What is Inborn errors of metabolism

LJ Mienie
Genetic defects

Numeric defects
- Die at an early age
- Structure abnormal
- Mental retardation
- Infections

Structural defects
- Die at an early age
- Structure abnormal
- Mental retardation
- Infections

Point mutations
- Die at an early age
- Structure abnormal
- Mental retardation
- Infections
Point mutations

Enzymes 100% active

Structural proteins 100% functional

50 %

50 %

50 %
Point mutations

Enzymes 50% active
No symptoms at birth
Recessive diseases

Structural proteins
Not functional
Symptoms at birth
Dominant diseases
Inborn errors of metabolism

Father

Child

Enzyme 0% activity

Mother
Metabolism

Food

Amino acids

Carbohydrates

Lipids

Nucleic acids

Enzyme A

Enzyme B

Enzyme C

Energy

Biomolecules
Inborn errors of metabolism

Food

Amino acids

Carbohydrates

Lipids

Nucleic acids

Enzyme A

Enzyme B

Enzyme C

Energy

Accumulation in cells

Spills into blood

Toxic effects

Biomolecules
Clinical effect

0% activity (homozygotes)

Toxic substance reaches toxic levels

50% activity (heterozygotes)

Toxic substance does not reach toxic levels

100% activity

Toxic substance does not reach toxic levels

(25% activity)

Toxic substance reaches toxic levels

(50% activity)

Toxic substance: reaches not toxic levels
Phenotype

0-15 years
- Die
- Neurological diseases
- Liver diseases
- Heart diseases
- Muscle problems
- Cancer
- Ear and Eye problems
- Abnormal behavior

20-60- years
- Die
- Neurological diseases
- Liver diseases
- Heart diseases
- Muscle problems
- Ear and Eye problems
- Abnormal behavior
- Cancer

No symptoms

Environment

1/1000 births

5 mutations/person 1/5 serious
Classification of IEM

- Organic acid metabolic defects
- Carbohydrate metabolic defects
- Amino acid metabolic defects
- Membrane transport defects
- Lipid metabolic defects
- Mitochondrial defects
- Purine & Pyrimidine metabolic defects
- Vitamin defects
- Lysosomal defects
- Peroxisomal defects
- Porphyrin metabolic defects
- Metal metabolic defects
- Hormonal defects
Other Defects

- Blood
- Immune and defense systems
- Connective tissue
- Cardiovascular system
- Kidney
- Muscle
- Lung
- Skin
- Neurogenetics
- Eye
- Multisystem inborn errors of development
- DNA repair defects
Diagnosis: Homozygotes

Food

Amino acids

Carbohydrates

Lipids

Nucleic acids

Energy

Biomolecules

Accumulation in cells

Spills into blood

And urine

Toxic effects

Enzyme A

Enzyme B

Enzyme C

Energy

Biomolecules

RFLP-analysis

Enzyme Analysis

GC

GC-MS

HPLC

MSMS

CE

TLC
Methods: Chemical analysis

Organic analysis – GC-MS
Amino acid analysis- GC-MS
Acylcarnitine analysis-ES-MSMS
Carbohydrate analysis-TLC GC-MS
Oligosaccharide analysis-TLC
Mucopolisaccharide analysis-Electrophoresis
Glycoprotein analysis-Isoelectrophoresis
Purine and Pyrimidine analysis-CE
Very long chain fatty acid analysis/phytanic acid-GC-MS
Bile acid analysis-ES-MSMS
DNA Repair analysis-Comet single cell eletrophoreses
Treatment and prevention: Homozygotes

**Reduce Intake**

**Inhibitors**

**Accumulation in cells**

**Spills into blood**

**Toxic effects**

**Detoxify**

**Supplementation**

**Prenatal diagnosis**

Food

Amino acids

Carbohydrates

Lipids

Nucleic acids

Enzyme A

Enzyme B

Enzyme C

Energy

Biomolecules

**Inhibitors**

**Supplementation**