About
ADH1

What is ADH1?

ADH1, or **A**utosomal **D**ominant **H**ypocalcemia Type **1**, is a form of hypoparathyroidism. It is an **inherited, lifelong condition**; can be found in children and adults; and is rare, affecting approximately 1 in 25,000 individuals.[1]

What is an inherited condition?

An inherited condition happens when a characteristic or trait is passed from one generation to another, such as from a parent to a child.[2-4]

What are other names for ADH1?

- Autosomal dominant hypocalcemia (ADH)[4,5]
- Autosomal dominant hypoparathyroidism[4]
- Familial hypercalciuric hypocalcemia[4]
- Familial hypocalcemia[4]
- Familial isolated hypoparathyroidism[5]
- Idiopathic hypoparathyroidism[6]

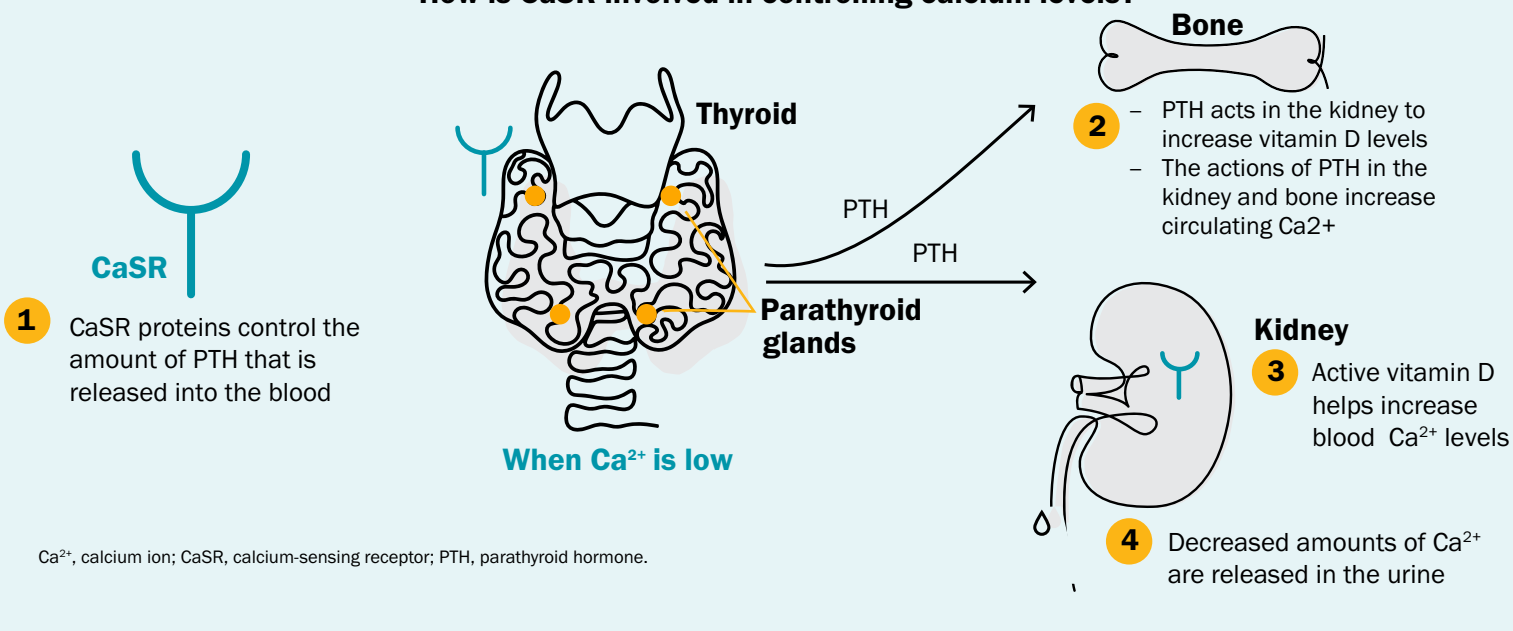
People with ADH1[4]:

- Will usually have low levels of calcium in the blood, known as hypocalcemia
- Have low levels of a hormone called parathyroid hormone, which helps control the amount of calcium in the blood
- Can have high levels of calcium in their urine, known as hypercalciuria, which can lead to calcium building up in the kidneys or the formation of kidney stones
- May also have the wrong amount of other important minerals in their body, such as too much phosphate or too little magnesium

What causes ADH1?

