Editorial:

Newborn screening for inborn errors of metabolism (IEM)

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Inborn errors of metabolism (IEM) are monogenic diseases resulting in deficient activity in a single enzyme in a pathway of intermediary metabolism. Sir Garrod, was the first to recognize heritable blocks in normal human metabolic flow that conformed to Mandelian mechanisms of inheritance, and gave the name **IEM**, at **1908**.

Single gene defects result in abnormalities in the synthesis or catabolism of proteins, carbohydrates, fats, or complex molecules. Most are due to a defect in an enzyme or transport protein, which results in a block in a metabolic pathway. Effects are due to toxic accumulations of substrates before the block, intermediates from alternative metabolic pathways, defects in energy production and use caused by a deficiency of products beyond the block, or a combination of these metabolic deviations. Nearly every metabolic disease has several forms that vary in age of onset (from few days after birth till adulthood), clinical severity, and, often, mode of inheritance.

The incidence collectively, is estimated to be approximately 1 in 4000 live births.

The international frequencies for each individual inborn error of metabolism vary. Of term infants who develop symptoms of sepsis without known risk factors, as many as 20% may have an inborn error of metabolism.

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There are over **300** gene disorders leading to specific biochemical defects of IEM,
a specific intervention that may prevent morbidity and/or is available in at least **1/3**$^{\mathbf{rd}}$ of the cases.

IEM may be implemented for sudden deterioration in a previously normal baby, of unexplained neonatal death. Older children with unexplained encephalopathy, mental retardation, epilepsy. Unexplained hepatomegaly, fulminant or chronic liver disease ending in cirrhosis, or at times hepatic carcinoma. Renal stones. Cardiomyopathy, rhabdomyolysis, maternal acute fatty liver of pregnancy.

Most of the diseases that exhibit clinical consequences manifest (or can be detected) in the newborn period or shortly after, on the other hand those that present early in the neonatal period are often lethal if proper treatment is not implemented, so early detection at least for some of these disorders has proven very effective in

treatment or management, avoiding later morbidity &/or mortality.

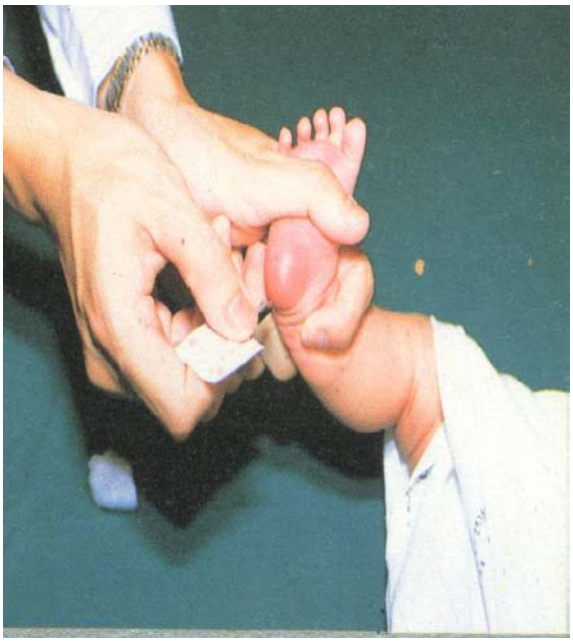
Newborn screening is the process of testing newborn babies for treatable metabolic,genetic, endocrinologic, and hematologic diseases. Robert Guthrie is given much of the credit for pioneering the earliest screening for phenylketonurea (one of the aminoacid metabolic disorders) in the 1960s using blood samples on filter paper obtained by pricking a newborn baby's heel on the second day of life to get a few drops of blood. Congenital hypothyroidism was the second disease widely added in the 1970s. The development of spectrometry screening by Edwin Naylor and others in the early 1990s led to a large expansion of potentially detectable congenital metabolic diseases reaching up to 30 diseases detected from a single blood spot sample, including most fatty acids, organic acids, aminoacids & urea cycle disorders, with a high sample throughput permitting the analysis of >100 samples in few hours. At present ,tandem mass spectrometry is being used as the screening technique for the diagnosis of IEM in newborns & sick infants in many clinical biochemical laboratories in USA, Europe, Australia & Japan, though the lists of screened diseases vary widely, according in part to the magnitude of the disease problem in that society.

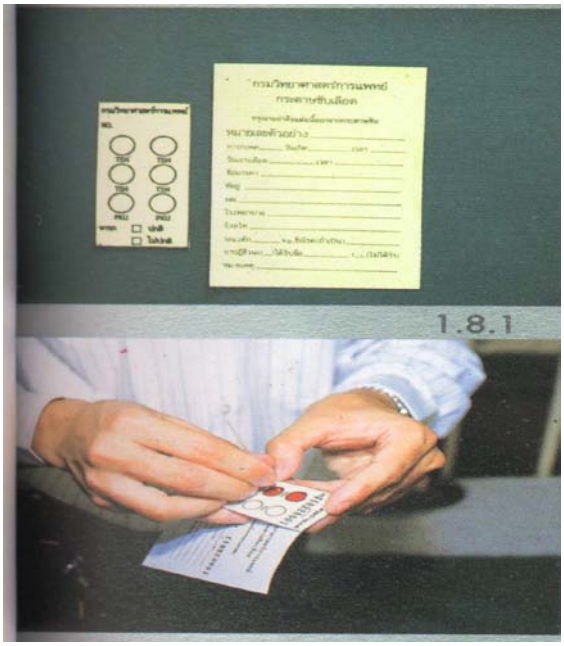
The current experiences in the Middle East and North Africa region (MENA), where the population is about 400 million, with high birth rate and an estimated 10 million newborns per year, the population is characterized by a high consanguinity (25-70%) and a high percentage of first-cousin marriages, so inherited metabolic disorders, neurogenetic disorders, Haemoglobin disorders and birth defects are relatively more common among this population, and numerous studies highlighted the need for newborn screening programs, despite that there is a slow progress in developing and implementing preventive genetic programs. There are only 4 countries that are executing national newborn screening. One of the earliest centers that applied tandem mass spectrometry in neonatal screening was the King Faisal Specialist Hospital & Research center in Riyadh / KSA that applied this technology since mid nineties.

In Iran, this technique started to be applied since 2002, in the Metabolic disease center in Tehran university, other modes of screening programmes were used since 1995, a second center was developed in Zanjan (Zanjan Metabolic Disease Center ZMDRC).

Lately, in Lebanon, international cooperation allowed the acquisition of this technology at the Newborn Screening Laboratory (NSL) of the Saint Joseph University (USJ) in the capital city of Beirut since 2006. NSL is currently screening up to 20% of all newborns in Lebanon.

In Iraq our Biochemical laboratories are not yet providing even the primary level of diagnostic tests with significant reliability, definitely they are not equipped yet with these newer diagnostic technologies , big steps need to be taken for developing national strategies for prevention and should learn from experiences at regional and international screening programs.

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