IN THE NAME OF GOD

Inborn Errors of Metabolism

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General characteristics

- They are rare disorders
- As a whole 1 of every 500 to 1000 live-borne babies may be affected
- In excess of 30% are associated with neurologic manifestations and MR

- They are either an acute and rapidly progressive or chronic, regressive, and disabling disorders
- Consanguineous marriage is a predisposing factor (AR)

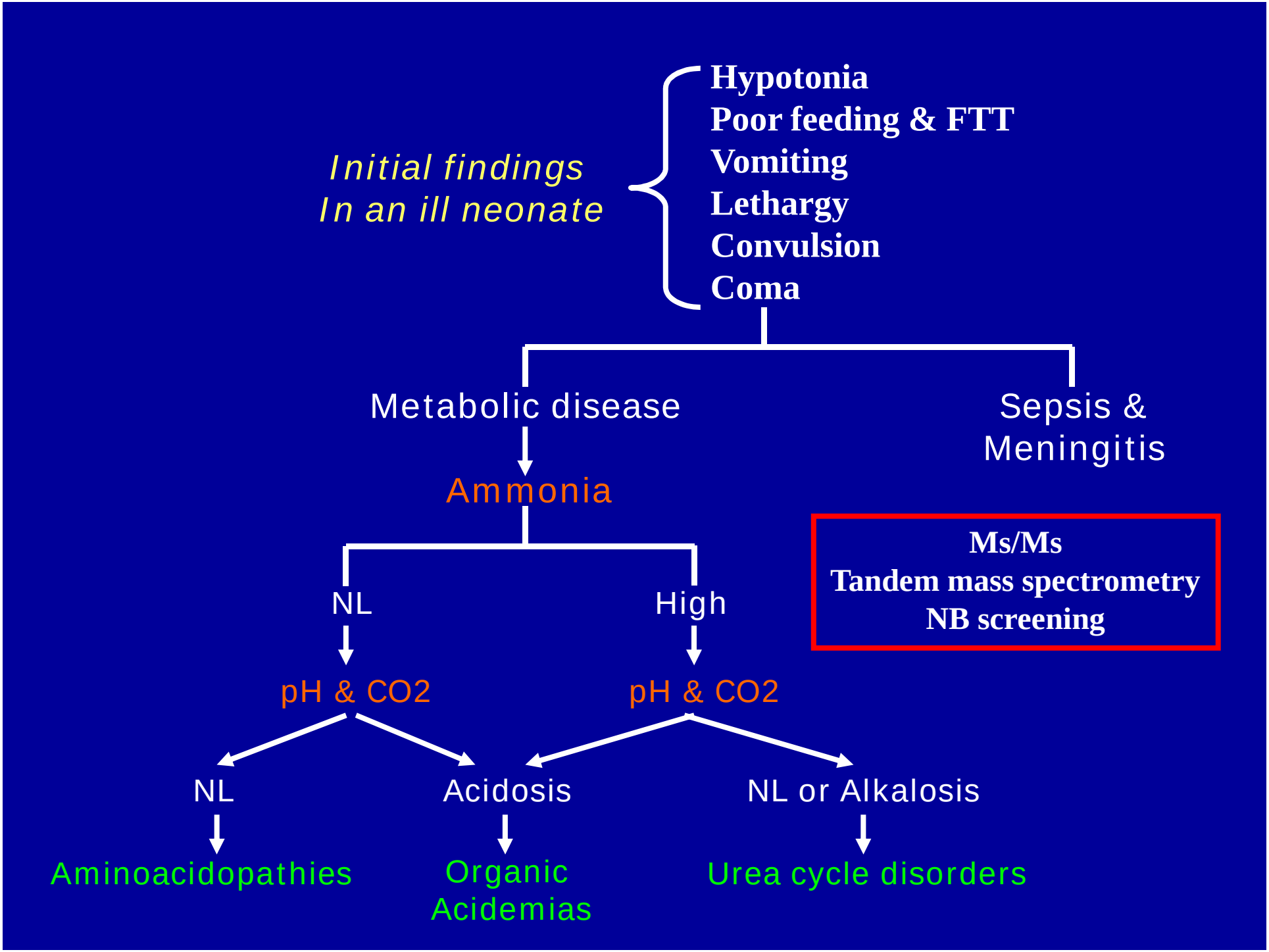
Family history

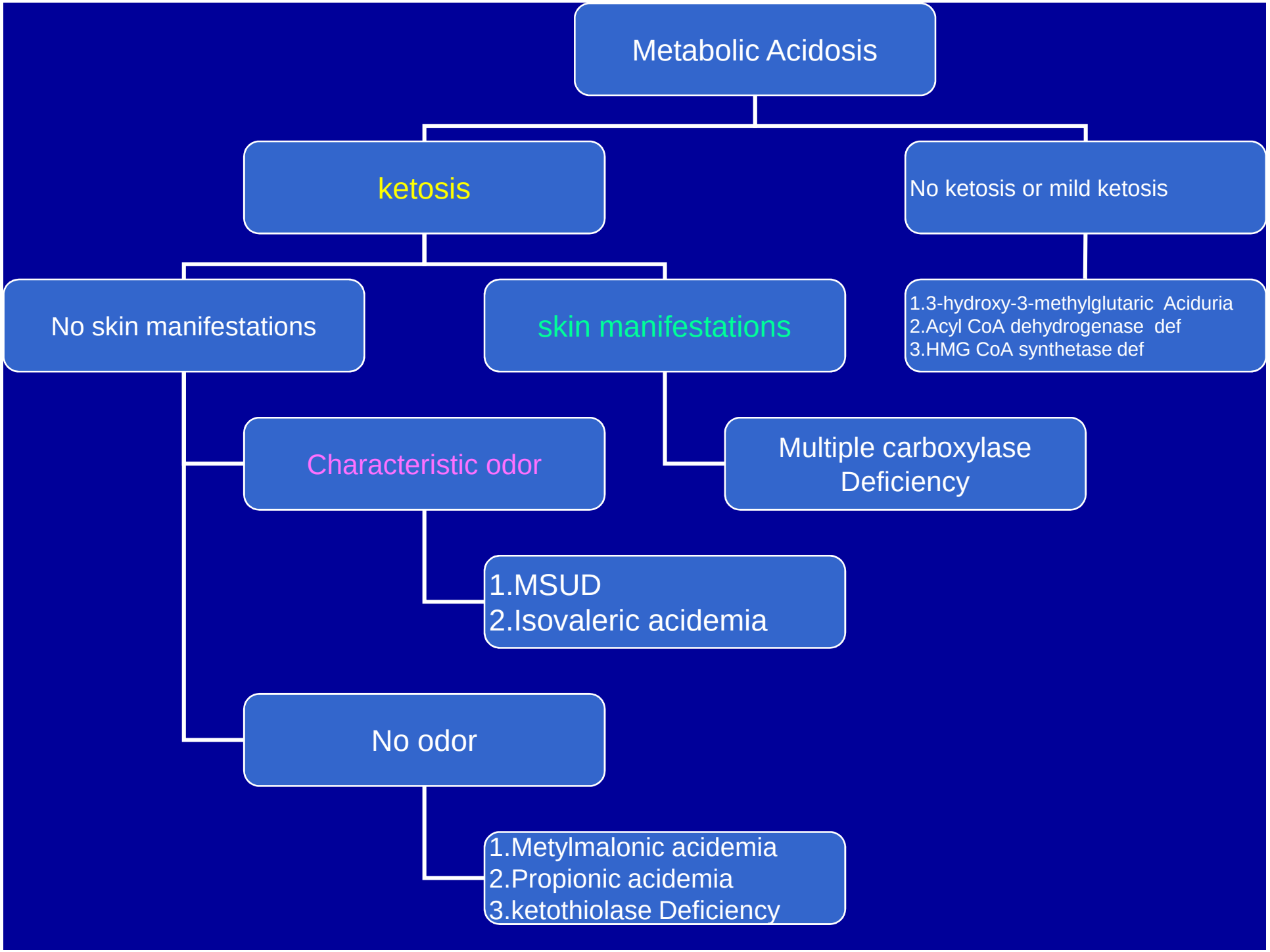
- History of consanguinity
- Death in the neonatal period
- Similar condition in other members of the family

- Ethnic background of the patient
- Severe reaction to mild disease
- Negative blood culture

