

## *Metabolic disorders*

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### **Metabolic disorders**

- Definition:
- Inborn errors of metabolism inherited traits result in the absence or reduced activity of a specific enzyme or co-factor.
- Most of them inherited as autosomal recessive traits.

### **Newborn screening**

- Most of metabolic disorders are associated with severe clinic. Illness ,appears soon after birth,as MR,sever neurologic involvement.
- Prenatal diagnosis for a family at risk.
- Or children for no apparent reason are lethargic,vomiting resp.distress or seizures-should be evaluated for undiagnosed metabolic disorder.

### **Newborn screening(cont.)**

- Tandem mass spectroscopy.
- Blood gases measurements.
- Electrolytes values.
- Blood glucose level.
- Plasma ammonia.
- Urine tests for ketons, reducing substances.

### **Newborn screening**

- Importance:
- Have offered opportunities for earlier diagnosis.
- Prevention of neurological crisis.
- Improve of intellectual and physical outcomes.

### **medical nutritional therapy**

- Goals :
- 1-maintain biochemical equilibrium for the affected pathway.

- 2-provide adequate nutrients to support social and emotional development.

### **Role of med. Nut.therapy**

- 1-restricting the amount of substance prior to the block.
- 2-supplementing the adequate amounts of end products.
- 3-supplementing the enzyme cofactor and vitamins.
- Remove toxic by-products accumulates,affecting metabolism, as carnitine.
- Combining any or all.

### **Classification of metabolic disorders:**

- Over 200 genetic disorders.
- 1-urea cycle disorders.
- 2-organic acidemias.
- 3-carbohydrates disorders.
- 4-amino acids disorders.

### **Urea cycle disorders**

- Rare .
- Clinically:vomiting,seizures,coma up to death.
- Treatment:acute =hemodialysis.
- Long term management=low protein diet.

### **Organic acidemias**

- Rare.
- Metabolic acidosis, increase ammonia level
- Vomiting,seizures,coma.
- Acute intervention:IV fluids,bicarbonates.
- Long term “ :low protein ,Kcal.

### **CHO disorders.**

- 1-galactosemia.

- 2-galactokinase deficiency.
- 3-glycogen storage disease.
- 4-hereditary fructose intolerance.
- Varied in :presentation,clinical course,outcome.
- All need early and aggressive nutritional therapy.

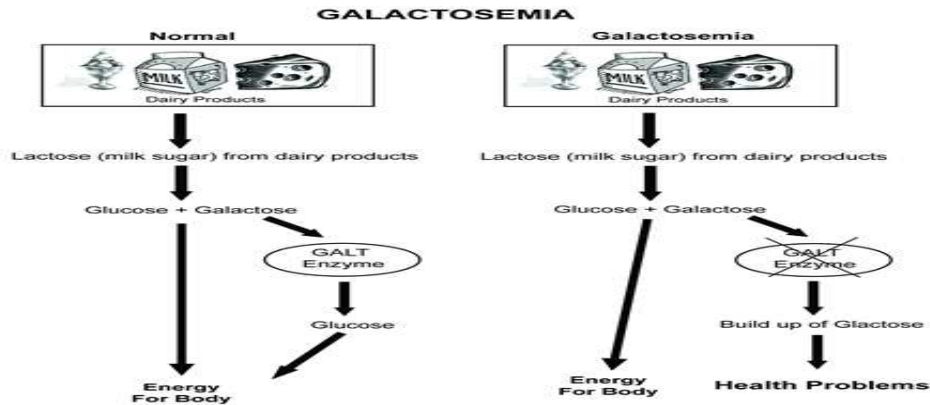
### galactosemia

- Disturbance in the conversion of galactose to glucose.
- Absence of galactose-1-phosphouridyl transferase .
- High level of plasma galactose-1-phosphate,combined with galactosuria.
- Manifest within first 2 weeks of life.

