CONDITION

Noonan syndrome with multiple lentigines

Noonan syndrome with multiple lentigines is an inherited condition affecting the skin, heart, hearing, growth, and development.

WHAT IT IS
Inherited condition affecting skin, heart, hearing, growth, and development

BODY SYSTEM
Skin, heart, hearing, growth, and development

MAIN SYMPTOMS
Lentigines, heart muscle thickening, short stature, hearing loss

WHAT CAUSES IT
Inherited or new gene change

HOW IT IS DIAGNOSED
Clinical assessment and genetic testing

MAIN TREATMENT
Heart monitoring and symptom-specific supportive care

CAN IT BE CURED?
No - the genetic change remains lifelong

IS IT AN EMERGENCY?
Sometimes - fainting, chest pain, or severe breathing trouble

LONG-TERM OUTLOOK
Many reach adulthood; heart involvement shapes long-term health

Overview

Noonan syndrome with multiple lentigines is a rare genetic condition. It belongs to a group of conditions called RASopathies , which affect signals that help cells grow and develop.

The condition can affect several parts of the body. Its main features include many small, dark skin spots called lentigines , thickening of the heart muscle, hearing loss, short stature, and distinctive facial features. Not everyone has all of these features.

The lentigines often appear during childhood and become more numerous around puberty. They are usually harmless. Heart involvement is more important for long-term health and is the main reason regular specialist follow-up is needed.

Older medical records may call this condition LEOPARD syndrome . This name came from an

acronym describing possible features, but Noonan syndrome with multiple lentigines is now the preferred term.

Symptoms

The condition affects each person differently. Some features may be present at birth, while others become clearer during childhood or adolescence.

Common skin findings include:

Lentigines may not appear until around age 4 or 5. A young child can therefore have the condition without the characteristic spots. Unlike freckles, lentigines do not usually fade during winter.

Heart findings may include hypertrophic cardiomyopathy , meaning abnormal thickening of the heart muscle. This can make it harder for the heart to fill or pump normally. Some people also have changes in the heart's electrical rhythm or a narrowed pulmonary valve, which controls blood flow from the heart to the lungs.

Heart involvement may cause no noticeable symptoms. When symptoms occur, they can include breathlessness, tiredness, chest discomfort, a racing or irregular heartbeat, dizziness, or fainting.

Other possible features include:

Most people do not have every feature. Intelligence is often within the usual range, although some children need help with learning, speech, attention, or coordination.

- Multiple brown or black lentigines, often on the face, neck, and upper body
- Café-au-lait spots, which are flat, light-brown patches
- Lentigines in areas that receive little or no sun
- Shorter-than-expected height
- Eyes that appear widely spaced
- Low-set or unusually shaped ears
- A broad or webbed neck
- A sunken or prominent chest
- Hearing loss caused by changes in the inner ear or hearing nerve
- Delayed speech, movement, or learning

- Feeding difficulties during infancy
- Undescended testicles in some boys
- Delayed puberty in some people

Causes and risk factors

Noonan syndrome with multiple lentigines is caused by a change in a gene involved in the RAS-MAPK pathway. This pathway carries signals that control how cells grow, divide, and mature.

Changes in the PTPN11 gene cause most identified cases. Changes in genes such as RAF1 or BRAF can also cause the condition. Genetic testing does not find a cause in every person with convincing clinical features.

The condition follows an autosomal dominant inheritance pattern. This means a person usually needs one changed copy of the gene to have the condition. A parent with the gene change has a 1 in 2 chance of passing it on with each pregnancy.

Sometimes the gene change is inherited from a parent who has mild or previously unrecognised features. In other cases, it is a new change that occurred in the egg, sperm, or early embryo. Nothing a parent did during pregnancy causes this new change.

Having an affected parent or sibling increases the chance of the condition. It is not caused by diet, infection, sun exposure, or lifestyle.

Diagnosis

Diagnosis usually begins with a review of medical history, growth, skin findings, facial features, hearing, development, and family history. Because the condition can resemble other RASopathies, assessment by a clinical genetics team can be helpful.

A genetic blood or saliva test can look for changes in PTPN11 and other related genes. Finding a disease-causing gene change can confirm the diagnosis. It may also help other family members decide whether to have testing.

A normal genetic test does not always rule out the condition. The available test may not detect every type of genetic change, and the responsible gene may not yet be known.

Tests used to assess how the condition affects the body may include:

Children may be reassessed over time because lentigines, heart changes, hearing loss, or

learning needs can become more apparent with age.

- An echocardiogram, which uses ultrasound to examine the heart
- An electrocardiogram, or ECG, which records the heart's electrical activity
- Formal hearing tests
- Growth and developmental assessments
- Eye examinations when there are vision concerns
- Blood tests or hormone assessments when growth or puberty is unusual

Treatment and management

There is no treatment that removes the underlying genetic change. Management focuses on finding and treating the features affecting the individual person.

Regular cardiology follow-up is important, even when there are no heart symptoms. The schedule depends on the type and severity of heart involvement. An echocardiogram and ECG may be repeated to check heart muscle thickness, valves, and rhythm.

Treatment for hypertrophic cardiomyopathy or rhythm problems is selected by a cardiology team. It may include medicines, procedures, or implanted heart devices. Some people need no active heart treatment beyond monitoring.

Hearing loss may be managed with hearing aids, classroom hearing systems, or cochlear implants, depending on its severity and cause. Regular hearing assessment is especially important for children because reduced hearing can affect speech and learning.

Early support can help with speech, movement, feeding, or school difficulties. This may involve speech and language therapy, physical therapy, occupational therapy, or an individual education plan.

Growth should be recorded over time. A specialist may investigate nutrition, thyroid function, puberty, or growth hormone levels when growth is slower than expected. Any treatment for short stature needs an individual specialist assessment, particularly when hypertrophic cardiomyopathy is present.

