Inborn errors of metabolism

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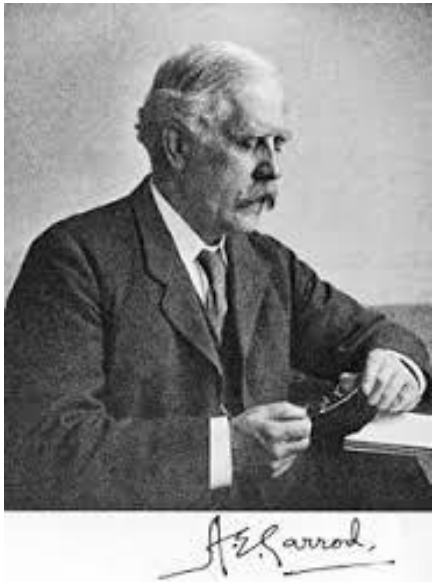
Garod 1908



Mckusick ,بیماری 334,1988

* Macro Molecule
Lysozomal
Peroxizomal –

*Intoxication
Org.Acid
U.C.D
Fructose Int.
Galactosemia

* Energy Deficiency
Gloconeogenesis Def
GSD
FAOD

Inborn errors of metabolism

- Aminoacidopathy
  - Organic acidemia
  - Urea cycle disease
- Defects in metabolism of lipids:
  - Fatty acid oxidation defect
  - Disorders of very long chain fatty acid (Proxidomal disorders)
  - Disorders of lipoprotein metabolism and transport
  - Lipidosis
  - Mucolipidosis

Inborn errors of metabolism…

- Defect in metabolism of Carbohydrates:
  - Glycogen storage disease
  - Defect in Galactose metabolism
  - Defects in Fructose metabolism
- Mucopolysaccharidosis

Inborn errors of metabolism

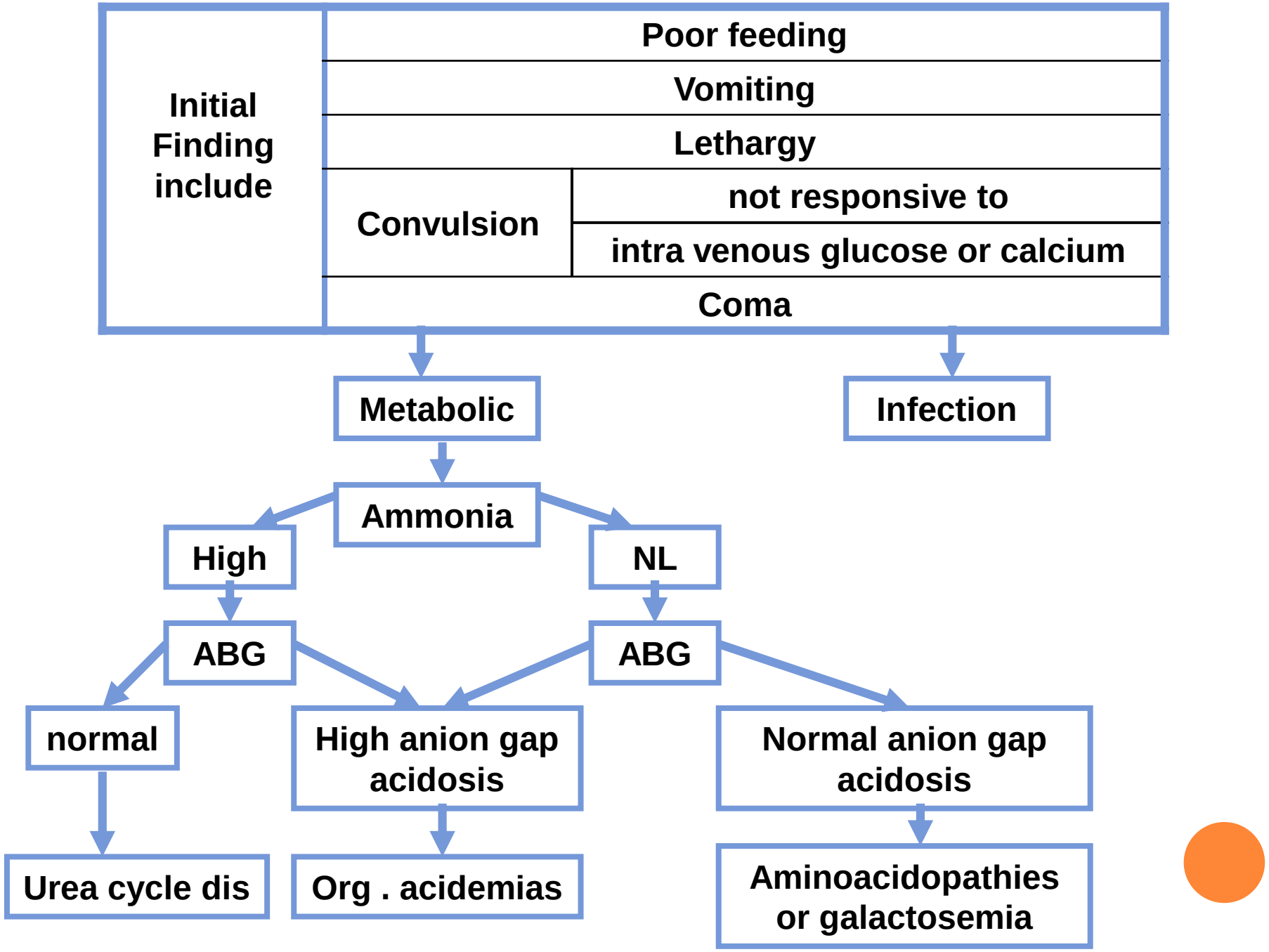
- Manifestation
- At birth
- Gen mutation
- Genetic polymorphism
- A.R.
- Sibling death
- screening

