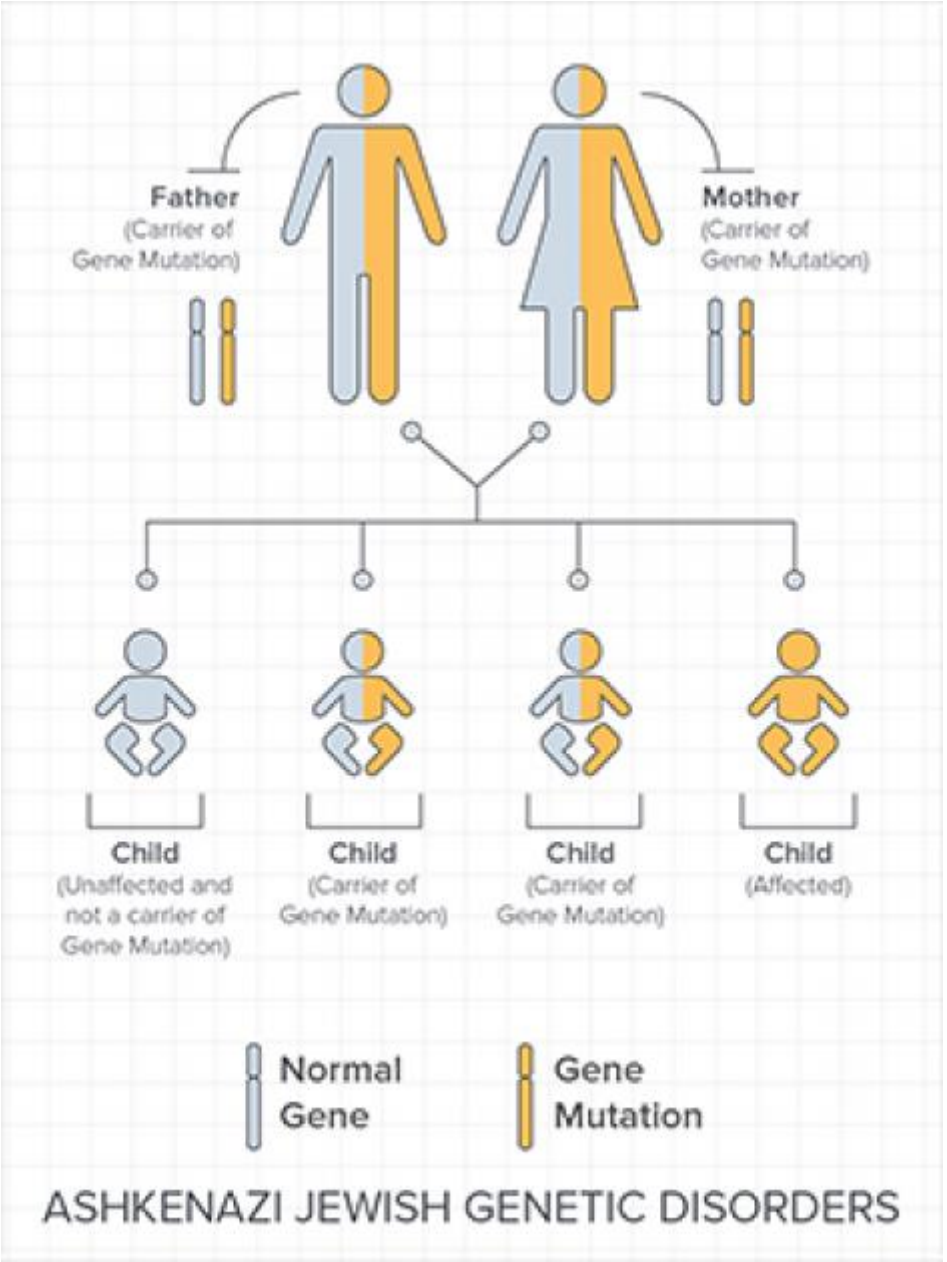
Maple Syrup Urine Disease
MSUD

MSUD

- Is a recessive genetic disease which means that:
  - Both parents must carry a mutation for the disease.
- Each person has two genes that code for enzymes.
  - If only one gene is mutated, then the person is just a carrier of MSUD.



(MSUD)
Also called branched-chain ketoacid-uria
(excessive amounts of ketone bodies in urine)

MSUD is:

- A rare genetic disease,
- Affects branched-chain amino acids.

- Caused by a deficiency of the:
  - Branched-Chain Alpha-Keto Acid Dehydrogenase enzymes (BCKAD enzyme).

❖ There are 3 BCAAs: leucine, isoleucine and valine.