Undescended testicles may require surgery. Skin treatment is not medically necessary for lentigines, but some people seek laser or other cosmetic treatment. Results can be incomplete, and spots may return.

Complications

Hypertrophic cardiomyopathy is the most significant potential complication. The thickened heart muscle can restrict blood flow, interfere with the heart's electrical system, or gradually reduce how well the heart works. The severity ranges from mild and stable to more serious disease requiring treatment.

Abnormal heart rhythms can cause palpitations, dizziness, or fainting. Rarely, a dangerous rhythm may occur. Personalised advice about exercise and follow-up is important when heart muscle thickening or rhythm changes are present.

Hearing loss can be permanent and may progress. Without suitable support, it can affect communication, education, work, and social participation.

Short stature and visible skin differences may affect confidence or emotional well-being. Children and adults may benefit from practical support at school or work and from contact with others who have a RASopathy.

Learning and developmental difficulties are usually managed through support rather than medical treatment. The level of help needed can change as school, work, and daily responsibilities become more complex.

Prevention

Noonan syndrome with multiple lentigines cannot be prevented through lifestyle changes because it is caused by a gene change.

Genetic counselling can explain how the condition may be inherited and what test results mean for relatives or future pregnancies. If the familial gene change is known, options such as testing during pregnancy or testing embryos created through in vitro fertilisation may be discussed. These are personal choices rather than ways to prevent the condition in someone who already has it.

Complications cannot always be prevented, but scheduled heart, hearing, growth, and developmental checks can identify changes before they cause larger problems. Following individual advice about physical activity can also reduce avoidable strain when heart disease is present.

Sun protection is still important for general skin health, but it does not prevent the inherited lentigines.

Living with it and what to expect

Noonan syndrome with multiple lentigines is lifelong. Its genetic cause does not go away, but its effects can change over time.

Café-au-lait spots may be visible in early childhood. Lentigines often appear later, increase through puberty, and remain during adulthood. The spots are generally harmless and do not need treatment unless their appearance is personally troubling.

Growth may remain below the average range. Developmental differences often become clearer during the preschool or school years, when speech, coordination, attention, and learning demands increase. Early support can improve access to education and daily activities, although each person's needs are different.

Heart findings may remain mild, become stable after a period of change, or require continued treatment. Hypertrophic cardiomyopathy can develop or become more apparent over time, so feeling well does not replace planned heart checks.

Some people live independently with few limitations. Others need continuing support for heart disease, hearing loss, education, or daily activities. Long-term outlook is shaped mainly by the severity of heart involvement and how well complications can be managed.

Adults may need continued cardiology and hearing follow-up rather than leaving specialist care after childhood. Before pregnancy, someone with the condition may benefit from genetic counselling and a heart assessment because pregnancy places extra demand on the heart.

When to get medical help

Arrange a routine appointment if you notice gradual changes such as reduced hearing, slower growth, feeding problems, school difficulties, delayed puberty, or new concerns about skin spots. These issues are not usually emergencies, but they deserve assessment.

Contact the usual medical team promptly for new palpitations, worsening breathlessness, reduced ability to exercise, swelling of the legs, or repeated dizziness. An infant who becomes sweaty, breathless, or unusually tired during feeding also needs prompt assessment.

Seek emergency help for:

These symptoms do not always mean there is a serious heart problem, but they should be assessed without delay.

- Fainting, especially during exercise
- Severe or sudden breathing difficulty

- Chest pain that is severe, persistent, or occurs with faintness
- A rapid or irregular heartbeat with collapse or marked weakness
- Blue or grey lips, severe unresponsiveness, or difficulty waking

Common questions

Is this the same as Noonan syndrome?

It is closely related but considered a distinct RASopathy. The two conditions can share facial features, short stature, heart problems, and developmental differences. Numerous lentigines, hypertrophic cardiomyopathy, and hearing loss are particularly associated with Noonan syndrome with multiple lentigines.

Can someone have it without lentigines?

Yes. Lentigines often do not appear until later in childhood and may take years to become numerous. Diagnosis in a young child may instead be based on heart findings, facial or growth features, family history, and genetic testing.

Do the dark spots turn into skin cancer?

The typical lentigines are benign, meaning they are not cancer. However, a spot that changes rapidly, bleeds, develops several colours, or looks different from the other spots should be checked in the same way as any changing skin lesion.

Can I pass it on to my children?

A person with a disease-causing gene change usually has a 1 in 2 chance of passing that change on with each pregnancy. The severity cannot be predicted from inheritance alone, even among relatives with the same gene change.

Can people with this condition exercise?

Many can take part in physical activity, but the safest type and intensity depend on heart muscle thickness, heart rhythm, and symptoms. A cardiology team can provide individual advice. Competitive or high-intensity exercise may need limits when significant heart disease is present.

Does it always cause learning disability?

No. Many people have intelligence within the usual range. Some have speech delay, attention difficulties, coordination problems, or specific learning needs. Hearing loss can also affect classroom progress if it is not recognised and supported.

Sources

- National Library of Medicine. MedlinePlus Genetics: Noonan syndrome with multiple lentigines . U.S. National Institutes of Health
- Orphanet. Noonan syndrome with multiple lentigines . ORPHA:500
- Sarkozy A, Digilio MC, Dallapiccola B. "LEOPARD syndrome." Orphanet Journal of Rare Diseases . 2008;3:13
- Roberts AE, Allanson JE, Tartaglia M, Gelb BD. "Noonan syndrome." The Lancet . 2013;381(9863):333-342
- Romano AA, Allanson JE, Dahlgren J, et al. "Noonan syndrome: clinical features, diagnosis, and management guidelines." Pediatrics . 2010;126(4):746-759