INTRODUCTION

Many inborn errors of metabolism are known to occur in immune defence systems. Most of these involve non-specific immunity, particularly the complement and neutrophil granulocyte systems. Inborn errors of specific immunity were not described until recently. In this discussion, we will review the two most important diseases in this latter group, deficiency of adenosine deaminase (ADA) and purine nucleoside phosphorylase (PNP). Lack of transcobalamin II, leading to hypogammaglobulinaemia, may represent a third disorder in this group but we will not consider this entity here.
ADA DEFICIENCY

Lack of ADA activity in children with severe combined immunodeficiency (SCID) was noted almost simultaneously by our group and the Danish investigators Dissing and Knudsen, each without knowing about the finding of the other. This association was so unexpected that these cases were not reported until our group happened to come upon the second case, again quite by accident (Dr Flossie Cohen's patient). Our finding was made in the process of searching for a bone marrow donor in a patient with SCID. SCID refers to a severe disorder of the immune system, in many instances inherited, in which both thymus-dependent (T cells) and cells belonging to the antibody-forming system (B cells) are malfunctioning. ADA is an enzyme in the purine reutilization pathway, and catabolizes adenosine to inosine by deamination. Inosine is further catabolized to hypoxanthine, and this latter metabolite may be degraded to uric acid or reutilized via the hypoxanthine guanine phosphoribosyl transferase (HGPRT) pathway (Figure 3.1).

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**Figure 3.1** A simplified scheme of purine metabolism. 1. Adenosine deaminase. 2. Purine nucleoside phosphorylase. 3. Hypoxanthine guanine phosphoribosyl transferase (deficient in the Lesch–Nyhan syndrome)