### Galactosemia



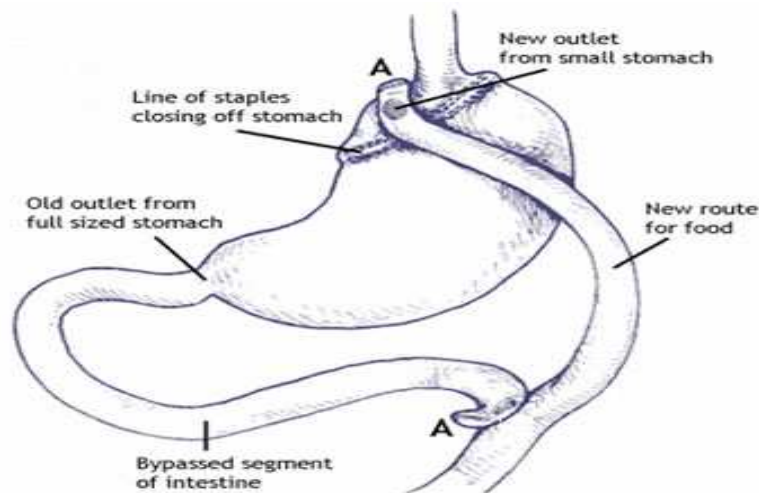
- Vomiting,diarrhea,lethargy,FTT,jundice, hepatomegaly,cataract,hypoglycemia+gram –ve bacterial infection.
- Untreated lead to MR or septicemia.
- Early diagnosis & ttt. >N.physical and motor development,however intellectual achievement depressed,visual perception and speech difficulty are common.
- Ovarian faliture in 95% in women with galactosemia.



## Galactosemia



The treatment for galactosemia is restriction of galactose and lactose for life.



## Medical nutritional therapy of galactosemia.

- Life long galactose restriction.
- All milk and milk products and lactose containing foods.
- Lactose ----→hydrolyzed to galactose & glucose.
- Breast milk.
- All fruits and vegetables contain significant amount of galactose.
- Dates ,papayas,tomatoes,watermelons ,contain more than 10 mg galactose\100g fresh wt of products.

### **Food of low galactose :**

- 1-milk and milk substitutes:  
Isomil(Ross)  
Proscabee (Johnson)  
Alsoy (carnation)  
Gerber soy (Gerber).

### **Food of low galactose:**

- Fruits and veg.:all except dates ,papayes,.....etc.
- All meat poultry,fish egg,nuts.(without unsafe additions as butter,cream
- Breads,cereals.
- Fats: oils.

### **Amino acids metabolic disorders**

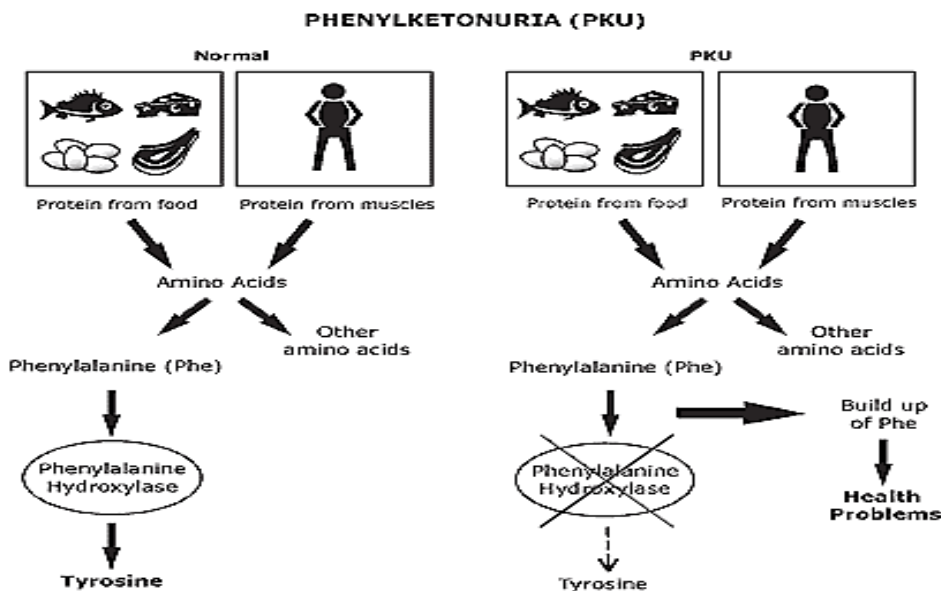
- 1-phenylketonuria :1:10,000.
- 2-tyrosinemias :rare  
acidosis,diarrhea,FTT,hepatomagaly,  
\*restrict tyrosine phenylalanine in diet.
- 3-maple syrup urine disease (MSUD):  
defect in ketoacid decarboxylase.  
early onset,seizures,acidosis,MR  
-restrict leucine,isoleucine& valine diet.
- 4-homocystinuria:rare  
defect in cystathionine synthase.  
-arterial,venous thromboses.,fair hair and skin,dislocated lens,MR.  
-high level of methionine &homocysteine.

