Foreword

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The first documented case of immune deficiency in man was reported in 1952 by Colonel Ogden Bruton, in a 4-y-old boy with recurrent infections and agammaglobulinemia. Since this original discovery, various immunologic deficiency disorders have been described throughout the world. This year's symposium, the fourth in a series that has attracted audiences nationwide, placed considerable emphasis on the recent advances made in defining the pathophysiology of primary immune deficiency diseases. The historical events that led up to our present-day understanding of the pathogenesis of these immune deficiencies were put into perspective by Richard Stiehm. An important advance, which has made earlier diagnosis possible, was the development of methods for prenatal diagnosis and genetic analysis of X-linked immune deficiency disorders. Jennifer Puck discussed the concept of linkage analysis of those gene defects that can be localized to the X chromosome for prenatal diagnosis. She also described the process by which female carriers can be detected in congenital X-linked inherited immune deficiency diseases and the process of X-chromosome inactivation in cell lineages targeted by the gene defect.

Two important advances in medicine, MAbs and molecular biotechnology, have tremendously enhanced our understanding of the pathophysiology of many immune deficiency diseases. Abnormalities of signal transduction and gene activation, as discussed by Roger Perlmutter and Erwin Gelfand, are important subjects that have opened up new doors toward achieving a better understanding of the pathogenic mechanisms of these diseases. These pathways of cell activation lead to the generation of effector molecules and soluble mediators that are important in regulating the immune response. Raif Geha and Warren Strober presented their exciting experiences in identifying cytokine deficiencies in some patients with immunodeficiency diseases.

A better understanding of abnormalities of immune regulation will enable a more precise therapeutic approach, perhaps through molecular genetic engineering. This latter concept is nicely exemplified by studies in patients with adenosine deaminase (ADA) deficiency. ADA deficiency was the first biochemically defined immune deficiency disorder whose mechanism was clearly related to a biochemical defect. Rochelle Hirschhorn was one of

the original contributors to investigations on ADA deficiency, which have increased our understanding of the purine salvage pathway and the relationship of the biochemical defects to immune dysfunction. In her presentation, she described the genetic and molecular bases of ADA deficiency. These biochemical and molecular genetic studies have provided new approaches to therapy in patients with this disorder. Michael Hershtfield summarized his studies on the use of enzyme replacement therapy using purified ADA conjugated to polyethylene glycol (PEG-ADA). Many aspects of ADA deficiency make this disease an ideal candidate for genetic engineering. In these terms, Michael Blaese described the early results of gene therapy in patients with ADA deficiency. This gene "replacement" therapy will be extremely important in laying the groundwork for the application of this concept to other metabolic and genetic diseases in man. An alternative approach, regulating the immune response through cytokine therapy, was described by Donald Leung.

This year's meeting was especially interesting because it presented two faces of the same coin: congenital immune deficiency disorders and AIDS. Although AIDS was first recognized in the early 1980s, its potentially epidemic proportions are just being recognized as a worldwide health problem. Despite the complexity of human immunodeficiency virus (HIV) infection, we now have a much better understanding of the pathogenesis of HIV disease, as outlined by Jay Levy, and the immune abnormalities associated with HIV infection, as discussed by Gene Shearer. During the last few years, particularly in third-world countries, the incidence of HIV infection in women of childbearing age has increased dramatically. This will not only lead to a rising incidence of HIV infection among heterosexual individuals, but also to an increase in infants infected with HIV. HIV infection has already become a leading cause of morbidity and mortality in childhood. Arye Rubinstein discussed the maternal-fetal transmission of HIV infection and the potential immune mechanisms for regulating transmission between mother and infant. Very few specific treatment modalities are available for HIV infection; supportive measures are used for the most part. The results of a large, recent, collaborative study, sponsored by the National Institutes of Health, on the use of i.v. immune globulin (IVIG) in the prevention of infections in children with symptomatic HIV infection were described by Lynne Mofenson.

The final segment of our symposium was devoted to immune mechanisms in the pathogenesis of autoimmune neuropathies and treatment with high-dose IVIG, discussed by Abdolmohamad Rostami and Shawke Souiedan, respectively. This group of clinical disorders, perhaps more than any other aside from congenital immune deficiencies and idiopathic thrombocytopenic purpura, offers investigators an opportunity to study the mechanisms by which IVIG modulates the immune and inflammatory responses.

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