NF Clinical Care Options

Bridging the Gap of NF Clinical Expertise

Neurofibromatosis 1 (NF1)

The Bottom Line

- NF1 is a medical condition that causes tumors of the nervous system and other complications.
- There is no single correct way to manage NF1. However failure to recognize NF1 or suboptimal care can lead to undesirable outcomes. These may be preventable with appropriate clinical management
- It is critical that NF1 be managed by an experienced NF1 clinical team. Experienced NF1 practitioners can also partner with clinicians in the community with limited NF experience
- NF Care Options CAN help people with NF and their physicians identify appropriate NF care
- NF Care Options CANNOT replace medical care and guidance from an experienced NF clinic

What is NF1 and Who is Affected?

- NF1 is the most common form of NF. It affects 1:2,500 births. Roughly half of NF1 cases are inherited; half are not. NF1 can affect ANY family.
- NF1 causes tumors to grow on nerves in different parts of the body and in the brain.
- NF1 can cause learning disabilities, bone abnormalities and a multitude of other complications.

When is NF1 Diagnosed and How Does it Develop?

- NF1 is most commonly diagnosed in young children, but it can be diagnosed at any age.
- The tumors and complications of NF1 can appear – or progress – throughout life.
- NF1 may require different clinical management approaches at different stages of life.

NF1 Notes

It is critical that NF1 is managed by an experienced NF1 clinical team, either directly or by partnering with clinicians in the community with more limited NF1 experience. For a list of NF1 clinics, see Resources Section I.

Signs of Possible NF1 - What To Look For

If someone develops these features, they may have NF1:

- Dark pigmented marks (called café-au-lait macules) on the skin
- Freckling in armpits, groin or skin folds
- Skin bumps called dermal neurofibromas

Clinical Diagnosis of NF1

A clinical diagnosis of NF1 requires TWO or more of the following to be present:

- Six or more café-au-lait macules >5 mm diameter (before puberty); or >15 mm (after puberty)
- Two or more neurofibroma tumors of any type, or one plexiform neurofibroma tumor
- Multiple freckles in the armpits or groin
- A distinctive abnormality of long bones, spine or orbit (eye socket)
- An optic pathway glioma (tumor)
- Two or more Lisch nodules (raised pigmented spots on the iris of the eye)
- A first-degree relative (parent, brother/sister) with clinically diagnosed NF1

SIDEBAR: *Do café au lait spots always mean NF1? NO they do not. These can signify some other condition (e.g. Legius Syndrome or Russell-Silver syndrome). This is another reason for suspected NF1 patients and their doctors to connect with an NF1 clinic. For a list of NF1 clinics and contact information, see Resources Section I.*

Tumor Types Seen in NF1

Not everyone with NF1 will develop all of the following tumor types, but people with NF should be alert to the possibility that these tumors may appear. It is critical that NF1 be managed or guided by an experienced NF1 clinic. For a list of NF1 clinics and contact information, see Resources Section I.

Dermal (or Cutaneous) Neurofibromas

Dermal neurofibromas include both subcutaneous (under the skin) and cutaneous (on top of the skin). The former can appear in toddlers, whereas the latter don't show up before puberty, often much later. They can number from a handful to hundreds. Benign; no cancer risk, but can be disfiguring and tender. People may opt for removal by surgery or electrodessication.

Plexiform Neurofibromas

Grow internally on nerves in 30%-50% of NF1 cases and can arise in childhood and grow throughout life, affecting health or quality of life. They may require surgery, although this can cause nerve damage and must be done by a surgeon experienced with NF1, as although plexiform neurofibromas are largely benign they can become malignant. Complete removal of these tumors is difficult and they can re-grow after surgery.

Malignant Peripheral Nerve Sheath Tumors (MPNSTs)

About 10% of people with NF1 will develop an MPNST in their lifetime, usually from an existing plexiform neurofibroma. Pain in a plexiform tumor is often the first sign of an MPNST. NF1 MPNSTs should only be treated by an oncology team experienced in sarcoma care.

