CONDITION

CHH

Learn how congenital hypogonadotropic hypogonadism affects puberty, fertility, bone health, and sexual development, and how it is diagnosed and managed.

WHAT IT IS
Congenital reproductive hormone signaling disorder

BODY SYSTEM
Hormone and reproductive systems

MAIN SYMPTOMS
Absent or delayed puberty, infertility, low sexual desire, reduced sense of smell

WHAT CAUSES IT
Genetic changes, sometimes unknown

HOW IT IS DIAGNOSED
Blood tests showing low sex hormones and low LH and FSH

MAIN TREATMENT
Hormone replacement and fertility hormone therapy

CAN IT BE CURED?
Sometimes - minority reverse, but relapse occurs

IS IT AN EMERGENCY?
No - CHH itself rarely causes emergencies

LONG-TERM OUTLOOK
Usually manageable with treatment, with fertility often needing separate hormone therapy

Overview

CHH stands for congenital hypogonadotropic hypogonadism . It is a condition present from birth in which the brain does not send enough hormonal signals to the ovaries or testes. As a result, the body produces too little estrogen or testosterone.

The signaling problem usually involves gonadotropin-releasing hormone, or GnRH. GnRH is made in the hypothalamus, a part of the brain that helps control hormones. It tells the pituitary gland to release luteinizing hormone, or LH, and follicle-stimulating hormone, or FSH. These hormones then stimulate the ovaries or testes.

When this pathway does not work normally, puberty may be absent, incomplete, or unusually late. CHH can also affect fertility, sexual function, bone strength, and emotional well-being.

Some people with CHH have a reduced or absent sense of smell. This form is commonly called Kallmann syndrome . Other people have a normal sense of smell. CHH may occur by itself or alongside features such as hearing loss, cleft lip or palate, unusual tooth development, involuntary mirror movements of the hands, or a missing kidney.

CHH is different from temporary delayed puberty, illness-related hormone suppression, or a pituitary tumor. A careful evaluation is needed because these conditions can initially look similar.

Treatment can usually produce the physical changes of puberty and maintain healthy sex hormone levels. Fertility often requires a different type of hormone treatment.

Symptoms

Symptoms depend on age, sex characteristics, and how much hormone signaling is present.

In infants with testes, early clues may include:

These signs are not specific to CHH. Most people are evaluated later, when puberty does not start or progress as expected.

In adolescents and adults with testes, possible features include:

People with ovaries may have:

A reduced or absent sense of smell may go unnoticed. Some people assume that their experience of smell is typical. Formal smell testing can sometimes identify a problem that was not previously recognized.

CHH can also affect mental and social health. Delayed puberty, differences in genital development, and fertility concerns may contribute to embarrassment, low self-esteem, anxiety, depression, or difficulty with relationships. These effects are important parts of the condition and can be discussed confidentially with a clinician.

- A penis that is smaller than expected
- One or both testes not descending into the scrotum
- Other congenital differences, such as cleft lip or palate
- Little or no testicular enlargement during puberty
- Limited facial, body, or pubic hair
- A voice that does not deepen as expected
- Reduced muscle development

- Low sexual desire
- Difficulty with erections
- Infertility or a very low sperm count
- Fatigue or reduced sense of well-being
- Little or no breast development
- Menstrual periods that never begin
- Periods that stop or remain very irregular because estrogen is low
- Low sexual desire
- Vaginal dryness or discomfort during sex
- Difficulty becoming pregnant

Causes and risk factors

CHH usually results from a problem with the development, movement, or function of the nerve cells that make GnRH. During fetal development, these cells normally travel from the developing nose area into the brain. Some genetic changes interfere with this process. Others affect the release of GnRH or the body's response to it.

Changes in many different genes can cause CHH. A person may have a change in one gene, changes in more than one gene, or no identifiable genetic cause. Inheritance can be X-linked, autosomal dominant, or autosomal recessive. These terms describe different ways a genetic change may be passed through a family.

The same genetic change can affect relatives differently. One family member may have absent puberty and no sense of smell, while another may have milder reproductive symptoms. Some people have no known family history because the genetic change is new, relatives were not diagnosed, or inheritance is complex.

CHH itself is congenital. However, other conditions can cause a similar pattern of low sex hormones with low or unexpectedly normal LH and FSH. These include major weight loss, undernutrition, intensive exercise, severe stress, chronic illness, high prolactin levels, certain medicines, pituitary disease, and damage to the hypothalamus.

Constitutional delay of growth and puberty is another important possibility in adolescents. This is a temporary pattern in which puberty begins later than average, often with a family history of late puberty. Distinguishing it from CHH can take time because no single test reliably separates every case.

Diagnosis

Diagnosis begins with a detailed medical and family history. The clinician may ask about growth, puberty, menstrual periods, erections, sexual interest, nutrition, exercise, long-term illness, medicines, sense of smell, and relatives with delayed puberty or infertility.

A physical examination evaluates growth and sexual development. Depending on the person's anatomy, this may include breast development, body hair, testicular size, penile development, and signs of an associated congenital condition.

Blood tests commonly measure:

In CHH, sex hormone levels are low while LH and FSH are low or not appropriately elevated. This is called hypogonadotropic hypogonadism . Results must be interpreted using age, stage of puberty, time of day, and the laboratory's reference ranges.

