

Galactosemia 101

An Introductory Overview

*a 'parent – to – parent' presentation for families
of children recently diagnosed with classic
galactosemia*

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GANES Mini-Conference

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Purpose

- To provide a lively, interactive, “upbeat, but honest” presentation of practical material and advice to parents who are new to the world of Classic Galactosemia from a parent who’s “*been there*”
- To provide a foundation from which parents can learn more together with their medical professionals

“Galactosemia 101”

- **Overview**
 - Definitions
 - A Very Brief History
 - Genetics
 - Metabolism
 - Normal
 - Galactosemic
- **Medical Management**
 - Doctors
 - What kinds
 - How often
 - Testing
 - What kinds
 - How often
- **Diet Management**
 - Newborn
 - Babies
 - Toddlers
 - Preschool age
 - Elementary school
 - Beyond
- **Medical / Developmental Complications**
 - Speech & Language
 - Neurological
 - Reproductive
 - Other
- **Emotional Impacts**
 - Personal
 - Family
 - Siblings
 - Extended family
 - Marital
- **Q&A / Discussion / Wrap-Up**

Intended Audience for Proposed Presentation

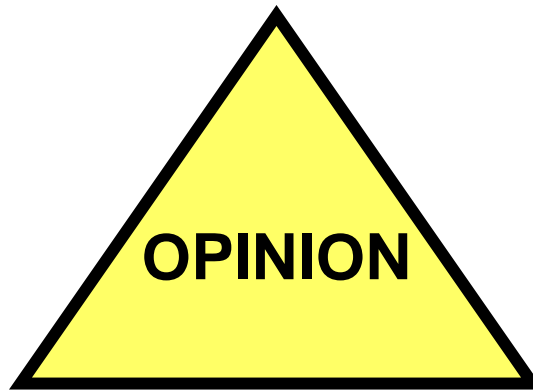
- Parents of small children (birth to two years) who need a practical introduction to “news they can use”
- Other Interested Adults Welcome !

Parents of older children have probably already heard this material, so they would likely be bored to sit through it again

*Children, especially children with galactosemia, should **NOT** be in the audience ... parents can decide for themselves when to expose their children to this material*

Important Caveat

The views expressed in the presentation are solely those of the presenter.



Important Caveat

GANES, Inc. neither guarantees nor reviews the accuracy of the material and is not responsible for any inadvertent inaccuracies presented.

Important Caveat

Parents should always discuss matters with their child's medical professionals before deciding on a course of action.

Definitions

Definitions

- **Galactosemia**

“*Galactose in the blood*”, a genetic disorder that is characterized by insufficient activity of the enzyme needed to properly metabolize galactose, resulting in the toxic accumulation of galactose in the blood that can cause medical and developmental complications.

Definitions

- **Metabolism**

A biochemical process that converts food for the body's purposes

Definitions

- **Enzyme**

A protein that makes a biochemical process happen

Galactose–1–Uridyl Transferase

GALT

GALT is the enzyme responsible for proper metabolism of galactose.

In Classic Galactosemia, GALT is missing.

Definitions

- **Enzymes related to Other Variants of Galactosemia**

Galactose–1–Uridyl Kinase

GALK

Galactose–1–Uridyl Epimerase

GALE

A Very Brief History

A Very Brief History

- Symptoms first noted in 1908,1917
- Specific enzyme defect isolated in 1956
- Newborn screening started in 1966
- Important research paper indicating ongoing medical and developmental complications in 1980s and 1990s
- 1st Support group formed in 1985

A Very Brief History

- *So What !?*

Now our kids usually live, and live better !

Now there is help !

But, it's still the *early* in the history of treatment for galactosemia

Genetics of Galactosemia

Genetics of Galactosemia

- Informal Gene Designators

Normal GALT production gene ==> **N**

Defective GALT production gene ==> **g**

Genetics of Galactosemia

- Everybody has 2 genes that determine GALT production

They inherit one gene from their biological mother's egg

They inherit one from gene their biological father's sperm

Genetics of Galactosemia

- Gene Combinations

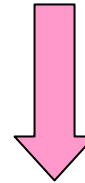
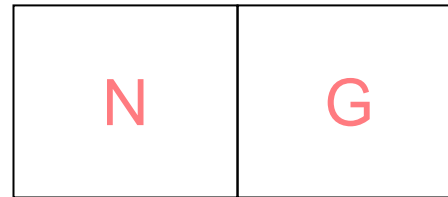
NN = normal GALT production

