# NUTRITIONAL MANAGEMENT OF METABOLIC DISORDERS: AN OVERVIEW

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# DISCLOSURES

- Clinical Trial Research
  - PTC Therapeutics
  - BioMarin Pharmaceutical Inc.

# OBJECTIVES

- Participants will be able to list three inborn errors of metabolism.
- Participants will be able to explain the difference between a complete and incomplete protein source in relation to metabolic nutrition.
- Participants will be able to recognize a metabolic diet in clinical practice.

https://extension.umd.edu/programs/family-consumer-sciences/nutrition-health-and-wellness/

# OUTLINE

- Phenylketonuria
- Urea Cycle Disorders
- Fatty Acid Oxidation Disorders
- Glycogen Storage Diseases
- Galactosemia

# PHENYLKETONURIA (PKU)

# NUTRITIONAL THERAPY FOR PKU

- Definition: inherited disorder that increases the amount of phenylalanine (PHE) in the blood

## Detected on NBS

- Classification
  - Severe (Classic): >19.8 mg/dL
  - Non-PKU: <2 mg/dL

## Goals:

- Treatment range: 2-6 mg/dL
- Growth & Development

https://globalgenes.org/raredaily/rhode-island-adds-immune-deficiency-newborn-screening-test/

# NUTRITIONAL MANAGEMENT OF PKU

- Diet:
  - Washout Period upon diagnosis
  - Complete ("intact") protein
    - <25% of protein requirements from food
  - Incomplete protein – PHE-free
    - Medical food - formula
  - Calorie intake
- Tracking Phe levels
  - Infants: weekly
  - Children: weekly to monthly
  - Adults: monthly
  - Pregnancy: weekly

# NUTRITIONAL MANAGEMENT OF PKU

- Adjusting PHE prescription
  - Frequent monitoring is needed
  - +/- 10%
  - +/- up to 25% if levels are <1 or >9.9 mg/dL
- Alternative Therapies
  - Sapropterin
  - Pegvaliase
  - Clinical Trials
    - Oral Medications
    - Gene therapy


https://www.amazon.com/BRISTOL-MYERS-NUTRITIONAL-INST-30087510003S/dp/B006ARSBQ0


https://shop.medicalfood.com/product/374/phenylade-essential-drink-mix


http://www.cambrooke.com/products/glytactin/rtd/15-chocolate/


https://www.nutriciametabolics.com/shop/pku-lophlex-lq


https://shop.medicalfood.com/product/321/phenylade-gmp-drink-mix


https://www.nestlehealthscience.co.uk/vitaflo/conditions/protegel

https://www.businesswire.com/news/home/20160920005138/en/Cambrooke-Therapeutics-launches-all-new%C2%A0Glytactin%E2%84%A2-Complete-Bar-medical


https://www.pkugolike.com/product-information


https://galenmedicalnutrition.com/products/pku-easy-microtabs/

# PKU Formulas

# Simplified PKU Diet

## Free Fruits

- Apples – fresh and dry
- Apricots – fresh and dry
- Bananas
- Berries (all varieties)
- Cherries
- Cranberries – fresh and dry
- Grapefruit
- Grapes
- Kiwi
- Lemons
- Limes
- Mango
- Melon (all varieties)
- Olives
- Oranges
- Papaya
- Peaches
- Pears – dry and fresh
- Pineapple
- Plaintains
- Plums
- Pomegranates
- Prunes

## Free Vegetables

- Acorn Squash
- Butternut Squash
- Cabbage
- Carrots
- Cauliflower
- Celery
- Chayote Squash
- Cucumber
- Green Beans
- Eggplant
- Jicama
- Leeks
- Lettuce
- Onions
- Parsnips
- Peppers (all varieties)
- Pumpkin
- Radishes
- Rutabaga
- Sauerkraut
- Spaghetti Squash
- Summer Squash (zucchini and yellow)
- Tomatoes
- Turnips
- Yuca (Cassava Root)

Please remember your NO foods are still NO foods

For any questions on specific items, please contact your metabolic dietitian.

