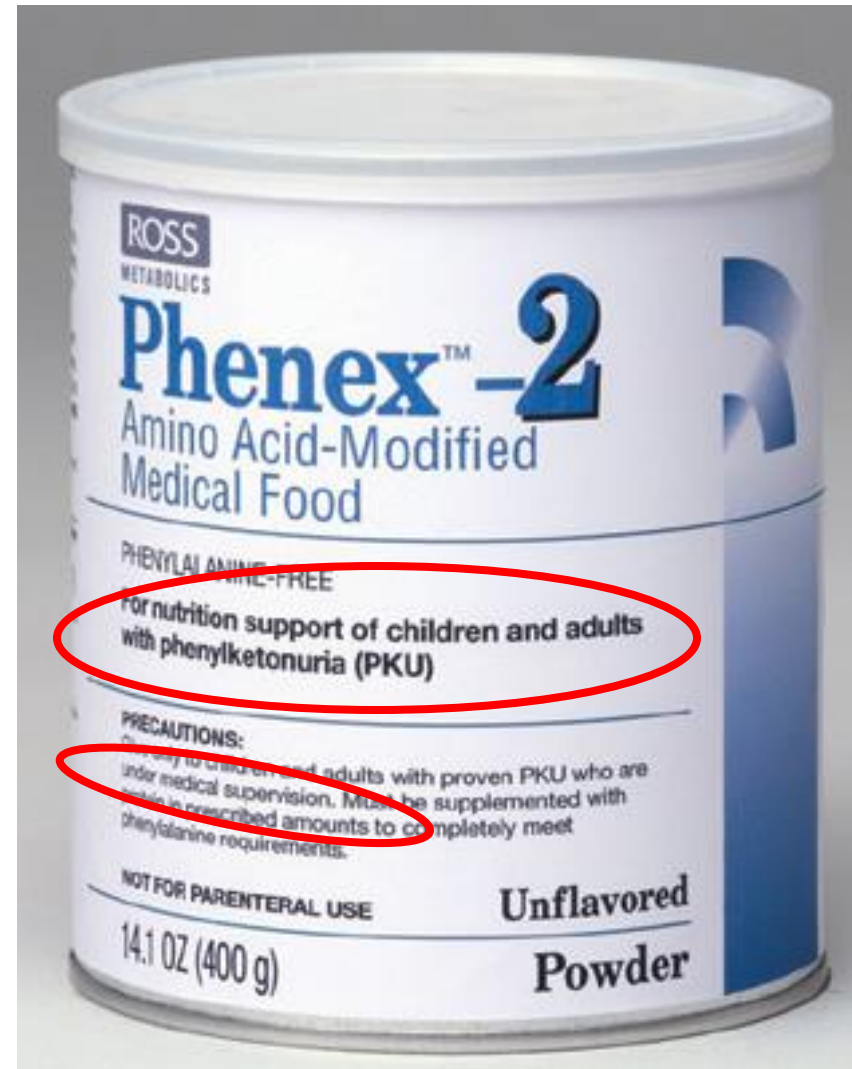


How do the statutes define medical foods?

- They are distinguished from the category of foods for special dietary use in that they
 - Are intended for the specific dietary management of a disease or condition (56 FR 60366 at 60377, November 27, 1991)
 - Meet distinctive nutritional requirements of a disease or condition
 - Used under medical supervision
- Specially formulated for the patient who is seriously ill or who requires the product as a major treatment modality
- Oral or tube feeding
- Does not pertain to all foods fed to sick patients

Medical Foods Labeling

- Labeled for the dietary management of a specific medical disorder, disease, or condition for which there are distinctive nutritional requirements
- Labeled for use under medical supervision



How are medical foods regulated?