Plexiform tumor surgery and clinical management should only be done by a surgeon experienced in NF1. These tumors can become malignant. Pain and rapid growth in a pre-existing tumor is often the first sign of malignancy and should be reported to your doctor IMMEDIATELY. NF1 MPNSTs are complex and MUST be managed by an experienced sarcoma oncologist.

Optic Nerve Pathway Gliomas and Other Brain Tumors
Optic pathway gliomas (OPGs) affect about 15% of children with NF1. These tumors may occur in children without NF, but need special clinical management when they occur in NF1. The first symptom may be reduced vision, a bulging eye or eye deviation. The optic pathway of children with NF1 should be evaluated at least annually by an experienced NF1 clinician and an ophthalmologist. Any abnormality detected by these professionals should trigger an MRI of the brain and orbits; clinical management must be guided by an experienced NF clinic. About half of OPGs will need intervention; chemotherapy is usually effective. Other brain tumor types can occur in NF1 and, as in the general population, are managed based on symptoms and progression.

Other Tumor Types Occasionally Seen In NF1
Less common tumors of NF1 include gastrointestinal stromal tumors (GISTs); pheochromocytoma of the adrenal medulla; juvenile xanthogranulomas (not rare); glomus tumors of the nailbed (not so rare); and giant cell granulomas (pretty rare). These rare tumor types should be managed by an experienced NF1 clinic.

Breast Cancer and NF1
Women with NF1 have a 2-4 fold increased risk of breast cancer and should consider starting annual breast exams earlier than general guidelines recommend.

NF1 Notes

Individuals with NF1 are predisposed to other medical complications including those listed below.

Other Medical Complications of NF1

Learning, Behavioral and Social Difficulties
Affect around two-thirds of NF1 cases. Usually diagnosed in childhood, but with lifelong impact. Usually respond to established medications used for children with parallel difficulties to those seen in NF1 (e.g. stimulants ADHD).

Bone Abnormalities
Affect about a quarter of people with NF1. Usually diagnosed in childhood; can include isolated long bone dysplasia and/or scoliosis. Require NF1 specialist orthopedic care.

Seizures and Epilepsy
Affect around 6-9% of NF1 cases - more than in the general population (4%). May require different treatment than in general population cases.

Headaches and Migraines
Affect many children and teens with NF1. The causes are not well understood. May respond to medicines used in the general population.

Other Medical Complications of NF1

Hypertension and Renal Artery Stenosis
May respond to established medications used in the general population. Note: hypertension with severe headaches may be due to a pheochromocytoma (see above) which should be investigated by an experienced NF1 clinic.

NF1 can cause a range of complications. Children with NF1 should be evaluated annually, and adults at least every three years, by an experienced NF1 clinical team, to assess for complications and tailor a treatment plan as needed. For a list of NF1 clinics and contact information, see Resources Section I.

New Treatment Options for NF1

There are no effective treatments for NF1, but medical research is advancing and potential treatments are being tested in clinical trials. Participating in an NF1 clinical trial is an opportunity to be involved in helping to evaluate promising treatments. More information on current NF clinical trials is available at http://nfcenter.wustl.edu/research/nf-clinical-trials/. One more good reason to connect with an NF1 clinic is that they can be a source of information on NF1 trials.

NF1 and Genetics Considerations

NF1 is caused by a gene mutation. This can happen spontaneously in any family, or it can be inherited by a child whose parent has NF1. A genetic test is not required to diagnose NF1, but if a genetic test is done, it MUST be interpreted by an experienced NF1 physician. If you have NF1 and are considering starting a family, you may have questions about passing NF1 on to your children. To learn more, contact an NF specialist clinic and schedule a discussion with a genetic counselor.

NF1 Notes

NF Care Options is intended for those with confirmed or suspected NF and their physicians. It provides an avenue for connecting with NF specialists to most effectively manage this complex genetic disorder. NF Care Options is not intended as a substitute for medical advice. More information is available at www.nfnetwork.org.