NG or **GN** = classic galactosemia carrier
reduced (but sufficient) GALT production

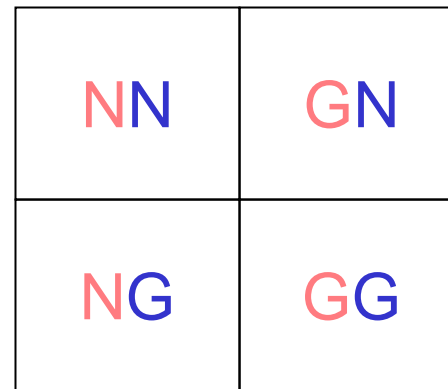
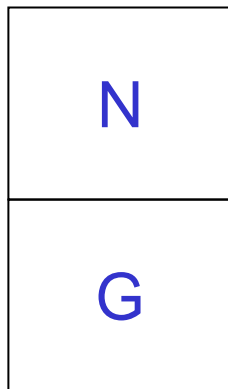
GG = classic galactosemic
insufficient GALT production

Genetics of Galactosemia

Biological Mother's Genes



Biological Father's Genes



Genetics of Galactosemia

- For a child conceived by biological parents who are both carriers of classic galactosemia (NG), there is:

a 25% chance of that that child will be completely unaffected by classic galactosemia (NN)

a 50% chance that that child will be a carrier of classic galactosemia (NG or GN)

a 25% chance that that child will have classic galactosemia (GG)

- Each conception is independent of other conceptions

Genetics of Galactosemia

- Details, Details, Details ...
 - Many individual defects have been identified that result in GALT deficiency
 - Defects have technical names that have to do with the type and location of the defect on the gene
 - e.g. Q188R, L195P, etc*
 - Unknown if there is or is not a correlation between any specific defect, or pair of specific defects, and outcome

Genetics of Galactosemia

Genetic (DNA) Testing

Blood test

Determines exact genetic defects present

No therapeutic value (currently)

No predictive value (currently)

Might help researchers someday

Genetics of Galactosemia

So What !?

This shows that it's not your fault !!

It's not 'catchy'