- Federal Food, Drug and Cosmetic Act and the Fair Packaging and Labeling Act
 - Exempt from nutrition labeling, health claims, and nutrient content claims requirements
 - Ingredients must be approved food additives for their intended use or if not Generally Recognized as Safe (GRAS), have an exemption for investigational use
- Medical foods do not require premarket review or approval by FDA
 - Manufacturers must be registered with FDA, must comply with cGMP, and are inspected every 2 years
- FDA does not maintain a list of medical food products

What about infant formulas for IEM?

- Considered to be medical foods but regulated as infant formulas
- Categorized as “Exempt” infant formulas
- Must meet the same regulatory requirements as standard infant formulas, except
 - They are not required to contain the offending nutrient
- Have strict labeling requirements
- New products require a 90-day premarket notification to FDA



FDA Draft Guidance for Industry 2013

Further clarified FDA thinking on medical foods

- Definition of medical foods narrowly constrains the types of products that fit within this category
 - Specially formulated and processed--as opposed to naturally occurring
 - For partial or exclusive feeding orally or enteral feeding by tube
 - For a patient with limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foods or certain nutrients *whereby dietary management cannot be achieved by modification of the normal diet alone*
 - Used to manage unique nutrient needs resulting from *a specific disease or condition determined by medical evaluation*
 - Intended for a patient receiving active, ongoing medical supervision
- Final guidance has not yet been released

What Medical Foods Are Not

They are not prescription drugs

- No premarket review or approval
- They do not have NDC codes
- They do not require a prescription
 - But, the regulation states that that they are to be used under medical supervision



They are not products developed for

- Pregnancy (unless the pregnant woman has PKU, for example), because *pregnancy isn't a disease*
- Diabetes because people with diabetes *can modify a normal diet*

What Do Medical Foods Cost?

A lot!

But a whole lot less than Kuvan® at \$200,000 per year for an adult with PAH deficiency

Estimated Costs Per Year for Medical Foods for IEM, by Selected Age Group

Age	Medical Foods with Protein Wholesale Cost (x 2.0 for markup) (A)	Foods Modified to be Low in Protein (B)	Total Cost for IEM Medical Foods (C=A+B)	Estimated Annual Expenditure for Foods (Non IEM) (D)	IEM-related MF Costs in Excess of Estimated Expenditure (C - D)
Infant < 1 yr	\$1,817 (\$3,634)	\$0 — minimal	\$3,634	\$1,380*	\$2,254
School-age (9-13)	\$6,249 (\$12,499)	\$2,200 + \$120 shipping	\$14,819	\$2,255*	\$12,564
Late teen male	\$9,551 (\$19,102)	\$5,000 + \$120 shipping	\$24,222	\$2,525*	\$21,700
Adult male or pregnant woman	\$11,021 (\$22,042)	\$4,500 + \$120 shipping	\$26,662	Ave family of 4 spent \$6,100** (\$2,000 for adult)	\$24,662

* Lino (2008). Estimates are based on the average of the highest and lowest income level.

**U.S. Census Bureau (2007).

What Medical Foods Cost to Families

- Costs per month paid out of pocket
 - 21% of parents paid >\$100 for medical formula (some >\$500)
 - 48% of parents paid >\$100 for low protein foods

How Patients Get Medical Foods

- Purchase out of pocket from pharmacies, hospitals, health departments, medical supply and medical food companies
 - Reimbursed by private insurance
 - Or not
- Programs administered by States
 - Medicaid/CHIP/WIC
- Military health benefits
- Newborn screening programs or metabolic clinics
- Many patients utilize multiple sources

Most medical food companies provide a small supply for newly diagnosed patients and cover some formula for pregnancies.