ADH1 is caused by an abnormal change in the **C**alcium-**S**ensing **R**eceptor (***CASR***) **gene**. The proteins made from this gene normally work together to detect and control the amount of calcium in the blood. In patients with ADH1, the proteins made from the abnormal *CASR* gene are more sensitive to calcium and do not work as well to control calcium levels, even when levels in the blood are low.[4] There are other abnormal genes that can cause forms of hypoparathyroidism similar to ADH1, but changes in the *CASR* gene are one of the most common.[7]

How is CaSR involved in controlling calcium levels?



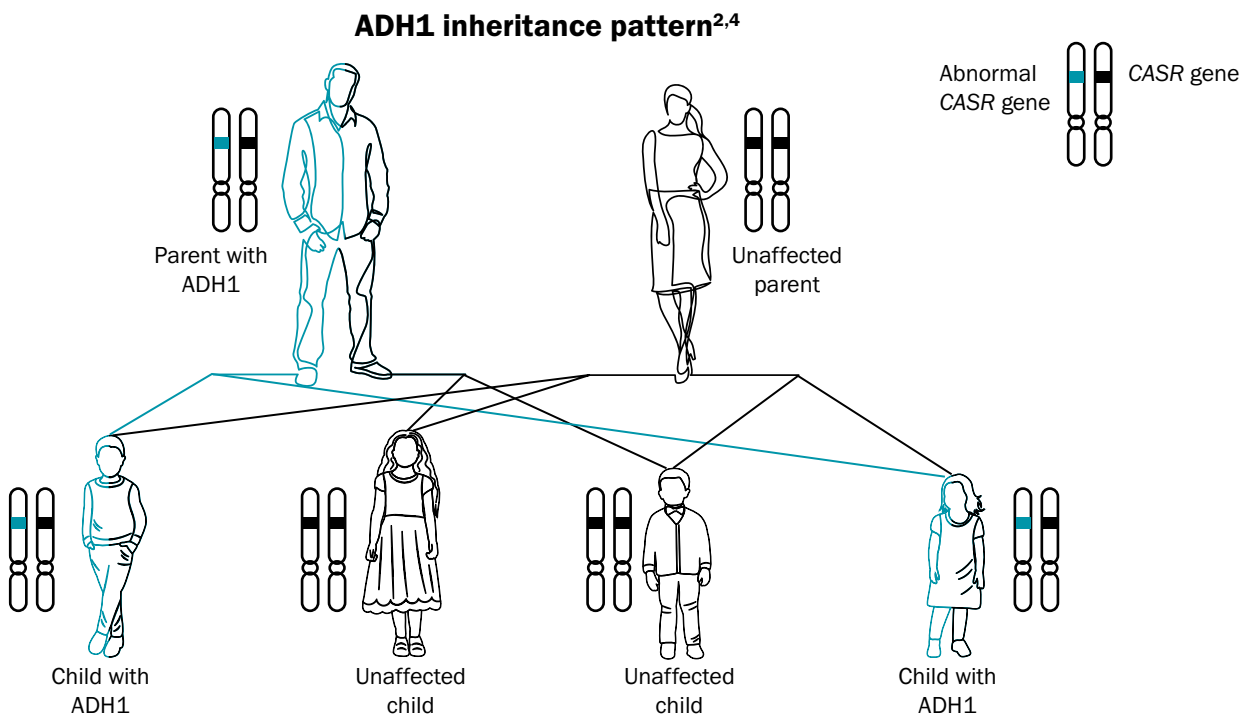
Ca^{2+}, calcium ion; CaSR, calcium-sensing receptor; PTH, parathyroid hormone.

Who gets or passes down ADH1?

