

# **METABOLIC DISORDER**

# INBORN ERRORS OF METABOLISM

- A group of diseases caused by
  - a defect in the activity of an enzyme that affect a wide variety of metabolic processes;
- defective processing or transport of amino acids, fatty acids, sugars or metals



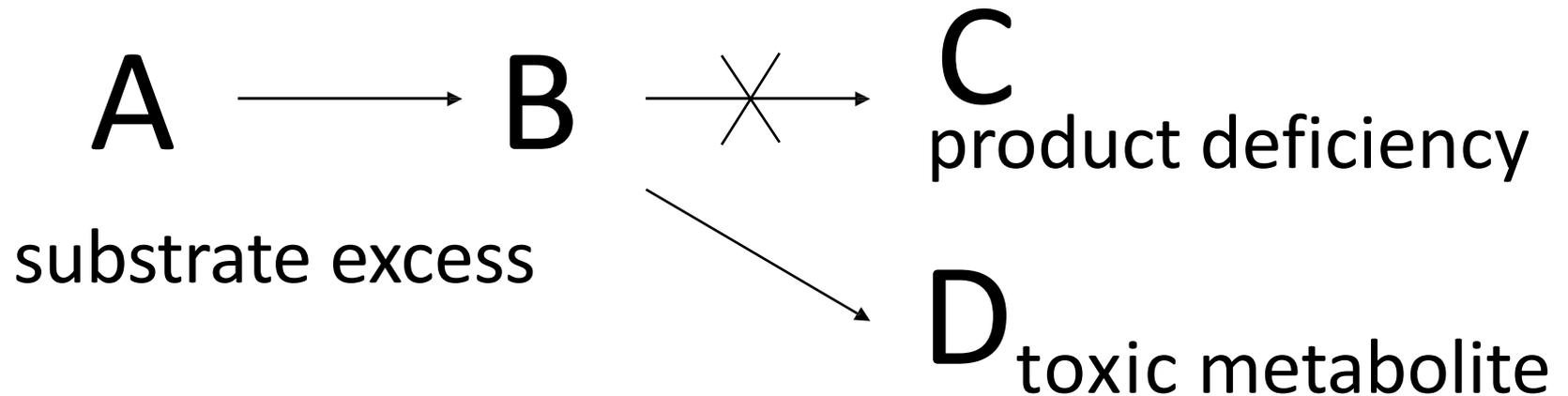
# INBORN ERRORS OF METABOLISM

- An inherited enzyme deficiency leading to the disruption of normal bodily metabolism
- Impaired formation of a product normally produced by the deficient enzyme
- Accumulation of a toxic substrate (compound acted upon by an enzyme in a chemical reaction)