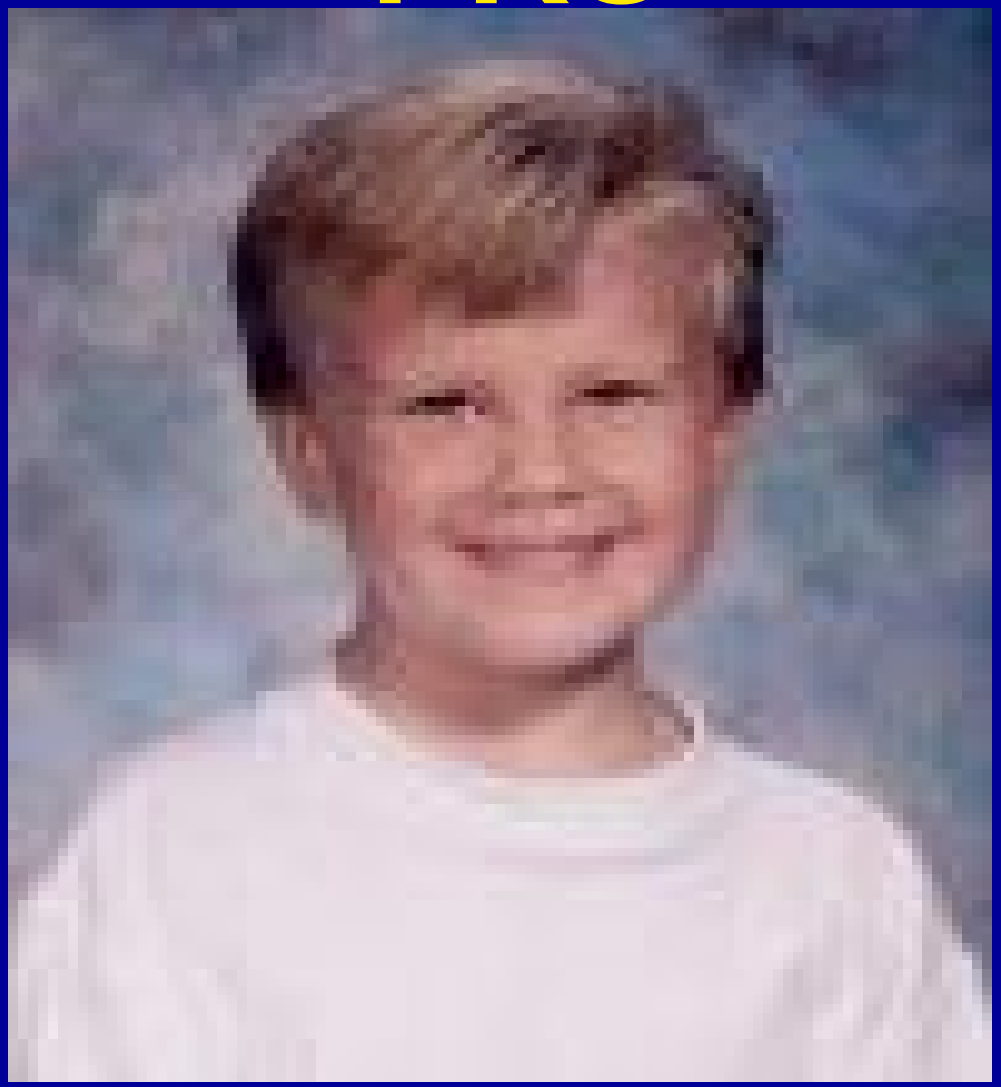
Physical examination

- Finding usually are nonspecific
- Central neurvous system problems
- Hepatomegaly
- Spelenomegaly
- Peculiar odor
- Jaundice
- Ascites
- Cataract

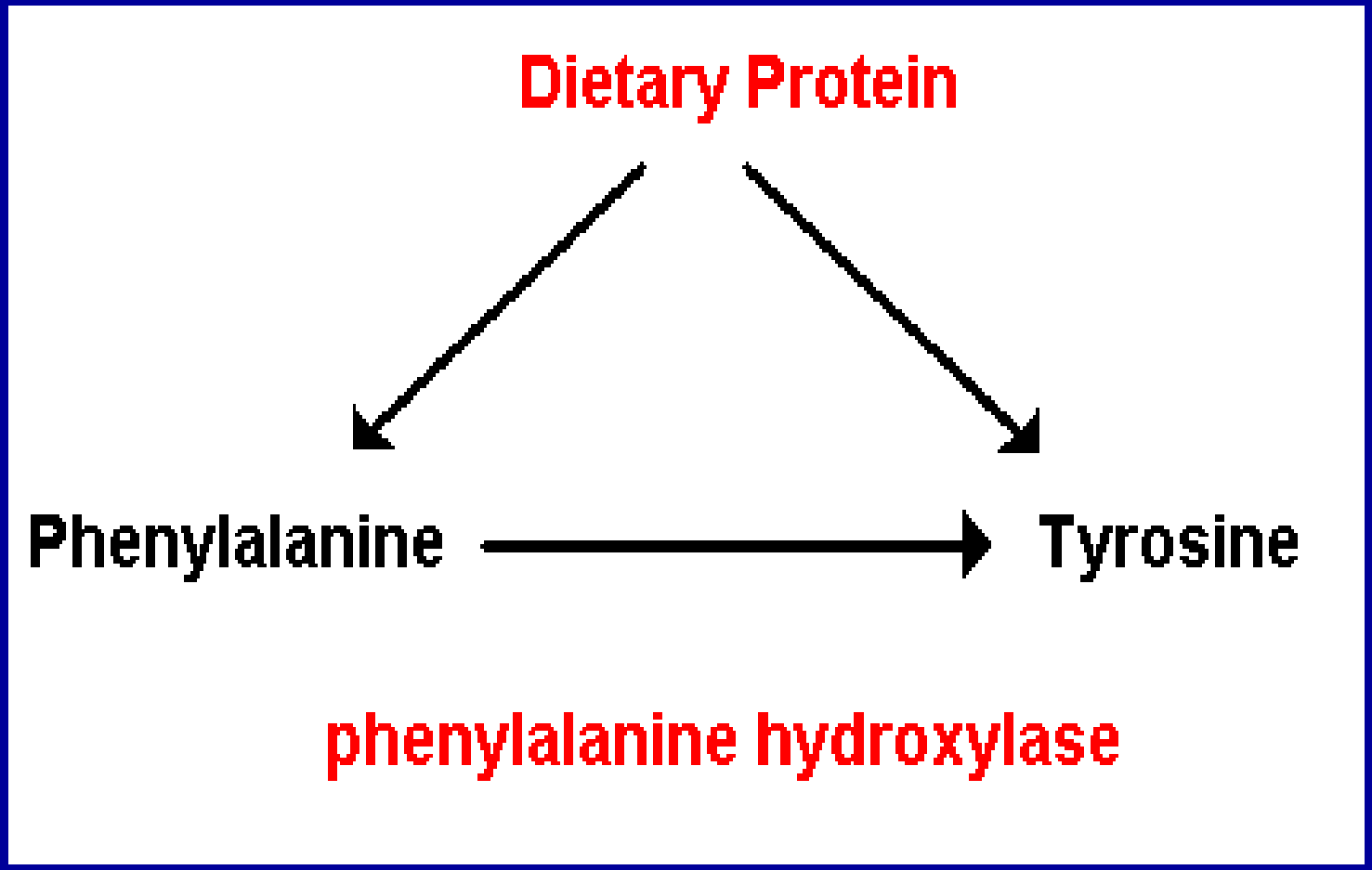




PKU



Phenylketonuria



CLINICAL MANIFESTATION

- Vomiting
- Delayed development(apparent in 4-9 month)
- MR(IQ<50),microcephaly,tremor,increased muscle tone,parkinsonian-like extrapyramydal symptoms
- Seizures
- Blond,blue eye,rough skin,eczema
- Hyperactivity,autism

- *PKU mathers* :
- Spontaneous abortion
- PA level >20mg/dl :fetal brain damage(MR,microcephaly),unusual facies : upturned nose ,underdeveloped philtrum,thin upper lip
- CHD,growth retardation
- Hypoplasia & partial agenesis of corpus calosum

- Neonatal screening:(12 hours after birth)
- Guthrie,spectroflorometry,ferric chloride
- If PA > 2-4 mg/dl : quantitative analysis of PA & tyrosine in blood

- Mild hyperphenylalaninemia:<10mg/dl
- Transient tyrosinemia : premature infants(tyrosine level increased much greater than PA)

MSUD

CLASSIC MSUD:

LEUCINE. ISOLEUCINE .VALIN.