In Neonatal Period

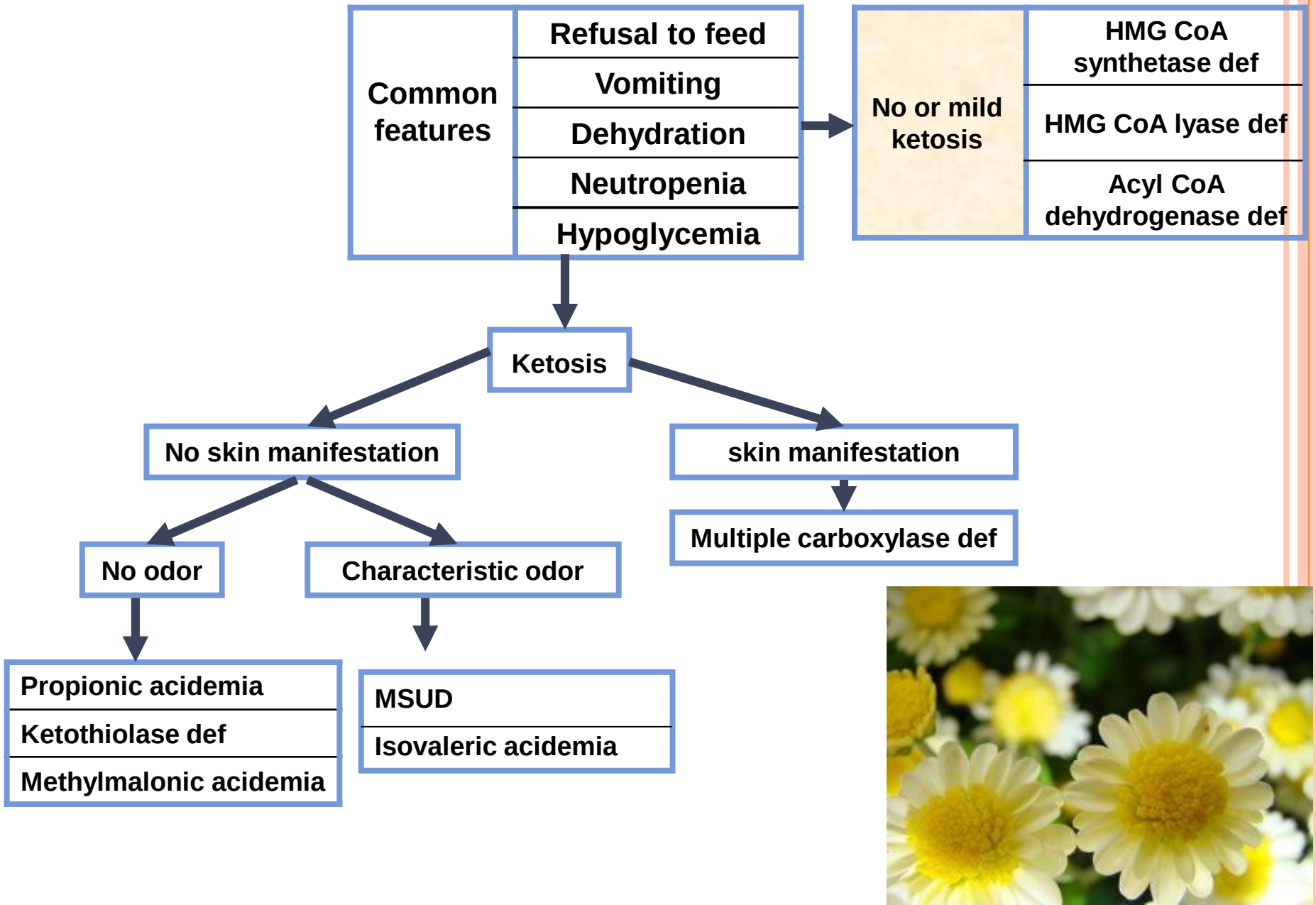
- Nonspesific manifestation similar to sepsis, hypoglycemia, hypocalcemia (lethargy ,poor feeding, convulsions, vomiting)
- Deterioration in a previously normal neonate
- Ph/Ex: nonspecific (CNS), hepatomegaly, peculiar odor.
- Initial tests, PH, Hco_3, ammonia, BS
- Most are lethal without treatment

