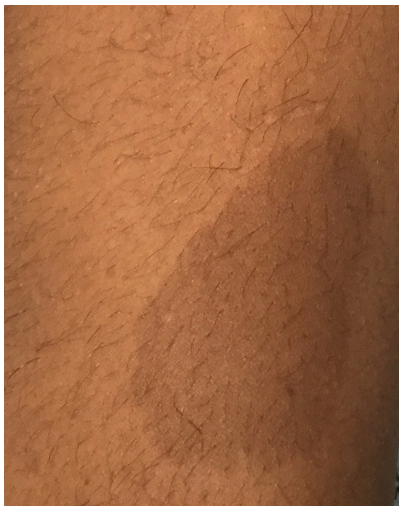
WHAT ARE CAFÉ-AU-LAIT SPOTS
AND DO I NEED TO BE CONCERNED?

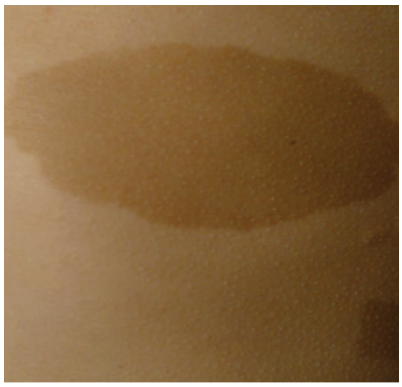
CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

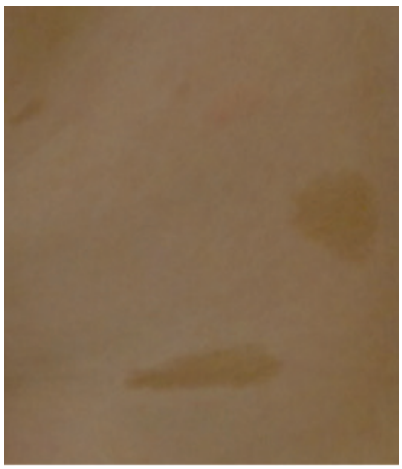
This resource is for families who are referred to a specialist due to multiple skin spots. Many children who are evaluated for multiple skin spots do not receive a definitive answer at their first evaluation. This does not necessarily mean an underlying condition does not exist; it simply means a diagnosis 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, pigmented 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 more than 5 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 (NF)?

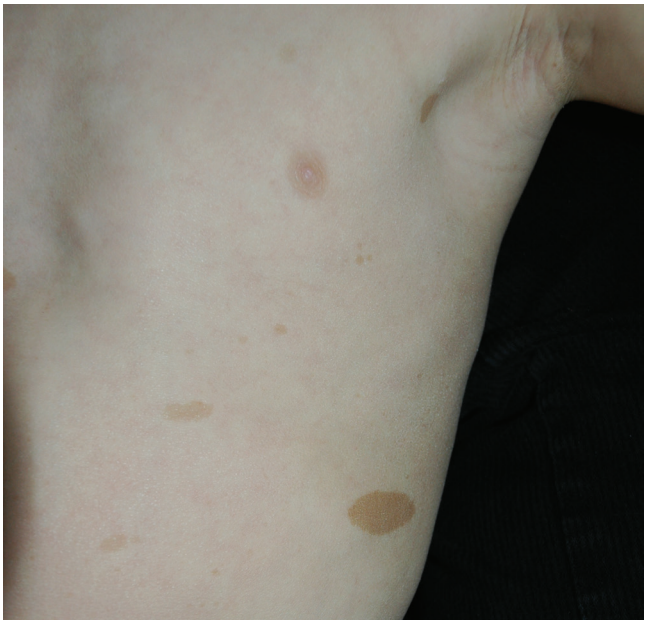
Neurofibromatosis (NF) is a term for three separate genetic conditions: neurofibromatosis type 1 (NF1), neurofibromatosis type 2 (NF2), and schwannomatosis. NF causes tumors to grow on nerves throughout the body, in addition to a variety of other features. When multiple CALS are present, doctors most commonly think about NF1 whereas NF2 and schwannomatosis have different symptoms.

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. The size of the spots varies, but most are greater than 0.5 cm in babies and children and greater than 1.5 cm in adolescents and adults.

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?

Clinical diagnosis



NF1 occurs in approximately one in every 3,000 individuals. Some of the most frequently observed features of NF1 also serve as criteria for medical professionals to make a diagnosis. An individual must have two or more of these features to have a clinical diagnosis of NF1:

1. Six or more light brown (café-au-lait) spots on the skin
   - Some CALS may be present at birth, but most develop in infancy and early childhood.
2. Freckling under the arms or in the groin area
   - Freckling typically develops at 3 to 5 years of age.
3. Presence of two or more growths (neurofibromas) or one or more complex tumor (plexiform neurofibroma)
   - Neurofibromas are the most common type of growth in NF1. They are benign and typically develop on or just underneath the surface of the skin, but may also occur in deeper areas of the body. Although they can appear at any age, neurofibromas most often develop during adolescence and pregnancy.
   - Plexiform neurofibromas grow more diffusely under the skin or 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. Pigmented bumps on the iris of the eye (Lisch nodules)
   - Lisch nodules do not affect vision and typically develop in late childhood or adolescence. 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 exam.
5. Tumor on the optic nerve (optic pathway glioma)
   - Optic gliomas typically develop before the age of 6. Vision loss or an early growth spurt/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. Skeletal abnormalities such as bowing of a bone (long bone dysplasia) or an underdeveloped eye socket (sphenoid dysplasia)
   - These findings are typically present at birth, but may not be noticed immediately.
   - Tibial or other bone dysplasia may increase the risk for fractures.
   - Sphenoid dysplasia often does not cause significant concerns.
7. Family history of NF1
   - Approximately half of individuals with NF1 have a first degree relative (parent, child, or sibling) with NF1.

If an individual has two or more of the above features, a clinical 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. Other times, families choose to pursue genetic testing.

Genetic testing

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
- Increased flexibility (joint hypermobility) which may lead to delays in motor development or fatigue/pain with activity
- Learning disabilities (usually not mental retardation/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 at risk need to be monitored over time at intervals deemed appropriate by their doctor.

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, 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 doctor

Although a diagnosis may not be able to be confirmed right away, it is important to follow your doctor's recommendations and realize that additional signs or symptoms of NF1 might appear with time, 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 your child's symptoms or the development of new symptoms
- Keep a list of questions to ask at your next doctor's 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 parents 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, or ask your doctor for other reliable websites and resources.

To locate an NF Clinic in your area, go to: http://www.ctf.org/understanding-nf/find-doctor.

CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

Written by:
Heather Radtke, MS, CGC | Children's Tumor Foundation, Medical College of Wisconsin, UW Cancer Center at ProHealth Care

Cristin Griffi s, MS, CGC | Medical College of Wisconsin

Photos submitted by: Donald Basel, MD and Gina Lewis, RN, MSN, PNP | Medical College of Wisconsin

This document has been reviewed and approved by the 2018 CTF Clinical Care Advisory Board.

1-800-323-7938 | ctf.org
Follow us online at @childrenstumor