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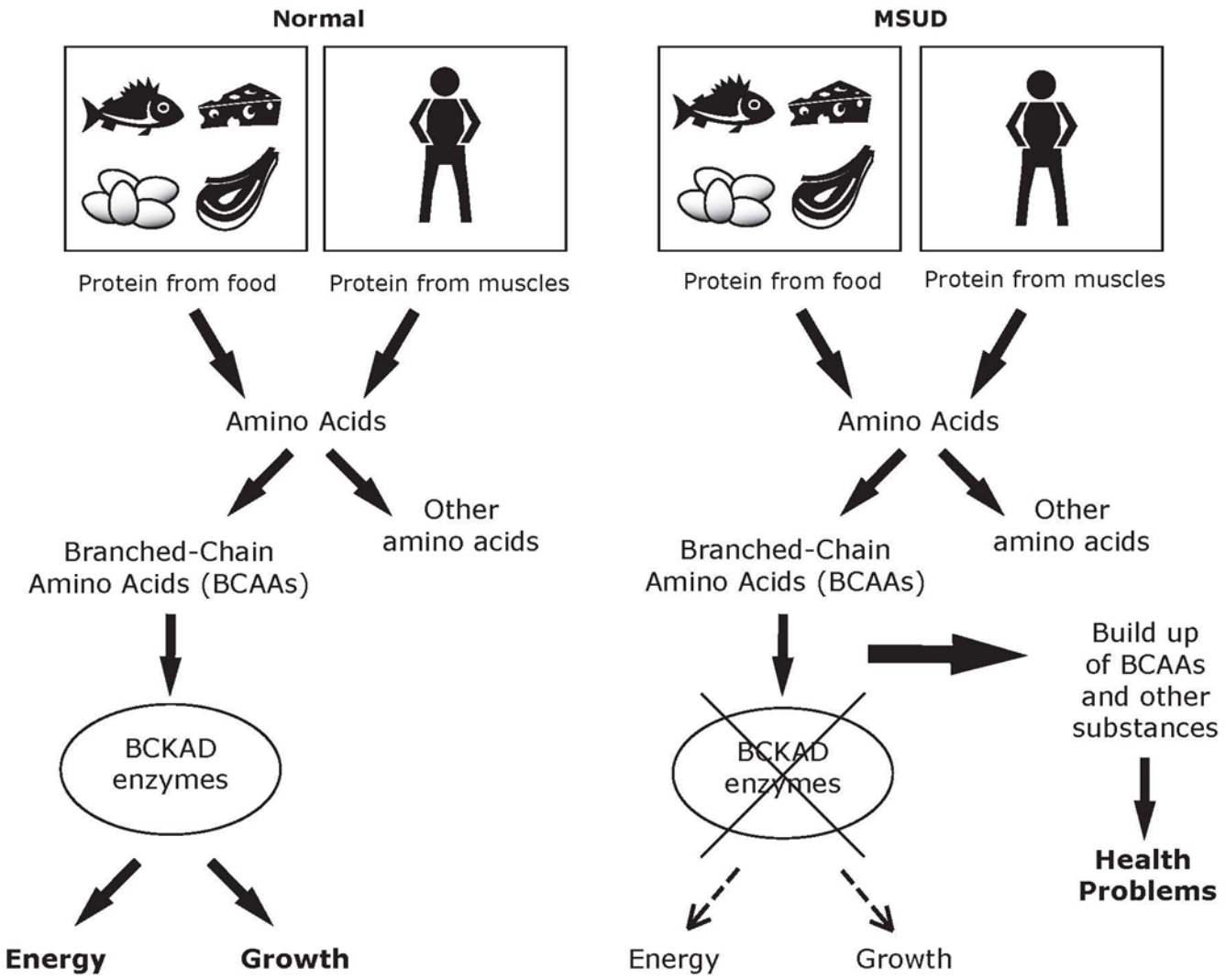
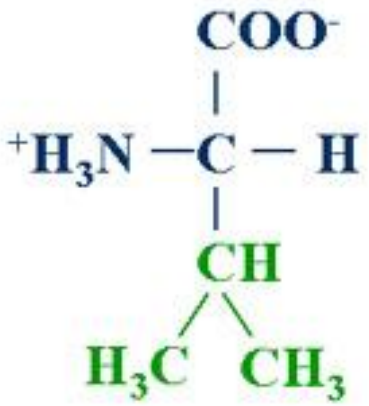
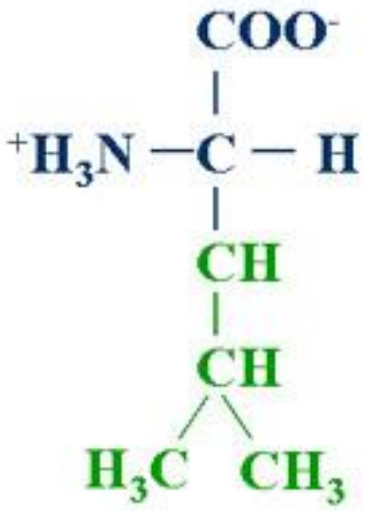
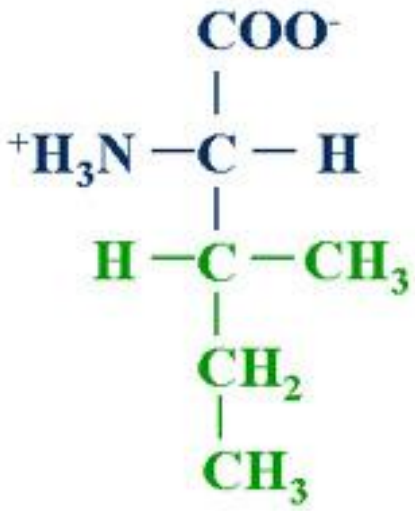




