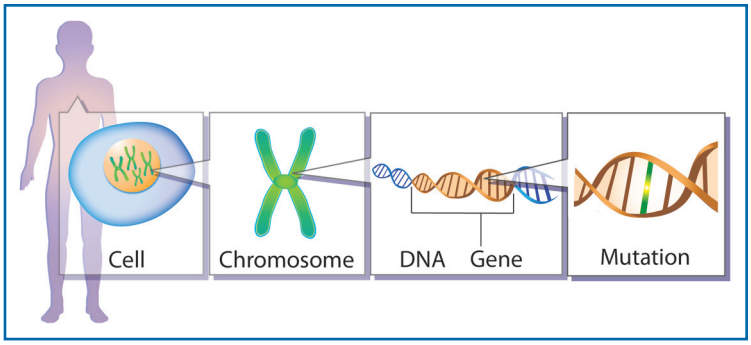
CEDS

What Is CEDS?

CEDS is a very rare genetic disorder of the immune system. CEDS stands for "caspase eight deficiency state." The disorder is characterized by an enlarged spleen and lymph nodes, recurrent sinus and lung infections, recurrent viral infections, and a low level of infection-fighting antibodies. CEDS is diagnosed based on clinical and laboratory findings as well as genetic testing.



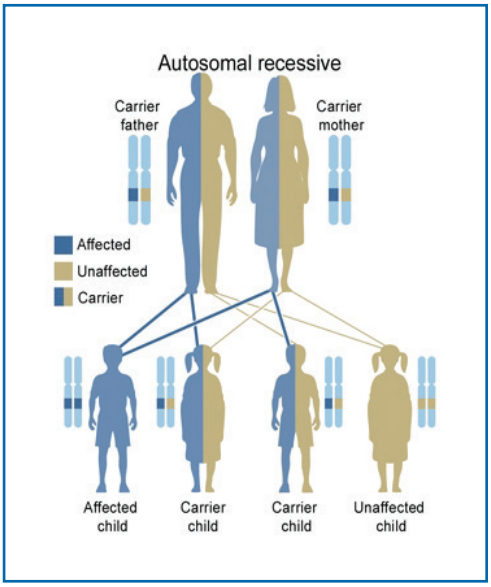
Genetics primer: All the cells in the body contain instructions on how to do their job. These instructions are packaged into chromosomes, each of which contains many genes, which are made up of DNA. Errors, or mutations, in the genes can cause diseases such as CEDS. Credit: NIAID

Genetics

CEDS is caused by mutations in the *CASP8* gene, which provides instructions for production of the protein caspase eight, which is also abbreviated as CASP8. The CASP8 protein is involved in programmed cell death, or apoptosis. The body must maintain a careful balance between proliferation of immune cells and apoptosis to defend against pathogens and avoid autoimmunity. The mutations that cause CEDS destabilize the CASP8 protein and block its function, leading to buildup of immune cells.

Inheritance

CEDS is inherited in an autosomal recessive manner. This means that affected people have a mutation on each of their two copies of *CASP8*—one inherited from their mother and one from their father. Sometimes the two copies have mutations that are identical, or homozygous. This often involves parents who are related to each other.



In this example, two unaffected parents each carry one copy of a gene mutation for an autosomal recessive disorder. They have one affected child and three unaffected children, two of which carry one copy of the gene mutation. Credit: U.S. National Library of Medicine

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Alternatively, the mutations in each copy of the *CASP8* gene are different. These are called compound heterozygous mutations.

In either case, parents of a child with CEDS are usually "carriers," meaning they have one mutated copy of *CASP8* and one normal copy. Carriers typically do not experience any symptoms of CEDS and lack immune-function abnormalities.

Clinical Symptoms

CEDS is related to autoimmune lymphoproliferative syndrome and used to be called ALPS type IIB. Although CEDS and ALPS share problems with apoptosis, CEDS is different from ALPS because of its additional immune deficiency symptoms. The symptoms of CEDS include splenomegaly (an enlarged spleen), lymphadenopathy (enlarged lymph nodes), recurrent sinopulmonary (sinus and lung) infections, recurrent mucocutaneous herpesvirus infections, persistent warts, molluscum contagiosum, and hypogammaglobulinemia (low antibody levels). Although immune cells called lymphocytes sometimes infiltrate certain organs, such as the lungs, liver, and kidneys, autoimmune problems are minimal. Lymphoma, a type of cancer, has not been observed in CEDS patients. However, people with ALPS are at increased risk of developing lymphoma.