HYPERTONICITY & HYPOTONICITY

OPISTHOTONUS

CONVULSION

HYPOGLYCEMIA

THIAMINE RESPONSIVE MSUD

Urea Cycle Disorders

- AMONIA >200 micromol
- DECREASE UREA
- ABG
- OTC IS THE MOST COMMON

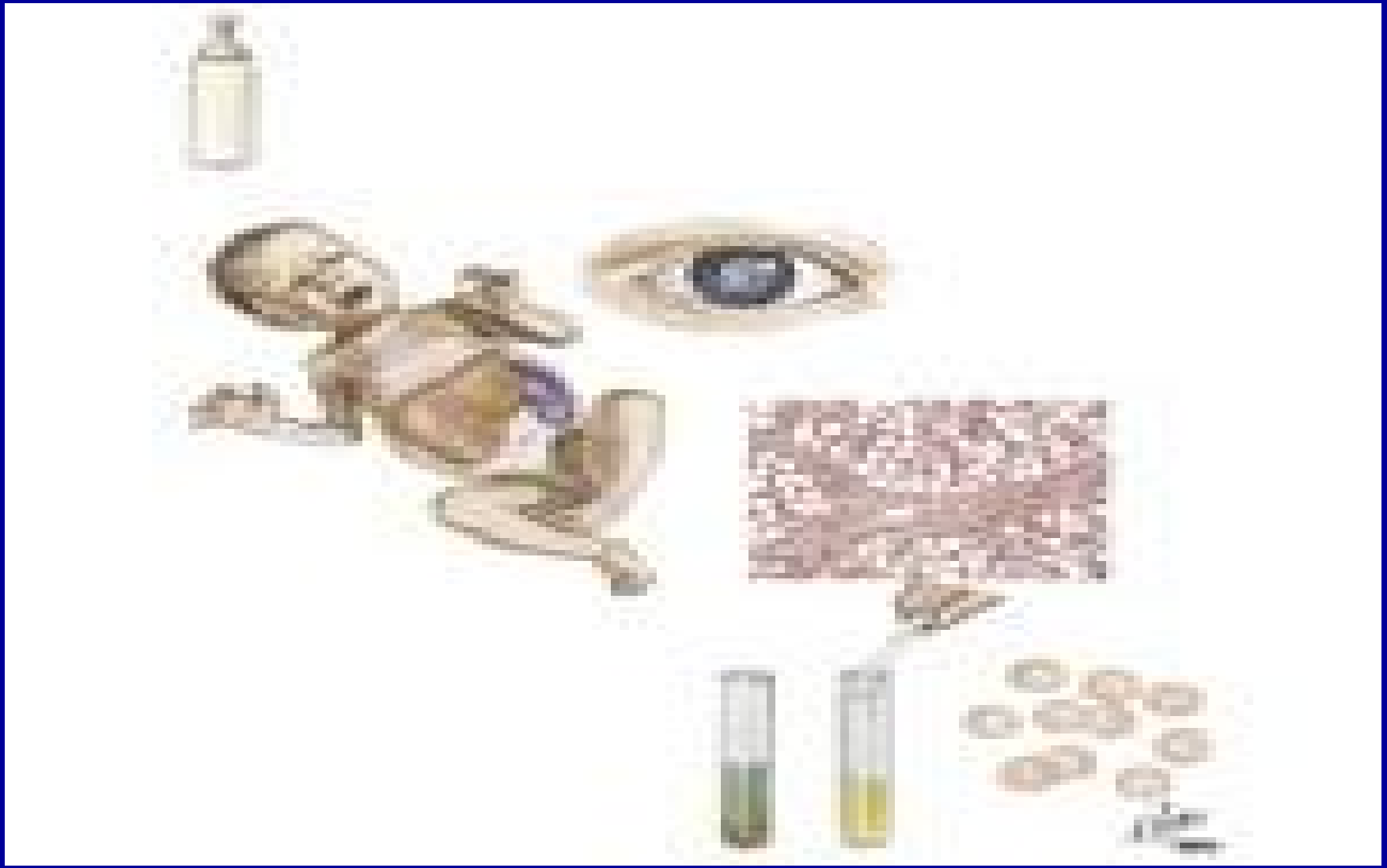
Urea Cycle Disorders

- POOR FEEDING
- VOMITTING
- TACHYPNEA
- CONVULSION
- COMA
- HEPATOMEGALY

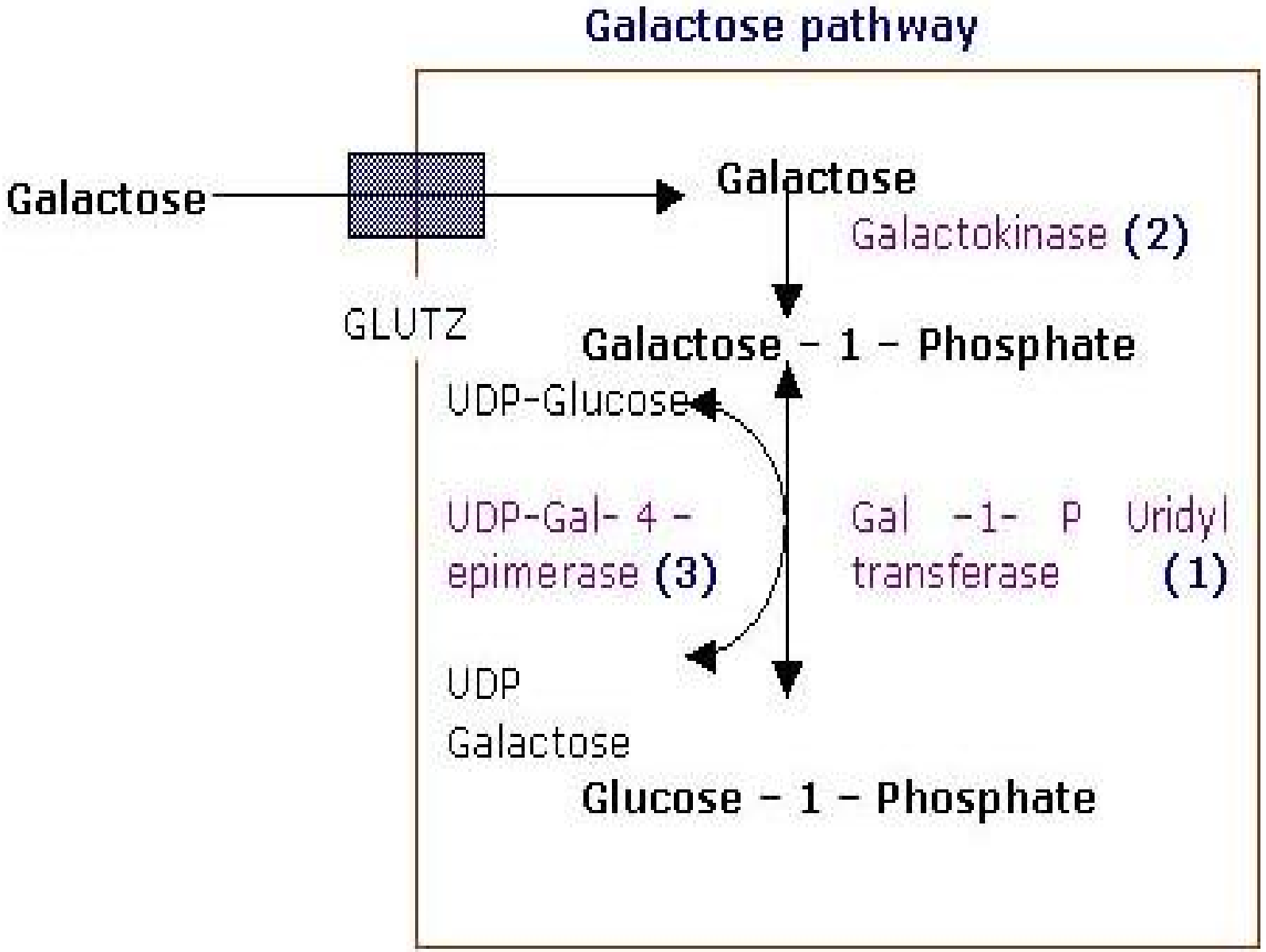
Mitochondrial disorders

- Multiple organe involvement
- Basal ganglial calcification
- Lactate / Pyruvate > 20

