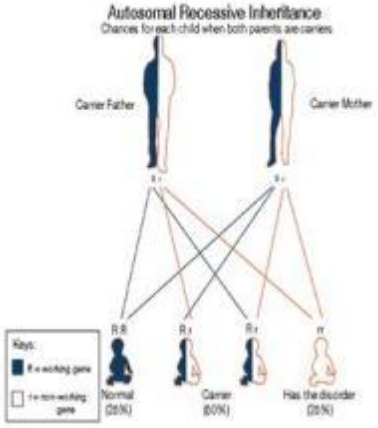
RARE METABOLIC DISORDERS IDENTIFIED IN THE NEWBORNS OF UAE

Metabolic Disorder/IEM

- Metabolic disorders/IEMs are caused when the body is unable to break down food properly, which then accumulate in the body and becomes toxic.
- When the concentration of toxic build-up increase they cross the blood-brain barrier and this leads to delayed development, brain damage and, in some cases, even death.
- Most infants with these disorders show no obvious signs of these disorders at birth, but the build-up can be rapid enough for the condition to become irreversible within a few weeks of birth.

Reason behind these Disorders

- These disorders follow an autosomal recessive inheritance pattern.
- Could skip generations.
- Parents are carriers.
- Happens when the two parents carry the gene 1:4 probability of having an affected child.



Newborn Screening

- **Newborn screening** is the process of testing newborn babies for treatable genetic, endocrinologic, metabolic and hematologic diseases.
- Screening is done to assist healthcare providers in detecting the existence of a number of treatable but clinically undiagnosed disorders, before symptoms occur, so that the most beneficial outcome can be achieved.

Early detection is very important

- Affected babies are identified quickly before symptoms appear.
- Cases of disease are not missed.
- The number of false-positive results is minimized.
- Early treatment can begin, that prevents the negative and irreversible health outcomes for affected newborns.
- Most treatments are inexpensive and may involve the addition of a vitamin to the diet, hormone supplementation, avoidance of certain foods and chemicals or a dietary change.

If screening is delayed

It could lead to lifelong complications:

- Mental Retardation.
- Motor Impairment.
- Physical Disability.

Every Newborn needs to be Screened

- Every Newborn (Routine screening).
- High Risk
  - Unexplained deaths of siblings.
  - Miscarriages & Aborted Fetuses.
  - Exhibit symptoms of IEMs.
  - Babies conceived by IVF.
  - Babies in NICU.
- Sick Children.

History of Newborn Screening

- Newborn screening began in South Carolina in the mid-1960's with testing for phenylketonuria (PKU) only (Kidshealth.org).
- Over the years, the test panel has expanded with increased use of tandem mass spectrometry (MS/MS) in newborn screening applications.
- Now almost all states screen for more than 30 disorders. (Kidshealth.org).
- Each year, at least 4 million babies in the United States are tested for these diseases, and severe disorders are detected in about 5,000 newborns. (Kidshealth.org).

Newborn Screening in UAE

- The national neonatal screening program started by screening for phenylketonuria in January 1995 (MOH, 2006).
- Screening for congenital hypothyroidism was introduced in January 1998 (MOH, 2006).
- By 2002, sickle cell anemia was identified by newborn screening program (MOH, 2006).
- In January 2005, Congenital Adrenal Hyperplasia has been included as part of the screening (MOH, 2006).
- Screening for newborns is still not mandatory for each child born in UAE.
- Only the sick babies are being tested due to a lack of awareness of the benefits and high costs.

Relative Incidence of disease

Since the Implementation of the screening program, From Jan 1995 until Dec 2005 by MOH: (MOH, 2006).