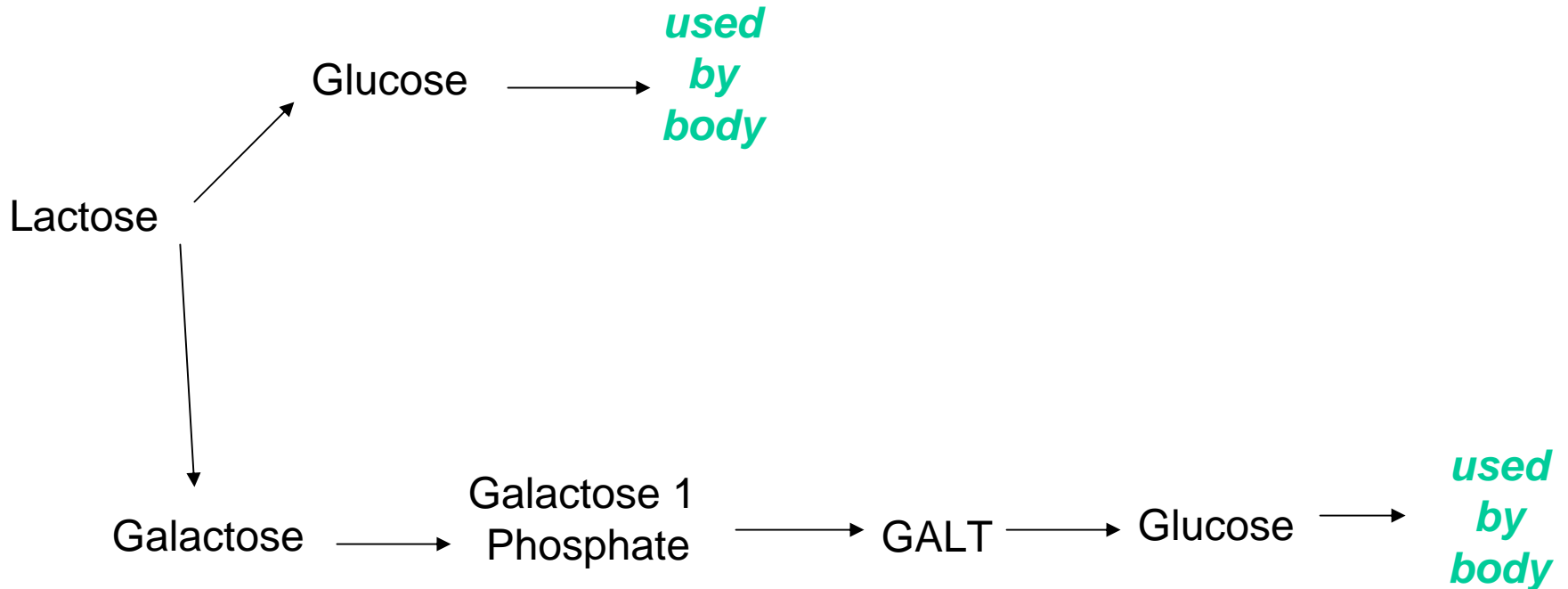
Knowledge is power

Metabolism

Metabolism

'Normal' metabolism of lactose & galactose

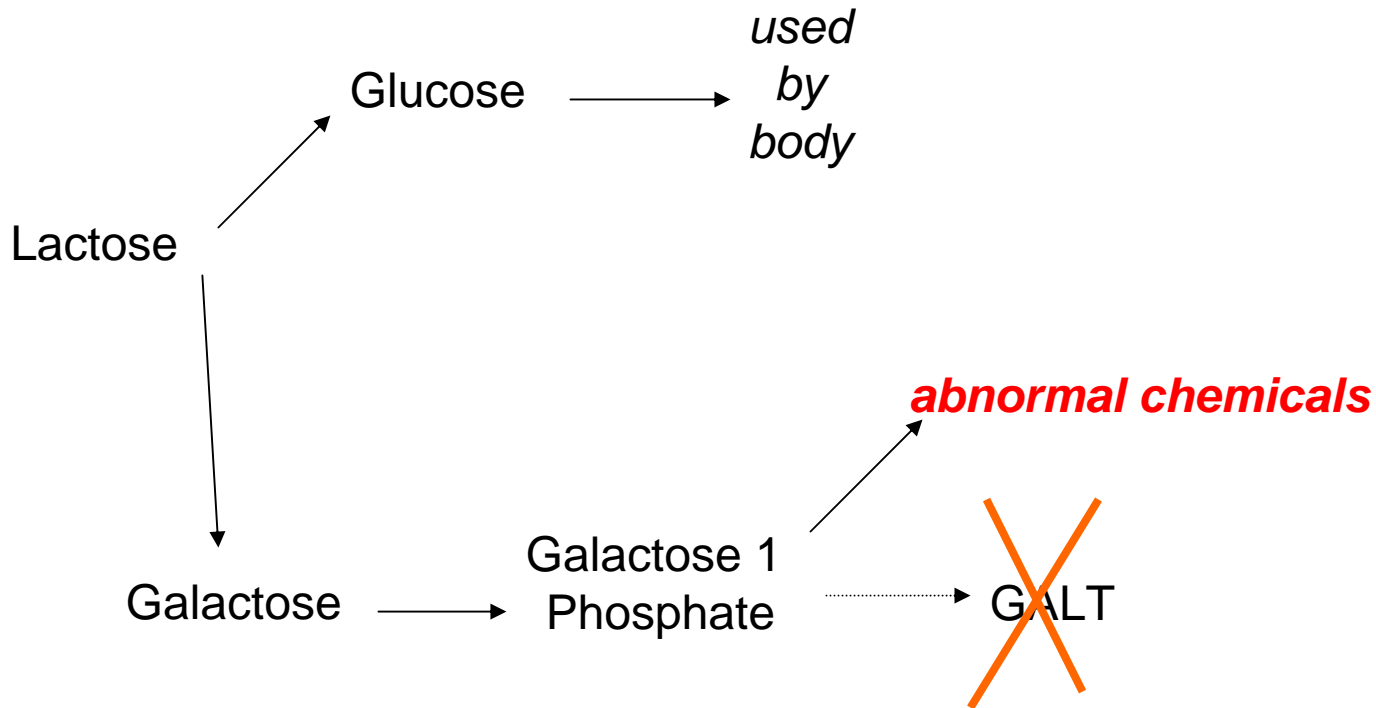
from "Understanding Galactosemia – A Diet Guide; Hartz, Pettis, Van Calcar