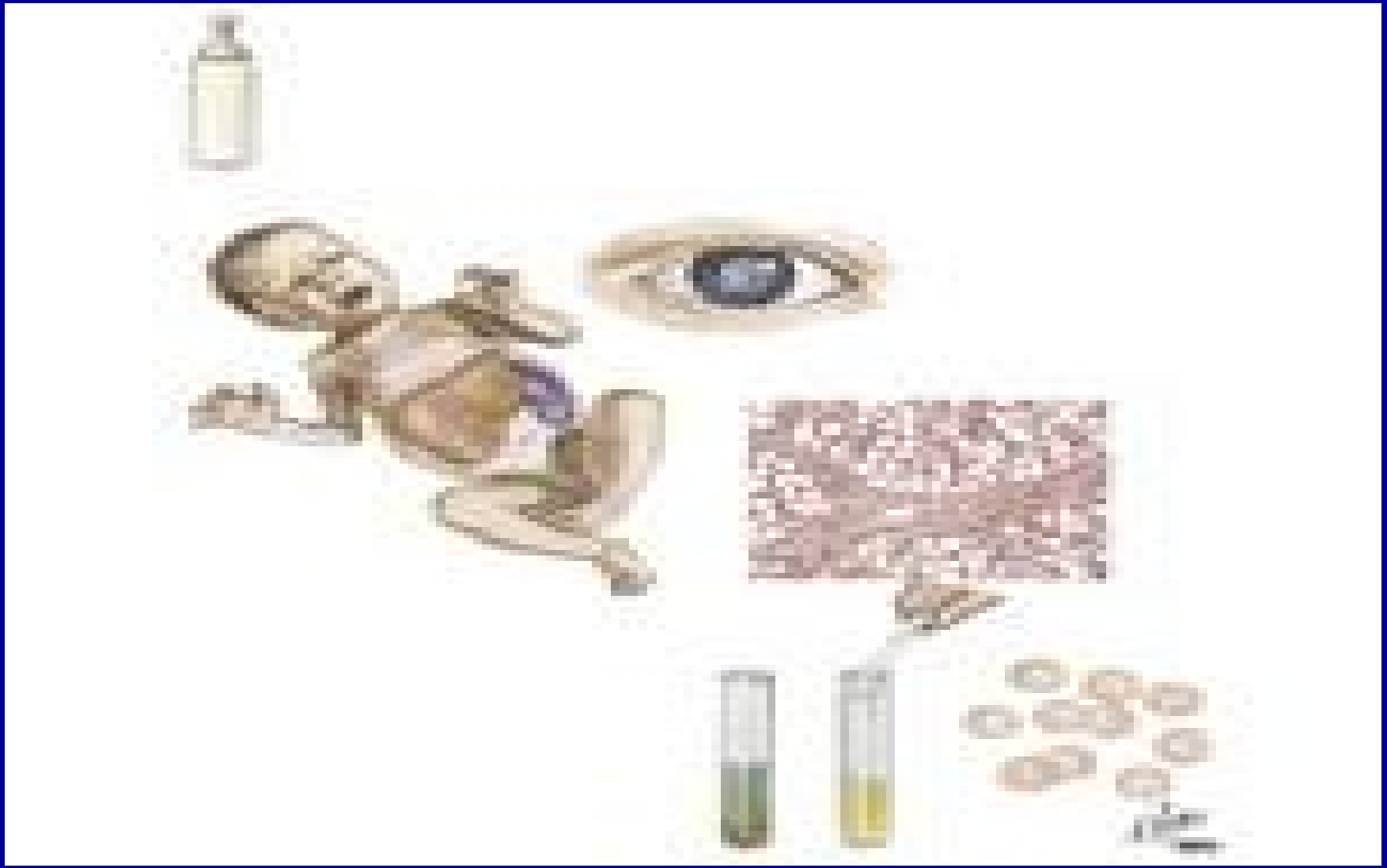
Clinical presentations



GALACTOSEMIA



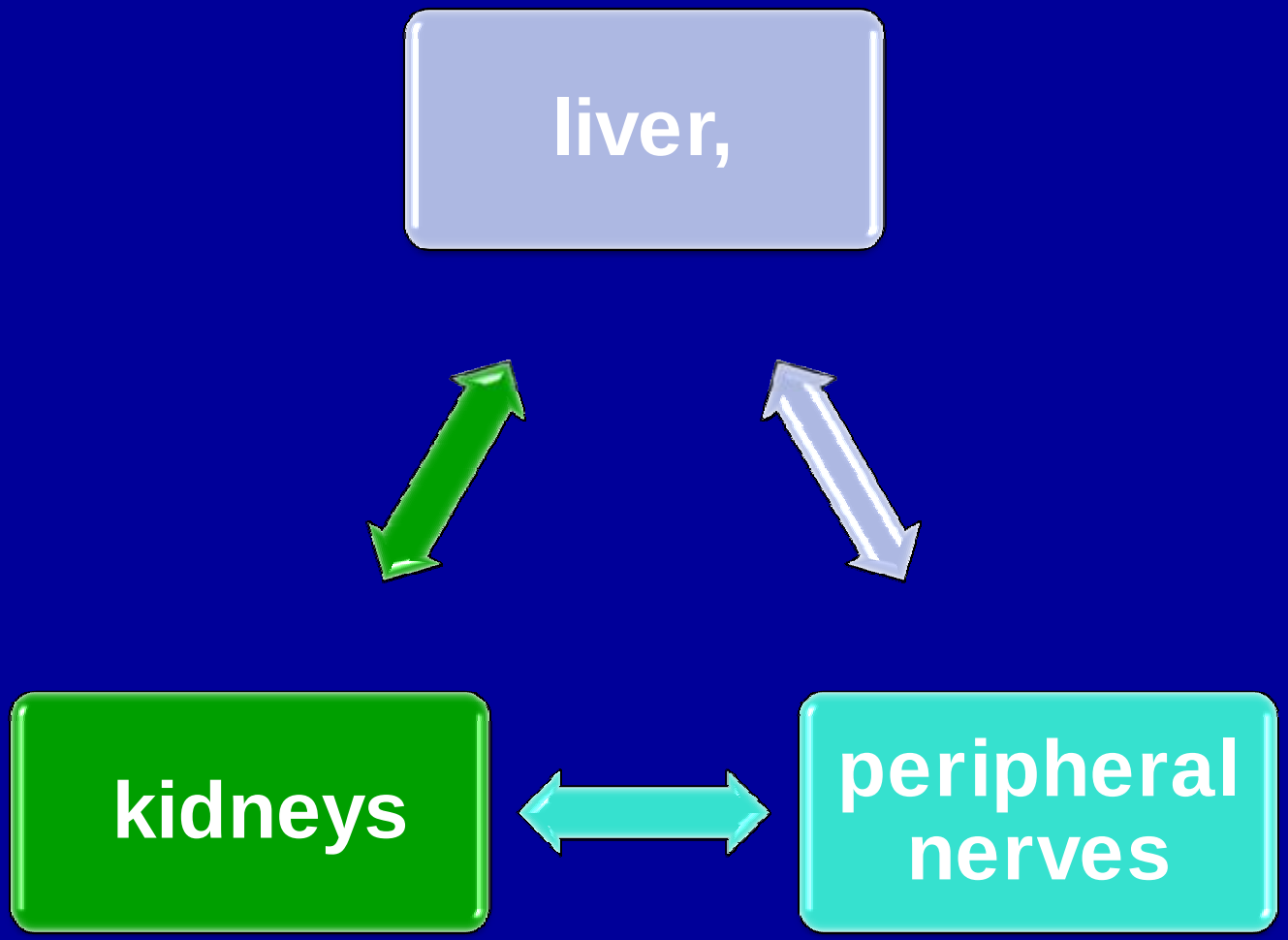
Clinical presentations



TYROSINEMIA

ÒHypertyrosinemia is observed with deficiencies of tyrosine aminotransferase, 4-hydroxy phenpyruvate dioxygenase (4-HPPD), or fumarylacetoacetate hydrolase (FAH).

major organs affected are :



TYROSINEMIA

acute peripheral neuropathy resembling acute porphyria occur in ~ 4 0 %of affected children

An acute hepatic crisis commonly heralds the onset of disease

Renal involvement is manifested as a Fanconi-like syndrome

Renal involvement is manifested as

- a Fanconi-like syndrome with normal anion gap metabolic acidosis,
- hyperphosphaturia,
- hypophosphatemia,
- and vitamin D-resistant ricket

Laboratory Findings

- a-Fetoprotein level is increased,
- liver-synthesized coagulation factors are decreased in most patients;
- serum levels of transaminases are increased,

Plasma tyrosine level is dependent on diet;

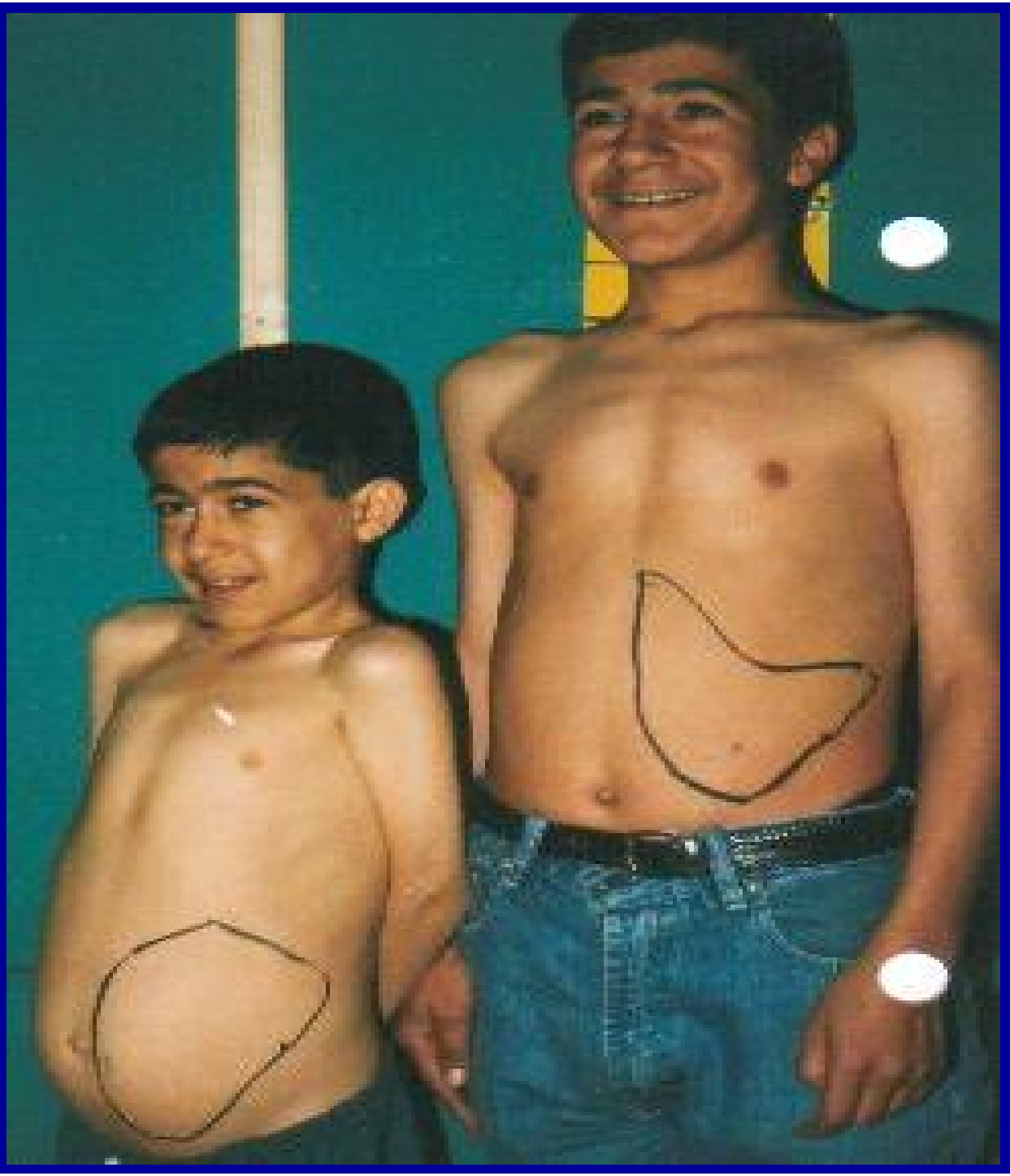
tyrosine level has less diagnostic value than that of succinylacetone