Valine



Leucine



Isoleucine

MSUD

Leads to a buildup of the branched-chain amino acids (leucine, isoleucine, and valine) and their toxic by-products in the blood & urine.

MSUD Diagnosis/Screening

In USA

- Mandatory State Screening Programs:
  - Every state tests infants for MSUD as part of their newborn screening program.
- Blood Tests to look at amino acid levels
  - BCAA and other disorders.

Characteristics of MSUD

- The disease is characterized by the:
  - Presence of sweet-smelling urine,
  - With an odor similar to that of maple syrup.
- Infants with this disease:
  - Seem healthy at birth but if left untreated
  - Suffer severe brain damage and eventually die.

Diagnostics for MSUD

The disease:

- Can usually be suspected from the characteristic odor of urine, and
- Is confirmed by the abnormal levels of:
  - Branched Chain Amino acids and keto acids in blood & urine.
- Other symptoms include:
  - Metabolic acidosis, and
  - Depressed serum alanine levels.

❖ Blood Leucine level is diagnostic.

Diagnostic tests for MSUD

- Normal leucine blood test value: < 4mg/dl

- Abnormal leucine blood test value: > 4mg/dl
- Suspected cases undergo more blood tests.

- If result of blood test is :
  - Leucine level = 3 to 4 mg/dl or 4 mg/dl
  - Interpretation: possible MSUD.

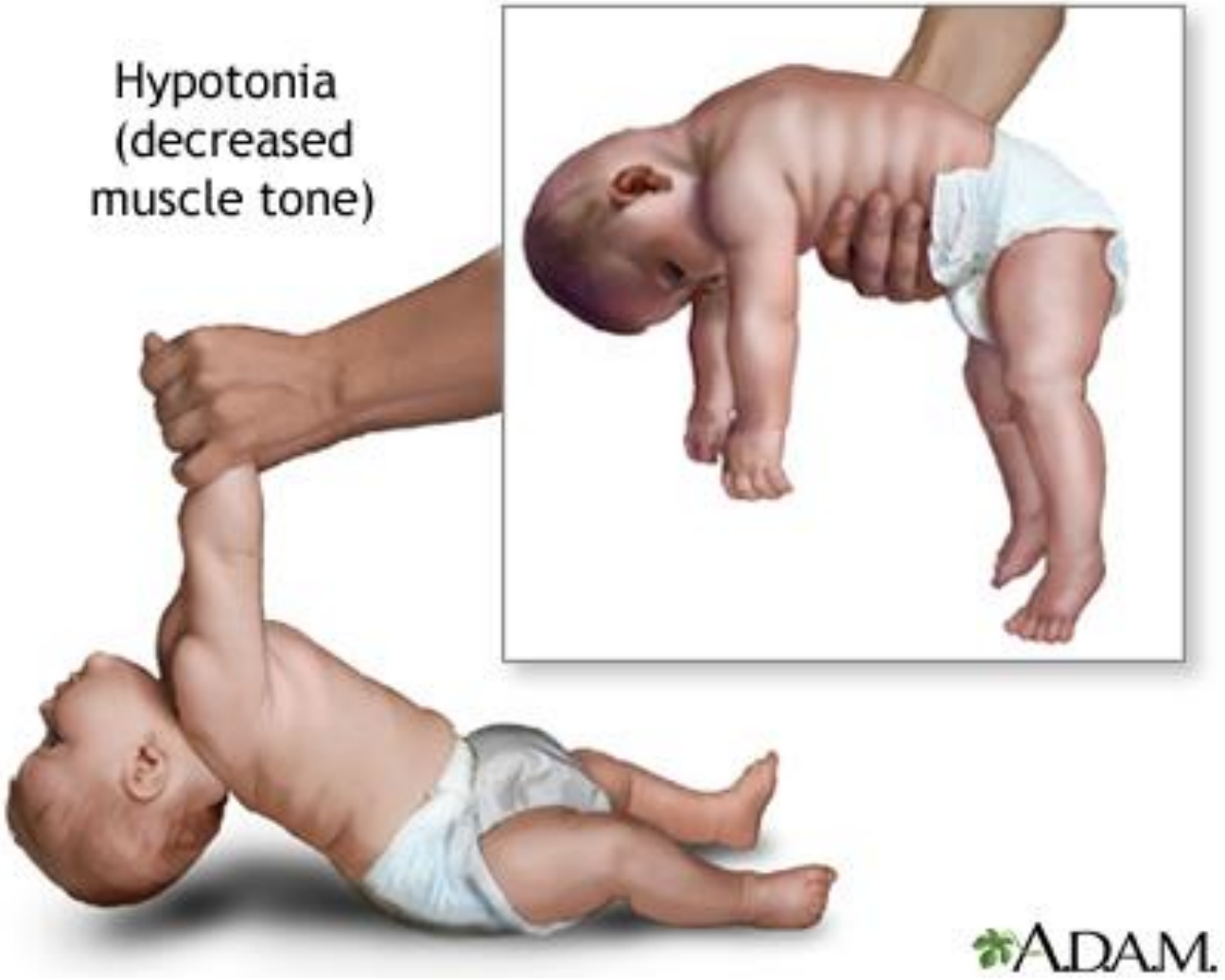
- Then undergo a confirmatory blood test:
  - Leucine = >4mg/dl
  - Interpretation: classic MSUD.

