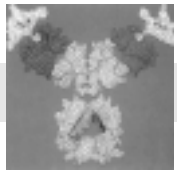

Immune Deficiencies: Introduction

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The primary immunodeficiency disorders reflect abnormalities in the development and maturation of cells in the immune system. The hallmark of these defects is an increased susceptibility to infections. Recurrent pyogenic infections occur with defects in the humoral immunity, and opportunistic infections with defects of cell-mediated immunity.

The last decade has been tremendously exciting for clinicians and scientists who treat and study primary immunodeficiency disorders. Prior to this, few genes were known and, for the majority of disorders, pathogenesis and diagnosis were based on proposed mechanisms and clinical observations. Using the new technical advances, the molecular and genetic basis for many primary immunodeficiency disorders was identified. This new information, coupled with enhanced understanding of basic human immunology, has provided insight into the function of these gene products in both the normal immune response and the pathologic conditions in which mutations in the genes were found [1]. In some disorders a genotype/phenotype correlation exists, while in other disorders no correlation was found. From the clinical point of view, this has resulted in improved diagnosis, a more precise definition of various syndromes, increased ability to predict prognosis, and accurate genetic consulting [2]. It also means that treatment protocols can be specifically tailored to the patient (like gene therapy) and allows the possibility for new strategies to be developed. To date, more than 95 different primary immunodeficiency disorders have been delineated, and the number increases every month [3]. Identifying the genetic defect in a given patient constitutes invaluable understanding of the importance of a given protein or cell in the normal immune system.

While each disorder may be relatively rare (between 1:10,000 and 1:100,000 persons), taken together as a group they represent a significant health problem. In the near future, research into more common aspects of the immune system, such as increased susceptibility to common infections and to specific infectious agents, will emerge as a new focus in the study of primary immunodeficiency disorders. Discovering the genetic basic of these more common diseases will ultimately yield critical information and eventually improve diagnosis and treatment of these patients.

Beginning in this issue of *IMAJ* is the first of a mini series on primary immunodeficiency disorders. Dr Anna Villa from Milan, who discovered the association between defects in RAG 1/2 and the Omenn syndrome, will discuss severe combined immunodeficiency due to mutations in the RAG genes. The importance of JAK3 in cases of autosomal recessive SCID was first reported by Prof. Luigi Notarangelo from Brescia, who will write on defects in the common gamma chain of the interleukin receptor (SCID-X1), the most common cause of SCID, and on its autosomal recessive equivalent mutations in JAK3. This mini series will also deal with other defects in the immune system. Dr. Hans Ochs from Seattle, who found the WASP, the defective protein in the Wiskott-Aldrich syndrome, will discuss this syndrome in depth. This series will also include reviews on hypogammaglobulinemia and bone marrow transplantation in immunodeficiency states. A survey of the incidence of primary immune deficiency in Israel will also be included.

The first article focuses on the exciting new field of gene therapy. The author, Prof. Fischer from Paris, was the first to successfully treat severe combined immunodeficiency with gene therapy in five children.

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Series Editor

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2. Conley ME, Notarangelo L, Etzioni A. Diagnostic criteria for primary immunodeficiency. *Clin Immunol* 1999;93:190–7.
3. Fischer A. Primary immunodeficiency diseases: an experimental model for molecular medicine. *Lancet* 2001;357:1863–9.

SCID = severe combined immunodeficiency