Additional evaluation may include a bone-age X-ray, which estimates skeletal maturity. A bone-density scan may be considered when sex hormone deficiency has been prolonged. Semen analysis can evaluate sperm production in adults with testes.

Magnetic resonance imaging, or MRI, may be used to examine the hypothalamus, pituitary gland, and smell-related brain structures. It is especially important when symptoms or laboratory results raise concern for an acquired brain or pituitary disorder.

Genetic testing may confirm a cause, identify related health concerns, or help with family counseling. A negative result does not rule out CHH because all genetic causes are not yet known. Genetic counseling can help people understand the limits of testing and what a result may mean for relatives or future children.

Clinicians may also assess hearing, kidney structure, dental development, or sense of smell when the person's history or genetic findings suggest a related feature.

- Testosterone or estradiol, depending on the clinical situation
- LH and FSH
- Prolactin
- Thyroid-related hormones
- Other pituitary or adrenal hormones when indicated

Treatment and management

Treatment is tailored to age, anatomy, health needs, and personal goals. Care may involve an

endocrinologist, pediatric endocrinologist, reproductive endocrinologist, urologist, gynecologist, genetic counselor, or fertility specialist.

Puberty induction and hormone replacement

For people with testes, testosterone can start and maintain male-pattern pubertal development. Treatment is generally introduced gradually in adolescents to better imitate natural puberty. Testosterone supports voice deepening, muscle and bone development, body hair growth, sexual function, and general well-being.

Testosterone treatment does not enlarge the testes substantially or stimulate sperm production. It can also suppress sperm production, so fertility goals should be discussed before and during treatment.

For people with ovaries, estrogen can begin and maintain breast development, support bone health, and help other estrogen-dependent tissues. It is usually introduced gradually during puberty induction. If a person has a uterus, a progestogen is generally added at an appropriate stage to protect the uterine lining.

Hormone therapy requires monitoring. The specific medicine, form, schedule, and treatment targets depend on the individual and should be decided with a clinician.

Fertility treatment

Fertility treatment aims to stimulate the ovaries or testes rather than simply replace sex hormones.

In people with testes, gonadotropin therapy may use hormones that act like LH and FSH. These treatments can increase testicular growth and support sperm production. Pulsatile GnRH therapy, delivered in timed small pulses by a pump, may be an option in specialized settings when the pituitary gland can respond normally.

Sperm production often takes time, and response varies. Previous undescended testes, very small testes, or absence of early-life hormone activity may affect treatment response, but they do not by themselves determine the outcome.

In people with ovaries, pulsatile GnRH or gonadotropin injections may stimulate egg development and ovulation. Gonadotropin treatment requires close monitoring because it can cause the ovaries to respond too strongly or can increase the chance of a multiple pregnancy.

Other aspects of care

Healthy nutrition, weight-bearing activity, adequate calcium and vitamin D intake, avoiding tobacco, and limiting excess alcohol support bone health. Supplements should be discussed with a clinician rather than started automatically.

Counseling or peer support may help with body image, relationships, sexual concerns, or

fertility-related stress. Treatment should address these concerns without assuming a person's gender identity, sexual orientation, or reproductive goals.

A minority of people experience a return of their own reproductive hormone activity after treatment. This is sometimes called reversal. Because relapse can occur, hormone therapy should not be stopped without medical supervision.

Complications

Without adequate treatment, prolonged low estrogen or testosterone can reduce bone mineral density and increase the risk of fragile bones. It may also affect muscle mass, body composition, energy, sexual comfort, and sexual function.

Infertility is common when the testes or ovaries are not being stimulated. Standard sex hormone replacement does not provide the same fertility effect as GnRH or gonadotropin treatment.

Undescended testes require separate assessment because they may affect fertility and carry other long-term risks. Associated kidney, hearing, dental, or neurologic differences may also need specific care.

The emotional impact can be substantial. Delayed diagnosis may leave a person feeling isolated or uncertain about their body. Recognizing and treating psychological distress is part of appropriate CHH care.

Follow up

Routine follow-up checks whether treatment is supporting pubertal development, sexual health, bone health, and personal goals. Visits may include a review of symptoms, growth or body changes, blood tests, and treatment effects. Bone-density monitoring may be appropriate when hormone deficiency was prolonged or other bone risks are present.

People planning a pregnancy should discuss fertility treatment early. Genetic counseling may also be useful before pregnancy, although genetic results cannot always predict whether or how severely a child would be affected.

Arrange a routine appointment if puberty has not started when expected, pubertal development begins but does not progress, menstrual periods do not begin, or there are concerns about sexual function or fertility. A reduced sense of smell or a family history of delayed puberty may be useful information to mention.

Contact the treating clinician promptly for significant treatment side effects, unexpected bleeding, new severe mood symptoms, or major changes in sexual or reproductive function.

CHH itself rarely causes an emergency. Seek urgent medical assessment for a new severe headache, sudden vision change, fainting, confusion, repeated vomiting, or severe weakness. These symptoms are not typical of stable CHH and could indicate a different pituitary, neurologic, or medical problem.

Sources

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