Developed by IMD Nutrition, Children's Hospital Colorado

# Simplified PKU Diet

## Measure and Count Phe/Protein

- Dried Fruit (except apples, apricots, craisins, pears, prunes, raisins)

- Artichokes
- Arugula
- Asparagus
- Avocado
- Broccoli
- Brussels Sprouts
- Corn
- Kale, mustard greens, Swiss chard
- Mushrooms
- Peas
- Potatoes
- Seaweed/Nori
- Sundried Tomatoes
- Spinach
- Yams/Sweet Potatoes

## Do Not Measure and Count Phe/Protein

- All other fruits and vegetables (see separate sheet for specific list)
- Low protein foods less than 20 mg of phe per serving from low protein food companies

Please remember your NO foods are still NO foods

For any questions on specific items, please contact your metabolic dietitian.

Developed by IMD Nutrition, Children's Hospital Colorado

# PKU: EXAMPLE DIET

10 year old
30 kg (66#)
RDA Protein: 36-45 g PRO (120-150% of 1g/kg/d)
RDA Calories: 2100 kcal/d (70 kcal/kg/d)

Diet Rx:

| | PRO (g) | ENERGY (kcal) |
|---|---|---|
| Formula: | | |
| Glytactin RTD 15 (3 cartons/d) | 45 g PE | 600 |
| Food Allowance: | 5 g | 1500 |
| Total: | 50 g | 2100 |
| Weight: 30 kg | 1.7/kg/d | 70/kg/d |

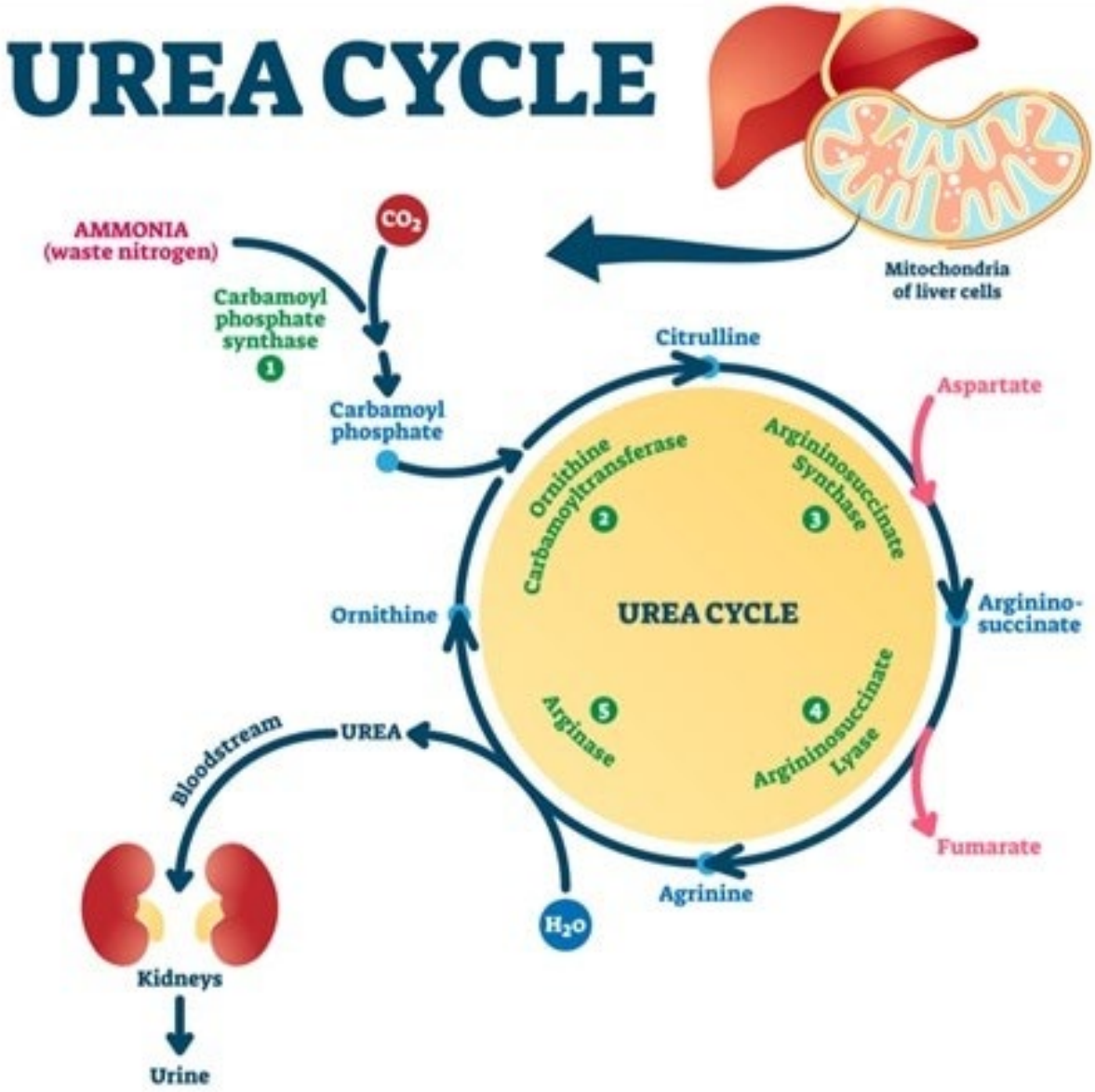
# UREA CYCLE DISORDERS (UCD)