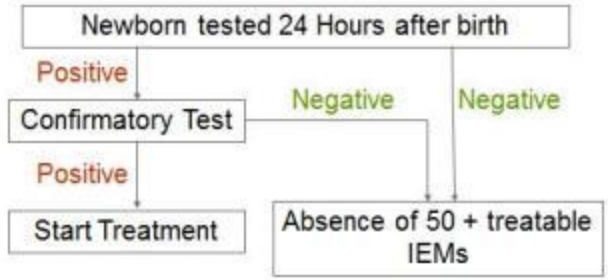
385,135 infants were screened with the relative incidence of:

- 1: 1963 for congenital hypothyroidism, 188 prevented from mental retardation.
- 1: 14,812 classic PKU, 26 prevented from mental retardation.
- 0.06% for sickle disease and 0.9% for sickle cell traits.

Disorders identified by Newborn Screening Program

- **ACYLCARNITINE PROFILE (Tandem Mass Spectrometry)**
  - I. Fatty Acid Oxidation Disorders
  - II. Organic Acid Disorders
- **AMINO ACID PROFILE (Tandem Mass Spectrometry)**
  - I. Amino Acid Disorders
  - II. Others
- **BIOCHEMICAL SCREENING (Enzyme Assay/Enz. immunoassay)**
  - I. Galactosemia
  - II. Congenital Hypothyroidism
  - III. Congenital Adrenal Hyperplasia
  - IV. G6PD Deficiency
  - V. Cystic Fibrosis
  - VI. Biotinidase Deficiency

Benefits of Newborn Screening for Metabolic Disorders



- The newborn screen has to be done only once in a lifetime.
- Speeds diagnosis and saves costs.
- Healthy child instead of sick or mentally retarded child.

Our Study

- 3,000 samples from newborns were screened by Tendem Mass Spectrometry from Sep, 2008 to Feb, 2010.
- Samples are collected randomly, from private hospitals of Dubai and from various population within 3-5 days of birth.
- 3,000 samples were screened for 45 inborn errors affecting the metabolism of urea cycle, amino acids, and organic acids and fatty acid oxidation.
- The same samples were analyzed for other disorders by regular biochemical analysis, for eg., G6PD Deficiency, Cystic Fibrosis, Galactosemia, Biotinidase, Congenital Hypothyroidism and Adrenal Hyperplasia , depending on patient and physician's request.

Time to do screening

- Anytime 24 hours AFTER birth (ideally within 1- 2 weeks).
- Baby needs to be fed at least 2 - 3 times before the specimen is taken.
- BEFORE developmental delay or other symptoms of mental retardation occur (best time is to screen a healthy baby).

Sample from baby's Heel

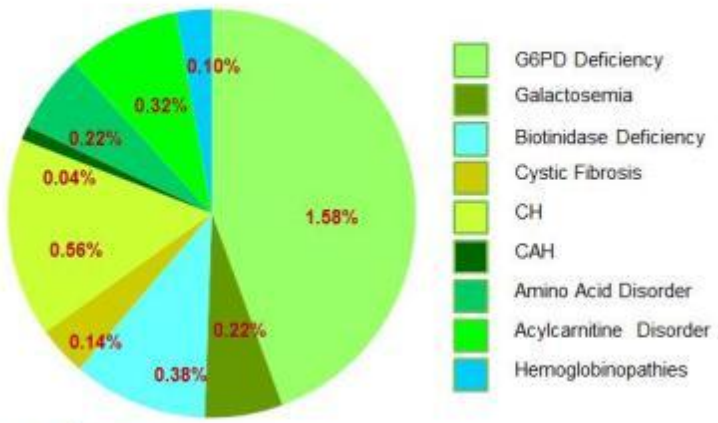
1. Puncture heel.
2. Lightly touch filter paper to LARGE blood drop.
3. Dry the sample & send to the laboratory.



