

# Immunodeficiency

## PRIMARY IMMUNODEFICIENCY

### Development of Population-Based Newborn Screening for Severe Combined Immunodeficiency

Chan K, Puck JM. *J Allergy Clin Immunol*. 2005;115:391–398

**PURPOSE OF THE STUDY.** To evaluate analysis of T-cell development as a potential population-screening method for severe combined immunodeficiency (SCID).

**STUDY POPULATION.** Twenty-three infants with SCID, 2 patients without SCID, 245 randomly selected infants, and several healthy adults.

**METHODS.** DNA was extracted from dried blood spots on standard newborn screening (Guthrie) cards. The DNA was subjected to polymerase chain reaction (PCR) to amplify and quantitate the number of T-cell receptor excision circles (TRECs), a marker of T-cell development in the thymus. For comparison, the  $\beta$ -actin gene was also amplified by PCR.

**RESULTS.** None of the SCID patients' blood spots contained detectable TRECs, whereas the infants without SCID had normal TRECs. Healthy adults had normal TRECs, and intentional depletion of T cells led to the disappearance of TRECs in simulated blood spots. Approximately 3% of randomly collected blood spots did not contain measurable TRECs but did contain  $\beta$ -actin.

**CONCLUSIONS.** Measurement of TRECs by PCR can accurately identify infants with SCID. The relatively high percentage (3%) of screened spots having the SCID profile indicates the need for further refinement of the method before a larger population study.

**REVIEWER COMMENTS.** Newborn screening for SCID is desirable because of the rapidly fatal nature of this disease and because of the good outcomes that may be obtained with the earliest possible diagnosis. The minimum estimate of the incidence of SCID is >1 per 100 000 births, comparable to other diseases that are already part of newborn screening programs. Almost all patients with SCID lack detectable TRECs. The ability to accurately measure them in dried blood spots represents a tremendous advance toward the possibility of effective newborn screening for this genetically very heterogeneous group of disorders. If the specificity of the analysis can be improved, this may soon be implemented in newborn screening programs.

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### Presenting Phenotype in 100 Children With the 22q11 Deletion Syndrome

Oskarsdottir S, Persson C, Eriksson BO, Fasth A. *Eur J Pediatr*. 2005;164:146–153

**PURPOSE OF THE STUDY.** To describe the clinical presentations of individuals having deletion of the 22q11 region.

**STUDY POPULATION.** The first 100 individuals <20 years old presenting to the Queen Sylvia Children's Hospital (Göteborg, Sweden) and found to have 22q11 deletion (from 1993–2002).

**METHODS.** All diagnoses were confirmed by fluorescence in situ hybridization. Clinical data collected at diagnosis included age and clinical findings in 8 categories (1, cardiac defects; 2, thymus size, infection history, autoimmune disease; 3, hypocalcemia; 4, feeding difficulties; 5, cleft lip/palate, speech/language impairment; 6, developmental delay, learning difficulties, behavioral abnormalities; 7, other malformations/deformities; 8, dysmorphic features). Those features that led (in particular) to the consideration of the diagnosis were distinguished.

**RESULTS.** The largest number was diagnosed by cardiologists (39) at a median age of 0.5 years old, with cleft palate or speech pathology specialists second (22) at a median age of 8 years, and neurologists or psychiatrists third (19) at a median age of 11.2. Note that 68 of the 74 children diagnosed after age 2 were born before the fluorescence in situ hybridization test was routinely available. The main findings are summarized in Table 1.

**CONCLUSIONS.** The authors offer diagnostic guidelines for testing for 22q11 deletion (for infants: any typical cardiac defect or 2 of the features in categories 2 through 5, 7, or 8; for preschool-aged children and adolescents: any 2 of the 8 categories either present currently or in the past medical history).

**REVIEWER COMMENTS.** 22q11 deletion leads to a spectrum of phenotypes most commonly called velocardiofacial syndrome and/or DiGeorge syndrome. Occurring in ~1 in 3000 to 4000 live births, it is among the most common syndromes associated with primary immunodeficiency. Serious infection occurs but is relatively rare. Early diagnosis is most desirable to prevent or mitigate morbidity arising from developmental and psychiatric complications in childhood and adolescence. Of the major clinical manifestations, the symptoms arising from velopharyngeal insufficiency (poor suck, nasal reflux) and various associated malformations seem to be significantly overlooked. The fact that all patients had subtle characteristic dysmorphisms that did not contribute very much to diagnosis shows how much our vision improves with the aid of molecular genetic glasses.

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