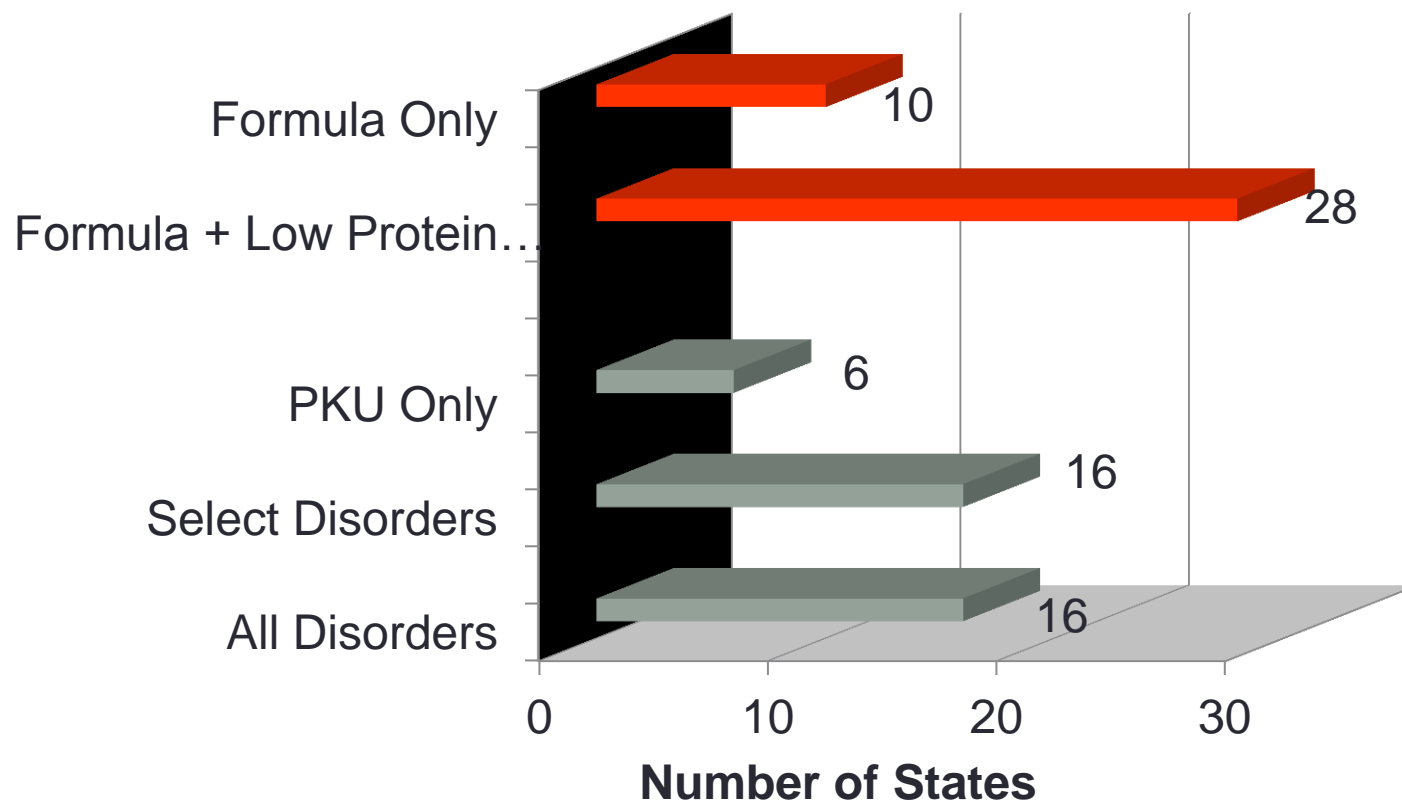
Who Pays?

Depends on:

- Who you are (age, disorder)
- Where you live
- What type of health benefits you have

State Insurance Mandates

Prior to ACA, 38 states had passed mandates for State or private payer plan coverage



Since ACA?

