

# PATHCHAT

by Cathy van Rooyen

Endorsed by the Ampath Immunology peergroup

## Newborn screening for severe primary immunodeficiencies (TREC<sub>s</sub> and KREC<sub>s</sub>)



**Screening for severe primary immunodeficiencies involving the cellular and humoral immune system allows early detection and treatment, potentially saving the lives of babies affected by the disease.**

During the past few years, neonatal screening assays have been developed to detect diseases hallmarked by the absence of T- or B-lymphocytes, classically seen in severe combined immunodeficiency (SCID) and X-linked agammaglobulinaemia (XLA)/Bruton's disease. Babies with SCID appear healthy at birth, but without early treatment, most of these babies die before the age of one year. A bone marrow transplant before the age of three months has the best chance of saving these babies' lives and curing this condition. It is crucial to make this diagnosis as early as possible, before the patients receive live vaccines or present with infections, as live vaccines and infections can be fatal, and also greatly diminish the success rate of the bone marrow transplant.

Patients with XLA usually present later in life, due to protective maternal antibodies, but are at great risk for live vaccines, like oral polio, which can lead to fatal infections. These patients are also at risk for severe infections, especially pulmonary infections. Pulmonary complications are the most common cause of mortality and morbidity in these patients. Early identification can prevent the administration of live

vaccines and aid in early initiation of immunoglobulin replacement therapy, which can prevent pulmonary and other infectious complications.

Although these diseases are rare (1:35 000 – 1:100 000 live births), screening is cost-effective compared to the vast amount of treatment the child will require if not quickly identified. At present, more than 30 states in the USA have mandatory neonatal screening for SCID, with excellent results being reported. This has also been implemented in many European countries and is currently under review by the European Union (EU) to develop European guidelines for all EU member states. South Africa has no current policies or guidelines, but as our neonates are exposed to live vaccines (BCG and polio) before being discharged from hospital, severely immunodeficient babies are at a greater risk and their mortality will be much higher. Parents should be informed of the risks involved and should be given the option to screen their newborns before the administration of live vaccines.

Ampath has implemented a qualitative real-time PCR assay to detect T-cell receptor excision circles (TREC<sub>s</sub>) and Kappa-deleting receptor excision circles (KREC<sub>s</sub>) in newborn blood. The reported sensitivity of PCR screening nears 100% with a specificity of 99.9%. TREC<sub>s</sub> are the best marker for the production of functional T-cells by the thymus and KREC<sub>s</sub> are the best marker for the production of functional B-cells by the bone marrow. Both of these markers are combined in one

screening assay and will be charged as a single PCR. Although this assay has primarily been developed for newborn screening, it can also be used in older patients and for other applications. In addition to identifying patients with SCID and XLA, this assay can also be used to identify patients with other severe immunodeficiency syndromes like ataxia telangiectasia and Nijmegen breakage syndrome.



## Who should be screened?

- Preferably all newborns, before the administration of live vaccines, dependant on the resources available.
- All babies with a family history of severe primary immuno-deficiency affecting B- or T-cells.
- Neonates or older babies/children where the diagnosis of a severe primary immunodeficiency affecting B- or T-cells is suspected.

## What specimen is required?

- EDTA blood (please ensure that there is no dilution of the specimen if collected from an intravenous line)
- A dried bloodspot on a Guthrie card obtained after a heel prick

## What are the limitations of this test?

- The screening test may be false positive in premature babies under 37 weeks. If the initial screen is positive in a premature baby, it is suggested that the test be repeated once 37 weeks corrected gestation is reached.

### For more information or clinical queries, contact:

Dr Cathy van Rooyen  
Tel: 012 678 0613/6  
Email: vanrooyenc@ampath.co.za

Dr Sylvia van den Berg  
Tel: 012 678 0613/7  
Email: vandenbergs@ampath.co.za

## CPD questions

1. Newborn screening using TRECS can be used to identify babies with severe combined immunodeficiency:

- True
- False

2. Newborn screening using KRECS can be used to identify babies with primary agammaglobulinaemia:

- True
- False

3. Which of the following conditions may cause a false positive screening test for SCID?

- Inborn errors of metabolism
- Prematurity
- Congenital hypothyroidism
- Selective IgA deficiency
- Rhesus incompatibility