overexpression of TSLP in the lungs or skin also promoted peripheral basophilia. This systemic basophilia resulted from TSLP-triggered expansion of bone marrow precursor cells through a mechanism independent of IL-3 signaling. Basophils were present in TSLP-deficient mice, indicating that TSLP was not essential for normal basophil development. In comparison with classical basophils induced by IL-3, TSLP-elicited basophils expressed higher levels of TH2-skewing cytokines and proinflammatory mediators. Furthermore, basophils obtained from patients with eosinophilic esophagitis, a disease associated with aberrant TSLP production, were phenotypically distinct from those found in healthy controls.

CONCLUSIONS. Abnormal TSLP production at 1 barrier surface may promote development of allergic inflammation at other sites by increasing the number and altering the function of circulating basophils.

REVIEWER COMMENTS. It is well known that patients with 1 allergic disorder are likely to develop others, but the mechanisms for this “atopic march” remain obscure. Here, the authors show an important role for the cytokine TSLP, which has been shown to be highly expressed in animal and human tissues with active allergen-driven inflammation. The ability of TSLP to expand and alter the phenotype of peripheral basophils may promote the development of allergic disease at other barrier surfaces and could explain why patients with atopic dermatitis frequently go on to develop asthma or food allergy. In addition to contributing to our understanding of the biology of allergic diseases, these studies also identify TSLP as a potentially important target for pharmacological blockade in vulnerable patients.


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PRIMARY IMMUNODEFICIENCY

Clinical Characteristics of Pediatric Patients Evaluated for Primary Immunodeficiency

PURPOSE OF STUDY. To investigate clinical characteristics of children evaluated for primary immunodeficiency (PID) and address the utility of the “10 Warning Signs of Primary Immunodeficiency” developed in 1994 by expert consensus and published by the Jaffry Modell Foundation (http://www.jfmworld.com).

STUDY POPULATION. The study included 141 children (birth to 21 years) evaluated in the Allergy/Immunology clinic at Children’s Hospital of Wisconsin for possible PID in 2004–2005. Patients were identified by International Classification of Diseases, Ninth Revision, codes indicative of immunodeficiency or recurrent infection.

METHODS. This was a retrospective chart review. Patients were classified with PID if they met published diagnostic criteria and were diagnosed with immunodeficiency. Those with PID were evaluated for the presence of warning signs and categorized as those who met 1 or more of the warning signs (WS+) and those who did not (WS−).

RESULTS. Twenty-three percent of patients were diagnosed with PID. Of those with PID, <70% met 1 or more criteria set forth in the warning signs. The most common warning signs met were recurrent otitis media, recurrent sinusitis, and need for intravenous antibiotics. Sensitivity of the warning signs was 63% and specificity was 23%.

CONCLUSIONS. “10 Warning Signs of Primary Immunodeficiency” were found to have low specificity and relatively low sensitivity. Study numbers were too small to draw conclusions regarding the utility of specific warning signs.

REVIEWER COMMENTS. The primary pediatrician’s question of when to refer a patient for workup of PID is a challenging one. The study suggests that this widely used screening tool has relatively low sensitivity and, therefore, the potential to miss PID cases. When clinical suspicion is high, immune evaluation should be considered even if a patient does not meet ≥1 of these 10 warning signs. Further studies are needed to develop a more optimal screening tool and to evaluate which specific signs are most relevant.

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The Wisconsin Approach to Newborn Screening for Severe Combined Immunodeficiency

PURPOSE OF THE STUDY. Severe combined immunodeficiency (SCID) is a life-threatening disease of infants that is curable with hematopoietic cell transplantation if detected early, whereas the outcome is less favorable if treatment is delayed. The study evaluated outcomes of a screening program in Wisconsin.

STUDY POPULATION. Newborns in Wisconsin over a 3-year period.

METHODS. Population-based screening for SCID by using the T-cell receptor excision circle (TREC) assay applied to samples obtained from routine newborn screening (Guthrie) cards has been underway in the state of Wisconsin since 2008.

RESULTS. Five infants with SCID or other forms of severe T-cell lymphopenia (TCL) have been detected out of a total
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Caroline Hobbs and Wesley Burks
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