

# WHAT ARE CAFÉ-AU-LAIT SPOTS AND DO I NEED TO BE CONCERNED?

This resource is for families who are referred to a specialist due to multiple skin spots. Many children who are evaluated for multiple skin spots do not receive a definitive answer at their first evaluation. This does not necessarily mean an underlying condition does not exist; it simply means a diagnosis cannot yet be confirmed. For many conditions associated with skin spots, features develop over time, so ongoing follow-up is necessary.



## WHAT ARE CAFÉ-AU-LAIT SPOTS?

Café-au-lait spots or macules (CALs or CALM) are flat, colored spots on the skin. They are commonly referred to as “birthmarks”, but are often not present at birth. The name café-au-lait spot is derived from the French term for coffee (café) with milk (lait) because they usually have a light brown color. These spots are always darker than the surrounding skin regardless of ancestry or race.

## WHY ARE CAFÉ-AU-LAIT SPOTS IMPORTANT?

Approximately 10% of the general population has one or two café-au-lait spots. However, having six or more café-au-lait spots (referred to as multiple CALs) is rare. Multiple café-au-lait spots alone do not lead to any health problems but may be associated with a number of different conditions that could cause other medical issues. Therefore, your physician may monitor your child and be suspicious in certain situations, such as if the number of spots exceeds five, additional spots appear over time, or your child has other physical, medical, or developmental concerns.

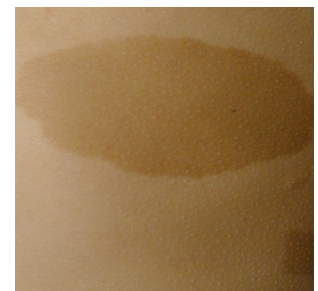
The most common condition associated with multiple CALs is called neurofibromatosis type 1 (NF1). Other conditions may look like NF1 so it is important to see a specialist who can make an accurate diagnosis.

## WHAT IS NEUROFIBROMATOSIS TYPE 1 (NF1)?

Neurofibromatosis type 1 (NF1) is a genetic condition that causes tumors to grow on nerves throughout the body, in addition to a variety of other features. When multiple CALs are present, doctors most commonly think about NF1, although these spots do sometimes appear in other related conditions, which are mentioned below. NF1 occurs in approximately one in every 2,500 individuals.

Individuals with NF1 almost always have six or more café-au-lait spots. CALs typically develop in the first few years of life and are usually the first noticeable sign of NF1. A specialist will evaluate the number of CALs greater than 0.5cm in children before puberty and the number greater than 1.5cm in adolescents and adults after puberty.

There are other signs of NF1 that may appear with time and may not be recognized without the aid of a trained medical professional. The other associated features may cause symptoms and potential medical issues which need monitoring. Therefore, if someone has multiple CALs or other signs of NF1, they should be followed for these concerns.



## HOW DO I KNOW IF MY CHILD HAS NF1?

Some of the most frequently observed features of NF1 also serve as criteria for medical professionals to make a diagnosis. A diagnosis of NF1 can be given if an individual has two or more of the following:

### 1. Six or more café-au-lait spots (CALs) or macules (CALM) \*

- CALs are light brown spots of a certain size on the skin.
- Some CALs may be present at birth, but most develop in infancy and early childhood.

### 2. Freckling in the axillary (under the arms) or inguinal (groin) areas \*

- Skin-fold freckling typically develops around 2 to 5 years of age.

### 3. Two or more neurofibromas of any type, or one plexiform neurofibroma

- Neurofibromas are benign nerve tumors and are the most common type of growth in NF1. Neurofibromas are most evident on or just underneath the surface of the skin, but may occur in any nerve of the body. Neurofibromas can appear at any age, although they most often develop during adolescence and pregnancy.
- Plexiform neurofibromas are more complex nerve tumors and tend to grow more widely on or under the skin as well as in deeper areas of the body. Unlike other neurofibromas, plexiform neurofibromas need to be watched more closely for the increased risk of cancer (malignancy). Plexiform neurofibromas are typically present at birth but may not be visible early on.

### 4. Two or more Lisch nodules or two or more choroidal abnormalities

- Lisch nodules are darkly colored bumps on the iris (colored circle) of the eye that do not affect vision and typically develop in mid-late childhood. An eye doctor uses a bright light with a microscope (called a slit lamp) to detect these because they are often too small to be seen on routine examination.
- Choroidal abnormalities occur within the vascular (blood vessel) layer of the eye (choroid). These abnormalities do not interfere with vision and are only seen with specialized equipment used by eye doctors.

### 5. Optic Pathway Glioma (OPG)

- OPGs are tumors that occur along the visual pathway in the brain. These are the most common type of brain tumors in NF1 and occur in approximately 20% of individuals, although only about 1/3 of individuals with an OPG requires treatment. They typically develop before the age of 6 years. Vision loss or an early growth spurt/early onset of puberty can be the first sign of an optic pathway glioma. Yearly eye exams are recommended for children with NF1 and for children in whom NF1 is suspected but a diagnosis is not yet confirmed.

