CONDITION

Pseudohypoparathyroidism

Pseudohypoparathyroidism is a rare condition in which the body does not respond properly to parathyroid hormone.

WHAT IT IS
Reduced response to parathyroid hormone

BODY SYSTEM
Hormones, bones, kidneys, and nervous system

MAIN SYMPTOMS
Muscle cramps, tingling, seizures, short fingers

WHAT CAUSES IT
Genetic or epigenetic changes affecting GNAS signaling

HOW IT IS DIAGNOSED
Calcium, phosphate, PTH, and genetic or epigenetic tests

MAIN TREATMENT
Active vitamin D, calcium, and hormone management

CAN IT BE CURED?
No - the signaling change remains

IS IT AN EMERGENCY?
Sometimes - seizures or breathing trouble from low calcium

LONG-TERM OUTLOOK
Often manageable with treatment and lifelong monitoring

Overview

Pseudohypoparathyroidism is a rare, long-term condition in which parts of the body do not respond properly to parathyroid hormone, usually shortened to PTH. PTH helps control calcium and phosphate levels in the blood.

In pseudohypoparathyroidism, the parathyroid glands usually make enough PTH. They may make extra PTH because the kidneys and bones are not responding to it as expected. This resistance can lead to low calcium and high phosphate levels.

Calcium is important for muscles, nerves, the heart, and bones. Very low calcium can cause painful muscle tightening, seizures, or heart rhythm problems. Treatment aims to keep calcium and PTH in a safe range and to identify other hormone problems early.

Some people also have physical features called Albright hereditary osteodystrophy. These can include short fingers or toes, short height, a round face, and areas of bone-like tissue under the skin. Weight gain, thyroid problems, growth differences, or learning difficulties may occur in certain forms.

The traditional names include pseudohypoparathyroidism types 1A, 1B, and 1C. Specialists may now group these and similar conditions under the name inactivating PTH/PTH-related peptide signaling disorders , or iPPSD . The older names are still widely used in medical records and test reports.

Symptoms

Symptoms differ according to the specific genetic or epigenetic change, the hormones involved, and how low the calcium becomes. Some people are diagnosed through routine blood tests before they notice symptoms.

Low calcium may cause:

Some people develop cataracts, which are cloudy areas in the lens of the eye, or dental problems such as delayed tooth eruption and weakened enamel.

Certain forms affect how the body responds to hormones other than PTH. Resistance to thyroid-stimulating hormone, or TSH, can cause an underactive thyroid. Possible symptoms include tiredness, constipation, dry skin, feeling cold, and slowed growth.

Other possible features include early weight gain, short adult height, delayed or incomplete puberty, reduced fertility, hearing problems, sleep apnea, and differences in learning or development. Not everyone has these features.

Shortened bones in the hands or feet may make one or more knuckles appear less prominent when making a fist. Bone-like deposits can also form under the skin or in deeper tissues. These deposits are different from the calcium deposits caused by high blood calcium.

- Tingling around the mouth or in the fingers and toes
- Muscle cramps, spasms, or stiffness
- Twitching of the face or other muscles
- Fatigue, weakness, or difficulty concentrating
- Seizures when calcium is severely low

Causes and risk factors

Pseudohypoparathyroidism is usually related to changes involving the GNAS gene. This gene helps cells pass hormone signals from the cell surface to the inside of the cell. When that signaling process does not work properly, tissues may resist PTH and sometimes other hormones.

Some people have a change in the DNA sequence itself. Others have an epigenetic change , meaning the instructions controlling how the gene is switched on or off are altered even though the underlying DNA sequence may be unchanged.

GNAS is affected by genomic imprinting . This means some effects differ according to whether a change came from the egg or the sperm. A change inherited from the mother can cause hormone resistance together with physical features in some forms. The same DNA change inherited from the father may cause physical features without PTH resistance, known as pseudopseudohypoparathyroidism.

The condition may be inherited, but it can also result from a new change that was not present in either parent. Some epigenetic forms occur without a clear family history.

Having an affected relative may increase the chance of the condition, but the inheritance pattern can be complicated. A genetics professional can interpret the specific test result and explain what it may mean for relatives or future pregnancies.

Diagnosis

Diagnosis usually begins with blood tests. The typical pattern is:

Calcium may be measured as ionized calcium, which is the active form, or interpreted alongside albumin, a blood protein that affects the total calcium result.

These results are not enough on their own. Vitamin D deficiency, kidney disease, severe magnesium abnormalities, medicines, and other causes of low calcium must be considered. Testing commonly includes magnesium, vitamin D, kidney function, thyroid function, and urine calcium.

Genetic testing can look for changes in GNAS and sometimes other genes involved in the same signaling pathway. A separate test may examine GNAS methylation, an epigenetic marker that controls gene activity. Both types of testing may be needed because standard DNA sequencing does not detect every cause.

Physical examination, growth measurements, hand or foot X-rays, and a review of development may help identify related features. An electrocardiogram, or ECG, may be used if

calcium is very low because calcium disturbances can affect the heart's electrical rhythm.

The combination of laboratory findings, physical features, family history, and genetic or epigenetic testing helps determine the specific form.

- Low calcium
- High phosphate
- High PTH

Treatment and management

Treatment does not correct the underlying signaling change. It can usually control low calcium and many associated hormone problems.

Active vitamin D medicines, such as calcitriol or alfacalcidol, help the intestines absorb calcium. Calcium supplements may also be used. The amount needed is based on blood and urine tests rather than symptoms alone.