Metabolism

Galactosemic metabolism of lactose & galactose

from "Understanding Galactosemia – A Diet Guide; Hartz, Pettis, Van Calcar



Metabolism

- Important aspects to keep in mind
 - Liver, not stomach
 - Alternate pathways of interest
 - Defective dietary metabolism not the only source of medical / developmental complications

Medical Management

Doctors

Testing

Medical Management

Procedure for Definitive Diagnosis - First Month

- Medical & Family History
- Physical examination - length, weight, head circumference
- Neurological examination
- Ophthalmologic examination

Medical Management

Procedure for Definitive Diagnosis - First Month

- Laboratory tests
 - a) GALT Activity levels
 - b) other enzyme analysis as indicated
 - c) Gal-1-P levels at first evaluation
- Nutritional consultation for galactose elimination diet, interpret diet prescription, explain diet records
- Social service assessment

Medical Management - Doctors

- What Kind / How Often
 - Pediatrician
 - Geneticist
 - Ophthalmologist
 - Endocrinologist
 - Gynecologist
 - Other MDs as needed
 - Neurologist
 - Other specialists
 - As needed

Medical Management - Doctors

- Pediatrician
 - Just like any other child for primary care
 - Probably not primary doctor for galactosemia
 - Help to educate your pediatrician
 - Point him at resources you have
 - Enlist him as an ally
 - Referrals for other doctors
 - Written letters when needed

Medical Management - Doctors

- Geneticist / Pediatric Metabolic Specialist
 - Find a clinic
 - They will order blood testing (Gal-1-P, etc)
 - 3 to 4 times per year first two years
 - Help detect galactosemia-related developmental issues
 - Twice per year until age 6
 - Annual until age 18 (?)
 - Galactitol (urine test) also available

Medical Management – Doctors

- Ophthalmologist
 - Two times per year first two years
 - if no complications
 - Annually
 - Cataracts are an indicator of diet non-compliance
 - Reversible when caught early

Medical Management – Doctors

- Gynecologist

Pediatric gynecology evaluation at ~9 years, or
sooner if indicated

- Endocrinologist

Can be seen for growth issues

Sometimes primary Galactosemia Specialist

Medical Management – Doctors

- Others (as needed)
 - Neurologist
 - Psychological / Developmental Assessment

Medical Management – Other Specialists

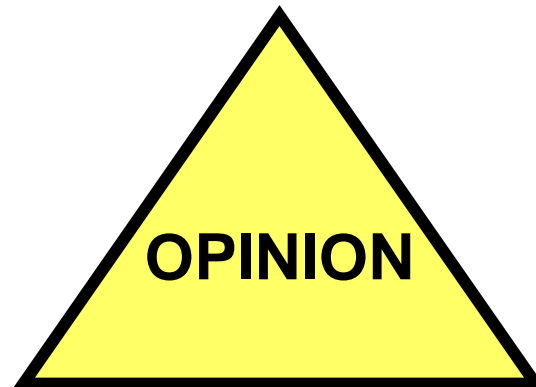
- Physical Therapist
- Speech Therapist
- Occupational Therapist

Medical Management - Testing

- What do results mean?
 - Low levels of Gal-1-P are an indication of good dietary compliance
 - Elevated levels are cause for investigation, not necessarily indicative of poor compliance
 - Newborns often take several months or more to have their levels stabilize at a low level
 - Some children have levels that do not correspond to diet

Medical Management - Testing

- DNA blood test
 - Once, maybe
 - Of no therapeutic value
 - May be of help to research
 - Often not covered by insurance



Diet Management

Newborn

Babies

Toddlers

Preschool age

Elementary School age

Beyond

Diet Management – newborns

- Couldn't be easier in most cases

Soy formula

- Decide about form

Powder, concentrate, ready-to-feed

- Look into reimbursement from Health Insurance

State-by-state coverage

Never easy, but worth it

Save those receipts !