Symptoms of MSUD

- Onset:

  Symptoms occur in newborns within the first 4-7 days of birth,

- Baby avoids food, poor feeding,
- Vomiting,
- Dehydration,
- Lethargy – deep sleep, sluggish,
- Hypotonia,
- Seizures – muscle spasms.



Elbows and knees loosely extended, head may fall to the side, backward, or forward.

Signs of MSUD

- Infants show poor weight gain due to improper feeding.
- Hypo-glycaemia,
- Ketoacidosis,
- Pancreatitis,
- Coma, and
- Neurological decline.

Management

- Keeping MSUD under control requires:
  - ✓ Careful monitoring of blood chemistry, and
  - ✓ Frequent testing.
  - ✓ Involves a special diet.

- A diet with minimal levels of the amino acids:
  - ➢ Leucine
  - ➢ Isoleucine
  - ➢ Valine
    - ✓ Must be maintained (lifelong) in order to prevent neurological damage, growth and intellectual impairment.

❖ The goal of dietary therapy is to normalize the level of branched-chain amino acids (particularly of leucine).

Metabolic Decompensation in MSUD

- Metabolic Decompensation in MSUD is:

  - Body's inability to cope with the high level of branched chain amino acids in blood.

  - An acute crisis which:

    - Is a potentially lethal medical emergency that:

    - Requires quick reduction in concentration of branched-chain amino acids in plasma.

Treatment of episodes of acute metabolic decompensation ((inability to cope with the build up).

- During episodes of metabolic decompensation (inability to cope),
  - Patients can be treated with intra-venous hyper-alimentation (total parenteral nutrition TPN):
    - ✓Initiate intravenous glucose infusions (5-8 mg/kg/min for infants) as rapidly as possible.
    - ✓Insulin infusions may be added to promote anabolism.

Treatment of episodes of acute metabolic decompensation ((inability to cope with the build up). Cont'd.

- Stop intake of branched-chain amino acids, but
- Resume intake as soon as plasma branched-chain amino acids normalize.
- Whenever possible,
  - ✓ Continue additional dietary support, including lipids and/or formulas free of branched-chain amino acid.
- In rare circumstances:
  - ✓ Hemodialysis or peritoneal dialysis is required to remove branched-chain amino acids and keto acids.

MSUD Special Foods

- Leucine, isoleucine, valine are required for proper metabolic function in all people, that is why:
  - Several special formulas and foods are available:
    - ✓ Without or with reduced levels of branched-chain amino acids to meet normal nutritional requirements without causing harm.
    - ✓ Products are available for infants, adolescents and adults, such as MSUD Express.
- The intake is calculated on an individual basis:
  - ✓ After measuring blood level of branched-chain amino acids.