After Neonatal Period

- **Episodic:**
- Unexphained, MR, regression, motor deficit, convulsions
- An usual odor
- Episodes of vomiting, acidosis, mental deterioration, coma
- Hepatomegaly
- Renal stone
- Muscle weakness or cardiomyopathy


Initial Finding include
Poor feeding
Vomiting
Lethargy
Convulsion
not responsive to
intra venous glucose or calcium
Coma
Metabolic
Infection
Ammonia
High
NL
ABG
ABG
normal
High anion gap acidosis
Normal anion gap acidosis
Urea cycle dis
Org . acidemias
Aminoacidopathies or galactosemia

Common approach to infants with organic acidemia



Laboratory finding helpful in the differential diagnosis of suspected metabolic disease in neonates

Finding	Diagnostic consideration
Acidosis	Fatty acid oxidation defect Gluconeogenesis defects Glycogene storage diseases Ketogenesis defects Ketolysis defects Krebs cycle defects Organic acidemiasis Respiratory chain defects
Alkalosis respiratory metabolic	Urea cycle defects stroid biosynthetic defects

Laboratory finding helpful in the differential diagnosis of suspected metabolic disease in neonates

Finding	Diagnostic consideration
Hepatic dysfunction	Amino acid defects Bile acid biosynthetic defects Carbohydrate defects Fatty acid oxidation defects Proxisomal disorders Respiratory chain defect Other (α_1 antitrypsin deficiency, Carbohydrate-deficient glycoprotein Syndrome)
hyperammonemia	Amino acid disorders ,fatty acid oxidation defects , urea cycle defects.

Laboratory finding helpful in the differential diagnosis of suspected metabolic disease in neonates

Finding	Diagnostic consideration
Hypoglycemia	Fatty acid oxidation defect Gluconeogenisis defects Clycogen storage disease Ketogenesis defects Organic acidemias
Ketosis/ketonuria	Amino acid defect Gluconeogenic defects Glycogen storage disease Ketolytic defects Organic acidemias
Pancytopenia	Organic acidemias Respiratory chain defects
Proximal renal tubular dysfunction	Amino acid defects Carbohydrate defects Respiratory chain defects

Initial laboratory screening of neonates with suspected metabolic disease

Body fluid	Laboratory studies
Blood	Blood cell count Electrolytes Blood gases Lactate and pyruvate Glucose Ketones (β-hydroxybutyrate and acetoacetate) Ammonia Uric acid
Urine	Smell Crystalluria Reduching substances PH Acetone α –ketoacids (diphenylhydrazone) Ferric chloride
CSF	Glucose Lactate and pyruvate