- Take time to *start* learning - *slowly*

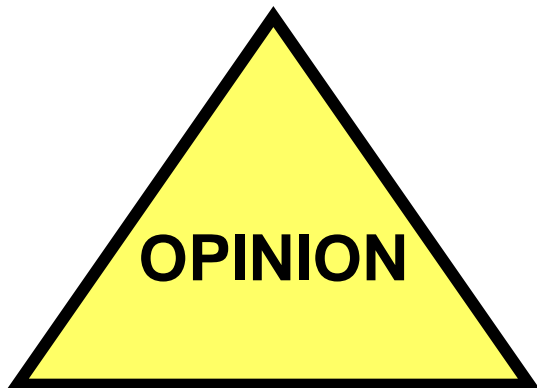
Diet Management – babies

- Start preparing before you are ready to start solids
 - Web resources
 - Written guidelines
- Start **LABEL READING**
 - Banned Ingredients lists
 - Restricted / limited foods
- Baby food lists
- Start **TEACHING**
 - yes food / no food

Diet Management – babies

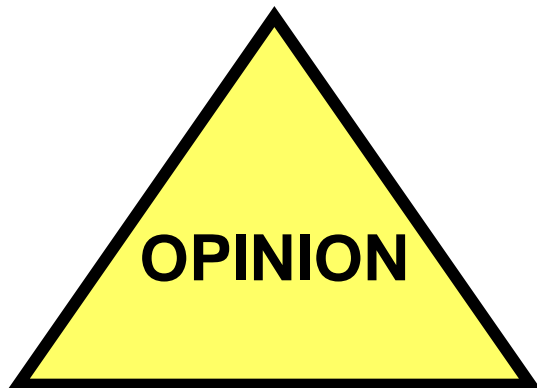
- Substitutes
 - Recipes
 - Specialty foods
- Decide about your household
 - Strongly recommend

Integration / Not Isolation



Diet Management – toddlers

- Introduce Variety & Substitutes
- Continue teaching through play
 - Yes food / No food
 - Red stickers / green stickers
 - Daycare
 - Provide written Guidance and supplies



Diet Management – pre-school

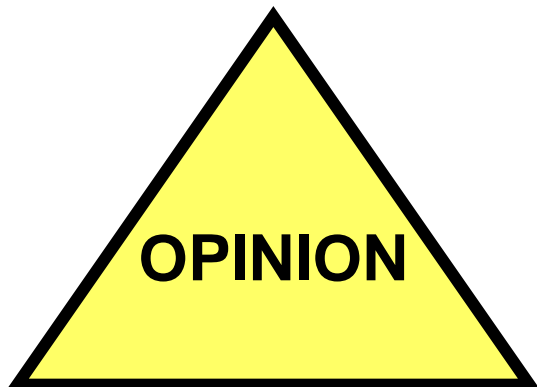
- Provide written guidance
 - Teachers
- Continue teaching
 - “Dairy” food / “Dairy-free” food
 - Red stickers / green stickers
 - Letter identification
 - Magnets with words on the fridge



OPINION

Diet Management – elementary

- Provide written guidance
 - Teachers, School nurse, Cafeteria
- Accidents happen
 - Monitor for gastrointestinal upset
 - Don't panic
 - Get to the bottom of it and see about corrective approaches



Diet Management – beyond

- Increase the child's independence in a way that matches their ability to conform
- Cheating happens
 - Hopefully rare
 - Hopefully “self-correcting”
 - Gastrointestinal ‘distress’



OPINION

Medical / Developmental Complications

- Newborn Medical Complications
- Speech & Language
- Neurological
- Reproductive
- Other

Newborn Symptoms

- Projectile Vomiting
- Jaundice
- Lethargy
- Hypotonia
- Failure to thrive

Newborn Medical Complications

- E. Coli Sepsis
- Organ damage
- Hemorrhage of the eye
- Cataracts

Potential Longer Term Complications

- Speech and Language
mild -> moderate -> severe
- Learning Disabilities
Low-average IQ compared to siblings
- Neurological
- Reproductive
- Other

Speech & Language

Articulation

Receptive Language

Expressive Language

Often Responsive to Speech Therapy

Speech & Language

Checklist for speech delays

- Exhibits minimal interest in talking
- Is not talking at all by age 2
- Has largely unintelligible speech, especially after age 3
- Has trouble producing many speech sounds
- Uses mostly vowel sounds
- Omits many consonants, especially after age 3
- Substitutes many sounds for others
- Has inaccurate speech sound pronunciation
- Consistently drops word endings after age 5
- Exhibits a slow labored rate of word pronunciation
- Exhibits rapid slurred speech
- Demonstrates oral inactivity
- Is drooling after 15 months