Maple Syrup Urine Disease Special Products

Product	*Age*	Characteristics
msud1-mix	*0 - 1 year*	special infant formula
msud1	*0 - 1 year*	amino acid mixture
msud 2-prima	*toddlers and children over 1 year*	amino acid mixture
msud2	*children, adolescents and adults over 1 year*	amino acid mixture
msud2-secunda	*children and adolescents over 9 years*	amino acid mixture
msud3-advanta	*adolescents and adults over 15 years*	amino acid mixture

MSUD MAXAMAID (MSUD AGES 1-8 YEARS)

MSUD Maxamaid is a leucine, isoleucine and valine free unflavoured powdered drink mix, containing a balanced mixture of the other essential and non-essential amino acids, carbohydrate, vitamins, minerals and trace elements. A food for special medical purposes.

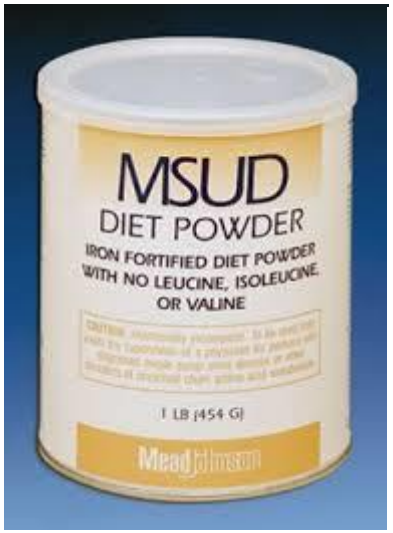
BRAND

CONDITIONS

Maple Syrup Urine Disease (MSUD)

CATEGORIES

Metabolic, Maple Syrup Urine Disease



Foods that are BCAAs Low or Free

- Fruits and vegetables are:
  - Naturally low in protein,
  - Therefore low in BCAA.

- Sugar, fats and oils are:
  - Protein free.

Management of MSUD

- Usually, patients are also monitored by a dietitian.
- Diet must be adhered to strictly and permanently.
- MSUD could lead to death if not treated, but it is manageable.

- With proper management,
  - ✓ Patients can live relatively healthy, normal lives and
  - ✓ Not suffer the severe neurological damage associated with the disease.