- Don't really know. No formal national survey of State practices has been undertaken
- ACA does not specifically address coverage of medical foods for IEM although newborn screening is a covered benefit without co-pay to families
- States with mandates may still have these mandates
 - Still may not apply to self-insured or Federal plans
 - Still have many inconsistencies and limited coverage

Here's What Metabolic Dietitians Report

- Patient with PKU lives in NH (has a mandate) but has an IL insurance plan (no mandate). The patient's IL plan rejected coverage for metabolic formula.
- Patient living in MD (has a mandate) has Federal BC/BS which does not cover medical food for patients over age 22 unless it is tube-fed or the sole source of nutrition so many adults are untreated.
- NJ has a comprehensive mandate, but Medicaid does not cover low protein foods.
- Patients in PA (has mandate for formula only) are not able to get low protein foods which affects their ability to fully comply with the diets.

How Outcomes Are Affected by State Policies

- NY is losing underinsured adults to care. It is hard to keep a patient motivated to seek care when they do not have a good paying job that has good insurance and the co-pays and co-insurances are prohibitive.
- This lack of access to medical foods and subsequent need to have multiple jobs to pay out-of-pocket leads to inconsistent metabolic control
- In VA state formula program became more restrictive after 2006 expanded NBS

Healthcare Common Procedure Coding System (HCPCS)

- Billing codes used by Medicare and monitored by CMS
- **B4162—Enteral formula for IEM administered through an enteral feeding tube, 100 calories = 1 unit**
 - CMS limits definition of “enteral” to tube feeding
 - Reimbursement units are based on calories
 - Calculations for diets for IEM are based on grams of protein
 - Products for older children and adults are high protein, low calorie so reimbursement falls way short of needs
- Private insurance companies may or may not adopt these codes

Efforts to Fix the Problem

Your Letters to the Secretary



May 19, 2009

- Committee reiterated 2007 recommendation to address gaps in coverage and reimbursement
 - More uniform approach and to amend Medicaid for uniform coverage by State programs
- Response on October 2, 2009
 - Enacting legislation is beyond the Department's authority

• June 14, 2010

- Committee recommended that health reform ensure access to medical foods and foods modified to be low in protein as essential health care services irrespective of the source of health coverage
- Interim Response on July 29, 2010
 - A response will be forthcoming
- Response on December 14, 2010
 - "I cannot adopt the Committee's recommendations at this time"; awaiting a DOL survey and IOM public workshop

Past Efforts--Legislative



- Medical Foods Equity Act (MFEA) of 2011 (S. 311; John Kerry)
 - Federal health programs and private insurance companies will cover
 - “medically necessary food” including formulas, pills, capsules, and bars;
 - Foods modified to be low in protein;
 - “pharmacological doses” of vitamins and amino acids as prescribed by a qualified medical provider.
 - Amends the Social Security Act definition of these products specifically for the treatment of conditions as recommended by the ACHDNC
- MFEA of 2013 (H.R. 3665; John Delaney)
 - Removed the requirement for private insurance companies to cover these products.

Past Efforts—Legislative



- American Health Security Act of 2011, 2013, 2015 (H.R. 1200 McDermott)
 - Provides coverage for medical foods and reiterated 1988 medical food definition
 - No committee action in any of the Congresses
- S.Res.324 – Designated December 3, 2015 as National Phenylketonuria Awareness Day
 - Multiple mentions of medical foods

Past Efforts—Advocacy Organizations

- NPKUA has advocated for coverage and reimbursement in a number of ways
 - Position statement on medical food coverage in the ACA
 - Educational information and resources on coverage under ACA for patients/families
 - Secured lead sponsors and led advocacy efforts for MFEA
- NORD hosted a conference on medical foods in Feb 2011
 - Address problems with HCPC codes
 - Revisit current definition of medical foods used by FDA
 - Support federal legislation
 - Investigate possibility of getting medical foods defined as essential health benefit in healthcare reform