presence of elevated levels of **succinylacetone in serum and urine is diagnostic**

Treatmen

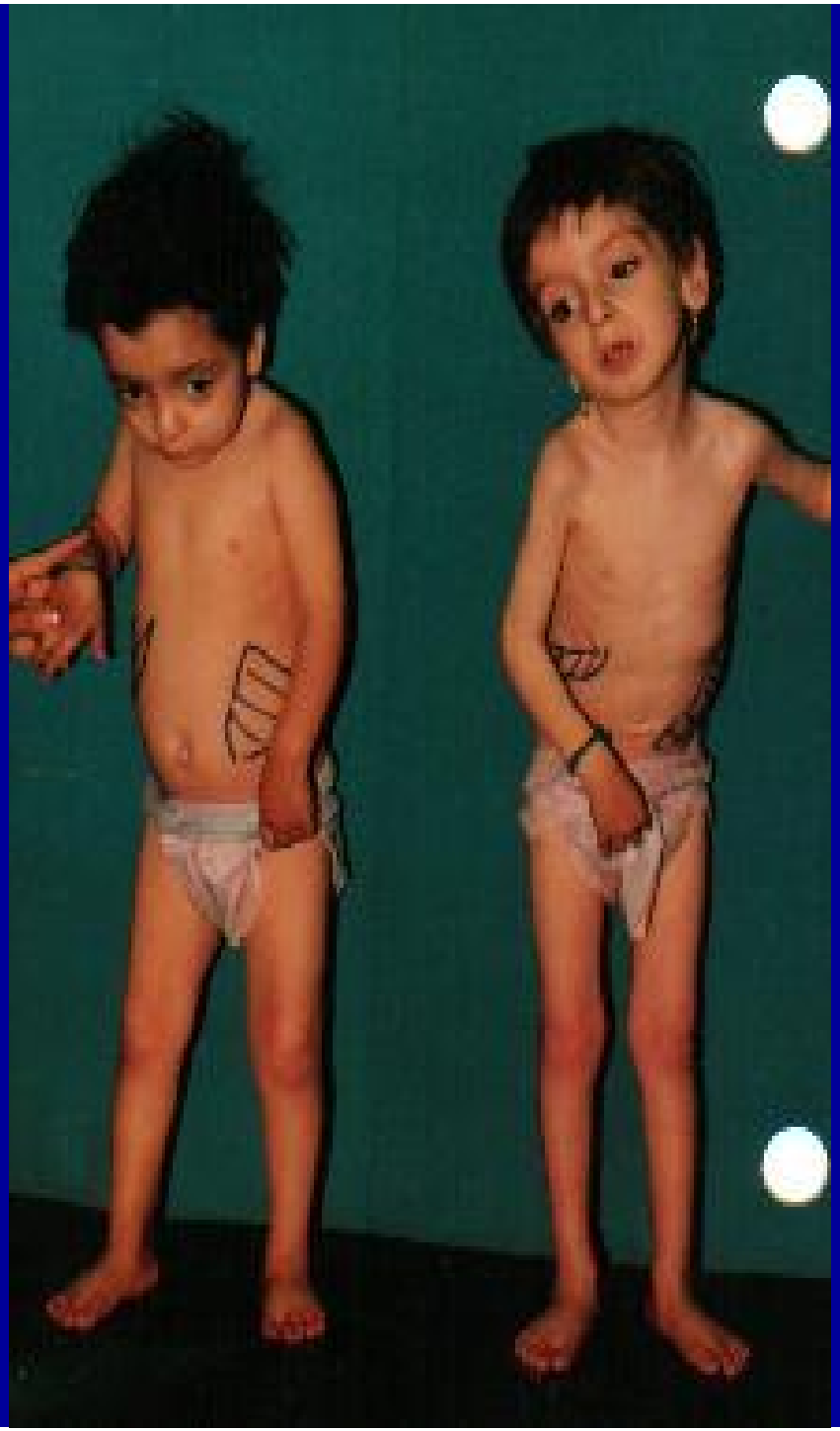
The treatment of choice is nitisinone (NTBC)

also prescribed a diet low in phenylalanine and tyrosine.