Galactosemia

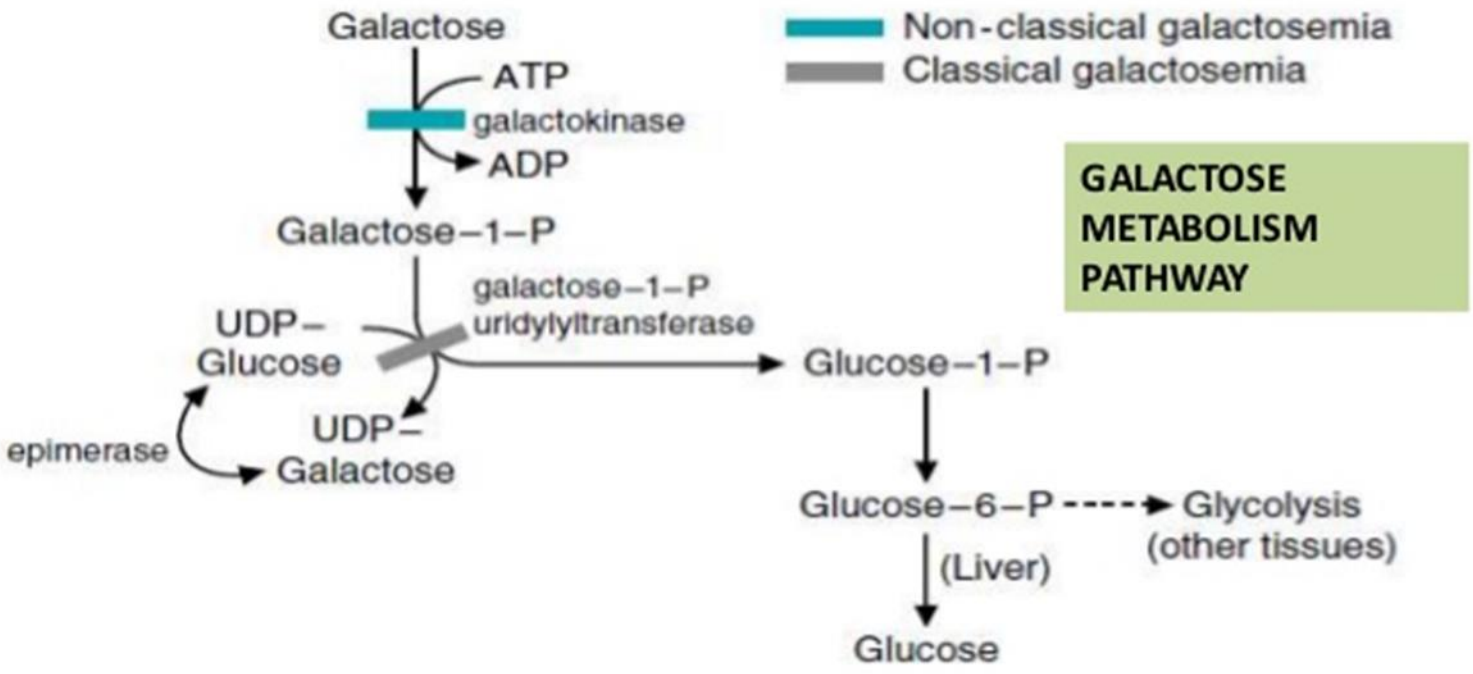
What is Galactosemia

- Galactosemia is a rare disorder that
- Affects the body's ability to break down galactose
- Normally the body breaks down lactose into galactose and glucose and uses these sugars for energy:
  - ✓ Galactose must be converted to glucose in order to be used for energy production.
- Most people with galactosemia are missing an enzyme (called GALT) that helps further break down galactose.
- Defects in galactose metabolism cause toxic chemicals to build up in cells of the body.

There are 3 forms of Galactosemia

- Deficiency of any of the following enzymes:

1. Galactose kinase,
2. Galactose-1 phosphate uridyl transferase,
3. Galactose-6-phosphate epimerase.



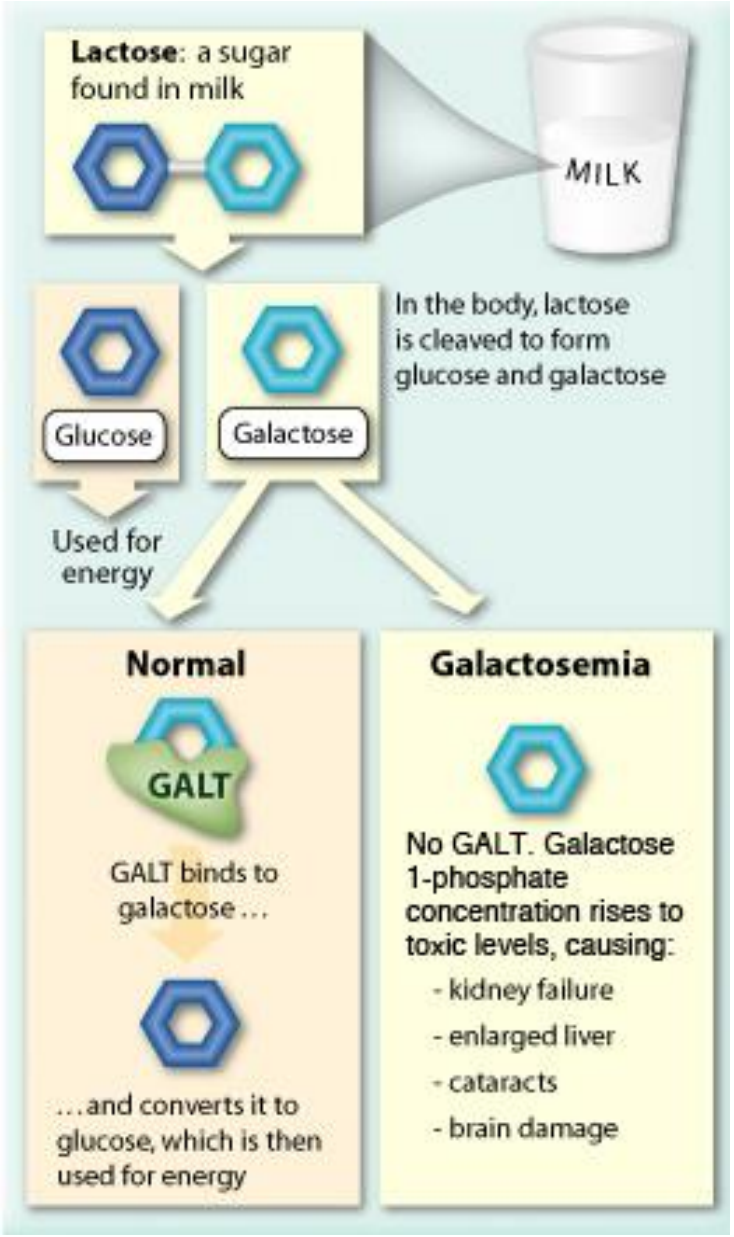
(1) Galactose + ATP —*galactokinase*→ Galactose-1-P + ADP

(2) Galactose-1-P + UDP-glucose —*galactose-1-P uridylyltransferase*→ UDP-galactose + glucose-1-P