Speech & Language

Checklist for language delays

- Shows minimal interest in communication, verbal or nonverbal
- Is not attempting to talk at any age over 18 months
- Is not using phrases by 2 ½ - 3
- Is not using sentences by age 3
- Does not follow 2 step instructions by age 2
- Is embarrassed, disturbed, or uncomfortable about speaking at any age
- Has difficulty organizing or expressing an idea or thought
- Exhibits an excessive amount of imitation and limited spontaneous production
- Often is 'searching' for words, or using 'empty' vocabulary
- Often talks 'around' a subject
- Has difficulty following 2 to 4 step instructions by age 3 or 4
- Has difficulty telling or retelling a story in sequence by age 4
- Has noticeably faulty sentence structure at age 5
- Has responses that are grammatically correct but not appropriate to a situation
- Has difficulty learning letters, numbers, sounds, rhymes, and reading

Speech & Language

Checklist for Voice

- Has excessive nasal, hyponasal, or denasal voice
- Has strained, harsh or hoarse voice, including evidence of frequent screaming
- Has breathy voice
- Has voice pitch that is too high or too low for age, size, gender
- Has minimal variation in intonation
- Uses excessively loud voice
- Consistently speaks too softly but not from shyness

Checklist for Fluency

- Uses excessive repetition of sounds in words
(e.g. “p-p-p-p-puppy”)
- Uses frequent prolongation of sounds in words
(e.g. “sssssssoap”)
- Uses excessive hesitations, pauses, and or hemming and hawing

Learning Disabilities

- Difficulties in School

Neurological

Ataxia

An inability to coordinate muscular movements that is symptomatic of some nervous disorders.

Tremors

Mostly hand / arm tremors, but also head and body
Seen mostly in young adults

Reproductive

Premature Ovarian Failure

Premature ovarian failure (POF) is defined as the cessation of menses associated with high levels of gonadotropins and low levels of estrogen before age 40

Effects a High Percentage of Adult Women with Galactosemia

Some Pregnancies Reported !

note – No Known Reproductive Problems For Adult Men with Galactosemia

Other

ADHD

*never fully studied regarding galactosemia
anecdotal only*

Fine / Gross Motor

Sensory Integration

noises, textures, etc.

Feeding Difficulties

rare

Emotional Aspects

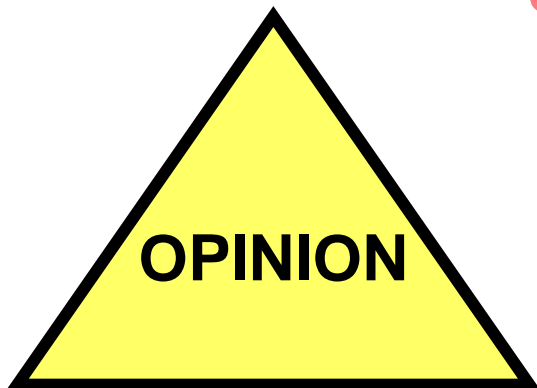
Emotional Aspects– Personal *Denial - Grieving – Acceptance*

Don't skip steps, but go through them as fast as you can

Respect your emotions, but don't be a slave to them

Don't judge others who don't feel what you feel

Don't let galactosemia define your life

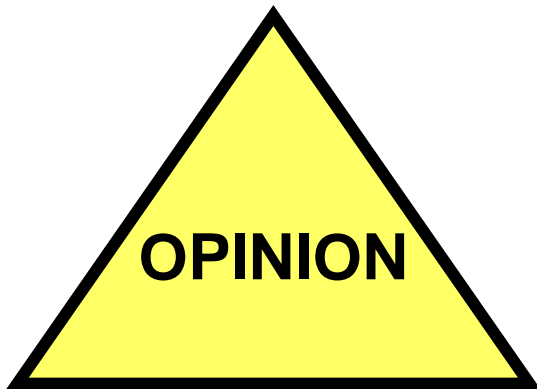


Emotional Aspects - Family

Siblings

Age Appropriate explanation

Don't let galactosemia define your family



Emotional Aspects - Family

Extended family

- Don't expect them to “get it”
ignore nonsense
- Try to educate them, especially if you need them
- Know when to stop trying

