Editorial

WORLD PI WEEK (WPIW)- 22 – 29 April 2014

A call for newborn screening to test for severe combined immunodeficiencies

The fourth World PI Week (WPIW) will take place on 22 – 29 April 2014, with its main aim to increase awareness of primary immunodeficiency conditions.

While in the past these conditions were thought to be rare, it is clear today that this is not the case anymore. A recent article showed that more than 6 million people around the world could be suffering from primary immunodeficiency conditions (1) (primary immunodeficiencies are not related to AIDS - 'acquired immunodeficiency syndrome'-,which is caused by a viral infection (HIV).

Although it is clear that early diagnosis will improve morbidity and mortality, there is a group of conditions in which early diagnosis is a medical paediatric emergency, and these are severe combined immunodeficiencies (SCID)(2). Most of these children are born after an uneventful pregnancy and delivery, but will be diagnosed in the first year of life after suffering from severe infections, which unfortunately may lead to death.

SCID is not a common condition (1:20,000 – 70,000) depending on the geographic area. It is clear that early diagnosis, before infections occur, is crucial in order to decrease mortality and morbidity in this group of infants. Several studies have showed that performing hematopoietic stem cell transplantation (HSCT) to SCID children before the age of 3 months has a success rate of 95% as opposed to around 70% if the procedure is done later in life (3). With this in mind, several newborn screening (NBS) tests were proposed in the past, but were not accurate enough.

The World Health Organization (WHO) adopted the Wilson and Jungner criteria to apply conditions to NBS and they are:

a. Disorder not readily identified by means of physical examination.
b. Disease must cause serious medical complications.
c. Early diagnosis and treatment of disease improves prognosis.
d. Prevalence warrants cost.
e. Acceptable, sensitive, specific, economic and proved screening test must be available.

SCID fulfills all these criteria and several years ago, Dr. Jennifer Puck was able to introduce an effective test (4). Using the normal Guthrie paper, one can extract DNA and look for a DNA biomarker of normal T cell development, the T cell receptor excision circles (TREC). This technique is a very accurate one. False positive results, mainly amplification failure of TREC in non-immunodeficiency newborns, were reported in less than 0.008% tests, which is similar to other newborn screening procedures (5). (Most of these false positive cases were in preterm babies weighing less than 1500gr). Furthermore, the cost of the screening was found to be covered by the difference in the high costs of HSCT of SCID which is performed later than 3 months of age.

After several pilot studies, which indeed proved that NBS for SCID fulfill all the Wilson and Jungner criteria, several states in the USA and the province of Ontario, Canada incorporated TREC testing as part of their newborn screening panels. So far more than one million newborns have been screened, and all cases of SCID have been detected and most transplanted successfully!

One can also apply kappa deleting recombination excision circle (KREC) to the same sample and detect cases of congenital hypogammaglobulinemia states.

Worldwide neonatal screening for SCID is needed. In Africa, it is urgent, as access to care is very limited. However, the situation in many African countries is problematic as the Guthrie test is not yet used even to the classic neonatal screening Africa. In Europe, no nation has yet incorporated SCID in their current NBS program, but in some countries like France, England and Germany, committees are actively discussing adding it to their national NBS panels. In Mexico and Brazil, screening for TRECS is in an advanced state of implementation.

We call on all countries around the world to take action and add SCID NBS to their respective programs. This will identify children born with this devastating disease and allow them to get the treatment they need to lead long, normal and productive lives. Newborn screening for Severe Combined immunodeficiency Disease saves lives.

References;

1. Bousfiha AA[1], Jeddane L, Ailal F, Benhsaien I, Mahlaoui N, Casanova JL, Abel L Primary immunodeficiency diseases worldwide: more common than generally thought. J Clin Immunol. 33;1-7,2013

2.Rosen FS. Severe combined immunodeficiency a pediatric emergency. J Pediat 130;345-6,1997.

3.Buckley RH. Transplantation of hematopoietic stem cells in human severe combined immunodeficiency: long term outcomes. Immunol Res. 49:25-43,2011.

4. Puck JM. The case for newborn screening for severe combined immunodeficiency and related disorders, Ann N Y Acad Sci 1246;108-17'2011

5. Somrch R, Etzioni A. A call to include severe combined immunodeficiency in newborn screening program. Rambam Maimonides Med J 5;1-8,2014.