CONDITION

Multiple lentigines syndrome

Multiple lentigines syndrome is an inherited condition that causes many dark skin spots and can affect the heart, hearing, growth, and development.

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

BODY SYSTEM
Skin, heart and circulation, hearing, growth, and reproductive system

MAIN SYMPTOMS
Many lentigines, heart changes, short stature, hearing loss

WHAT CAUSES IT
Inherited changes in RAS-MAPK pathway genes

HOW IT IS DIAGNOSED
Clinical assessment, heart tests, hearing tests, and genetic testing

MAIN TREATMENT
Heart care, hearing support, skin care, and developmental support

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

IS IT AN EMERGENCY?
No, except fainting, chest pain, or severe breathing trouble

LONG-TERM OUTLOOK
Many lead active lives with lifelong specialist monitoring

Overview

Multiple lentigines syndrome is a rare inherited condition that affects several parts of the body. Medical literature often calls it Noonan syndrome with multiple lentigines , or NSML.

Lentigines are small, flat, brown or black skin spots. They resemble freckles but are usually darker and do not appear only on sun-exposed skin. People with this condition often develop hundreds or thousands of them.

The skin spots themselves are usually harmless. The condition matters mainly because it can also affect the heart, hearing, growth, genital development, and learning. The combination and severity of these features differ greatly between people, including members of the same family.

Heart involvement deserves particular attention. Some people develop thickening of the heart muscle, known as hypertrophic cardiomyopathy . Others have abnormalities of the heart's electrical system or a narrowed valve leading from the heart to the lungs.

Regular follow-up helps identify these changes even when you feel well. Early assessment can also provide access to hearing support, learning assistance, and other useful care.

Symptoms

Features may be present at birth or appear gradually during childhood. A baby may have heart or growth differences before lentigines become obvious.

The characteristic lentigines usually begin in early childhood. They often increase through puberty and may cover the face, neck, upper body, arms, and legs. The lips and other moist surfaces inside the body are usually not affected. Larger light-brown patches, called café-au-lait spots , may appear before the lentigines.

Possible features include:

Not everyone has all these features. Intelligence is often within the usual range, although some people need support with learning, speech, attention, or movement skills.

Heart changes may cause no symptoms. When symptoms occur, they can include breathlessness, reduced exercise tolerance, chest discomfort, a racing or irregular heartbeat, dizziness, or fainting.

Hearing loss may be present from birth or develop later. Signs in a child can include delayed speech, unclear speech, difficulty following instructions, or seeming not to respond to quiet sounds.

- Thickened heart muscle or other structural heart differences
- An irregular heartbeat or abnormal electrical signals on an electrocardiogram
- Shorter-than-expected height
- Hearing loss, usually involving the inner ear or hearing nerve
- Widely spaced eyes, low-set ears, or other characteristic facial features
- A broad or sunken chest
- Delayed learning, speech, or motor skills in some children
- Undescended testicles or delayed puberty in some males

Causes and risk factors

Multiple lentigines syndrome results from a genetic change affecting the RAS-MAPK pathway . This is a communication system that helps cells grow, divide, and respond to signals. Conditions involving this pathway are sometimes called RASopathies.

Most confirmed cases involve a change in the `PTPN11` gene. Changes in `RAF1` and `BRAF` can also cause the condition. Different genetic changes may be associated with somewhat different patterns, but a gene result cannot predict a person's exact future health.

The condition usually has an autosomal dominant inheritance pattern. This means that one altered copy of the gene is enough to cause it. A person with the condition has a 1 in 2 chance of passing the altered gene on during each pregnancy.

Sometimes the genetic change is inherited from a parent who has clear or very mild features. In other cases, it occurs for the first time in the egg, sperm, or early embryo. This is called a de novo genetic change.

The condition is not caused by anything someone did during pregnancy. Sun exposure does not cause the syndrome, although sunlight may make existing lentigines look darker.

Diagnosis

Diagnosis begins with a detailed medical and family history and a physical examination. A clinician looks at the pattern of lentigines and checks for heart, hearing, growth, chest, facial, and genital features.

Because the skin changes may not appear until later childhood, diagnosis can be difficult in babies and young children. Heart findings or a family history may lead to testing before the spots develop.

Assessment commonly includes:

Finding a disease-causing change in a related gene can confirm the diagnosis. However, a negative genetic test does not always rule it out. Testing may not detect every possible genetic change, and the meaning of some results remains uncertain.

A clinical genetics team can help interpret results and distinguish this condition from others that cause many pigmented spots. These include Noonan syndrome, neurofibromatosis type 1, Legius syndrome, and Carney complex.

A skin biopsy is not usually needed because lentigines can generally be recognised by their appearance.

- An echocardiogram , which uses ultrasound to examine heart structure and muscle thickness
- An electrocardiogram , or ECG, which records the heart's electrical activity
- Formal hearing tests
- Growth and developmental assessment
- Genetic testing, often using a panel of genes linked to RASopathies

Treatment and management

There is no treatment that removes the underlying genetic change. Care is directed at the particular features affecting you or your child.

Heart care is a central part of management. Follow-up may include repeat echocardiograms, ECGs, or longer heart-rhythm recordings. How often these are needed is based on age, previous findings, symptoms, and family history.

Hypertrophic cardiomyopathy may be managed with medicines, procedures, or implanted heart devices when appropriate. A narrowed pulmonary valve may sometimes be treated with a catheter procedure or surgery. Exercise advice should be based on the specific heart findings rather than the skin diagnosis alone.