# UREA CYCLE DISORDERS

Definition: genetic disorder caused by a mutation that results in a deficiency of one of the six enzymes in the urea cycle

Enzymes:

- NAGS – N-Acetyl Glutamate Synthetase
- CPS I – Carbamoyl Phosphate Synthetase
- OTC – Ornithine Transcarbamoylase
- ASS – Arginosuccinic Acid Synthetase (Citrullinemia)
- ASL – Argininosuccinate Lyase (Argininosuccinic Aciduria)
- ARG - Arginase




https://www.news-medical.net/health/The-Urea-Cycle-Step-by-Step.aspx

# NUTRITION THERAPY FOR UCDS

- Limit Protein
- Prevent Catabolism
- Supplement Amino Acids
- Use Medications

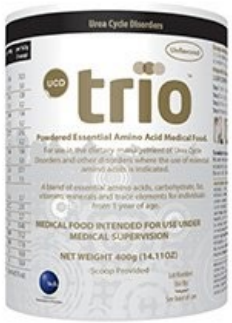
# NUTRITION THERAPY FOR UCDS

- Limit Protein
- Essential amino acids (EAA)
  - From formula
  - ~ 50% of total protein
    - Difficult to get EAA from food alone
    - Promotes normal growth
- Prevent Catabolism
- Amino Acid Supplementation
  - L-citrulline used in CPS and OTC
  - L-arginine used in ASA and ASL

| Age (years) | Total Protein (g/kg/d) for UCD |
|---|---|
| 0-1 | 1.2-2.2 |
| 1-7 | 1.0-1.2 |
| 7-19 | 0.7-1.4 |
| >19 | 0.5-1.0 |

R.H. Singh Nutritional Management of UCDs


https://abbottnutrition.com/cyclinex-1




https://www.nestlehealthscience.us/vitaflo-usa/inborn-errors-of-metabolism/protein-metabolism/urea-cycle-disorders/ucd-trio


https://shop.medicalfood.com/product/120/essential-amino-acid-mix


https://www.healthproductsexpress.com/89202600-89202600-Infant-Toddler-Formula-WND-2-1-lb-Can-Powder.html

# UCD Formulas

# ACUTE NUTRITIONAL MANAGEMENT OF UCDS

- Sick day diet plan
  - Diet plan is given to each family
    - No protein diet
    - Half protein diet
    - Usual Diet
- Hyperammonemia
  - Reverse catabolism
  - Medications

# UCD: EXAMPLE DIET

2 month old with Citrullinemia

4.56 kg (10#)

RDA Protein (if unaffected): 2.2 g/kg/d

RDA Calories (if unaffected): 108 kcal/kg/d

SICK DAY DIET PLAN:

| Step | ProPhree(g) | WND 1 (g) | Enfamil Infant Powder(g) | total vol (mL) | total cals | cals/kg | Cc/kg | cal/oz | total Pro (g) | Pro/ kg |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 126 | 0 | 0 | 800 | 642.6 | 140.6 | 175.1 | 24.1 | 0 | 0.00 |
| 2 | 78 | 29 | 19 | 800 | 639.7 | 140.0 | 175.1 | 24.0 | 3.804 | 0.83 |
| 3 | 32 | 57 | 38 | 800 | 642 | 140.5 | 175.1 | 24.1 | 7.543 | 1.65 |

**Goal Recipe (Step 3):** 32 g ProPhree + 57 g WND 1 + 38 g Enfamil Infant + water to 800 mL total volume
**Goal regimen**: 100 ml q 3 hrs - Offer PO x 30 minutes then give remainder via G-tube.