Neonatal – onset inborn errors of metabolism characterized by abnormal plasma amino acid patterns

Disorder	Finding
Amino acid disorders Maple syrup urine disease Nonketotic Hyperglycinemia Phenylketonuria Hereditary tyrosinemia	↑Isoleucine, leucine, valine ↑Glycine ↑Phenylalanine ↑Tyrosine, methionine Alanine

Neonatal – onset inborn errors of metabolism characterized by abnormal plasma amino acid patterns

Disorder	Finding
Organic acidemias	
Methylmalonic acidemia	↑Glycine
Isovaleric acidemia	↑Glycine
Propionic acidemia	↑Glycine
Urea cycle defects	↑Glutamine, arginine and …
Argininosuccinic aciduria	↑ASA, Citruline
Citrullinemia	↑↑Citrulline
CPS and OTC deficiency	↓Citrulline

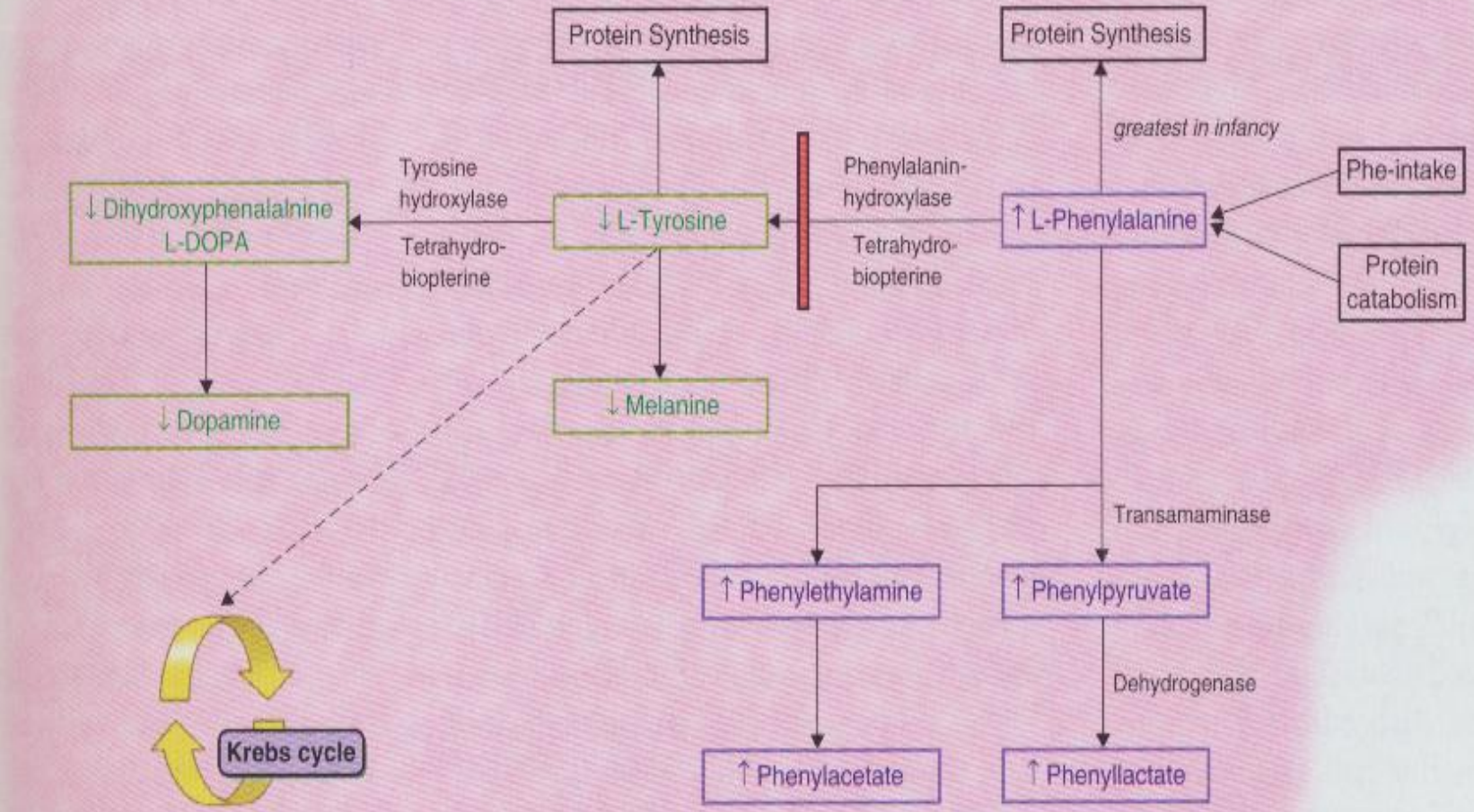
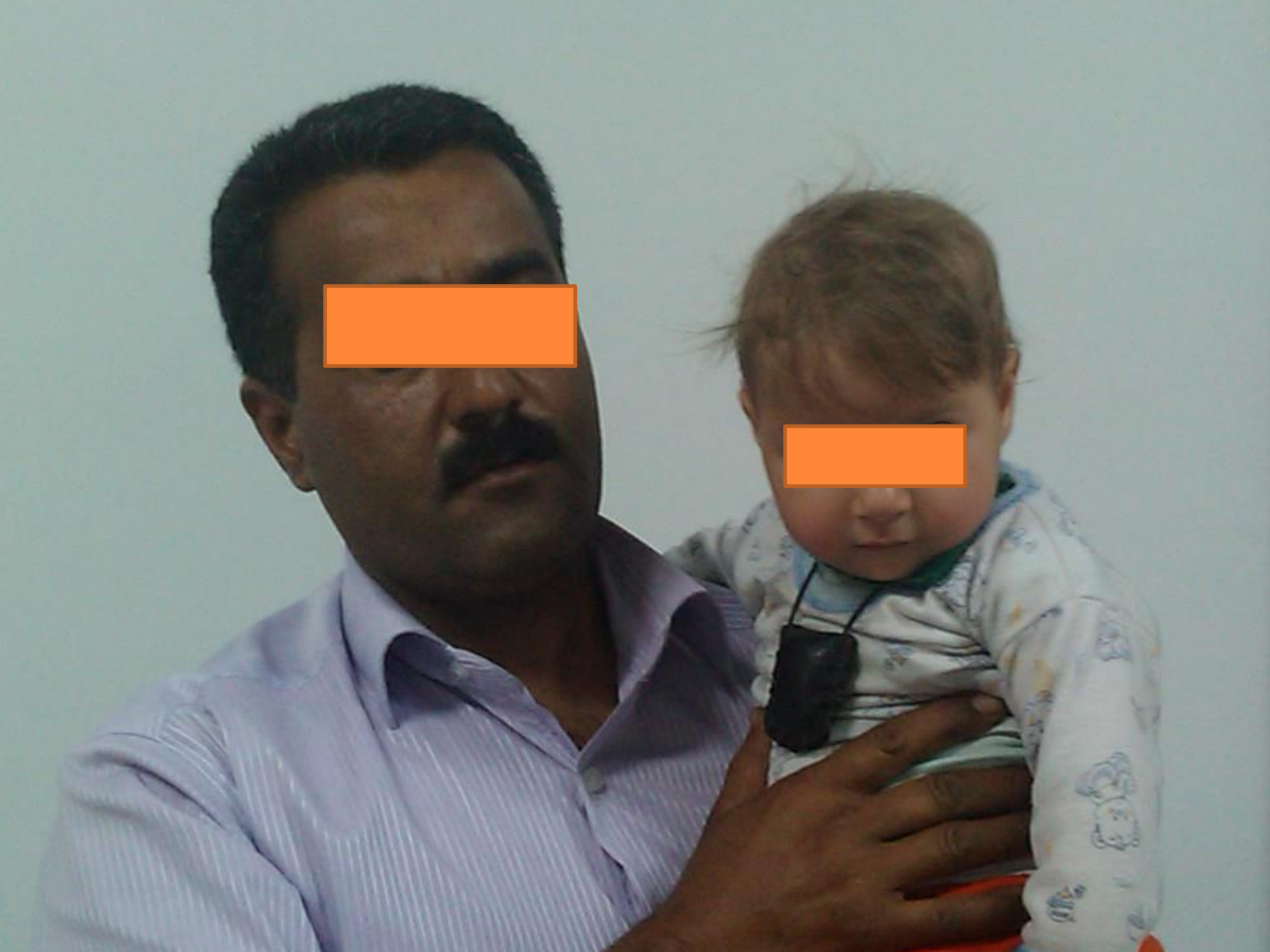
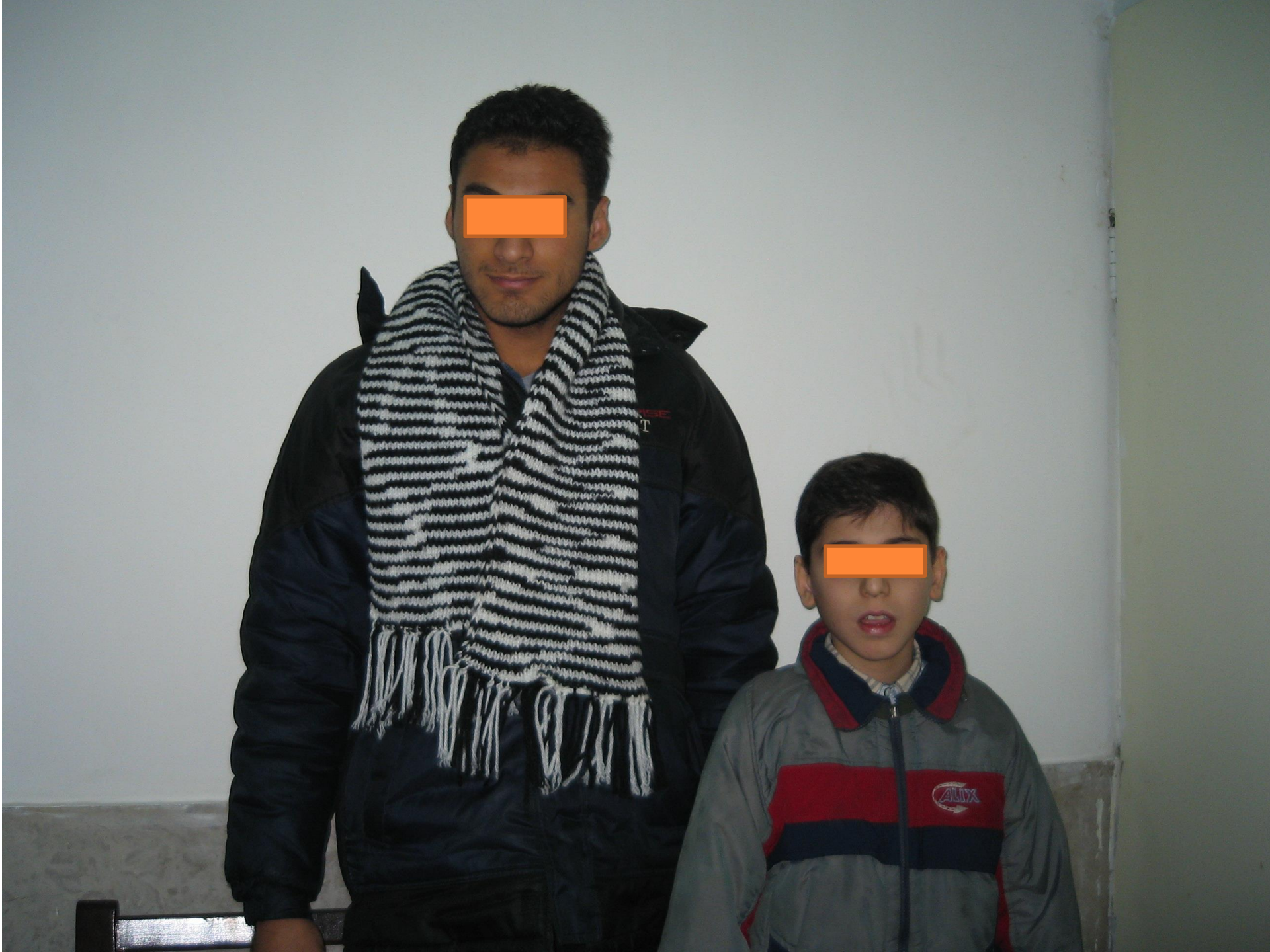
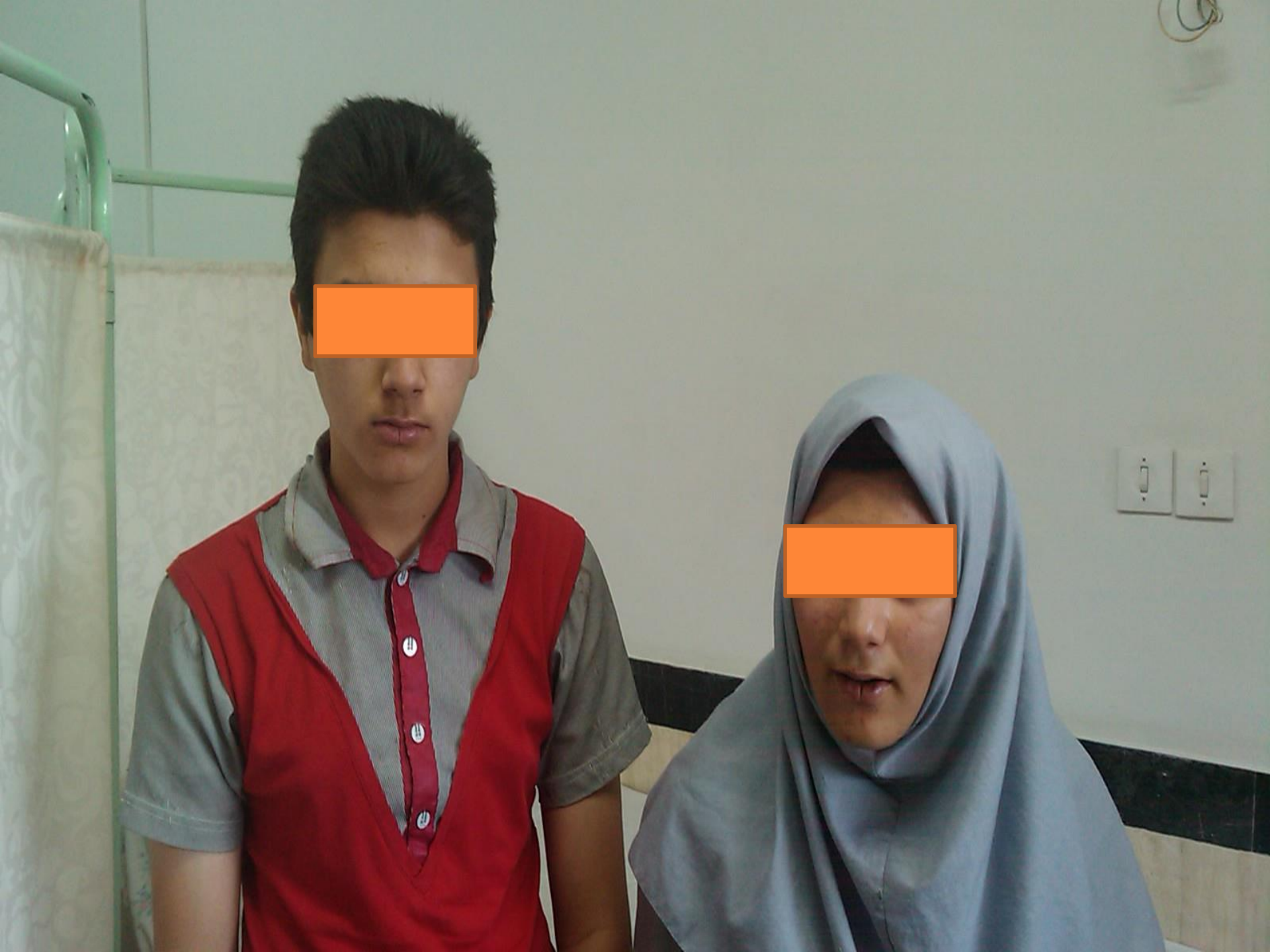


