Combined pituitary hormone deficiency

Combined pituitary hormone deficiency is a condition that causes a shortage (deficiency) of several hormones produced by the pituitary gland, which is located at the base of the brain. A lack of these hormones may affect the development of many parts of the body. The first signs of this condition include a failure to grow at the expected rate and short stature that usually becomes apparent in early childhood.

People with combined pituitary hormone deficiency may have hypothyroidism, which is underactivity of the butterfly-shaped thyroid gland in the lower neck. Hypothyroidism can cause many symptoms, including weight gain and fatigue. Other features of combined pituitary hormone deficiency include delayed or absent puberty and lack the ability to have biological children (infertility). The condition can also be associated with a deficiency of the hormone cortisol. Cortisol deficiency can impair the body’s immune system, causing individuals to be more susceptible to infection.

Rarely, people with combined pituitary hormone deficiency have intellectual disability; a short, stiff neck; or underdeveloped optic nerves, which carry visual information from the eyes to the brain.

Frequency

The prevalence of combined pituitary hormone deficiency is estimated to be 1 in 8,000 individuals worldwide.

Causes

Mutations in at least eight genes have been found to cause combined pituitary hormone deficiency. Mutations in the \textit{PROP1} gene are the most common known cause of this disorder, accounting for an estimated 12 to 55 percent of cases. Mutations in other genes have each been identified in a smaller number of affected individuals.

The genes associated with combined pituitary hormone deficiency provide instructions for making proteins called transcription factors, which help control the activity of many other genes. The proteins are involved in the development of the pituitary gland and the specialization (differentiation) of its cell types. The cells of the pituitary gland are responsible for triggering the release of several hormones that direct the development of many parts of the body. Some of the transcription factors are found only in the pituitary gland, and some are also active in other parts of the body.

Mutations in the genes associated with combined pituitary hormone deficiency can result in abnormal differentiation of pituitary gland cells and may prevent the production of several hormones. These hormones can include growth hormone (GH), which is needed for normal growth; follicle-stimulating hormone (FSH) and luteinizing hormone
(LH), which both play a role in sexual development and the ability to have children (fertility); thyroid-stimulating hormone (TSH), which helps with thyroid gland function; prolactin, which stimulates the production of breast milk; and adrenocorticotropic hormone (ACTH), which influences energy production in the body and maintains normal blood sugar and blood pressure levels. The degree to which these hormones are deficient is variable, with prolactin and ACTH showing the most variability. In many affected individuals, ACTH deficiency does not occur until late adulthood.

Most people with combined pituitary hormone deficiency do not have identified mutations in any of the genes known to be associated with this condition. The cause of the disorder in these individuals is unknown.

Inheritance Pattern

Most cases of combined pituitary hormone deficiency are sporadic, which means they occur in people with no history of the disorder in their family. Less commonly, this condition has been found to run in families. When the disorder is familial, it can have an autosomal dominant or an autosomal recessive pattern of inheritance.

Autosomal dominant inheritance means one copy of an altered gene in each cell is sufficient to cause the disorder.

Autosomal recessive inheritance means both copies of a gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of a mutated gene, but they typically do not show signs and symptoms of the condition. Most cases of familial combined pituitary hormone deficiency are inherited in an autosomal recessive pattern.

Other Names for This Condition

- CPHD
- panhypopituitarism

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
• Genetic Testing Registry: Pituitary hormone deficiency, combined 4

• Genetic Testing Registry: Pituitary hormone deficiency, combined 5

• Genetic Testing Registry: Pituitary hormone deficiency, combined 6

Research Studies from ClinicalTrials.gov
• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22combined+pituitary+hormone+deficiency%22+OR+%22Hypopituitarism%22

Other Diagnosis and Management Resources
• GeneReview: PROP1-Related Combined Pituitary Hormone Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1347

• Great Ormond Street Hospital for Children (UK): Growth Hormone Deficiency
  https://www.gosh.nhs.uk/conditions-and-treatments/conditions-we-treat/growth-hormone-deficiency

• MedlinePlus Encyclopedia: ACTH
  https://medlineplus.gov/ency/article/003695.htm

• MedlinePlus Encyclopedia: FSH
  https://medlineplus.gov/ency/article/003710.htm

• MedlinePlus Encyclopedia: Growth Hormone Deficiency
  https://medlineplus.gov/ency/article/001176.htm

• MedlinePlus Encyclopedia: Prolactin
  https://medlineplus.gov/ency/article/003718.htm

• MedlinePlus Encyclopedia: TSH Test
  https://medlineplus.gov/ency/article/003684.htm

• MedlinePlus Medical Tests: Adrenocorticotropic Hormone (ACTH)
  https://medlineplus.gov/lab-tests/adrenocorticotropic-hormone-acth/

• MedlinePlus Medical Tests: Cortisol Test
  https://medlineplus.gov/lab-tests/cortisol-test/