The aim is not simply to raise calcium as high as possible. Treatment also seeks to lower excessive PTH while avoiding too much calcium in the blood or urine. Regular monitoring may include calcium, phosphate, PTH, kidney function, vitamin D, and urine calcium. Kidney imaging may be considered if there is concern about stones or calcium deposits.

Severe symptomatic hypocalcemia may require calcium through a vein in hospital, with heart and blood-test monitoring.

Other care is matched to the person's needs. It may include:

Bone-like tissue under the skin does not usually improve with calcium treatment. Surgery is considered carefully because deposits can return, and tissue injury may sometimes encourage further bone formation.

- Thyroid hormone treatment for an underactive thyroid
- Growth assessment and specialist treatment for significant growth problems
- Support for puberty, menstrual, or fertility concerns
- Developmental, educational, hearing, or speech support
- Dental and eye care
- Assessment for sleep apnea and weight-related health problems
- Physiotherapy or specialist review for movement-limiting bone formation

Complications

Untreated or poorly controlled low calcium can cause repeated muscle spasms, seizures, and abnormal heart rhythms. High PTH over a long period may affect bone strength.

Treatment also needs monitoring. Too much calcium or active vitamin D can cause high blood calcium or excess calcium in the urine. Over time, this can contribute to kidney stones or calcium deposits in the kidneys.

Other possible complications relate to the specific form of the condition. These include persistent hypothyroidism, reduced adult height, delayed puberty, fertility problems, obesity-related health concerns, dental abnormalities, cataracts, hearing loss, and sleep apnea.

Bone formation in the skin or deeper tissues can cause pain, limit joint movement, or interfere with daily activities. Severe progressive bone formation is more typical of related GNAS conditions than of every form of pseudohypoparathyroidism.

Not everyone develops these complications. Regular follow-up is intended to detect changes before they cause lasting problems.

Prevention

Pseudohypoparathyroidism cannot currently be prevented. Genetic and epigenetic changes are not caused by something a person ate, did, or failed to do during pregnancy or childhood.

Once the condition is known, consistent treatment and monitoring can help prevent complications from low calcium, high PTH, thyroid dysfunction, and treatment-related high calcium.

Genetic counselling cannot prevent the condition, but it can clarify whether a particular form may run in a family. Testing may also help relatives decide whether they want their own calcium, hormone, or genetic assessment.

Living with it and what to expect

Pseudohypoparathyroidism is usually lifelong. The genetic or epigenetic change does not disappear, although symptoms and treatment needs can change over time.

Hormone resistance may become more apparent during childhood rather than being obvious at birth. Growth, weight, thyroid function, calcium balance, puberty, learning, and development may therefore need repeated review. Adults still need monitoring even if their treatment has

been stable for years.

Many people can attend school, work, exercise, and take part in family and social life. Some need additional educational, mobility, hearing, or daily-living support. The course cannot be predicted from the diagnosis alone because different forms affect people in different ways.

Taking medicines consistently matters because calcium levels can fall without clear early symptoms. Keeping an up-to-date medicine list and sharing the diagnosis before surgery or hospital treatment can help prevent missed doses and unexpected calcium problems.

Illness, pregnancy, breastfeeding, major dietary changes, and starting certain medicines can alter calcium needs. These situations usually call for planned blood testing rather than automatically changing treatment.

Routine follow-up is commonly coordinated by an endocrinology team. Genetics, kidney, dental, eye, hearing, sleep, growth, reproductive, or rehabilitation services may also be involved when relevant.

When to get medical help

Arrange routine medical review if you develop new tingling, recurring cramps, unusual fatigue, constipation, dental problems, changes in growth, menstrual changes, or symptoms of an underactive thyroid. These symptoms have many possible causes, so blood tests are needed rather than assuming they come from calcium.

Seek prompt medical advice if vomiting, diarrhea, illness, or missed medicine makes it difficult to continue your usual treatment. Advice is also needed for symptoms that could mean calcium is too high, such as persistent nausea, marked thirst, frequent urination, confusion, or worsening weakness.

Seek emergency care for:

These symptoms can occur with severe calcium disturbance and need urgent testing and monitored treatment.

- A seizure
- Trouble breathing or severe throat tightening
- Fainting or a sustained irregular heartbeat
- Severe muscle spasms affecting the whole body
- Sudden confusion or reduced responsiveness

Common questions

Is pseudohypoparathyroidism the same as hypoparathyroidism?

No. In hypoparathyroidism, the parathyroid glands do not make enough PTH. In pseudohypoparathyroidism, PTH is present, but the body does not respond to it properly. Both can cause low calcium, but their monitoring and long-term management differ.

Does "pseudo" mean the condition is not real?

No. "Pseudo" refers to the way it resembles hypoparathyroidism even though PTH levels are usually high rather than low. The hormone resistance and calcium disturbance are real medical findings.

Is pseudohypoparathyroidism inherited?

Some forms are inherited, while others result from a new genetic or epigenetic change. Because GNAS is imprinted, the effects can differ according to which parent passes on the change. A specific laboratory result is needed to estimate the chance for relatives.

Can calcium supplements alone treat it?

Not always. Many people need an active form of vitamin D so the body can absorb and use calcium effectively. Treatment must be guided by blood and urine tests because excessive calcium can also cause harm.

Does pseudohypoparathyroidism affect intelligence?

Some forms are associated with learning or developmental differences, but this is not true for everyone. Abilities range widely. Early assessment can identify useful educational, speech, occupational, or developmental support.

Can someone with pseudohypoparathyroidism live a full life?

Many people manage the condition with regular medicine and monitoring. Long-term needs differ according to hormone resistance, growth, development, and bone formation. Ongoing care helps identify treatable problems and support independence.

Sources

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