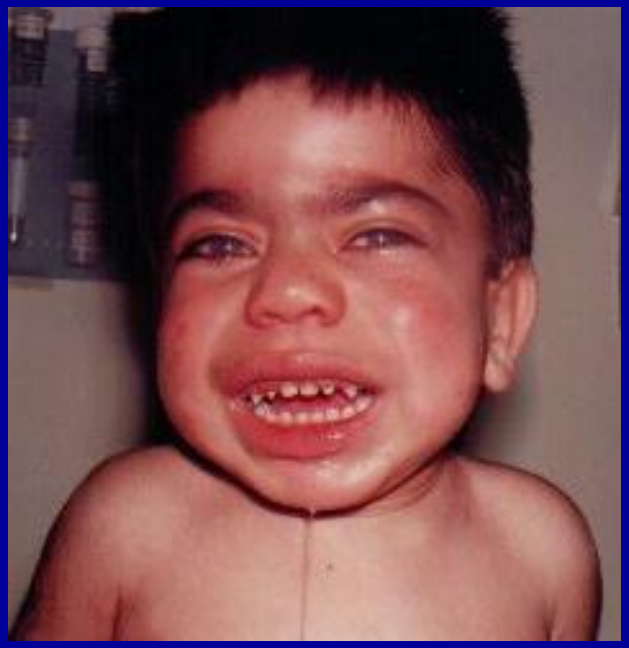


Gaucher disease

Acid β-glucosidase, 1q21-23



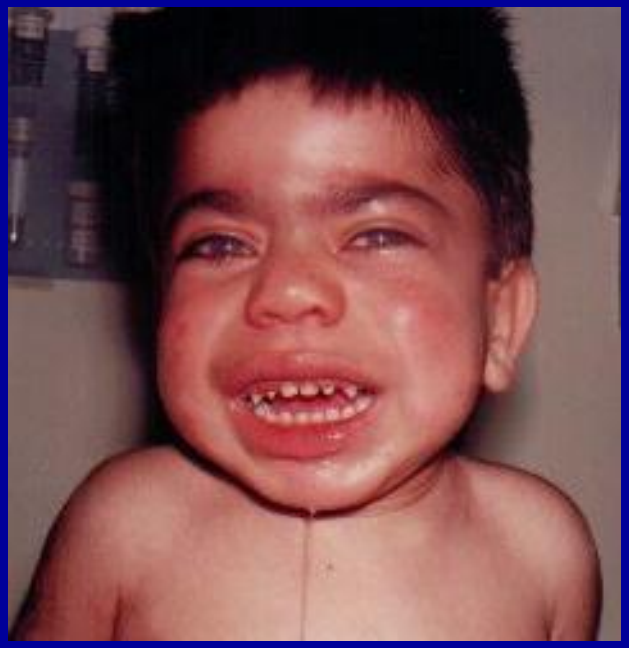
Niemann-Pick disease



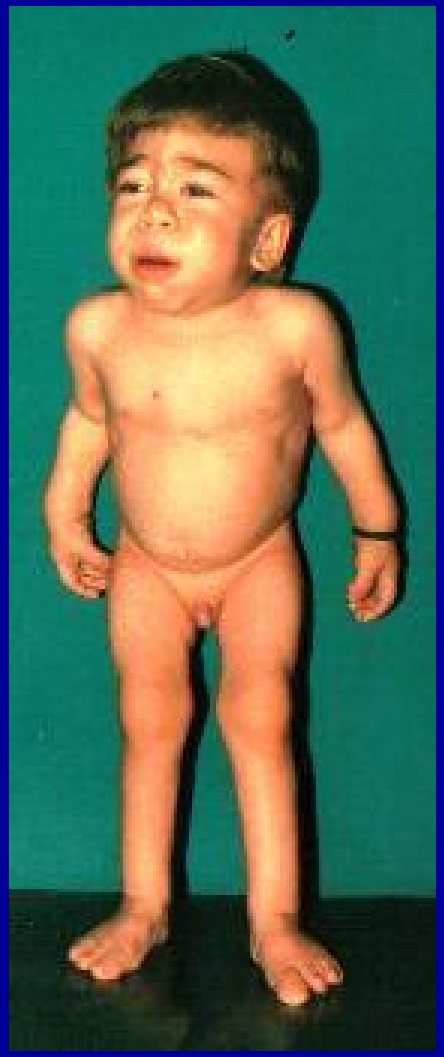
Mucopolysaccharidoses

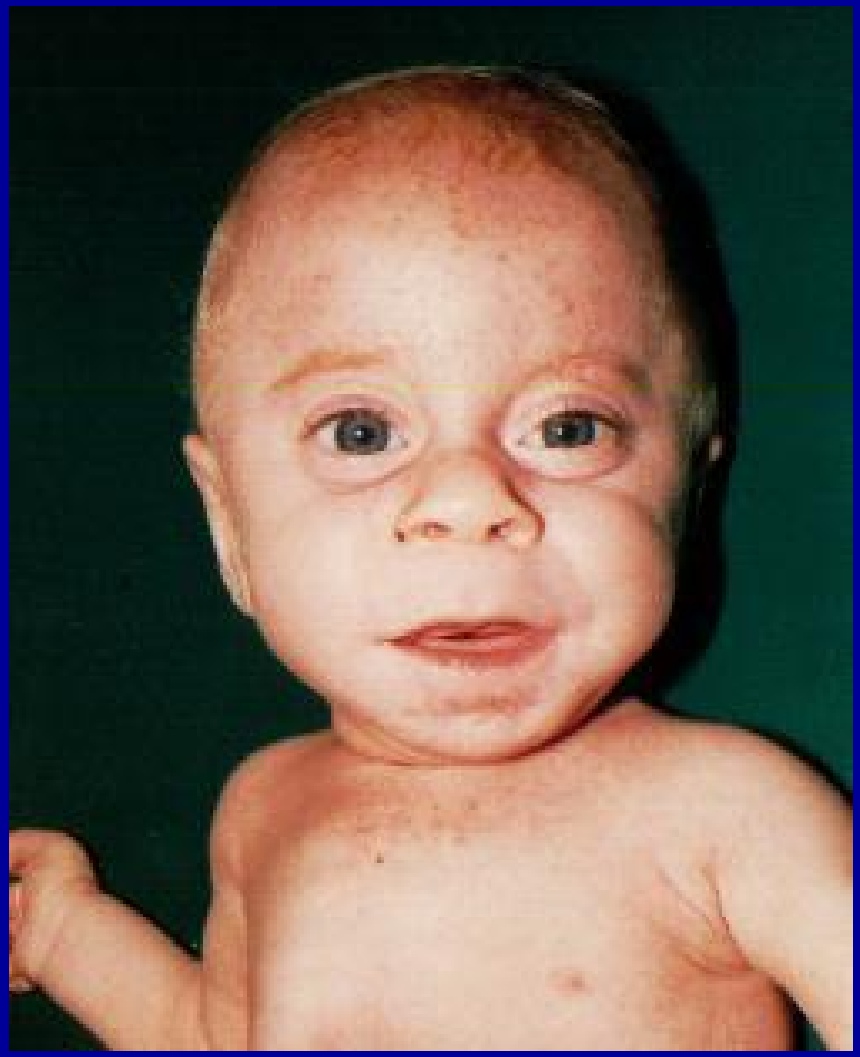
MPS type I (Hurler's syndrome)

