

variably combines a mild T-cell immune deficiency with a more severe B-cell immune deficiency, coarse face, digestive disease, and mild mental retardation. A diagnostic feature is the detection by cytogenetic analysis of multiradial aspects in multiple chromosomes (most frequently 1, 9, and 16) corresponding to an abnormal DNA structure secondary to defective DNA methylation. It is the consequence of a deficiency in most cases in the DNA methyltransferase DNMT3B, ZBTB24, CDCA7, or HELLS.

T-Cell Primary Immunodeficiencies with Hyper-IgE Several T-cell PIDs are associated with elevated serum IgE levels (as in Omenn syndrome). A condition sometimes referred to as *autosomal recessive hyper-IgE syndrome* is notably characterized by recurrent bacterial infections in the skin and respiratory tract and severe skin and mucosal infections by pox viruses and human papillomaviruses, together with severe allergic manifestations. T and B lymphocyte counts are low. Mutations in the *DOCK8* gene have been found in many of these patients. This condition is an indication for HSCT.

A very rare, related condition with autosomal recessive inheritance that causes a similar susceptibility to infection with various microbes (see above), including mycobacteria, reportedly results from a deficiency in Tyk-2, a JAK family kinase involved in the signaling of many different cytokine receptors.

Autosomal Dominant Hyper-IgE Syndrome This unique condition, the *autosomal dominant hyper-IgE syndrome*, is usually diagnosed by the combination of recurrent skin and lung infections that can be complicated by pneumatoceles. Infections are caused by pyogenic bacteria and fungi. Several other manifestations characterize hyper-IgE syndrome, including facial dysmorphism, defective loss of primary teeth, hyperextensibility, scoliosis, and osteoporosis. Elevated serum IgE levels are typical of this syndrome. Defective T_H17 effector responses have been shown to account at least in part for the specific patterns of susceptibility to particular microbes. This condition is caused by a heterozygous (dominant) mutation in the gene encoding the transcription factor STAT3 that is required in a number of signaling pathways following binding of cytokine to