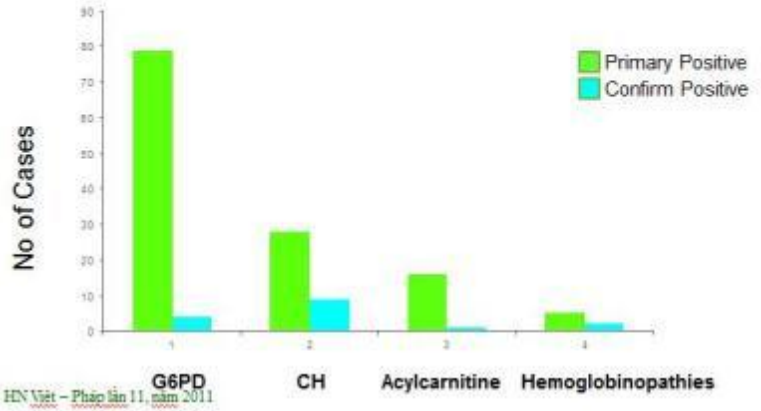
Confirmation of the Primary result

Name of disorder	Primary Abnormal Report	Confirmed positive cases with Repeat Analysis	False Positive cases with Repeat Analysis	Samples Not Repeated
G6PD Deficiency	79	17	9	53
Galatosemia	11	Unknown	2	9
Biotinidase Deficiency	19	Unknown	7	12
Cystic Fibrosis	7	Unknown	4	3
Congenital Hypothyroidism (CH)	28	1	10	17
Congenital Adrenal Hyperplasia (CAH)	2	Unknown	Unknown	2
Amino Acid Disorder	11	Unknown	5	6
Acylcarnitine Disorders	19	1	6	12
Hemoglobinopathies	5	2	Unknown	3

Positive cases with primary screening



Comparative study of primary and confirmed results



Summery of the Study

- Many Metabolic disorders exist in the mixed population of the babies born in UAE remain undetected.
- Number of false positive is quite common which need to be conveyed to the parents.
- Physicians must advice the parents to repeat the analysis for confirmation.
- Parents must come back and take necessary action without making delay.
- It is beneficial to check for these rare metabolic disorders along with the routine biochemical analyses as part of the Newborn Screening by using Tandem Mass Spectrometry.

Challenge Faced

- Difficult to explain the episodic nature of metabolic illness.
- The wide range of clinical symptoms that are associated with more common conditions like infection or sepsis.
- The low incidence of these disorders.
- The consequent lack of experience among the pediatric sub-specialties.
- The need for specialty testing.

Counseling completes the Screening Analysis

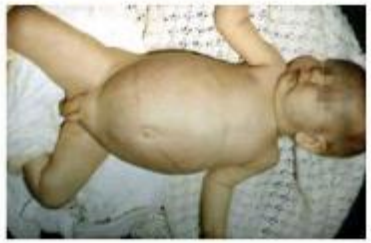
- ❖ Advice parents to screen the baby even he looks healthy.
- ❖ Answer all the queries of the parents.
- ❖ Families are given clear explanations and told how to find information about their child's condition.
- ❖ Explain them that if the initial follow-up shows an abnormal value, repeat analysis needs to be done.
- ❖ Assure parents that the Confirmatory testing is required in case of repeated abnormal value.
- ❖ Prompt referral of patients with confirmed or suspected disorders.

Our Comprehensive Newborn Screening

- ❖ Educational Material given to parents immediately after the birth of baby OR during Antenatal Sessions by Gynaecologists.
- ❖ Provide comprehensive training to the nurse and technician how to collect the sample from the newborn.
- ❖ Supply the sample collection cards to individual hospitals and arrange collection of sample every alternate days.
- ❖ Counsil parents to understand the report and help them to go further if the result is positive.

Future Direction

- Additional conditions are already under consideration for adding to screening panels: SCID, lysosomal storage disease, fragile X syndrome and other.
- Expansion of treatable disease criteria.
- Considering the identification of unaffected "carriers", or conditions.



Way Forward

- ❖ Governments need to take measures to make NBS mandatory for each and every baby born in the region.
- ❖ Technical information needs to be conveyed to people by counselors.
- ❖ Consider Tendem Mass Spectrometry to widen the scope of the program.
- ❖ Systematically evaluate all phases of the program.

Conclusion

All babies have equal right to live healthy lives

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We need to create the platform for them