Neurofibromatosis Resources

I: How to find an NF Clinic for NF Clinical Care and Information
II: NF Clinical Trials and Clinical Research
III: National NF Support Organizations
IV: Further Reading on NF

I. How to find an NF Clinic for NF Clinical Care and Information

The following is a list of some of the clinics in the United States that offer experienced NF clinical care. All of these clinics have notified the NF Network that they are happy to be contacted by NF patients or families, or by clinicians seeking to learn more about NF or refer a patient.

If you need guidance in making initial outreach to a clinic, you are encouraged to contact the NF Network at (630)-510-1115 or email: admin@nfnetwork.org

All of the clinics listed below see a large number of NF patients. The staff members of these clinics are experienced and knowledgeable about NF. Some of these clinics will primarily see children with NF, others will mainly see adults; some clinics will have particular expertise in managing certain forms of NF or in managing specific NF complications. However these clinics are in frequent communication with each other. So if you reach out to one clinic, and they feel another clinic may be more helpful for you, they can help you connect.

All of these clinics are members of the national Neurofibromatosis Clinical Trials Consortium (NFCTC - http://www.uab.edu/nfconsortium/). This is a network of NF clinics who work together to test new treatments and clinical care approaches. Therefore these clinics will be up to date on the latest available treatments for NF.

STATE: Alabama CITY: Birmingham

University of Alabama at Birmingham
Department of Genetics
Kaul Human Genetics Building
1530 3rd Ave. S, Birmingham, AL 35294

Principal Investigator: Bruce R. Korf, MD, PhD; Study Coordinator: Elizabeth Davis, RN

Appointments and questions: 205-934-5376
Email: lvdavis@uab.edu
Website: http://www.uab.edu/medicine/genetics/

STATE: California CITY: Los Angeles

The Children's Hospital of Los Angeles (CHLA) Neurofibromatosis Clinic
The CHLA NF Clinic is coordinated through the Division of Neurology and the Division of Medical Genetics. Patients may be referred to either department. Contact information for both is below.

Division of Neurology
4650 Sunset Blvd, MS# 82, Los Angeles, CA 90027
Tena Rosser, MD
Clinic Coordinator: Lisa Betesh, RN, BSN
(323-361-3727 Mon, Tues, Thurs)
Phone: 323-361-2471
Email: trosser@chla.usc.edu; lbetesh@chla.usc.edu

Division of Medical Genetics
4650 Sunset Blvd #90, Los Angeles, CA 90027
Linda Randolph, MD
Clinic Coordinator: Tina Liu, MS, LCGC
Phone: 323-361-2178
Email: tiliu@chla.usc.edu; lrandolph@chla.usc.edu

STATE: District of Columbia CITY: Washington, DC

Children's National Medical Center: Gilbert Family Neurofibromatosis Institute
Department of Neurology
111 Michigan Avenue, NW, Washington, DC 20010

Appointments: Peter Shibuya (pshibuya@childrensnational.org, 202-476-4598) or Julie Albert (jalbert@childrensnational.org, 202-476-2359)

Questions: Roger J. Packer, MD (rpacker@childrensnational.org or 202-476-5973) or Maria Acosta, MD, NF Clinical Director (macosta@childrensnational.org or 202-476-5513)

STATE: Illinois CITY: Chicago

Ann & Robert H. Lurie Children's Hospital of Chicago
225 East Chicago, Box 30, Chicago, IL 60611

Physicians: Robert Listernick, MD; Joel Charrow, MD; Clinic Coordinator: Emily Sites, MS

Appointments and questions: 312-227-6776, 312-227-6120
Website: https://www.luriechildrens.org/en-us/care-services/specialties-services/genetics-birth-defects-metabolism/programs/Pages/neurofibromatosis-program.aspx

STATE: Illinois CITY: Chicago

University of Chicago
Pediatric Neurology MC 3055
5841 S. Maryland Avenue, Chicago, IL 60637

Physician: James Tonsgard, MD; Clinic Coordinator: Cynthia MacKenzie, RN

Appointments and questions: 773-203-2344
Email: cmackenzie@peds.bsd.uchicago.edu
Website: http://www.uchicagokidshospital.org/specialties/neurology/patient-guides/neurofibromatosis/index.html

