

Note: Italics denote less common disorders.

■ APS-1

APS-1 (Online Mendelian Inheritance in Man [OMIM] 240300) has also been called autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED). Mucocutaneous candidiasis, hypoparathyroidism, and Addison’s disease form the three major components of this disorder. However, as summarized in [Table 389-1](#), many other organ systems can be involved over time. APS-1 is rare, with <500 cases reported in the literature.

The classical form of APS-1 is an autosomal recessive disorder caused by mutations in the *AIRE* gene (autoimmune regulator gene) found on chromosome 21. This gene is most highly expressed in thymic medullary epithelial cells (mTECs) where it controls the expression of tissue-specific self-antigens (e.g., insulin). Deletion of this regulator leads to decreased expression of tissue-specific self-antigens and is hypothesized to allow autoreactive T cells to avoid central deletion, which normally occurs during T-cell maturation in the thymus. The *AIRE* gene is also expressed in epithelial cells found in peripheral lymphoid organs, but its role in these extrathymic cells remains controversial. To date, >100 mutations have been described in this gene, and there is a higher frequency within certain ethnic groups including Iranian Jews, Sardinians, Finns, Norwegians, and Irish. Recently, several autosomal dominant mutations have been identified and are localized primarily in the PHD1 domain of the *AIRE* gene, rather than the CARD region, where the autosomal recessive mutations have been found. Individuals with this nonclassical form of APS-1 may have a later onset of symptoms and less aggressive disease, without the full spectrum of autoimmune components being expressed.

Clinical Manifestations Classical APS-1 develops very early in life, often in infancy ([Table 389-2](#)). Chronic mucocutaneous candidiasis without signs of systemic disease is often the first manifestation. It affects the mouth and nails more frequently than the skin and esophagus. Chronic oral candidiasis can result in atrophic disease with areas suggestive of leukoplakia, which can pose a risk for future