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Editorial

# Newborn Screening Program for Oman: The Time is Here and Now

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The WHO defines newborn screening as a public health program, aimed at an early identification of conditions, for which early and timely interventions can lead to the elimination or reduction of associated mortality, morbidity, and disabilities.[1] The diseases included in a screening program do not manifest at birth and have a window period of a few days to months. This gives an opportunity to detect the condition by performing a screening test, which if positive need to be confirmed by a diagnostic test, and to initiate treatment at the pre-clinical stage thereby achieving the best possible outcome.

The history of newborn screening dates back to 1959 when Dr Robert Guthrie developed a test to detect high phenylalanine levels by microbiological bacterial inhibition test on the dry blood spot (DBS) sample collected on a filter paper (Guthrie card) to diagnose phenylketonuria in the newborn babies.[2] The test was highly successful in case finding leading to early treatment of disease by dietary modification thus preventing severe mental retardation. Guthrie test became a routine in USA in 1962. The approach was so successful that in 1975, Dussault introduced screening for congenital hypothyroidism.[3] Subsequently, more diseases like congenital adrenal hyperplasia, galactosemia, biotinidase deficiency, G6PD deficiency, and cystic fibrosis were included in the screening program. The real breakthrough in the screening for inborn errors of metabolism came in 1990 when a new technique of Tandem Mass Spectrometry (TMS) was introduced by Millington.[4] The TMS could identify about 30 different metabolic diseases belonging to aminoacidopathies, urea cycle disorders, organic acidemia, and fatty acid oxidation disorders by analyzing amino acids and acylcarnitine levels on DBS sample. The technique was subsequently automated and a computer program was added to flag only abnormal values.[5] TMS also detects some untreatable diseases and can miss some treatable disorders in each category, thus one should set up the instrument and computer program to flag only the diseases selected in individual screening program.

In addition to TMS, it is also desirable to add 3 more techniques for a complete screening program: 1) Gas chromatography and mass spectrometer for urine organic acid analysis to confirm diagnosis of organic acidemia and certain fatty acid oxidation disorders; 2) An amino acid High Performance Liquid Chromatography (HPLC) to confirm diagnosis of aminoacidopathies; and 3) AutoDELFIA system for the diagnosis of disease that cannot be identified by TMS namely congenital hypothyroidism, biotinidase deficiency, galactosemia, congenital adrenal hyperplasia, cystic fibrosis, etc.

Selection of diseases in the screening panel should be based on the priorities of the individual country. In this regard, the Wilson and Jungner criteria can serve as a useful guide.[6] Basically, consideration should be given to disease prevalence and the cost *vs.* benefit of screening and treatment. From the experience of running metabolic disease services in Oman,[7] a program is proposed incorporating common diseases that can be treated by simple and cost effective means. After a period of 3 to 5 years' experience, more diseases can be added gradually to reach an expanded program.

**A. Initial program**

***TMS tests:*** Phenylketonuria, Isovaleric Acidemia, Type 1 Glutaric Aciduria, Medium Chain Acyl CoA Dehydrogenase (MCAD) deficiency, HMG CoA lyase deficiency.

***AutoDELFIA tests:*** Congenital Hypothyroidism, Galactosemia, Biotinidase deficiency, Congenital Adrenal Hyperplasia.
Hematological diseases: Sickle Cell Disease, Thalassaemia, G6PD deficiency.

**B. Expanded program**

***TMS tests:*** Phenylketonuria, Homocystinura, Maple Syrup Urine Disease, Arginino Succinic Aciduria, Citrullinemia, Propionic Acidemia, Methyl Malonic Acidemia, Isovaleric Acidemia, Beta Ketothiolase deficiency, Glutaric Aciduria types 1 & 2, Medium Chain Acyl-CoA Dehydrogenase deficiency, Very Long Chain Acyl CoA Dehydrogenase deficiency, HMG-CoA Lyase deficiency.

***AutoDELFIA tests:*** Galactosemia, Biotinidase deficiency, Cystic fibrosis, Hypothyroidism, Congenital Adrenal Hyperplasia.
Hematological diseases: Sickle Cell Disease, Thalassaemia, G6PD deficiency.

Some other diseases that can be diagnosed by simple tests prior to discharge of a baby from the hospital are also important to include in the Expanded Screening Program: 1) Screening for congenital deafness by Oto-accoustic Emission testing,[8] 2) Screening

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for cyanotic congenital heart diseases by pulse oxymetry,[9] and 3) Bilirubin check to predict risk for hyperbilirubinemia using Bhutani's nomogram.[10]

It is also important to decide the timing to perform the screening test. The best time is after 48 hours of normal feeding so that enough metabolites are accumulated for detection and to avoid TSH surge following the birth stress. At the present time, there is a tendency to discharge mother and baby within 24 hours of normal delivery; in such cases, the test must be done just prior to discharge after the baby has consumed at least 3 normal feeds.

Oman has a good healthcare network of 57 hospitals and 136 health centers. The National Congenital Hypothyroidism screening has been in operation since 2004. Tandem MS has been in operation at the Sultan Qaboos University Hospital for metabolic diagnostic services since 2002 giving the institution a wealth of clinical and technical expertise.[11] It is therefore, quite possible that this screening program can be easily broadened to successfully accommodate the proposed screening program.

Main barriers to screening program in Oman are cost, availability of diagnostic and treatment facilities, public and healthcare worker education, difficulties in reaching many geographical locations, and recalling positive cases. With the recent establishment of a Genetic Centre at MoH and availability of services of three new genetic-metabolic specialists, such a task would not be difficult. However, the full commitment of the Ministry of Health to bear the cost of screening and disease management is necessary.

Like other Gulf countries, Oman has 52% consanguinity and metabolic diseases are at least 3 to 5 times more common. Birth rate in the country is about 45,000 per annum, which will require at least 123 screening tests per day. This will require a medium size-screening laboratory.

In the Gulf region,[12] Qatar has already been running a full newborn screening program since 2004 in collaboration with the University Children Hospital of Heidelberg, Germany. Until recently, Saudi Arabia had a program covering only 25% of all newborns through selected hospitals; however, the Ministry of Health has recently given the permission to launch a nationwide screening program. UAE has also expanded its screening program in 2010. It can therefore be categorically said that the time for newborn screening for Oman is here and now. The investment in screening will certainly be rewarded many times over in terms of money spent over the care of handicapped children, improved quality of life, and reducing the high burden of genetic disease.

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