STATE: Indiana CITY: Indianapolis

Indiana University School of Medicine
705 Riley Hospital Drive, Indianapolis, IN 46202

Physician: Wade Clapp, MD, Michael Ferguson, MD, MS, Fabio Nunes, MD; Clinic Coordinator: Cindy Dwight

Appointments and questions: 317-274-4928
Email: nfstudy@iu.edu
Website: http://www.indiananf.com/

STATE: Massachusetts CITY: Boston

Boston Children's Hospital
Multidisciplinary Neurofibromatosis Program
300 Longwood Avenue - Boston, MA 02115

Physicians: David Miller, MD, PhD (Director), Nicole Ullrich, MD, PhD (Associate Director, Director Clinical Trials), Mayra Martinez Ojeda, MD; Clinical Coordinator: Caroline McGowan, MS, CGC, LGC

Appointments and questions: 857-218-4018
Email: NFClinic@childrens.harvard.edu
Website: www.childrenshospital.org/nf

STATE: Michigan CITY: Grand Rapids

Helen DeVos Children's Hospital
Children's Outpatient Center
330 Barclay NE, Suite 203, Grand Rapids, MI 49503

Physicians: Bernard Eisenga, MD, internist; Cynthia Hingtgen, MD, neurologist; Karen VanderLaan, MD, pediatrician

Other Specialists & Support Staff: Steven Pastyrnak, PhD, child psychologist; Brittany Barber-Garcia, PhD, child psychologist; Kathleen Delp, MSW, CGC, genetic counselor; Heather Hardiman, LMSW, clinical social worker; Carol Nicholas, RN, nurse & scheduler Rosemary Anderson & Kristin Bradley, patient advocates

Appointments: 616-391-2414
Fax: 616-391-2505
Information: 616-451-3699
Clinic Hours: Thursday, 8:00-4:30 pm (adults seen in mornings only)
Website: http://www.nfsupport.org/nf-clinic--helen-devos-childrens-hospital.html

STATE: Missouri **CITY: St. Louis**

Washington University
NF Center, Washington University School of Medicine/
St. Louis Children's Hospital,
One Children's Place, St. Louis, MO 63110

Physician: David H. Gutmann, MD, PhD; Clinic Coordinator: Anne C. Albers, PNP

Appointments and questions: 314-454-6120, 314-454-2523
Website: http://nfcenter.wustl.edu

The Washington University NF Center website has a wealth of NF information including further information on the medical complications of NF, up to date information on NF clinical trials and information for physicians seeking to make NF patient referrals. http://nfcenter.wustl.edu

STATE: New York **CITY: New York**

New York University Langone Medical Center
Hassenfeld Clinic, 160 East 32nd Street, New York, NY 10016

Director: Jeffrey Allen, MD; Co-Director: Kaleb Yohay, MD; Clinic Coordinator: Carole Mitchell, MS RN OCN CORLN

Appointments and questions: 212- 263-9695
Email: carole.mitchell@nyumc.org
Website: http://hassenfeld.med.nyu.edu/patient-care/neurofibromatosis-center

STATE: Ohio **CITY: Cincinnati**

Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue - ML 4006, Cincinnati, OH 45229-3039

Physicians: Elizabeth Schorry, MD; Brian Weiss, MD, Robert Hopkin, MD, Howard Saal, MD, Trent Hummel, MD
Clinic Coordinator: Anne Lovell, RN, MSN

Appointments and questions: 513-636-4760, 513-636-8773, 513-636-2047

STATE: Pennsylvania **CITY: Philadelphia**

Children's Hospital of Philadelphia
3400 Civic Center Blvd., Philadelphia, PA 19104

Physician: Michael Fisher, MD; Clinic Coordinator: Jenn Foster

Appointments and questions: 215-590-2800
Website: www.chop.edu

STATE: Utah **CITY: Salt Lake City**

University of Utah
Division of Medical Genetics, Department of Pediatrics
2C412 SOM, 50 N. Mario Capecchi Drive, Salt Lake City, UT 84132

Physician: David Viskochil, MD, PhD; Clinic Coordinator: Heather Hanson, BS, CCRC

Appointments and questions: 801-587-9017
Email: heather.hanson@hsc.utah.edu

II. About NF Clinical Trials and Clinical Research

As NF research makes advances, there will be an increasing opportunity for people with NF to participate in clinical trials. These will be testing the safety and effectiveness of new drugs or treatments to improve the outcome of different aspects of NF. At any time, only a limited number of NF clinical trials will be recruiting participants, so there may not always be an opportunity for participation.