Laboratory Findings

Doctors may perform immunologic studies to look for features that suggest CEDS. For example, they may assess serum immunoglobulin, or antibody, levels; antibody function; and lymphocyte activation. Patients with CEDS have hypogammaglobulinemia and develop poor antibody responses to certain vaccines. In addition, their immune cells, including B cells, T cells, and NK cells, do not activate well in response to stimuli.

Prognosis and Treatment

Given the rarity of CEDS, the prognosis for and optimal treatment of people with this condition remain unclear. People with CEDS have done well while taking intravenous immunoglobulin and prophylactic acyclovir, an antiviral drug, to prevent sinopulmonary infections and mucocutaneous herpesvirus outbreaks. Investigators at the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, are conducting clinical studies to identify new approaches for the diagnosis and treatment of this disorder. More information can be found on clinicaltrials.gov, using the study identifiers NCT00246857 and NCT00001467.

CEDS and Your Family

Living with CEDS can be difficult not only for the person who has it but for their family members as well. It is important for families to talk openly about CEDS and about how the family is dealing with it so misconceptions can be corrected and children can learn to cope with their reactions. Some children with CEDS have to work hard to develop their self-confidence and sense of security.

Everyone benefits from being reminded that they have many positive characteristics, but this is especially important when a child's appearance attracts attention (for example, due to large lymph nodes).

Some children who have siblings with the disease feel anxious about their brother or sister being in pain or even dying from the disease. Some think that they may develop symptoms because they look or act like a sibling who has the disease or that the disease is contagious. Some children struggle with how much time their parents spend with their sick sibling. Many families benefit from meeting or talking to other families affected by the same rare disease. Patient organizations such as the Immune Deficiency Foundation (www.primaryimmune.org) are also great resources for providing useful information and support. Counseling can also help families cope with the challenges of CEDS.

At the same time, many families say that the disease has brought them closer together. Through their experiences with the disease and its treatment, family members learn about controllable and uncontrollable aspects of life. Although certain aspects of the disease cannot be controlled, how a family responds to the stress of any illness is controllable and an important aspect of managing CEDS. Children also learn who they can turn to for support and how to solve problems. Acknowledging both the challenges and opportunities that CEDS presents helps children develop resilience.

Glossary

Apoptosis—Programmed cell death, an important part of a healthy immune system.

Autoimmunity—A process during which a person's immune system attacks healthy cells, organs, and tissues.

B cells—Immune cells that present antigens to T cells and produce antibodies, or immunoglobulins.

Cell—The basic unit of living organisms. Human cells consist of a nucleus (control center) and cellular organs, called organelles, enclosed by a membrane. Groups of cells with similar structure and function form tissues.

Chromosome—A thread-like structure made up of DNA that is tightly coiled around supporting proteins. Chromosomes reside in the control center, or nucleus, of a cell.

DNA (deoxyribonucleic acid)—A self-replicating material present in nearly all living organisms. It is the carrier of genetic information.

Gene—A unit of heredity that is transferred from parent to child. Genes are made up of DNA.

Hypogammaglobulinemia—A type of immune deficiency that is characterized by a reduction in all types of gamma globulins, or infection-fighting antibodies.

Immune system—A system of biological structures and processes within the body that protects it against "foreign" threats such as bacteria or viruses.

Lymphadenopathy—Enlarged lymph nodes.

Lymphocytes—A class of white blood cells that are part of the immune system.

Lymphoma—A type of cancer that occurs when certain immune cells start dividing uncontrollably and no longer behave like normal immune cells.

Molluscum contagiosum—A viral skin infection that results in round, firm, painless bumps.

Mucocutaneous herpesvirus—An infection of the skin or mucus membranes (mouth, nose, eyes, genitals) with herpesvirus.

Mutation—A change in the DNA sequence that is associated with disease or susceptibility to disease.

NK cells—Small lymphocytes that are part of the first line of immune defense.

Phenotype—A person's observable characteristics.

Proliferation—The rapid reproduction of cells.

Sinopulmonary infections—Infections of the sinuses and/or lungs.

Splenomegaly—Enlarged spleen.

T cells—Lymphocytes produced or processed by the thymus (a small organ located in the upper chest under the breastbone) that are actively involved in the immune response.

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