# Medical Low Protein Food

https://zoiahealthcare.org/store/marketplace/

# FATTY ACID OXIDATION DISORDERS (FAOD)

# FATTY ACID OXIDATION DISORDERS

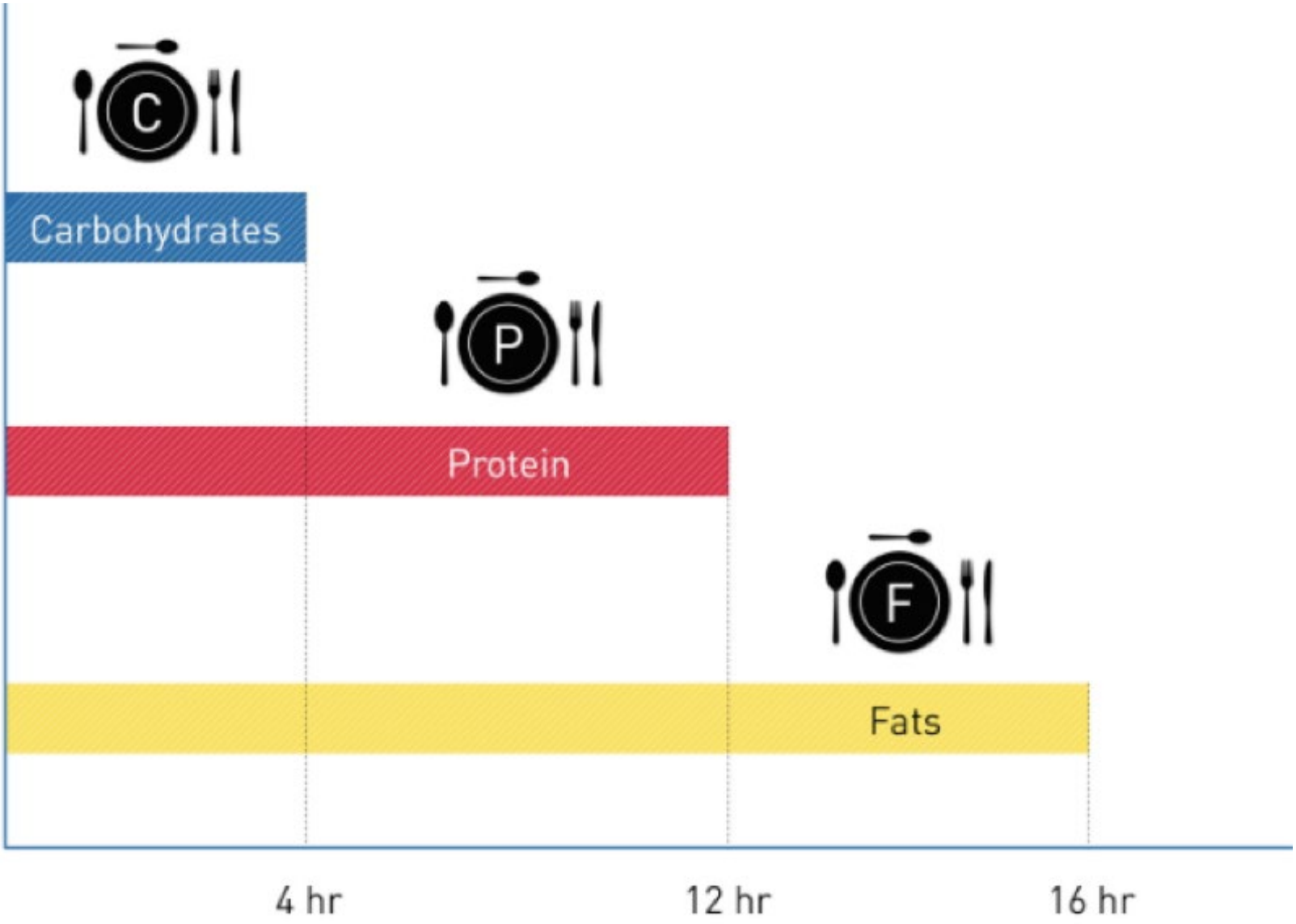
Definition: metabolic conditions where the body has the inability to produce or utilize enzymes that oxidize fatty acids