FIGURE 13-1. Defect and accumulating metabolites in phenylketonuria.







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Case Report

A Methylmalonic Acidemia Case Presenting with Acrodermatitis Enteropathica

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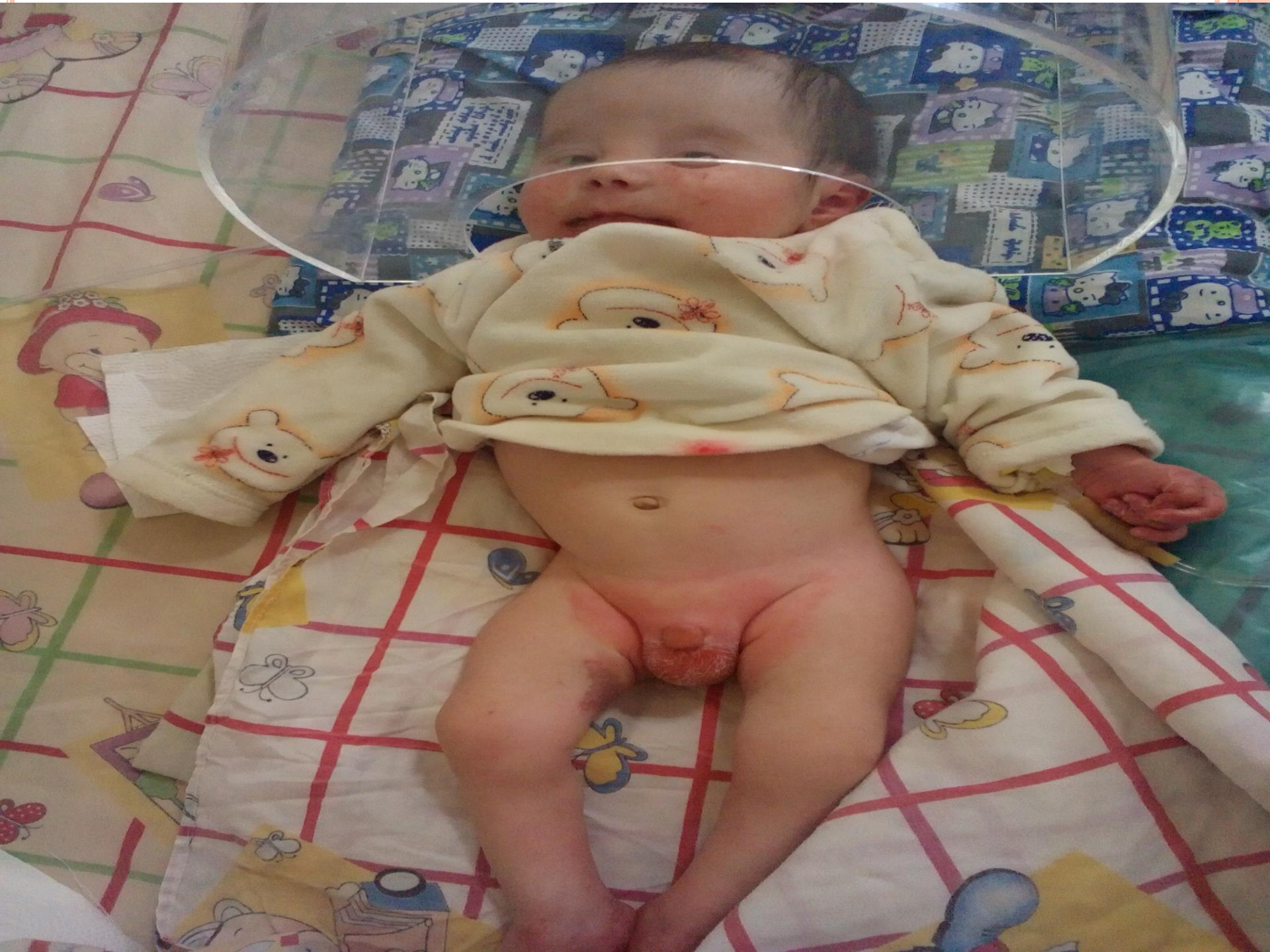
Abstract

We encountered a patient with methylmalonic aciduria associated with skin lesions resembling acrodermatitis enteropathica. This child was being fed with a low-protein diet when the skin disorder developed. A deficiency in plasma levels isoleucine, was confirmed. Supplementation of a high-caloric, protein-rich diet led to a prompt improvement of skin lesions. We assume that in our patient the skin lesions were the result of malnutrition, rather than being primarily associated with the underlying metabolic disease. To our knowledge, few reports are so far available concerning methylmalonic aciduria complicated by skin eruptions.

Keywords: Acrodermatitis Enteropathica, Children, Methylmalonic acidemia.




Thanks for your attention