It is important to discuss your interest in NF clinical trials with an experienced NF clinician to fully understand what participation means and what the outcomes might be.

1. For the latest information on ongoing NF clinical trials, vis-it the Washington University NF Center website, updated quarterly: **http://nfcenter.wustl.edu/research/nf-clini-cal-trials/**

2. For general information on what it means to participate in a clinical trial, and what the different 'Phases' of clinical trials are, visit **http://clinicalcenter.nih.gov/participate.shtml**

III. National NF Support Organizations

There are national organizations that can provide a range of resources for individuals with NF and their families, and offer a way for those affected by NF to connect with each other. These organizations also support NF research, both with direct funding, and indirectly by advocating the federal government to support NF research. People with NF and their families can find it very empowering to connect with each other, and to participate together in NF awareness and research fund-raising. You are encouraged to explore these organizations' websites and contact them if you wish to learn more.

Neurofibromatosis Network
www.nfnetwork.org
213 S. Wheaton Ave, Wheaton, IL 60187
Phone: (630)-510-1115
Email: admin@nfnetwork.org

About: *The leading national organization advocating for federal funding for NF research and the development of local NF organizations. Programs include educational materials for those affected by NF, including where to find NF care; advocacy to promote federal funding for NF research; an annual NF Camp for children with NF; and dissemination of information about NF medical research.*

NF Network Regional Affiliates

Neurofibromatosis Arizona
www.nfarizona.org

Neurofibromatosis California
www.nfcalifornia.org

Neurofibromatosis Central Plains
www.nfcentralplains.org

Neurofibromatosis Michigan
www.nfsupport.org

Neurofibromatosis Midwest
www.nfmidwest.org

Neurofibromatosis Northeast
www.nfincne.org

Washington State NF Families
www.wsnfsupport.org

Children's Tumor Foundation
www.ctf.org
120 Wall Street, 16th Floor, New York, NY 10005
Phone: (212)-344-6633 or toll free (1-800)-323-7938
Email: info@ctf.org

IV. Further Medical Reading on NF

NF is diagnosed by the appearance of specific physical symptoms. The recognized clinical critieria for the different forms of NF are described in the following documents.

NF1:

- National Institutes of Health Consensus Development Conference Statement: Neurofibromatosis. Arch Neurol Chicago 1988;45:575-8.
- Update: Gutmann et al. (1997) JAMA. The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. JAMA. Jul 2;278(1):51-7.

NF2:

- Gutmann et al. (1997) JAMA. The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. JAMA. Jul 2;278(1):51-7.
- Update: Baser et al. (2002) Evaluation of clinical diagnostic criteria for neurofibromatosis 2. Neurology. Dec 10;59(11):1759-65.

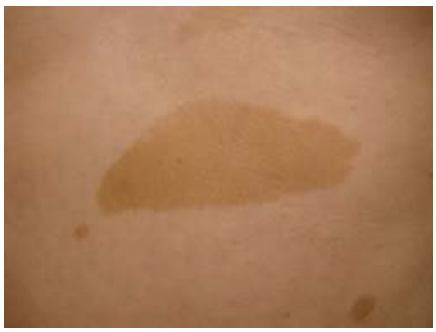
Schwannomatosis:

- MacCollin M et al. (2005) Diangnostic Criteria for Schwannomatosis. Neurology Jun 14;64(11):1838-45.
- Update: Plotkin SR et al. (2013) Update from the 2011 International Schwannomatosis Workshop: From genetics to diagnostic criteria. Am J Med Genet A. Mar;161A(3):405-16.