ADH1 is inherited, or passed from one generation to the next, in an **autosomal dominant** pattern.[4,6] In an autosomal dominant inheritance pattern, one copy of the *CASR* gene with an abnormal change is enough to cause the condition.[4] In most cases, a person with ADH1 gets the abnormal *CASR* gene from one parent with ADH1.[4] Each child of someone with ADH1 has a 50% chance of inheriting the abnormal gene for ADH1.[2]

- Some people do not inherit ADH1. Instead, ADH1 can be caused by a spontaneous change in the *CASR* gene. Thus, people can develop ADH1 with no history of the condition in their family[4]
- If someone is diagnosed with ADH1, their parents also should be tested for the abnormal *CASR* gene[3]

ADH1 inheritance pattern[2,4]



What are the symptoms of ADH1?

The symptoms of ADH1 may be **different from person to person** and may affect children and adults differently. Symptoms can appear at any age and may change over time.[6,8] One of the most common symptoms of ADH1 is sudden, strong muscle tightening, known as **muscle spasms**, in the hands and feet.[4,6] Sensations of **muscle cramping; prickling or tingling**, known as paresthesia; or twitching of the nerves and muscles in various parts of the body are also common.[4,6] People with serious ADH1 may develop short periods of uncontrolled movements, known as **seizures**, usually in infancy or childhood.[4,6]

Most common symptoms of ADH1

Brief or sudden symptoms of ADH1[6,9,10]

- Symptoms affecting the brain and muscles
  - Seizures
  - Intermittent muscular spasms, known as tetany
  - Paresthesia
  - Muscle cramps/spasms
  - Pain in bones or where bones connect, known as joints
  - Feeling tired all over, known as fatigue
- Symptoms affecting a person's thoughts
  - Fear or worry, known as anxiety
  - Problems with thinking, remembering, or concentrating, known as brain fog

Long-term potential consequences of ADH1[4,6,9,10]

- Affecting the kidneys
  - Kidney stones
  - Too much calcium in the kidneys
  - Damaged kidneys that can't properly filter blood, known as chronic kidney disease
- Affecting other parts of the body
  - A buildup of calcium on important regions of the brain
  - Breaks in bones, known as bone fractures
  - Feeling sad or hopeless and having little interest in activities, known as depression
  - Heart beating too fast or too slow, known as arrhythmia

Talk to your doctor, early detection is important to treat symptoms caused by ADH1.[7]
Ask your doctor about genetic testing if you think you or your child may have ADH1.

What is the purpose of clinical research?

Clinical studies or medical research studies look at new ways to prevent, detect, or treat conditions. Treatments may be new drugs or new combinations of drugs, or new ways to use existing treatments. The goal of clinical trials is to determine if a new medicine or treatment is safe and works well.[10] Talk to your doctor about currently ongoing clinical trials for patients with ADH1.

References: 1. Roszko et al. *JBone Miner Res*. 2022;37:1926-1935. **2.** National Human Genome Research Institute. https://www.genome.gov/genetics-glossary/Autosomal-Dominant-Disorder. Updated July 24, 2023. Accessed July 24, 2023. **3.** MedlinePlus. https://medlineplus.gov/ency/article/002049.htm. Accessed July 24, 2023. **4.** MedlinePlus. https://medlineplus.gov/genetics/condition/autosomal-dominant-hypocalcemia. Accessed July 24, 2023. **5.** Cinque et al. *J Clin Endocrinol Metab.* 2017;102:3961-3969. **6.** Mannstadt et al. Poster presented at: ENDO 2023; June 15-18, 2023; Chicago, IL. **7.** Mannstadt et al. *J Bone Miner Res.* 2022;37:2615-2629. **8.** Rejnmark et al. *Endocrinol Metab (Seoul).* 2015;30:436-442. **9.** MedlinePlus. https://medlineplus.gov/genetics/gene/casr. Accessed July 24, 2023. **10.** Johns Hopkins Medicine. https://www.hopkinsmedicine.org/research/understanding-clinical-trials/clinical-research-what-is-it.html. Accessed July 24, 2023.