Past Efforts—Literature and Professional Organizations

- Journal articles (e.g., Huntington 2009, Weaver 2010; Camp 2012; Berry 2013; Therrell 2014)
- SIMD & GMDI—Policy statements on Medical Foods 2007; SIMD updated in 2016; others, e.g. AAP
- ACMG—Management guidelines
 - PAH Deficiency—“Treatment for life mandates the need for medical insurance to provide coverage for medications and medical foods regardless of age.” (Vockley GIM 2014)
- GMDI—Management guidelines
 - PAH Deficiency—“Ensure access to medical and modified low-protein foods.” (Singh GIM 2014)

National Institutes of Health

- Consensus Statement on Phenylketonuria, 2000
 - “Uniform policies need to be established to remove from the individual and the family financial barriers to the acquisition of medical foods and modified low-protein foods”
 - Reimbursement should be covered by third-party providers. (Pediatrics 2001 108:972)
- PKU Scientific Review Conference, 2012
 - Full access across the lifespan to medical foods and foods modified to be low in protein provides the tools to succeed in managing PKU effectively on a daily basis. However, availability is inconsistent due to a patchwork of state laws and state programs that impact access (Camp and Parisi, et al. MGM 2014 112:87)

The Players

- Congress—legislation
 - FDA—regulation
 - CMS—Medicare, Medicaid, and CHIP; HCPCS
 - HRSA—health services
 - NIH—research
 - USDA—funds states to administer WIC programs
 - States—legislation; health services, WIC, etc.
-
- Patients/families/advocacy organizations
 - Professional societies and organizations
 - Clinicians and researchers
 - Medical food and pharmaceutical companies

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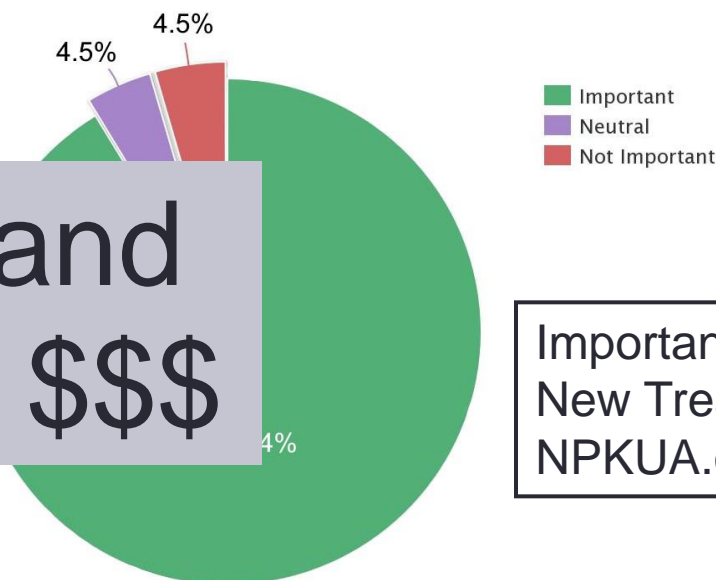
Thoughts on Where We are Now

- IEM are screened conditions because treatments are available--but not for everyone
- Patients and families continue to be saddled with high costs for medical foods
- Clinicians spend significant time dealing with coverage and reimbursement, leaving less for patient care and research
- Families spend significant time dealing with coverage and reimbursement, leaving less time to play with their kids
- > 50% of adults with PKU are not being followed (Berry 2013)
- Effect of the ACA on coverage and reimbursement nationally for medical foods is not known at this time
- Bills introduced but Congress has taken no action

The Future

- New treatments
- Patient

Decades and
Billions of \$\$\$



Importance of
New Treatments
NPKUA.org

- Meanwhile, almost 500 babies are born each year with an IEM requiring medical foods as the primary management modality
- A small percentage of all children but it's 100% to patients and their families

A Way Forward – Access for All

- Understand the current status of State mandates
- Efforts currently being undertaken
- Policy makers at the Federal and State level recognize the changes that need to be made
- Everyone gathers together to chip away at the barriers and challenges
- Other thoughts?

Regardless, it will take leadership, commitment, and persistence to navigate the complexities that lie ahead

Thank You



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