| # of Carbons | Category | Where oxidation occurs | Associated Disorders |
|---|---|---|---|
| 2-4 | Short chain | Mitochondria ✖ carnitine | Short chain acyl Co-A deficiency (SCADD) |
| 6-12 | Medium chain | Mitochondria ✖ carnitine | Medium chain acyl Co-A deficiency (MCADD) |
| 14-20 | (Very) Long chain | Mitochondria ✸ carnitine | Very long chain acyl Co-A deficiency (VLCADD)<br>Long chain hydroxy-acyl ca-A deficiency (LCHADD) |

# NUTRITION THERAPY FOR FAODS

- Avoid long chain fats as an energy source
  - Avoid prolonged fasting
  - Modify diet composition
    - Provide alternative energy sources
    - Supplement with Medium Chain Triglycerides (MCT)

# Avoid Prolonged Fasting




Bernstein L et al. Visual Teaching Aids, Vitaflo USA

# MODIFYING DIET COMPOSITION FOR LCHADD AND VLCADD

- Restrict long chain fat (LCT)
- Supplement with MCT

- Total fat: 30% of diet
  - LCT: 10%
  - MCT: 20%


https://www.dojolvi.com/dosing/


https://www.nutriciametabolics.com/shop/liquigen


https://www.nestlehealthscience.com/vitaflo/conditions/mctprocal-hcp


https://www.pureformulas.com/product/mct-oil-100-pure-by-pureformulas/1000038103?srsltid=AfmBOopereJH9sDL-iNY50T7q6e3CItHVte7JaUK4SkUy76ocggH18t2

# GLYCOGEN STORAGE DISEASES (GSD)

# GSD

Definition: a metabolic disorder caused by enzyme deficiencies which impair the synthesis or degradation of glycogen

Symptoms:

- Liver affected genetic defect:
  - Hypoglycemia
- Muscle affected genetic defect:
  - Weakness
  - Difficulty with exercise

# NUTRITIONAL THERAPY FOR GSD TYPE I

- Frequent feedings to avoid fasting
  - Infants: every 2 hours
  - Children/Adults: every 4 hours
- Limit/exclude sucrose, fructose, and galactose
- Cornstarch Therapy
  - Mixed in sucrose-/lactose- free drink
    - 1g CS: 2-3 mL fluid
  - By mouth or via G-tube
  - Glycosade
  - Individualized dosing


https://www.hy-vee.com/grocery/PD6244209/Argo-100-Pure-Corn-Starch


https://www.vitaflousa.com/products/glycosade

# GSD 1A: EXAMPLE DIET

6 year old
22 kg (48.4#)

Diet Rx (prior to starting Glycosade):
16g UCCS Q4H (6am, 10am, 2pm, 6pm, 10pm, 2am)

Current Diet Rx (with Glycosade):
20 g Glycosade Q8H (6am, 2pm, 10pm)

**UCCS = uncooked corn starch

# GALACTOSEMIA

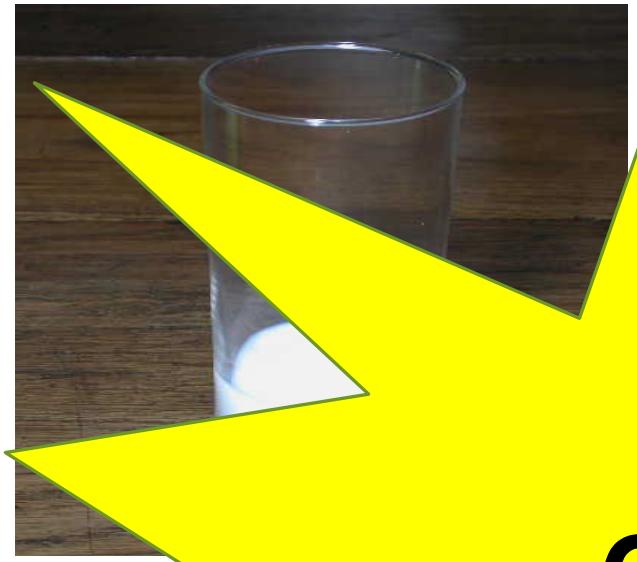
# Current Diet Restrictions for Galactosemia