(3) UDP-galactose —*UDP-glucose epimerase*→ UDP-glucose

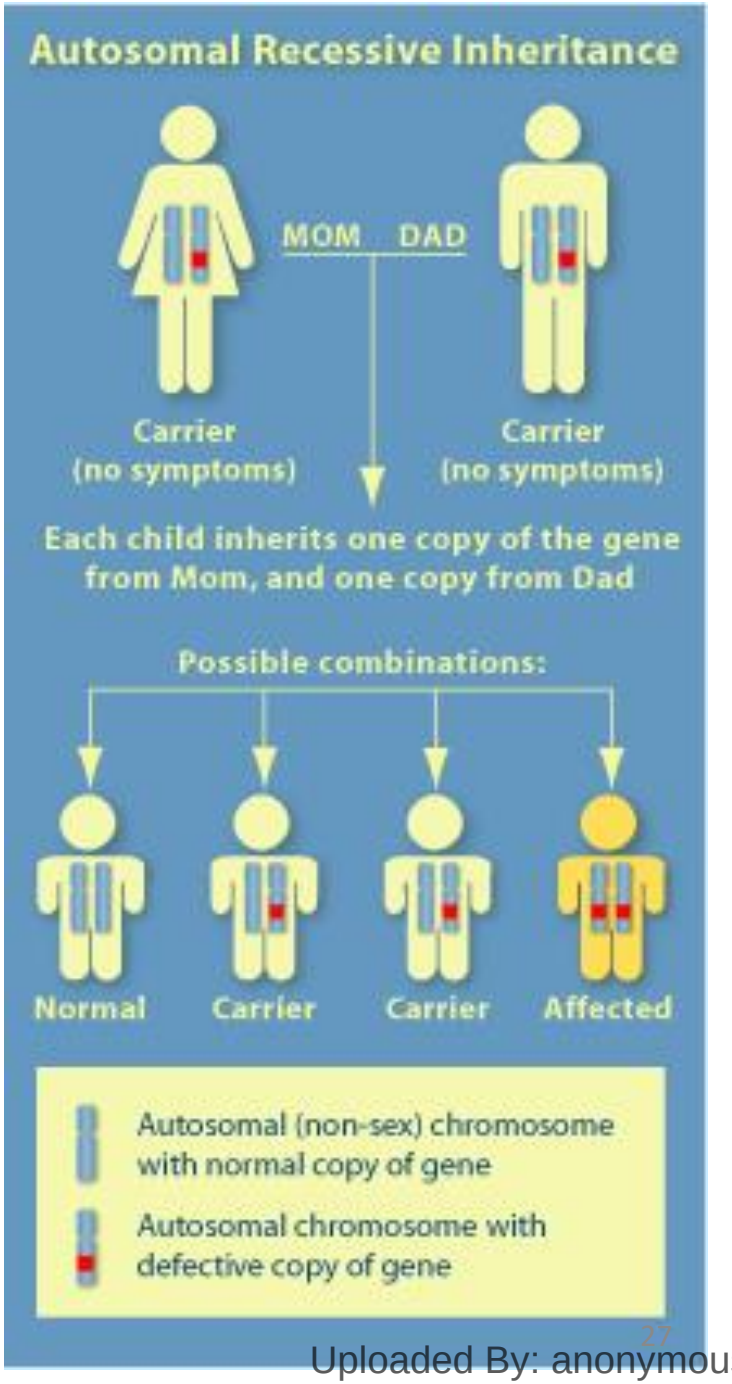
Net Equation: Galactose + ATP ⟶ Glucose-1-P + ADP

- Galactose-1 phosphate uridyl transferase deficiency:
  - ➢ Classic galactosemia,
  - ✓ The most common and most severe form).
- Galactose makes up ≈ 50% of lactose.



How do People get Galactosemia?

- To get the disorder, a child must inherit one defective gene from each parent.
- Inheriting one normal gene and one mutated gene makes a person a carrier.
- A carrier produces less of the GALT enzyme than normal, but is still able to break down galactose and avoid having symptoms of galactosemia.
- However, carriers can still pass on the mutated gene to their children.



How do Doctors Diagnose Galactosemia?

- Babies are tested for galactosemia at birth.
  - ✓ Using a tiny blood sample taken from the baby's heel, the test checks for low levels of the GALT enzyme.
  - ➢ This allows for prompt treatment, which can substantially prevent the serious symptoms of this disorder.
- For those families with a history of the disorder:
  - Doctors can determine during a woman's pregnancy whether her baby has galactosemia:
    - ✓ By taking a sample of fluid from around the fetus (amniocentesis), or
    - ✓ By taking a sample of fetal cells from the placenta (chorionic villus sampling or CVS).

Some Facts about Galactosemia

- Newborns with galactosemia:
  - ✓ Seem normal at first but,
  - ✓ Within a few days or weeks:
    - ➢ Lose their appetite, vomit, become jaundiced, have diarrhea, and stop growing normally.
    - ➢ White blood cell function is affected, and serious infections can develop.
    - ➢ If treatment is delayed, affected children remain short and become intellectually disabled or may die.

