Development Of
Neonatal Screening Program
In Iran

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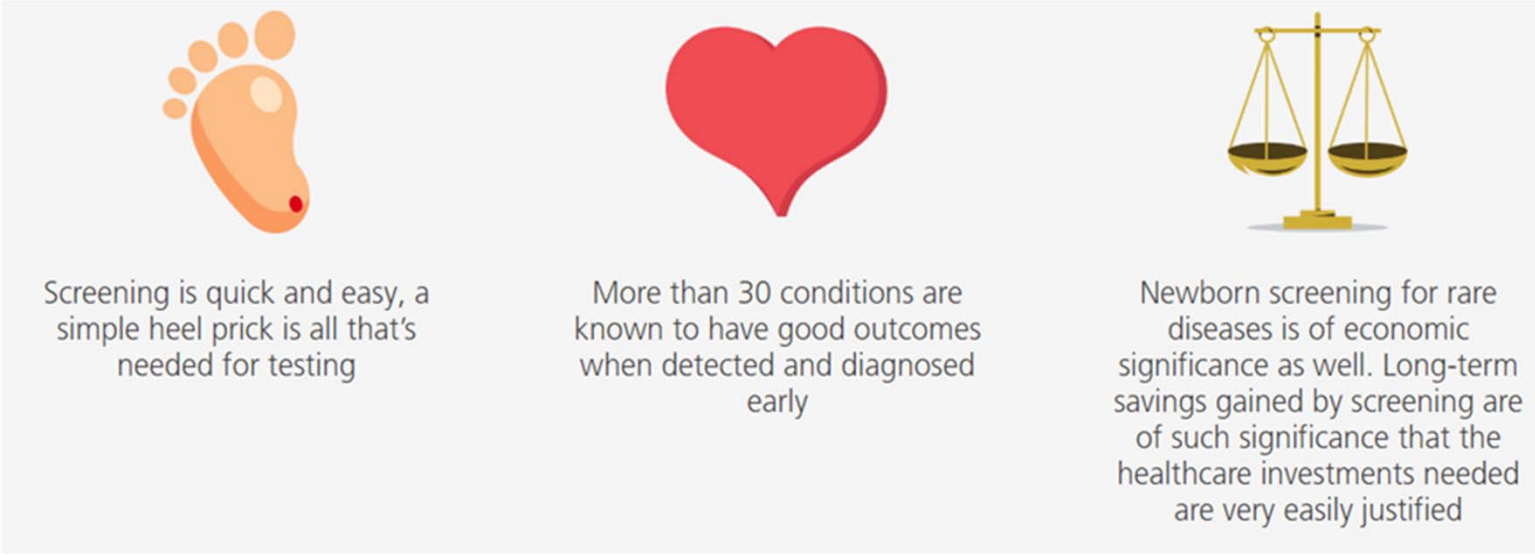
What is newborn screening?

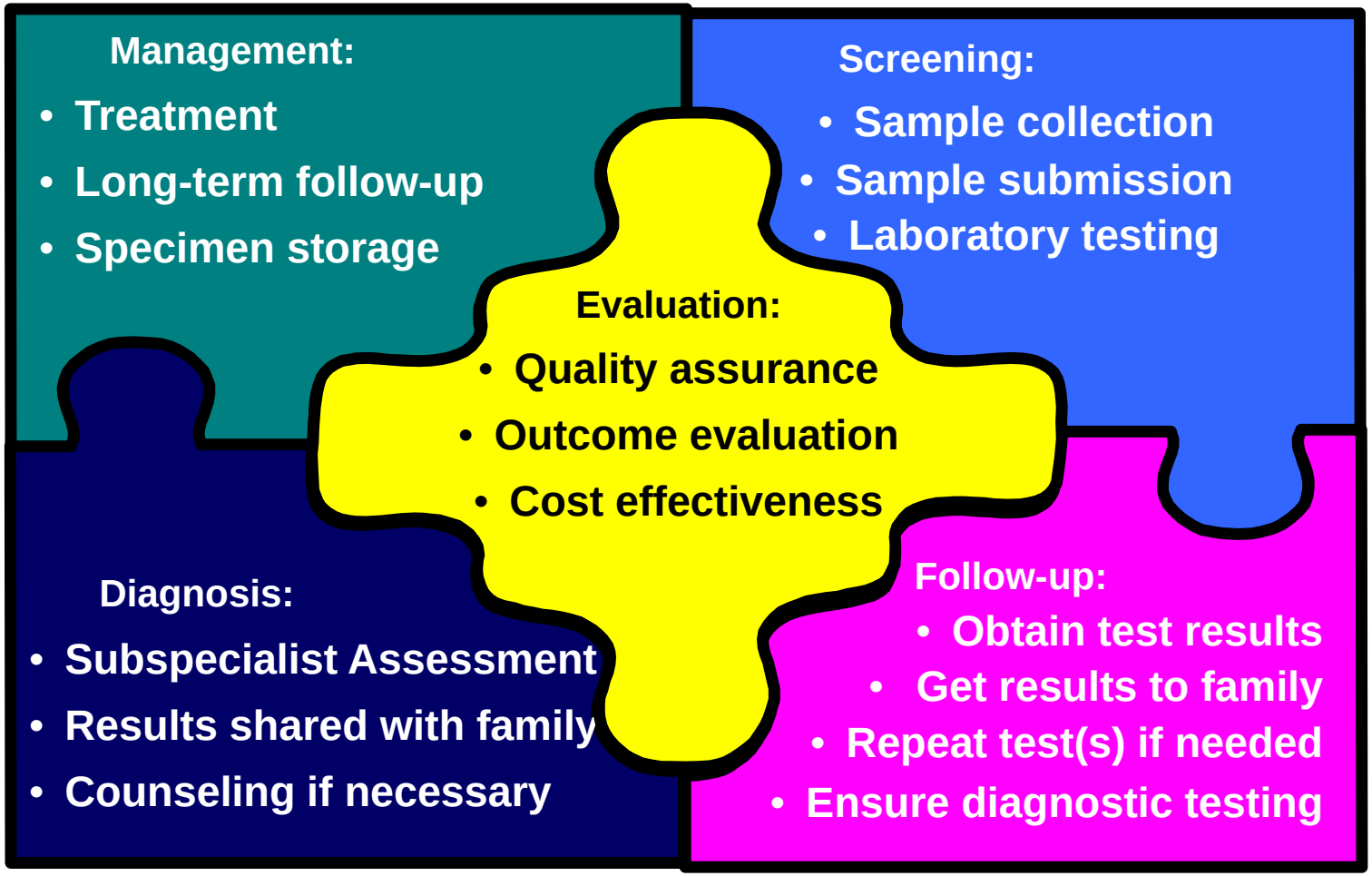
- An essential public health program that prevents catastrophic health consequences through early detection, diagnosis and treatment.