a-L-Iduronidase, 4p16.3

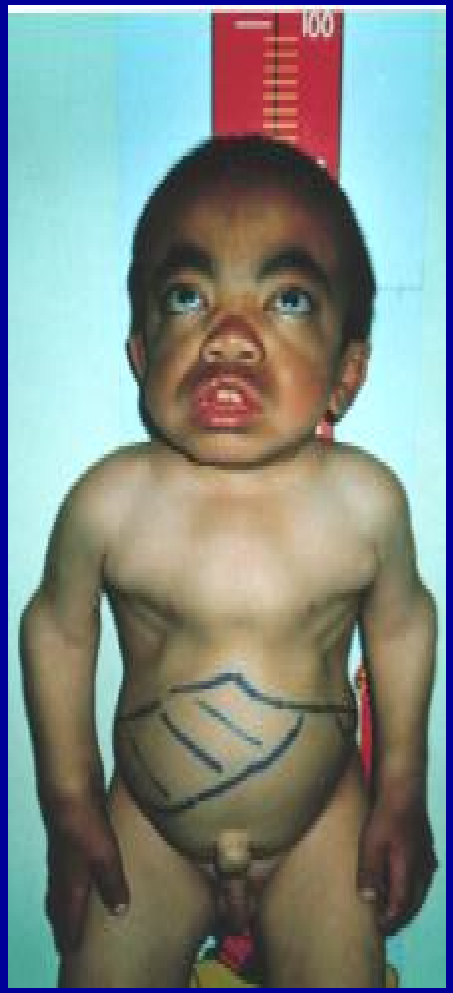


Mucolipidosis II & III
N-acetylglucosamin-1-phosphotransferase

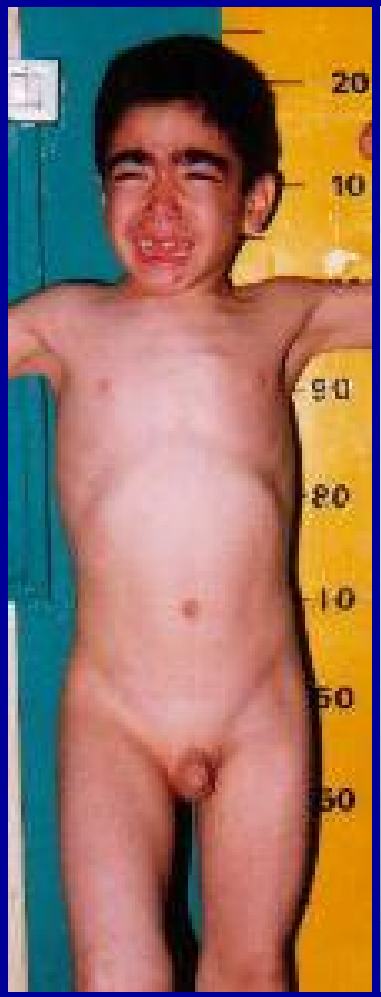




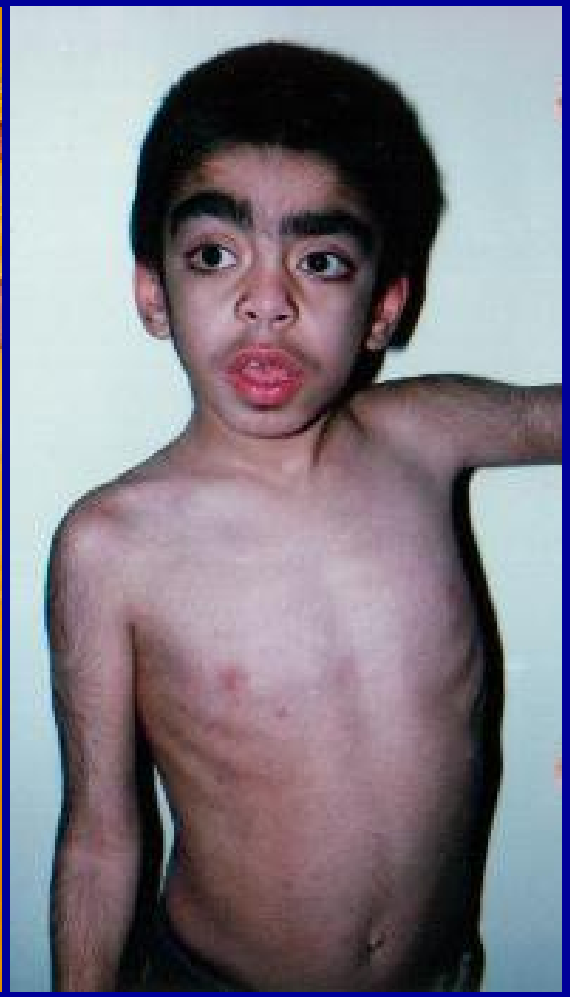
MPS VI



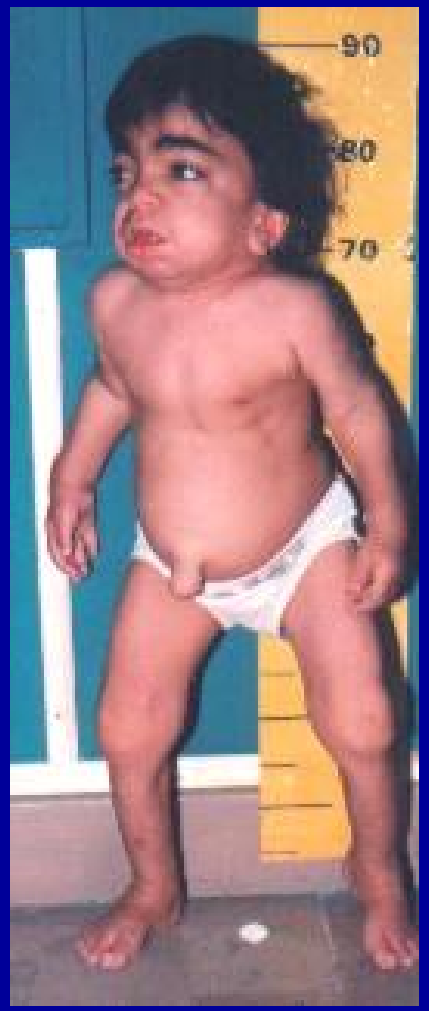
MPS IIIB



MPS IIIA

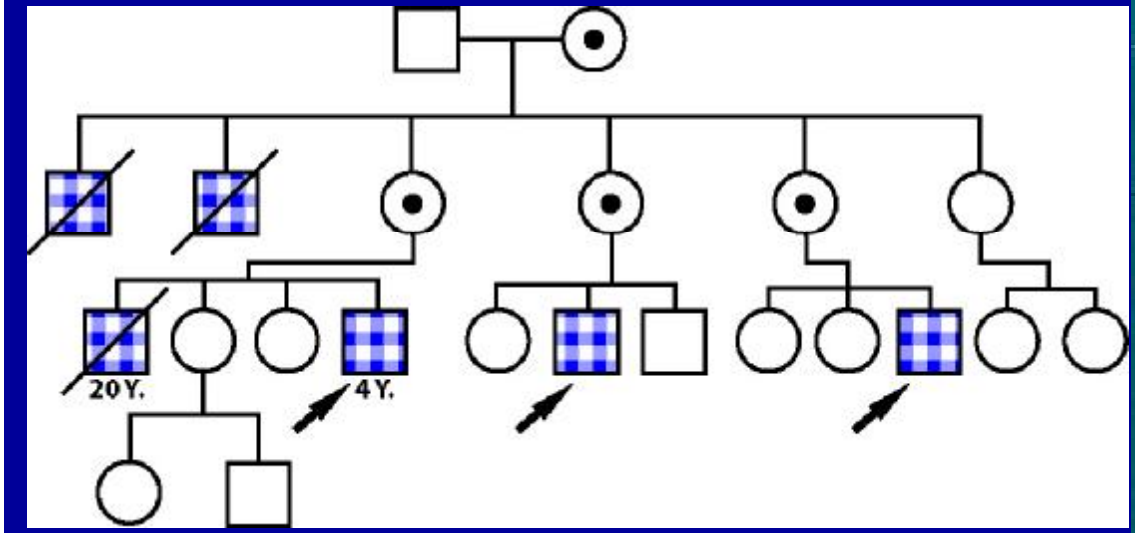


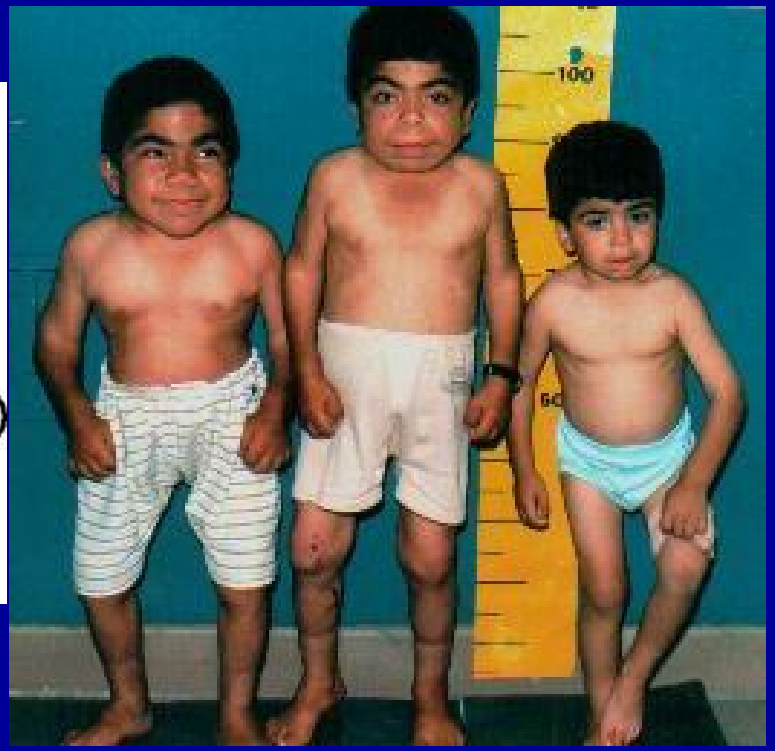
MPS I



MPS type II (Hunter's disease)

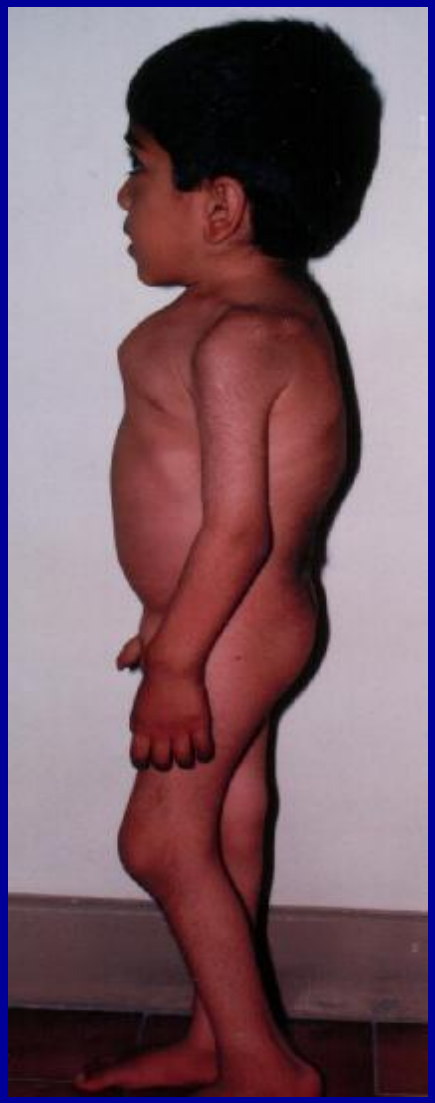
Iduronate sulfatase, XLR, Xq28

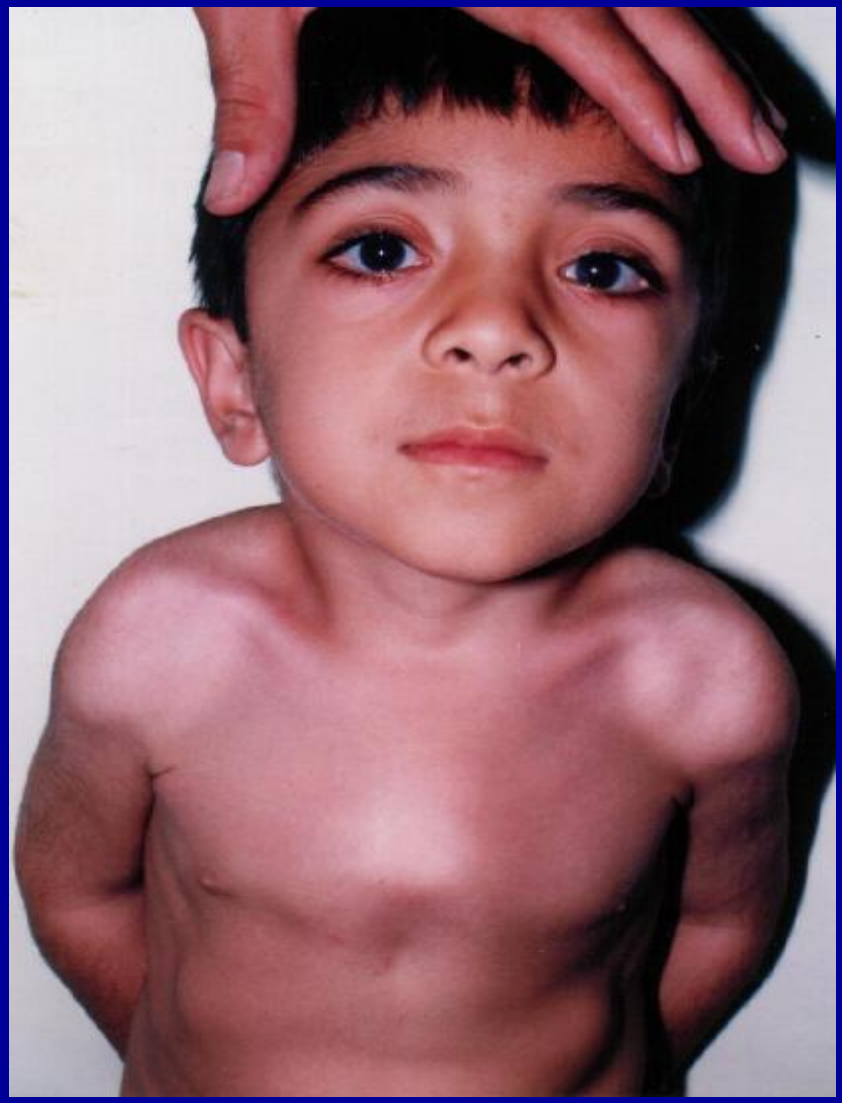




MPS type IV (Morquio Disease)