# What is a metabolic disease?

- Garrod's hypothesis

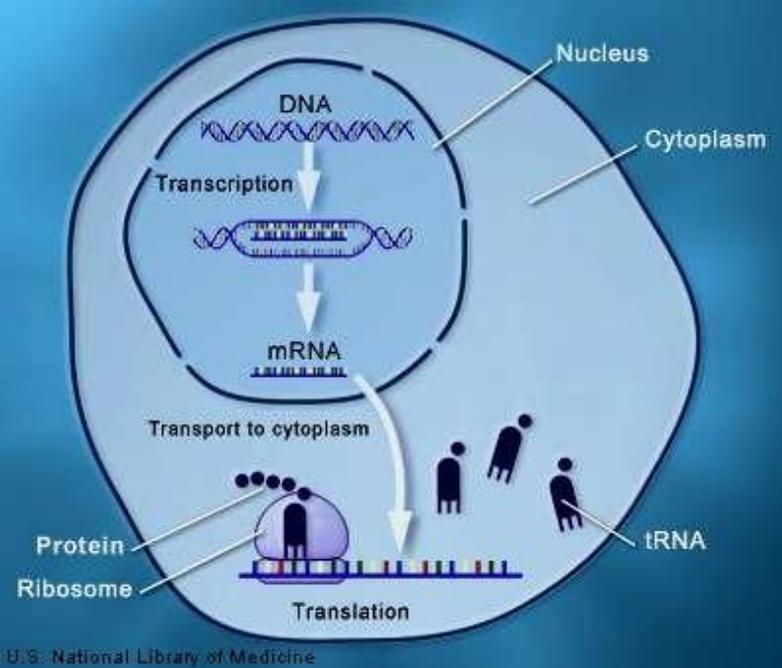


# OUR GENETIC BACKGROUND

- **Total genes 25000 in pairs**
- **Genetic disorders 7000**

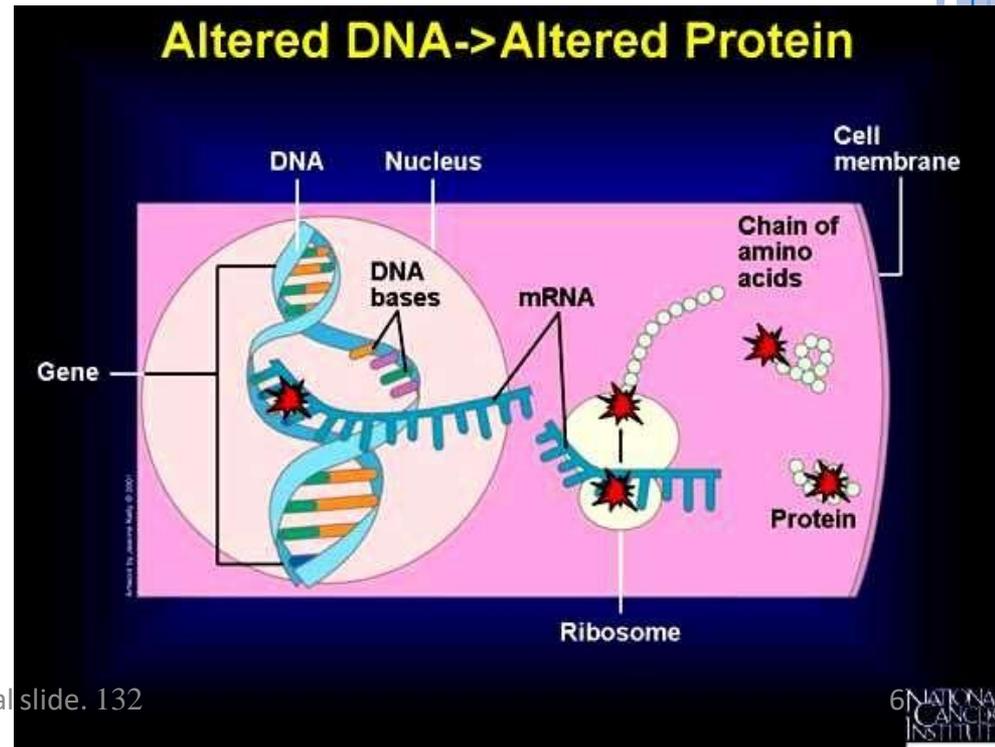


# GENETIC BASIS OF INHERITED DISORDERS



Point mutations,  
Insertions, Deletions,  
Missense Mutations  
and Rearrangements