### **phenylketonuria (PKU)**

- 1:10,000.



- Phe metabolised to tyrosine (Tyr), if decreased or no phe hydroxylase lead to phe blood conc. increase more than 6-10 mg/dl. And Tyr. Blood conc. less than 3 mg/dl.



### Diag. criteria & outcome:

- 1-screening bacterial inhibition test, if +ve, then qualitative & quantitative tests done.
- No clinical manifestation immediately after birth, so it is v. imp.
- IQ (intellectual quotient) will be quite normal if ttt. started immediately, compared to IQ=40, if delayed diagnosis.

### Medical nutritional therapy:

#### 1- infants & children:

- Planned around the use of:
- Formula/medical food with phe removed from proteins. + energy needed + CHO sources + fat + calcium, iron, and all necessary vit. & minerals.
- Phe formulas:
- 1-phenex 1,2.
- Phenyl-free 1,2.
- Periflex.
- Phe free formulas is supplemented with breast milk, reg. milk or cow milk in early childhood. why?

- To provide (HBV)pr.+non-essential a.a.
- Phe free formula +milk mixture should provide 90% of protein,80% of energy needed.
- Adequate hydration should be considered.
- Maintain serum phe at 2-6 mg/dl.
- Phe containing foods are offered as tolerated as long as bl.conc. Within the range.
- Child rate of growth and mental, emotional development are carefully monitored.

### **Fig.45-3 p.1155**

- Blood phe conc.,checked regularly.
- If phe level increase=1-excess intake  
2-tissue catabolism.
- ie,trauma of illness,infection--→pr. Breake down,release of phe.
- Also,anorexia of illness---→less energy intake.
- Maintain med.nut.therapy.

### **Therapy in adolescence:**

- Therapy must continue for life.
- To maintain normal cognitive functions.
- Phe level must kept at 1-6mg/dl.and not more than 10mg/dl at any stage of life.
- Otherwise,learning difficulties,poor attention span,and behavioral changes.
- Phe level more than 20mg/dl=best predictors of IQ loss (Diamon,1994)

### **Nutritional care in maternal PKU**

- Pregnancy lead to amplified a.a. transport via placenta.
- Fetus exposed to twice phe conc.the mother.
- Cardiac defects,retarded  
growth,microcephaly...
- The higher the mother phe blood level,the more sever damage will be.
- So,strict control of phe level before conception and throughtout preg. At 1-5mg/dl....

### **Daily requirements for dietary components**

phenylalanine	1-5 mo=47-90	1-10y=200-500
energy	1-5mo=108kcal	70-102kcal/kg
water	100ml/kg	1000ml/kg
CHO	Kcal*0.5/4=g/d	same
Total pr.	2.2-1.6g/kg	16-18g/kg
fat	Kcal*0.35/9=g/d	same

Table 45-4 p.1152

<http://special-needs.org>