Criteria for Newborn Screening

- Important condition
- Acceptable treatment available
- Facilities for diagnosis and treatment
- Difficult to recognize early
- Suitable screening test
- Natural history known
- Cost-effective to diagnose and treat

Newborn screening is more than testing



History of Newborn Screening in Indiana

- 1965: PKU only condition included in newborn screen
- 1978: Hypothyroidism added
- 1985: Galactosemia, homocystinuria, maple syrup urine disease (MSUD), and hemoglobinopathies added
- 1999: Biotinidase deficiency and congenital adrenal hyperplasia added
- 2003: Screening further expanded to include disorders detected by tandem mass spectrometry (MS/MS)
- 2007: Cystic fibrosis was added to the panel in some states

- **Currently, all infants born in Indiana are screened for 29- over 50 conditions (including hearing loss)**

Robert Guthrie

The Father of Newborn Screening
(1916-1995)

Expanded NBS – 29 conditions

- 20 inborn errors of metabolism
- 3 hemoglobinopathies
- 2 endocrine disorders
  - ✓Congenital hypothyroidism
  - ✓Congenital adrenal hyperplasia
- 3 other metabolic disorders
  - ✓Cystic fibrosis
  - ✓Galactosemia
  - ✓Biotinidase deficiency
- Hearing loss

Recommended screening for

- **Core panel of 29 diseases**
- **Secondary targets of 25 diseases**
- **Total of 54 diseases should be included in NBS test panels**

History of Newborn Screening
In Iran

1990s:The beginning of newborn screening started with thalassemia as an inherited single-gene disorder

2000: Screening of Hypothyroidism in newborns

2005: Establishing PKU screening as the first metabolic disorder

2011: Development of the comprehensive newborn screening map simultaneous with entrance of LC-MS/MS technologies in Iran.

History of Newborn Screening
In Iran

2014: Introducing the standards, training programs, and future directions for newborn screening.

2015: Establishment of the first metabolic disorder newborn screening program in Sari and Babol.

Tandem Mass Spectrometer (LC-MS/MS)