Galactose-6-sulfatase and β-galactosidase, 16q24.3





Clinical features

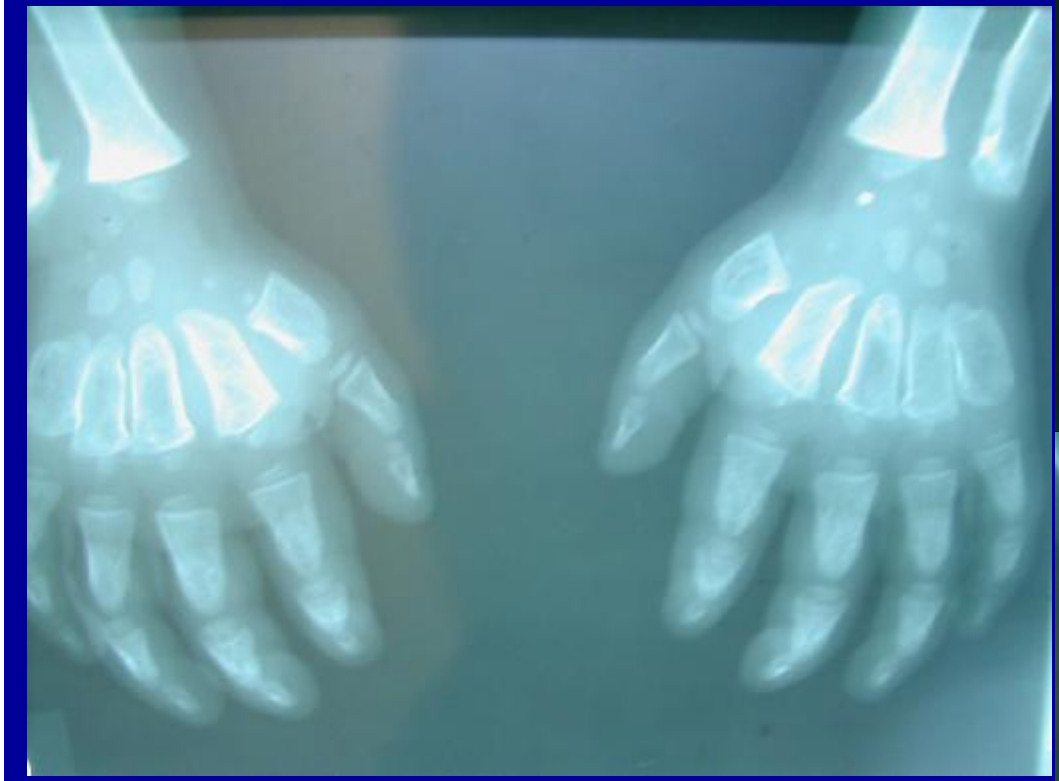
- Developmental delay
- Macro-Hydrocephaly
- Recurrent respiratory infection and noisy breathing
- Obstructive airway disease
- Combind hearing loss
- Hernias
- Neurologic regression
- Deafness

Radiographic findings
(Dysostosis multiplex congenita)

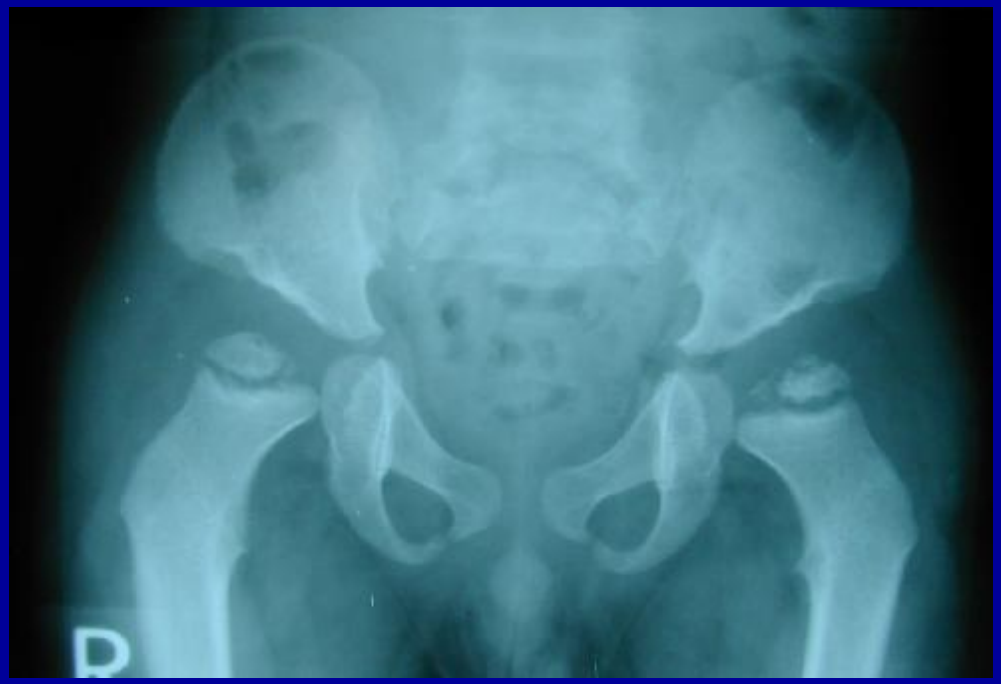
- Large thickened calvarium
- Large J-shaped sella
- Shallow orbits
- Ant. Spinal beaking
- Flaring of the pelvis
- Acetabular hypoplasia
- Fan like metacarpals
- Widening of the diaphyses

Large j-shaped sella

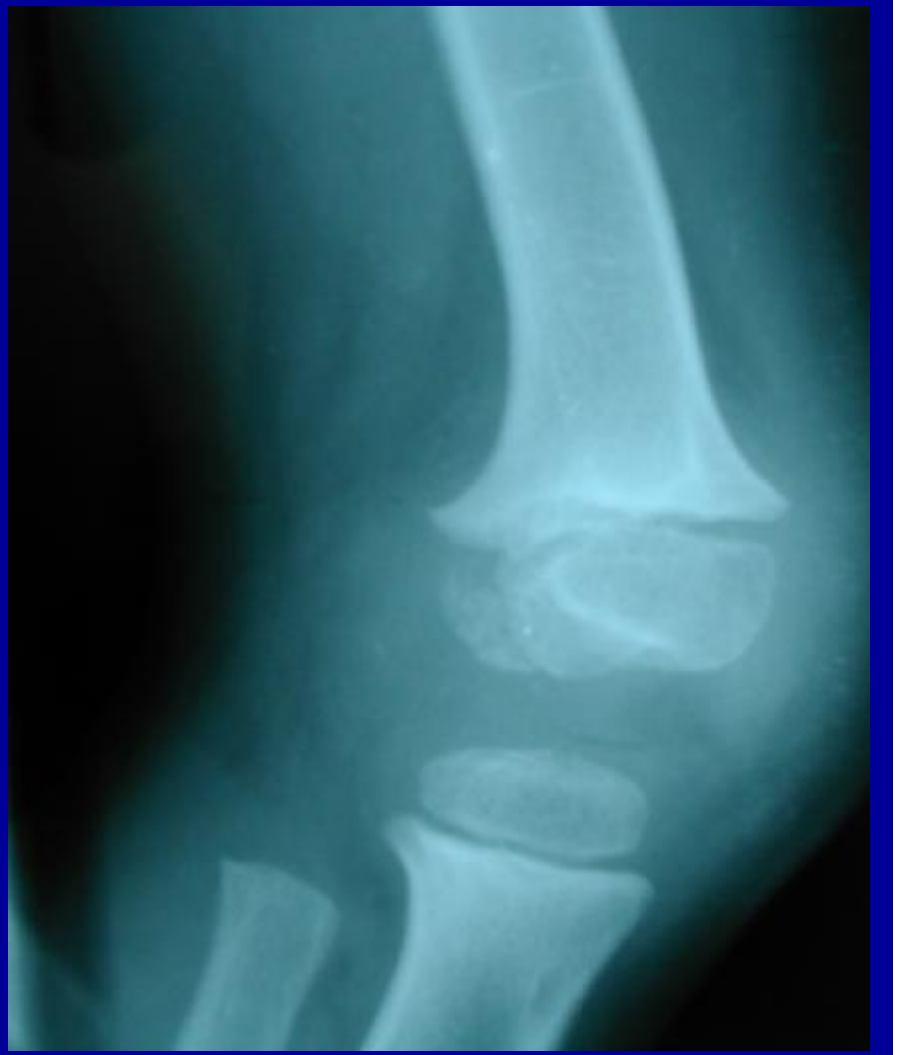
Fan like metacarpal bones



Tapering and flaring of iliac bones



Widening of metaphyses and Diaphyses



They are rare disorders, but not too much rare that we forget them at all

Thanks