You can't control people's actions, you can only control your reactions

Your children learn more from your reactions than from the actions of others



OPINION

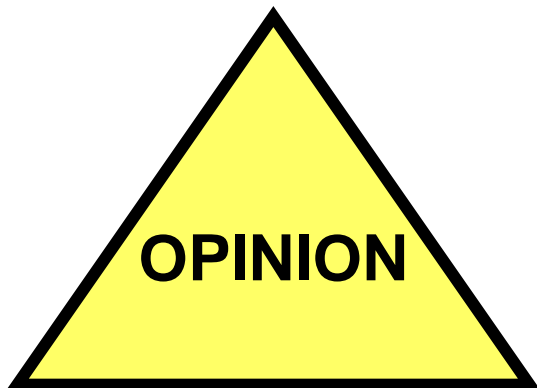
Emotional Aspects - Marital

Do your part

Help each other

Accept & Respect that your spouse might
be handling this differently

*Don't let galactosemia define your
marriage*



Q& A / Discussion / Wrap-up

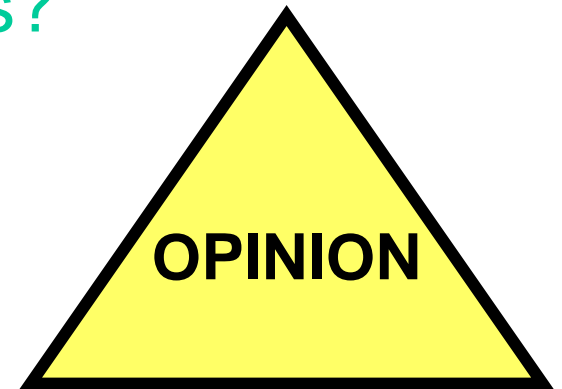
What did I miss?

A Cure - Definition

Let's try to define what we mean by “a cure” for galactosemia

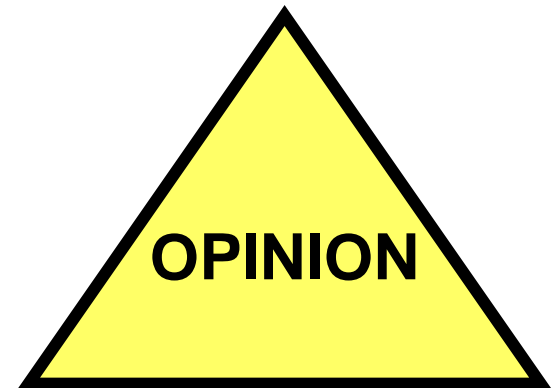
Is it the ability to eat restricted / limited items without consequence?

Is it elimination and reversal of medical and developmental complications?



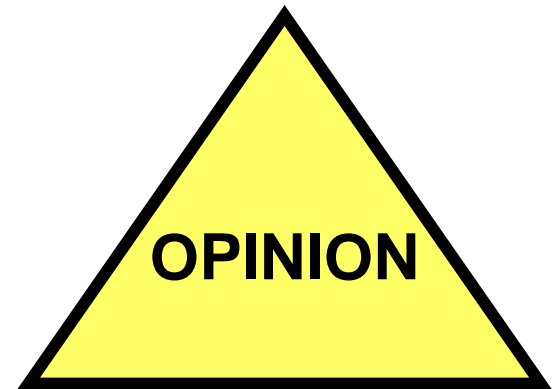
A Cure - Paths

- Let's try to understand the steps that might have to be taken in order to arrive at "a cure"
 - Internal enzyme infusion
 - Gene therapy to bring about internal enzyme synthesis



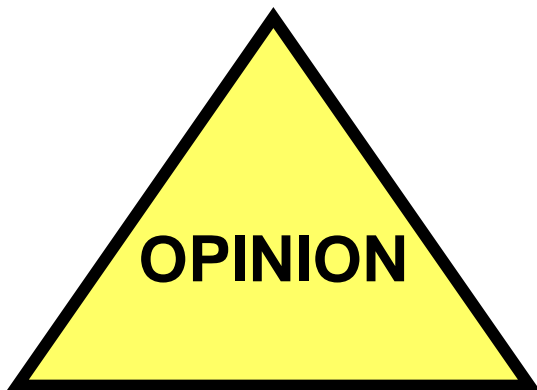
A Cure - Steps

- Potentially dangerous testing
- Is the path to the 'cure' worse than the 'disease'
- \$\$\$\$\$\$
 - Better spent elsewhere



Instead of *A Cure* ...

- How about more research into better management?
- How about researching treatments for complications from a galactosemia point of view?



One Last Thing

- Get Involved !!
- Nothing feels as good or provides as much benefit as being part of a community of people

Others can help you

You can help others