| Allowed Foods and Ingredients | Menu planning ideas |
|---|---|
| *Soy-based infant formulas containing soy protein isolate, amino acid-based elemental infant formulas | |
| *All fruits, vegetables and their juices, pickled fruits and vegetables | Fruit salad, smoothies, herbed vegetables, pickled cucumbers |
| *All legumes (e.g. navy beans, kidney beans, garbanzo beans, soybeans) | Hummus, chili, burritos, black bean soup |
| *Soy-based products that are not fermented (soy milk, tofu, textured soy protein, hydrolyzed vegetable protein, soy protein concentrate, meat analogs) | Veggie burgers, tofu stir-fry, soy cheesecake |
| *Aged Cheeses: Jarlsberg, Emmentaler, Swiss, Gruyere, Tilsiter, Parmesan aged > 10 months, 100% Parmesan cheese powder, sharp cheddar cheese | Grilled cheese sandwich, spaghetti sauce topped with parmesan, Caesar salad |
| *Sodium and calcium caseinate | |
| *All cocoa products except milk chocolate | Hot chocolate, brownies, chocolate cake |
| *Additional ingredients: natural and artificial flavorings, all gums including carrageenan | Herbs, spices, extracts, even if the flavoring sounds like it might be made from milk. Given the extremely small amounts of flavorings added to foods, restriction is not necessary. |
| **Restricted Foods and Ingredients** | **Examples of foods to avoid** |
| Breast milk, all milk-based infant formulas | |
| All milk- based foods and beverages except for caseinates and aged cheeses, listed above | Sour cream, puddings, ice cream, yogurt |
| All milk- based ingredients including buttermilk solids, casein, dry milk protein, dry milk solids, hydrolyzed whey protein, hydrolyzed casein protein, lactose, lactalbumin, whey | Butter, whipped toppings, many packaged baked goods |
| All cheese and cheese-based products except those listed above | Soft cheeses such as ricotta, cottage or cream cheese |
| Organ meats, meat-by-products | Hot dogs (Kosher all-beef hot dogs are o.k.), some lunch meats, liver |
| Soy products that are fermented (e.g. miso, natto, tempeh, sufu)[1] | Miso soup |
| Soy sauce[2] | |

*Indicates foods or ingredients that were previously restricted or considered questionable by some clinics.
[1]These products are restricted until further analysis becomes available.
[2]Fermented soy sauce contains approximately 400 mg galactose/100 mL; the amount of soy sauce used in foods needs to be considered when determining acceptability.

IMD Clinic and Galactosemia Task Force
December 2013
*Publication Pending*

25 mL milk



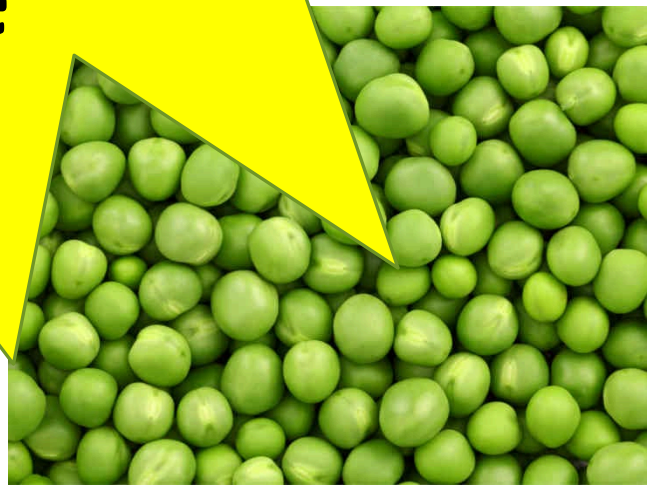
5.5 lbs tomatoes

=

**600 mg**

**galactose**

16.5 l



# FUTURE

- Clinical trials
  - New therapies
    - Gene therapy
    - Medications
- Adding to NBS
- At home monitoring

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# CEU Evaluation