

# Autoimmune Polyendocrinopathy-candidiasis-ectodermal Dystrophy

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Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) is an inherited condition that affects many of the body's organs. It is one of many autoimmune diseases, which are disorders that occur when the immune system malfunctions and attacks the body's own tissues and organs by mistake.

Keywords: genetic conditions

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## 1. Introduction

In most cases, the signs and symptoms of APECED begin in childhood or adolescence. This condition commonly involves three characteristic features: chronic mucocutaneous candidiasis (CMC), hypoparathyroidism, and adrenal gland insufficiency. Affected individuals typically have at least two of these features, and many have all three.

CMC is a tendency to develop infections of the skin, the nails, and the moist lining of body cavities (mucous membranes) caused by a type of fungus called *Candida*. These infections, which are commonly known as yeast infections, are chronic, which means they recur and can last a long time. CMC is usually the first of the three characteristic features of APECED to become apparent in people with this disorder. Almost all affected individuals develop infections of the oral cavity (known as thrush). Infections of the tube that carries food from the mouth to the stomach (the esophagus) are also common, while the skin and nails are affected less often. In women, vaginal infections frequently occur.

Other features of APECED result from the body's immune system attacking the network of hormone-producing glands (the endocrine system). The second characteristic feature of the disorder is hypoparathyroidism, which is a malfunction of the parathyroid glands. These glands secrete a hormone that regulates the body's use of calcium and phosphorus. Damage to the parathyroid glands leads to reduced parathyroid hormone production (hypoparathyroidism). Hypoparathyroidism can cause a tingling sensation in the lips, fingers, and toes; muscle pain and cramping; weakness; and fatigue. Serious effects of hypoparathyroidism, such as spasms of the voicebox (larynx) leading to breathing problems and seizures, can be life-threatening.

Damage to the small hormone-producing glands on top of each kidney (adrenal glands) results in a third major feature of APECED, adrenal gland insufficiency (autoimmune Addison disease). Reduced hormone production by the adrenal glands leads to signs and symptoms that can include fatigue, muscle weakness, loss of appetite, weight loss, low blood pressure, and changes in skin coloring. Other endocrine problems that can occur in APECED include type 1 diabetes resulting from impaired production of the hormone insulin; a shortage of growth hormone leading to short stature; problems affecting the internal reproductive organs (ovaries or testes) that can cause inability to conceive children (infertility); and dysfunction of the thyroid gland (a butterfly-shaped tissue in the lower neck), which can result in many symptoms including weight gain and fatigue.

Autoimmune problems affecting non-endocrine tissues can lead to a variety of additional signs and symptoms in people with APECED. These features occur more often in North American populations than in European populations. Rashes that resemble hives (urticarial eruptions) are common and often occur in infancy and early childhood. Other early signs and symptoms may include thin enamel on the teeth (enamel hypoplasia) and chronic diarrhea or constipation associated with difficulty in absorbing nutrients from food. Additional features that occur in people with APECED, many of which can lead to permanent organ and tissue damage if left untreated, include stomach irritation (gastritis), liver inflammation (hepatitis), lung irritation (pneumonitis), dry mouth and dry eyes (Sjogren-like syndrome), inflammation of the eyes (keratitis), kidney problems (nephritis), vitamin B12 deficiency, hair loss (alopecia), loss of skin color in blotches (vitiligo), high blood pressure (hypertension), or a small (atrophic) or absent spleen (asplenia).

## 2. Frequency

APECED occurs in about 1 in 90,000 to 200,000 people in most populations studied, which have been mainly in Europe. This condition occurs more frequently in certain populations, affecting about 1 in 9,000 to 25,000 people among Iranian Jews, Sardinians, and Finns.

## 3. Causes

Mutations in the *AIRE* gene cause APECED. The *AIRE* gene provides instructions for making a protein called the autoimmune regulator. As its name suggests, this protein plays a critical role in regulating certain aspects of immune system function. Specifically, it helps the body distinguish its own proteins and cells from those of foreign invaders (such as bacteria, fungi, and viruses). This distinction is critical because to remain healthy, a person's immune system must be able to identify and destroy potentially harmful invaders while sparing the body's normal tissues.

Mutations in the *AIRE* gene reduce or eliminate the function of the autoimmune regulator protein. Without enough of this protein function, the immune system's ability to distinguish between the body's proteins and foreign invaders is impaired, and it may attack the body's own organs. This reaction, which is known as autoimmunity, results in inflammation and can damage otherwise healthy cells and tissues. Autoimmune damage to the adrenal glands, parathyroid glands, and other organs underlies many of the major features of APECED.

Studies suggest that *AIRE* gene mutations also result in immune substances (antibodies) mistakenly attacking proteins involved in an immune process called the IL-17 pathway, which is important in the body's defense against *Candida*. This pathway, which depends on specialized proteins called IL-17 cytokines for signaling, creates inflammation, sending additional cytokines and white blood cells to fight foreign invaders and promote tissue repair. In addition, the IL-17 pathway promotes the production of certain antimicrobial protein segments (peptides) that control growth of *Candida* on the surface of mucous membranes. By damaging IL-17 cytokines, *AIRE* gene mutations are thought to impair the IL-17 pathway's function, resulting in CMC in people with APECED.

Researchers believe that differences in the effects of specific *AIRE* gene mutations as well as variations in other genes that have not been identified may help explain why the signs and symptoms of APECED can vary among affected individuals and populations.

### 3.1. The gene associated with Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy

- AIRE

## 4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

In rare cases, people with one copy of certain *AIRE* gene mutations in each cell have some features of APECED, such as CMC, hypoparathyroidism, or vitamin B12 deficiency, but do not have the full pattern of signs and symptoms that typically characterize the disorder. These individuals usually have one similarly-affected parent.

## 5. Other Names for This Condition

- AIRE deficiency
  - APECED
  - APS type 1
  - APS1
  - autoimmune polyendocrinopathy syndrome type 1
  - autoimmune polyendocrinopathy with candidiasis and ectodermal dystrophy
  - autoimmune polyglandular syndrome, type 1
  - PGA I
  - polyglandular autoimmune syndrome, type 1
  - polyglandular type I autoimmune syndrome
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