Hypohidrotic ectodermal dysplasia

Hypohidrotic ectodermal dysplasia is one of more than 100 types of ectodermal dysplasia. Starting before birth, these disorders result in the abnormal development of ectodermal tissues, particularly the skin, hair, nails, teeth, and sweat glands.

Most people with hypohidrotic ectodermal dysplasia have a reduced ability to sweat (hypohidrosis) because they have fewer sweat glands than normal or their sweat glands do not function properly. Sweating is a major way that the body controls its temperature; as sweat evaporates from the skin, it cools the body. Reduced sweating can lead to a dangerously high body temperature (hyperthermia), particularly in hot weather. In some cases, hyperthermia can cause life-threatening health problems.

Affected individuals tend to have sparse scalp and body hair (hypotrichosis). The hair is often light-colored, brittle, and slow-growing. Hypohidrotic ectodermal dysplasia is also characterized by several missing teeth (hypodontia) or teeth that are malformed. The teeth that are present erupt from the gums later than usual and are frequently small and pointed.

Some people with hypohidrotic ectodermal dysplasia have distinctive facial features, including a prominent forehead, thick lips, and a flattened bridge of the nose. Additional features of this condition can include thin, wrinkled, and dark-colored skin around the eyes; chronic skin problems such as eczema; and a bad-smelling discharge from the nostrils (ozena).

Intellectual ability and growth are typically normal in people with hypohidrotic ectodermal dysplasia.

Frequency

Hypohidrotic ectodermal dysplasia is the most common form of ectodermal dysplasia. It is estimated to occur in 1 in 20,000 newborns worldwide.

Causes

Hypohidrotic ectodermal dysplasia is a genetic condition that can result from mutations in one of several genes. These include *EDA*, *EDAR*, *EDARADD*, and *WNT10A*. *EDA* gene mutations are the most common cause of the disorder, accounting for more than half of all cases. *EDAR*, *EDARADD*, and *WNT10A* gene mutations each account for a smaller percentage of cases. In about 10 percent of people with hypohidrotic ectodermal dysplasia, the genetic cause is unknown.

The *EDA*, *EDAR*, and *EDARADD* genes provide instructions for making proteins that work together during embryonic development. These proteins form part of a signaling pathway that is critical for the interaction between two cell layers, the ectoderm and the

mesoderm. In the early embryo, these cell layers form the basis for many of the body's organs and tissues. Ectoderm-mesoderm interactions are essential for the formation of several structures that arise from the ectoderm, including the skin, hair, nails, teeth, and sweat glands.

Mutations in the *EDA*, *EDAR*, or *EDARADD* gene prevent normal interactions between the ectoderm and the mesoderm, which impairs the normal development of skin, hair, nails, teeth, and sweat glands. Mutations in any of these three genes lead to the major signs and symptoms of hypohidrotic ectodermal dysplasia described above.

The *WNT10A* gene provides instructions for making a protein that is part of a different signaling pathway known as Wnt signaling. Wnt signaling controls the activity of certain genes and regulates the interactions between cells during embryonic development. Signaling involving the WNT10A protein is critical for the development of ectodermal structures, particularly the teeth. The *WNT10A* gene mutations that cause hypohidrotic ectodermal dysplasia impair the protein's function, which disrupts the development of teeth and other structures that arise from the ectodermal cell layer.

When hypohidrotic ectodermal dysplasia results from *WNT10A* gene mutations, its features are more variable than when the condition is caused by mutations in the *EDA*, *EDAR*, or *EDARADD* gene. Signs and symptoms range from mild to severe, and mutations in the *WNT10A* gene are more likely to cause all of the permanent (adult) teeth to be missing.

Inheritance Pattern

Hypohidrotic ectodermal dysplasia has several different inheritance patterns. Most cases are inherited in an X-linked pattern and are caused by mutations in the *EDA* gene. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females, who have two copies of the X chromosome, one altered copy of the gene in each cell often leads to less severe features of the condition. Signs and symptoms can include a few missing or abnormal teeth, sparse hair, and mild problems with sweat gland function. However, some females with one copy of the mutated gene have more severe features of this disorder.

Less commonly, hypohidrotic ectodermal dysplasia has an autosomal dominant or autosomal recessive pattern of inheritance. Mutations in the *EDAR*, *EDARADD*, or *WNT10A* gene can cause either autosomal dominant or autosomal recessive hypohidrotic ectodermal dysplasia.

Autosomal dominant inheritance means one copy of the altered gene in each cell is sufficient to cause the disorder. Some affected individuals inherit the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Autosomal recessive inheritance 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. Some mutation carriers have mild signs and symptoms of hypohidrotic ectodermal dysplasia, including a somewhat reduced ability to sweat and less severe dental abnormalities.