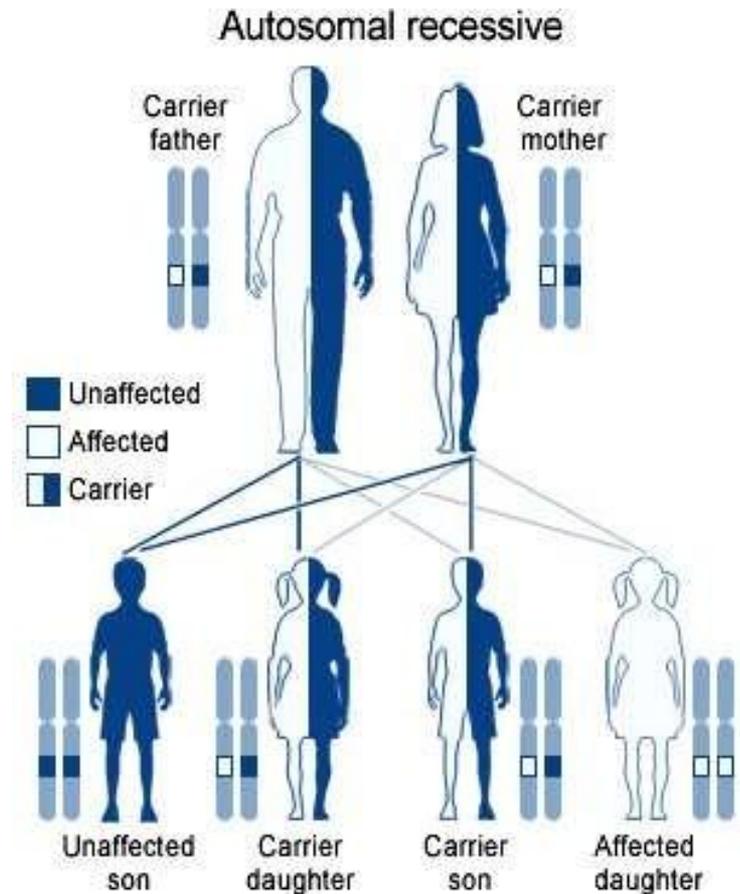
15 August 2019



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# EPIDEMIOLOGY AND INHERITANCE

- Although each individual IEM is rare, cumulatively they occur ~ **1:5000 live births**
- Majority of IEM follow an **autosomal recessive** mode of inheritance



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# CLASSIFICATION OF METABOLIC DISEASES

## Small molecule disease

- **Carbohydrate**
- **Protein**
- **Lipid**
- **Nucleic Acids**
- **Minerals**
- **Vitamins**

## Organelle disease

- **Lysosomes**
- **Mitochondria**
- **Peroxisomes**
- **Cytoplasm**



# METOBOLIC DISORDERS

- **Aminoacid Metabolim**
- **Lipid Metabolism**
- **Carbohydrate Metabolism**
- **Mitochondrial Energy Metabolism**
- **Vitamin Metabolism**
- **Metal Transport**
- **Nucleic acid and Heme Metabolism**
- **Organelles – lysosomes , peroxisomes**



# METOBOLIC DISORDERS

- **Defects in Amino and Organic Acid Metabolism**
- **Defects in Carbohydrate Metabolism**
- **Errors in Fatty Acid Metabolism**
- **Defects in Cholesterol and Lipoprotein Metabolism**
- **Mucopolysaccharide and Glycolipid Disorders**
- **Defects in Nucleotide Metabolism**
- **Disorders in Metal Metabolism and Transport**
- **Porphyrias and Bilirubinemias**
- **Diseases Associated with Defective DNA Repair**



# Categories of IEMs

## **Disorders of protein metabolism**

(amino acidopathies, organic acidopathies, and urea cycle defects)

**Disorders of carbohydrate metabolism** (eg, carbohydrate intolerance disorders, glycogen storage disorders, disorders of gluconeogenesis and glycogenolysis)

**Fatty acid oxidation defects**

**Lysosomal storage disorders**

**Mitochondrial disorders**

**Peroxisomal disorders**



# Protein metabolism disorders

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- **Organic acidemias**
- **Aminoacidurias**
- **Urea cycle defects**



# Carbohydrate metabolism disorders

- **Glycogen storage disease**
- **Galactosemia**
- **Fructose intolerance**
- **Glucose malabsorption**



# Fat metabolism disorders

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- **Hypertriglyceridemia**
- **Hyperlipidemia**
- **Fatty acid oxidation defects**



# VITAMIN DISORDERS

- **Biotinidase deficiency**



# MINERAL DISORDERS

- **Wilson disease**
- **Menkes disease**
- **Cystinosis**