General reading:
For a recent book that reviews more recent updates on NF clinical guidelines, see "Neurofibromatosis in Clinical Practice". Authors: RE Ferner, SM Huson and DGR Evans. 2011. Springer-Verlag (London) Limited.

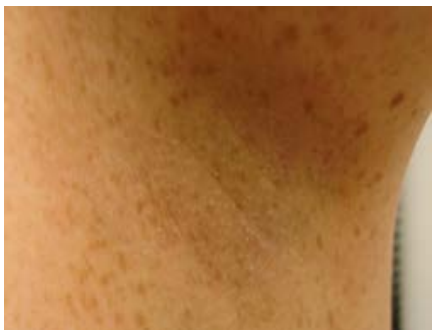
The Network Edge:
Every few months, the NF Network publishes The Network Edge, a summary of the latest publications in NF research to keep you abreast of advancements in treatment and clinical care for all forms of NF. Read The Network Edge at **http://www.nfnetwork.org/understanding-nf/the-network-edge-science-column.**

Image Glossary



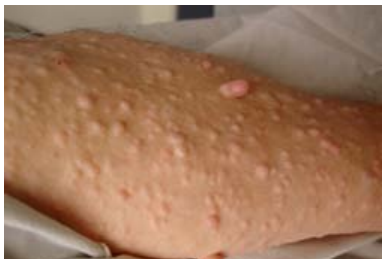
Café-au-lait Macules

Flat, darkly pigmented spots of birthmarks on the skin, typically present at birth.



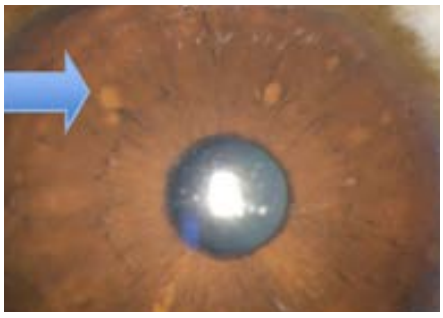
Skinfold Freckling

These freckles are commonly seen in areas of the body not exposed to the sun, like the armpits and groin. They also may be found under the neck or under the breasts in women.



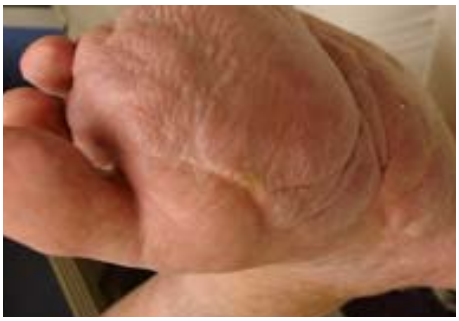
Neurofibromas

Benign growths which typically develop on or just underneath the skin but may also occur within the body. These are seen in nearly all adults with NF1. These tumors are not contagious. NF is progressive, and the majority of people will experience increases in tumor numbers and size. Regular evaluations in a coordinated care clinic specializing in NF1 is necessary to identify and address potential problems early.



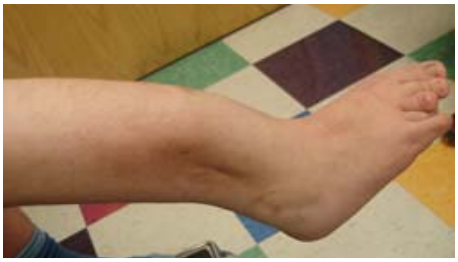
Lisch Nodules

These nodules are benign pigmented growths on the iris (the colored portion of the eye). They are usually found in both eyes but do not interfere with vision.



Plexiform Neurofibromas

25 to 30 percent of individuals with NF1 will develop a larger, more diffuse type of neurofibroma, termed a plexiform neurofibroma, which can grow to large proportions and affect adjacent structures and organs. Rarely, these tumors can become malignant.



Bone Abnormalities

Children with NF1 are prone to the development of bone deformities involving the lower leg, forearm and eye socket. Deformities of the lower leg and forearms can cause a bowing of these bones and lead to repeated fractures. Bone problems involving the eye socket can affect the way the eye sits in the socket. All of these deformities are typically noticed early in childhood and are treated promptly.