Other Names for This Condition

- anhidrotic ectodermal dysplasia
- Christ-Siemens-Touraine syndrome
- CST syndrome
- HED

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Autosomal dominant hypohidrotic ectodermal dysplasia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1720965/
- Genetic Testing Registry: Autosomal recessive hypohidrotic ectodermal dysplasia syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0406702/
- Genetic Testing Registry: Hypohidrotic X-linked ectodermal dysplasia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0162359/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22hypohidrotic+ectodermal+dysplasia%22+OR+%22Anhidrotic+Ectodermal+Dysplasias%22+OR+%22Christ-Siemens-Touraine+Syndrome%22

Other Diagnosis and Management Resources

- Ectodermal Dysplasia Society (UK): Coping with ED
  https://edsociety.co.uk/support/coping-with-ed/
- GeneReview: Hypohidrotic Ectodermal Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1112
- National Foundation for Ectodermal Dysplasias: Diagnosis
  https://www.nfed.org/learn/diagnosis/
- National Foundation for Ectodermal Dysplasias: Treat
  https://www.nfed.org/treat/

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Ectodermal dysplasia
  https://medlineplus.gov/ency/article/001469.htm
- Encyclopedia: Ozena
  https://medlineplus.gov/ency/article/001627.htm
- Encyclopedia: Sweating - absent
  https://medlineplus.gov/ency/article/003219.htm
- Health Topic: Skin Conditions
  https://medlineplus.gov/skinconditions.html
- Health Topic: Tooth Disorders
  https://medlineplus.gov/toothdisorders.html

Genetic and Rare Diseases Information Center

- Hypohidrotic ectodermal dysplasia
  https://rarediseases.info.nih.gov/diseases/76/hypohidrotic-ectodermal-dysplasia
- Hypohidrotic ectodermal dysplasia autosomal dominant
  https://rarediseases.info.nih.gov/diseases/2048/hypohidrotic-ectodermal-dysplasia-autosomal-dominant
- Hypohidrotic ectodermal dysplasia autosomal recessive
  https://rarediseases.info.nih.gov/diseases/2057/hypohidrotic-ectodermal-dysplasia-autosomal-recessive
- Hypohidrotic ectodermal dysplasia with hypothyroidism and ciliary dyskinesia
  https://rarediseases.info.nih.gov/diseases/2049/hypohidrotic-ectodermal-dysplasia-with-hypothyroidism-and-ciliary-dyskinesia
- X-linked hypohidrotic ectodermal dysplasia
  https://rarediseases.info.nih.gov/diseases/10427/x-linked-hypohidrotic-ectodermal-dysplasia

Educational Resources

- MalaCards: hypohidrotic ectodermal dysplasia autosomal recessive
  https://www.malacards.org/card/hypohidrot
  ic_ectodermal_dysplasia_autosomal_recessive
- MalaCards: hypohidrotic ectodermal dysplasia with immunodeficiency
  https://www.malacards.org/card/hypohidrot
  ic_ectodermal_dysplasia_with_immunodeficiency
- Orphanet: Autosomal dominant hypohidrotic ectodermal dysplasia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1810

- Orphanet: Autosomal recessive hypohidrotic ectodermal dysplasia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=248
- Orphanet: Hypohidrotic ectodermal dysplasia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=238468
- Orphanet: X-linked hypohidrotic ectodermal dysplasia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=181
- UC Davis Children's Hospital
  https://health.ucdavis.edu/children/clinical_services/cleft_craniofacial/anomalies/ectodermal.html

Patient Support and Advocacy Resources

- Ectodermal Dysplasia Society (UK)
  https://edsociety.co.uk/
- National Foundation for Ectodermal Dysplasias
  https://www.nfed.org/learn/types/hypohidrotic-ectodermal-dysplasia/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/hypohidrotic-ectodermal-dysplasia/
- Resource List from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/ectoderm.html

Clinical Information from GeneReviews

- Hypohidrotic Ectodermal Dysplasia
  https://www.ncbi.nlm.nih.gov/books/NBK1112

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Ectodermal+Dysplasia%5BMAJR%5D%29+AND+%28%28hypohidrotic+ectodermal+dysplasia%5BTIAB%5D%29+OR+%28anhidrotic+ectodermal+dysplasia%5BTIAB%5D%29+OR+%28christ-siemens-touraine+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

- ECTODERMAL DYSPLASIA 1, HYPOHIDROTIC, X-LINKED
  http://omim.org/entry/305100
- ECTODERMAL DYSPLASIA 10A, HYPOHIDROTIC/HAIR/NAIL TYPE, AUTOSOMAL DOMINANT
  http://omim.org/entry/129490

- ECTODERMAL DYSPLASIA 10B, HYPOHIDROTIC/HAIR/TOOTH TYPE, AUTOSOMAL RECESSIVE
  http://omim.org/entry/224900
- ECTODERMAL DYSPLASIA 11A, HYPOHIDROTIC/HAIR/TOOTH TYPE, AUTOSOMAL DOMINANT
  http://omim.org/entry/614940
- ECTODERMAL DYSPLASIA 11B, HYPOHIDROTIC/HAIR/TOOTH TYPE, AUTOSOMAL RECESSIVE
  http://omim.org/entry/614941

Medical Genetics Database from MedGen

- Hypohidrotic ectodermal dysplasia
  https://www.ncbi.nlm.nih.gov/medgen/310309
- Hypohidrotic Ectodermal Dysplasia, Dominant
  https://www.ncbi.nlm.nih.gov/medgen/893601
- Hypohidrotic Ectodermal Dysplasia, Recessive
  https://www.ncbi.nlm.nih.gov/medgen/893648
- Hypohidrotic X-linked ectodermal dysplasia
  https://www.ncbi.nlm.nih.gov/medgen/57890

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Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/hypohidrotic-ectodermal-dysplasia

Reviewed: November 2018
Published: December 11, 2018

Lister Hill National Center for Biomedical Communications
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