How is Galactosemia Treated?

- The only way to treat galactosemia is through dietary restriction of galactose through:

  - ✓ Eliminating : all milk, milk-containing products (including dry milk),
  - ✓ Avoiding: other foods that contain galactose depending on blood test results.

- Galactosemia diet is lifelong.
- It is essential to read product labels in case they contain milk.

❖ Diet is not a galactose free diet.

Foods that Contain Galactose

Non- alpha glucans (non digestible oligosaccharides [NDOs]):

- Raffinose: sucrose + galactose
  - ✓ Found in: beans, cabbage, Brussels sprouts broccoli, asparagus, other vegetables, and whole grains.

- Stachyose: sucrose + 2 galactoses
  - ✓ Found in numerous vegetables and plants. (e.g. green beans, soybeans and other beans).

- Verbascose: sucrose + 3 galactoses:
  - ✓ Found in many legumes.

Medical Foods for Galactosemia

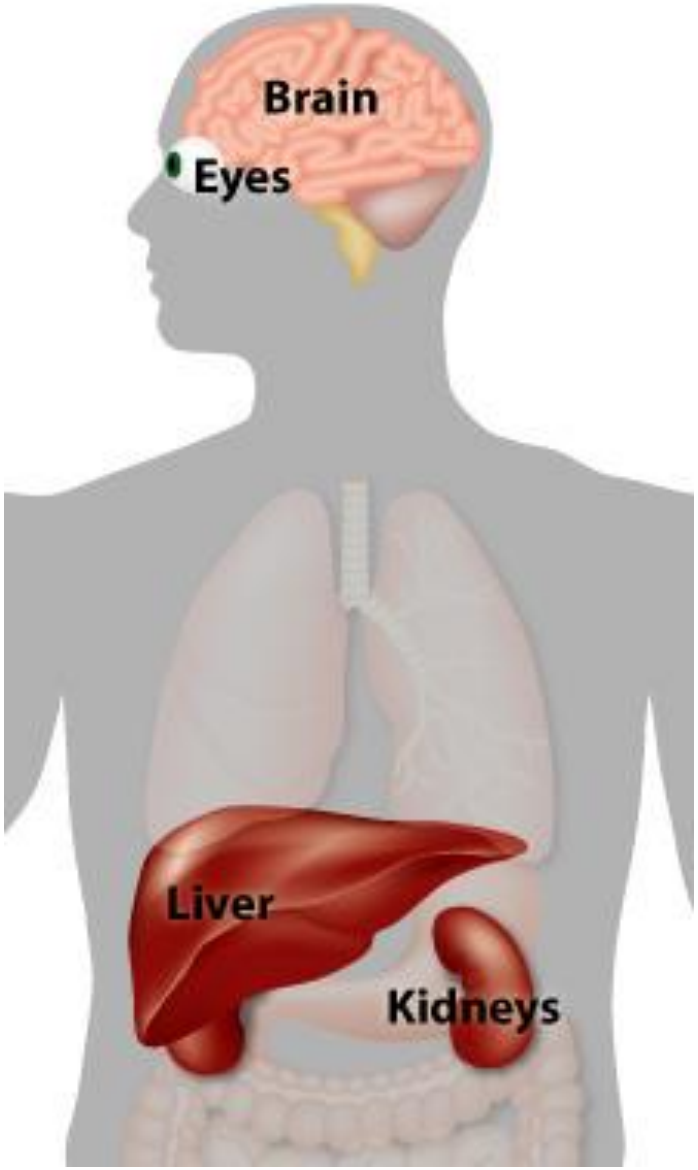
Alternative formulas for infant:

- ✓ Since breast milk and regular baby formulas have to be eliminated:
- ✓ Infants can be fed with specially designed formulas such as:
  - Meat-based formula
  - Lactose-free formula
  - Soy based formula
- ✓ Calcium supplements are recommended.

Galactosemia Prognosis

- People who:
  - Are diagnosed early, and
  - Strictly eliminate milk products:
  - Can live a relatively normal life.
- However they may develop:
  - Mild intellectual impairment.

Organs Affected by Galactosemia



Possible Complications

- Cataracts: clouding of the eye lens,
- Hepatomegaly: abnormal enlargement of the liver,
- Cirrhosis of the liver,
- Renal failure,
- Delayed speech development.

Possible Complications Cont'd.

- Irregular menstrual periods, reduced function of ovaries leading to ovarian failure,
- Mental retardation, Intellectual disability,
- Severe infection with bacteria (*sepsis*),
- Tremors and uncontrollable motor functions,
- Death (if no galactose restriction).