SHIMADZU
Excellence in Science

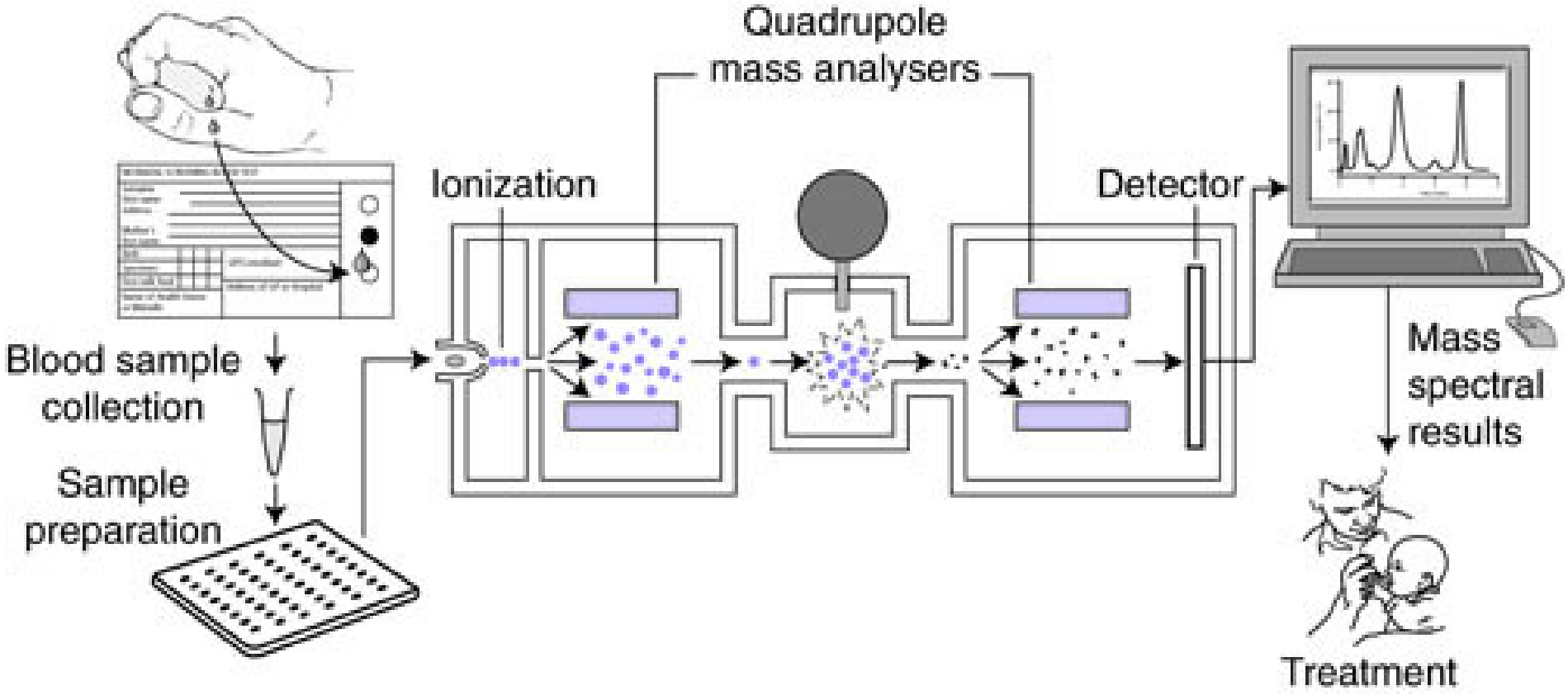
Liquid Chromatograph Mass Spectrometer

LCMS-8045

—Best in class sensitivity

Made In Japan

Tandem Mass Spectrometer (LC-MS/MS)



MS/MS Methodology

- Blood spots punched (1.36 inch disc)
- Stable isotope internal standards added (deuterated)
- Butyl esters derivatives made
- Automatic injection into MS/MS via 96 well plates
- Sample set up determines which masses and therefore which compounds are detected
- 2 minute analysis time
- Automated data processing for results

Gas Chromatograph-Mass Spectrometer

Inherited Metabolic Disorders

- Amino acid metabolism disorders and Urea cycle disorders include
- Fatty Acid Oxidation Disorders include
- Organic Acid Disorders include

Amino Acid Disorders

- AA that are not used to make proteins are recycled by their specific metabolic pathways.
- Diagnosed by plasma amino acids, urine amino acids, and/or urine organic acids (takes 2-5 days)

1. PKU: severe, permanent ID
2. MSUD: ID, hallucinations, ataxia
3. HCY: connective tissue damage (joints, heart), ID, psychiatric disturbances
4. CIT: risk of hyperammonemia → ID, coma, death
5. ASA (Argininosuccinic acidemia): brittle hair, liver disease ID
6. TYR I: acute or chronic liver disease, liver cancer, neurologic pain crises

Organic Acid Disorders

- Organic acids are breakdown products of protein and fatty acid metabolism
- Diagnosed by urine organic acids and/or plasma acylcarnitines

1. IVA: Isovaleric acidemia
2. GA I: Glutaric acidemia type I
3. HMG: 3-OH 3-CH3 glutaric aciduria
4. MCD: Multiple carboxylase deficiency
5. MUT: Methylmalonic acidemia (mutase deficiency)
6. 3MCC: 3-Methylcrotonyl-CoA carboxylase deficiency
7. Cbl A,B: Methylmalonic acidemia
8. PROP: Propionic acidemia
9. BKT: Beta-ketothiolase deficiency

Fatty Acid Oxidation Disorders

- Breakdown of fatty acids in mitochondria is an essential part of body's ability to produce energy.
- Disorder: inability to break down fatty acids.
- Decompensate with any catabolic stress

1. Carnitine uptake defect (CUD)
2. Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
3. Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)
4. Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)
5. Trifunctional Protein Deficiency (TFP)

Summary

✓Specific diagnosis must be confirmed
- In coordination with the state Newborn Screening Program

✓Careful monitoring of medical and nutritional status must be on-going
- By the metabolic team

✓Nutritional intervention
- Must be specific to the disorder
- Specific to the child

Thank You