• MedlinePlus Medical Tests: Follicle-Stimulating Hormone (FSH) Levels Test
  https://medlineplus.gov/lab-tests/follicle-stimulating-hormone-fsh-levels-test/

• MedlinePlus Medical Tests: Luteinizing Hormone (LH) Levels Test
  https://medlineplus.gov/lab-tests/luteinizing-hormone-lh-levels-test/
Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: ACTH
  https://medlineplus.gov/ency/article/003695.htm
- Encyclopedia: FSH
  https://medlineplus.gov/ency/article/003710.htm
- Encyclopedia: Growth Hormone Deficiency
  https://medlineplus.gov/ency/article/001176.htm
- Encyclopedia: Prolactin
  https://medlineplus.gov/ency/article/003718.htm
- Encyclopedia: Short Stature
  https://medlineplus.gov/ency/article/003271.htm
- Encyclopedia: TSH Test
  https://medlineplus.gov/ency/article/003684.htm
- Health Topic: Pituitary Disorders
  https://medlineplus.gov/pituitarydisorders.html
- Medical Tests: Adrenocorticotropic Hormone (ACTH)
  https://medlineplus.gov/lab-tests/adrenocorticotropic-hormone-acth/
- Medical Tests: Cortisol Test
  https://medlineplus.gov/lab-tests/cortisol-test/
- Medical Tests: Follicle-Stimulating Hormone (FSH) Levels Test
  https://medlineplus.gov/lab-tests/follicle-stimulating-hormone-fsh-levels-test/
- Medical Tests: Luteinizing Hormone (LH) Levels Test
  https://medlineplus.gov/lab-tests/luteinizing-hormone-lh-levels-test/

Genetic and Rare Diseases Information Center

- Combined pituitary hormone deficiencies, genetic forms
- Pituitary hormone deficiency, combined 1
  https://rarediseases.info.nih.gov/diseases/10601/pituitary-hormone-deficiency-combined-1
- Pituitary hormone deficiency, combined 3
  https://rarediseases.info.nih.gov/diseases/10603/pituitary-hormone-deficiency-combined-3
- Pituitary hormone deficiency, combined 4
  https://rarediseases.info.nih.gov/diseases/10604/pituitary-hormone-deficiency-combined-4
Educational Resources

- Boston Children's Hospital: Growth Hormone Deficiency in Children
  http://www.childrenshospital.org/conditions-and-treatments/conditions/g/growth-hormone-deficiency
- Kids Health from Nemours: What Is a Growth Disorder?
- MalaCards: combined pituitary hormone deficiency
  https://www.malacards.org/card/combined_pituitary_hormone_deficiency
- Merck Manual Consumer Version: Overview of the Pituitary Gland
- Orphanet: Combined pituitary hormone deficiencies, genetic forms
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=95494
- Teens Health from Nemours: Delayed Puberty

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD): Growth Hormone Deficiency
  https://rarediseases.org/rare-diseases/growth-hormone-deficiency/
- The MAGIC Foundation: Growth Hormone Deficiency in Children
  https://www.magicfoundation.org/Growth-Disorders/Growth-Hormone-Deficiency-in-Children/

Clinical Information from GeneReviews

- PROP1-Related Combined Pituitary Hormone Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1347

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28combined+pituitary+hormone+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- PITUITARY HORMONE DEFICIENCY, COMBINED, 1
  http://omim.org/entry/613038
- PITUITARY HORMONE DEFICIENCY, COMBINED, 2
  http://omim.org/entry/262600
• PITUITARY HORMONE DEFICIENCY, COMBINED, 3
  http://omim.org/entry/221750
• PITUITARY HORMONE DEFICIENCY, COMBINED, 4
  http://omim.org/entry/262700

Medical Genetics Database from MedGen
• Pituitary hormone deficiency, combined 1
• Pituitary hormone deficiency, combined 2
• Pituitary hormone deficiency, combined 3
• Pituitary hormone deficiency, combined 4
• Pituitary hormone deficiency, combined 6

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19837867
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2806371/
• Kelberman D, Turton JP, Woods KS, Mehta A, Al-Khawari M, Greening J, Swift PG, Otonkoski T,
  Rhodes SJ, Dattani MT. Molecular analysis of novel PROP1 mutations associated with combined
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19128366
• Mody S, Brown MR, Parks JS. The spectrum of hypopituitarism caused by PROP1 mutations. Best
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12464226
• Reynaud R, Gueydan M, Saveanu A, Vallette-Kasic S, Enjalbert A, Brue T, Barlier A. Genetic
  screening of combined pituitary hormone deficiency: experience in 195 patients. J Clin Endocrinol
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16735499
• Vieira TC, Boldarine VT, Abucham J. Molecular analysis of PROP1, PIT1, HESX1, LHX3, and LHX4
  shows high frequency of PROP1 mutations in patients with familial forms of combined pituitary
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18157385

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