Hearing loss may be managed with hearing aids, classroom listening equipment, communication support, or cochlear implants. Early hearing assessment is important for speech and language development.

Children with developmental or learning differences may benefit from speech therapy, physical therapy, occupational therapy, or tailored support at school. Growth and puberty can also be assessed over time. Undescended testicles may require surgery.

Lentigines do not usually need medical treatment. Camouflage cosmetics can reduce their appearance if desired. Laser or light-based treatments may help some people, but spots can return and treatment can cause lighter or darker skin patches. A dermatologist can explain realistic benefits and risks.

Sun protection does not stop the inherited tendency to develop lentigines. It is still useful for reducing sunburn, premature skin ageing, and ordinary skin cancer risk.

Complications

The most important possible complications involve the heart. Thickening of the heart muscle can make it harder for the heart to fill or pump normally. It may also increase the chance of abnormal heart rhythms. In some people, heart disease becomes the main long-term health concern.

Symptoms do not always match the degree of heart involvement. Someone may feel well despite a significant change on an echocardiogram, which is why planned monitoring remains important.

Other possible complications include:

Lentigines are generally benign, meaning non-cancerous. A new spot that looks different from the others should still be assessed in the same way as any unusual skin lesion. Warning changes include persistent bleeding, an irregular shape, several colours, or rapid enlargement.

Tumours have been reported in people with RAS-MAPK pathway conditions, but the cancer risk associated specifically with multiple lentigines syndrome is not fully defined. Screening should be based on the gene finding, personal history, and specialist advice rather than the number of lentigines.

- Progressive or unrecognised hearing loss
- Speech, learning, or coordination difficulties
- Delayed puberty or fertility problems in some males
- Emotional distress related to visible skin differences
- Reduced exercise tolerance caused by heart disease

Prevention

Multiple lentigines syndrome cannot be prevented through diet, exercise, medicines, or choices during pregnancy. It is caused by an inherited or newly occurring genetic change.

Genetic counselling can explain how the condition is passed on and what a test result may mean for relatives or future pregnancies. Options such as testing during pregnancy or testing embryos created through in vitro fertilisation may be available to some families. These are personal choices rather than required steps.

Routine healthy habits cannot prevent the condition, but avoiding smoking, staying physically active within any heart-related limits, and attending planned follow-up can support general and cardiovascular health.

Living with it and what to expect

Multiple lentigines syndrome is lifelong, but its effects can change with age. The lentigines usually become more numerous during childhood and puberty. They often remain visible in adulthood and may become a major cosmetic concern for some people, while others are not troubled by them.

Heart changes may be identified in infancy, childhood, or later. They can remain stable or progress, so a normal early test does not always remove the need for future review. Hearing can also change over time.

Many children attend mainstream school, sometimes with support for hearing, speech, attention, or learning. Many adults work, form relationships, and live independently. The amount of medical support needed is mainly shaped by heart disease, hearing loss, development, and other individual features.

Visible lentigines can lead to unwanted questions or self-consciousness. Practical options include skin camouflage, counselling, and contact with communities for people with genetic or visible-difference conditions.

Before pregnancy, someone with the condition may be offered genetic counselling and a heart assessment. Pregnancy places extra demand on the heart, so the care plan is guided by any cardiomyopathy, valve problem, or rhythm disturbance.

Routine follow-up commonly involves cardiology, hearing, growth, development, and genetic review. Dermatology, endocrinology, reproductive care, or mental health support may be added when relevant.

When to get medical help

Arrange a routine medical appointment if you notice possible features of the condition, especially many lentigines together with short stature, hearing problems, heart findings, or a family history. This does not confirm the diagnosis, but it may justify assessment.

If you already have the condition, seek earlier advice for:

Get urgent medical help for fainting, particularly during exercise, or for a sustained fast or irregular heartbeat with dizziness.

Call emergency services for severe breathing difficulty, severe or persistent chest pain, collapse, or a person who is unresponsive. These symptoms can have several causes, but they require immediate assessment.

Routine surveillance appointments are different from urgent care. Do not wait for the next planned review if significant new heart symptoms develop.

- New breathlessness, reduced stamina, or frequent palpitations
- Dizziness or near-fainting
- A change in hearing
- Concerns about a child's speech, learning, growth, or puberty
- A skin spot that bleeds, changes rapidly, or looks unlike the others

Common questions

Are lentigines the same as freckles?

No. Both are flat, pigmented spots, but freckles usually become darker with sun exposure and may fade when sunlight is limited. Lentigines tend to remain present and can occur on areas that receive little sun.

Are the dark spots cancerous?

The typical lentigines in this condition are benign. They do not usually become skin cancer. Any spot that changes rapidly, bleeds, develops several colours, or looks different from the others should still be checked.

Is multiple lentigines syndrome contagious?

No. It is caused by a genetic change and cannot spread through touch, saliva, sex, or shared belongings.

Will my child definitely have heart problems?

Not everyone develops the same heart findings. However, heart involvement is common enough that assessment and continued monitoring are important, even when a child has no symptoms.

Can the lentigines be removed?

Cosmetic camouflage, laser treatment, or other light-based procedures may make some spots less visible. Results are not always permanent, and treatment can alter skin colour. Removing spots does not affect the condition elsewhere in the body.

Can I pass the condition to my children?

A person with an autosomal dominant gene change has a 1 in 2 chance of passing it on during each pregnancy. The severity in a child cannot be predicted from the parent's symptoms.

Sources

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