### 6. A distinctive bone lesion such as: sphenoid wing dysplasia; anterolateral bowing of the tibia (tibial dysplasia); or pseudarthrosis of a long bone

- These findings are typically present at birth, but may not be noticed immediately.
- Sphenoid dysplasia involves an abnormality in the structure of the eye socket and often does not cause significant concerns.
- Tibial dysplasia is curving of the lower leg that may increase the risk for fractures with poor healing.
- Pseudarthrosis is a weakened area of a bone that can result from poorly healed fractures.

### 7. A pathogenic NF1 variant

- Genetic testing identifies a change or variant (previously called a mutation) in the gene known to cause NF1.

### 8. A parent with NF1 based on diagnostic criteria

- Approximately half of individuals with NF1 have a parent with NF1.

If an individual has two or more of the diagnostic criteria above, a diagnosis of NF1 is confirmed. However, at young ages, many of these features are not present. Some doctors and families take the “wait and see” approach to monitor the child over time to see if additional features of NF1 develop. Genetic testing may also be an option.

\*At least one of the two pigmentary findings (café-au-lait spots or freckling) should be bilateral (present on both sides of the body).



## Genetic testing

Genetic testing for NF1 is available. If your healthcare provider suspects NF1, a genetic test may be recommended to look for the underlying genetic change in the gene that causes NF1. Testing is typically performed by analyzing the *NF1* gene in a blood or saliva sample and may include testing for other conditions that have similar features. Genetic testing does not detect all individuals with NF1, therefore a normal test result does not exclude the possibility of having the condition. In most cases, genetic testing cannot predict what features of NF1 will be present or the severity of those features. Talk to your medical provider or genetic counselor for more information.

## Other symptoms of NF1 may include:

- Large head size (macrocephaly)
- Height less than expected based on height of parents (short stature)
- Speech and/or language delays
- Hypotonia (low muscle tone) and increased flexibility (joint hypermobility) which may lead to delays in motor development or fatigue/pain with activity
- Learning disabilities (usually not significant intellectual disability)
- Attention deficit disorder with or without hyperactivity (ADD/ADHD)
- Curvature of the spine (scoliosis)
- High blood pressure (hypertension)

NF1 is an extremely variable condition. The severity ranges from very mild cases in which the only signs of the condition in adulthood may be multiple café-au-lait spots and a few neurofibromas, to more severe cases in which more serious complications develop. The signs and symptoms of NF1 may progress slowly over time and may even go undetected for many years. Individuals with NF1 need to be monitored over time at intervals deemed appropriate by their healthcare provider.

## DOES NF1 RUN IN FAMILIES?

In 50% of individuals with NF1, there is no family history of the condition. In this case, NF1 is a new, or *de novo*, genetic change; therefore, a negative family history of NF1 does not exclude the diagnosis.

An individual with NF1 has a 50/50, or 1 in 2, chance of having a child with NF1. If there is no family history, the parents of a child with NF1 have a less than 1% chance to have another child with NF1. Talk to your doctor or genetic counselor if you have specific questions.

## CAN MULTIPLE CALS BE CAUSED BY SOMETHING OTHER THAN NF1?

Although NF1 is the most common cause of multiple CALS, they are also a feature of other conditions including Legius syndrome, Noonan syndrome with multiple lentigines (formerly called LEOPARD syndrome), chromosome abnormalities, McCune-Albright syndrome, *NF2*-related schwannomatosis, and others. Each of these conditions has features that overlap with NF1, but other features that distinguish them. Rarely, multiple CALS can be seen as an isolated feature and not associated with an underlying condition.

A specialist in NF is often required to determine if multiple CALS are isolated or caused by a genetic condition.



## WHAT CAN I DO?

### Follow-up with your child's healthcare provider

Although a diagnosis may not be able to be confirmed right away, it is important to follow your healthcare provider's recommendations and realize that additional signs or symptoms of NF1 might appear with time, eventually leading to a confirmed diagnosis.

Recommendations may include the following:

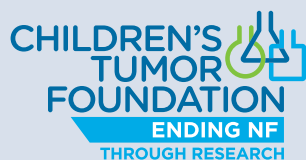
- Schedule an eye exam with a specialized eye doctor (ophthalmologist) annually
- Note any changes in current symptoms or the development of new symptoms
- Keep a list of questions to ask at your next clinic visit
- Continue to follow with a trained medical professional such as a pediatrician, geneticist, dermatologist, neurologist, or NF-specialty center

### Take care of yourself

For many parents, this is a scary time and it may be helpful to talk with someone. If you are feeling overwhelmed, reach out to your NF providers or seek professional counseling.

Some people may want more information about NF1. You should determine if this will be helpful to you at this time. Sometimes detailed information can be overwhelming, especially since the internet may have incorrect information or highlight the most severe scenarios. If you do search for additional information, please visit [www.ctf.org](http://www.ctf.org), or ask your healthcare provider for other reliable websites and resources.

To locate an NF Clinic in your area, go to: [ctf.org/doctor](http://ctf.org/doctor).



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