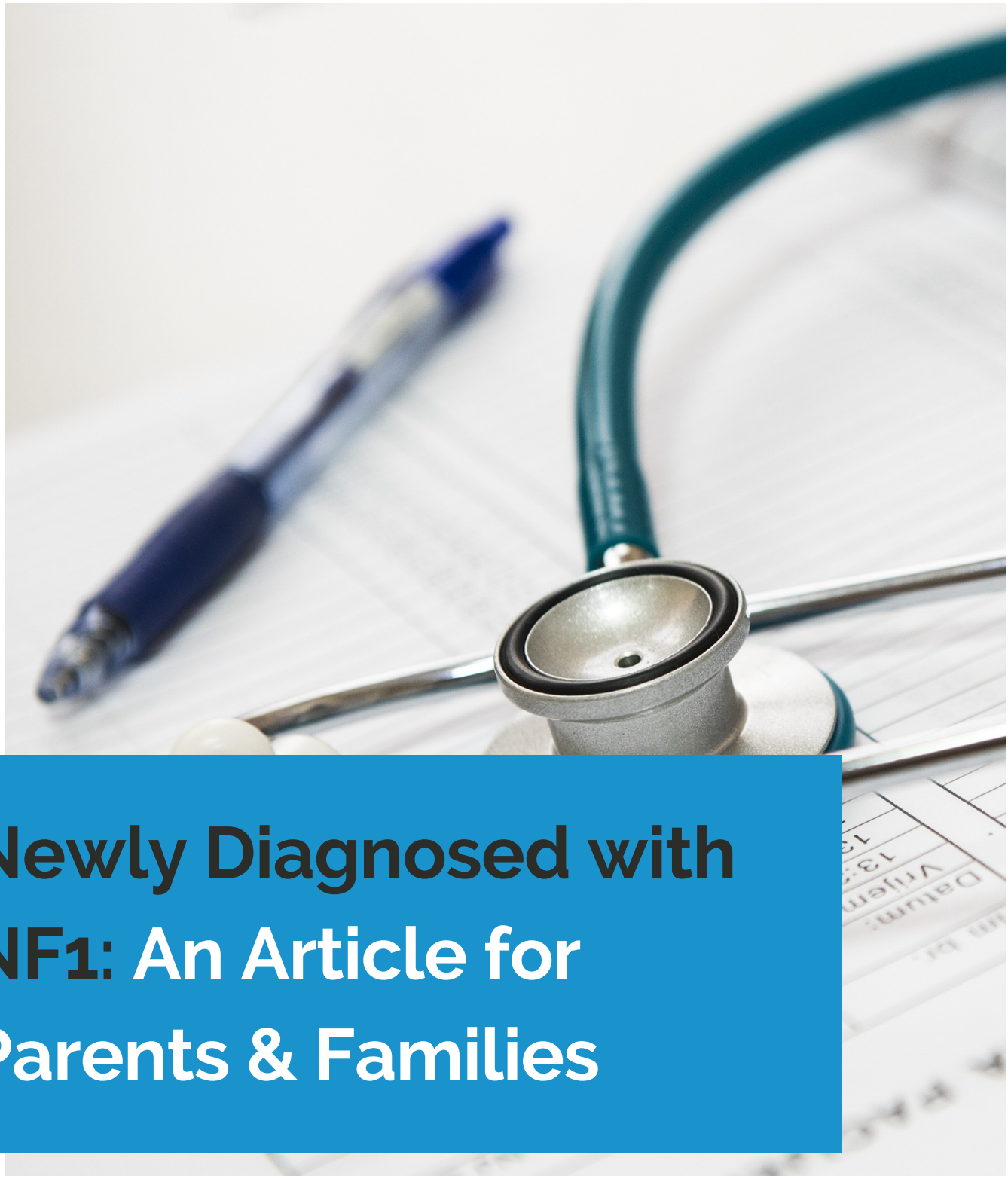

Newly Diagnosed with NF1: An Article for Parents & Families

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INTRODUCTION

Neurofiber... What?

Most people have never heard of neurofibromatosis, so when your doctor suggests this diagnosis for you or a family member, getting a grasp on what it is and what it means down the road can be scary and difficult. Even some of the basic facts and ideas are confusing and seemingly contradictory. A certain level of anxiety about any new medical diagnosis is natural, but with NF that gets magnified for many reasons. First, the diagnosis often is made in young children so what it means "down the road" has many implications. Also, there is a lot of variation in the features of NF from one person to the next so trying to predict what will happen is challenging. There can be serious tumors and cancers, there can be problems with growth and development, there can be little effect on daily life or a lot, "my doctor does not know much about NF…", and the list goes on.

Most NF-related problems take place over many years…the course of development, with chronic concerns that evolve very slowly. Then there are some types of problems that are acute and intermittently recur, and require contingency plans, for example migraine headaches or seizures. Only a few NF problems are urgent / emergent conditions, mainly relating to tumors in very sensitive areas, like the brain or spine. No one can learn everything about NF1 as a crash course. Understanding how it evolves during different phases of life takes time and experience, and often, by learning from what other people with NF have gone through. As a starting point, try to learn what are the most relevant concerns for your loved one with NF. Rely on your doctors to guide you and teach you those things. Use expert advice provided through online libraries and booklets from the national sources like CTF and NF Network. They use world renowned experts to write this material. Expect that as time goes by your understanding of the various aspects of NF1 in the broader sense will come into focus.

- Learn to look at your set of problems...look at the details.
- Learn to look at the big picture, too.
- Learn how to provide support. Expect your child to grow and develop, and figure out how best to help them do that despite the potential hurdles of NF1.

This is a brief guide to getting started at understanding NF.

NEUROFIBROMATOSIS – WHAT IS IT?

NF Type 1 (NF1), the most common form of neurofibromatosis, is a genetic disorder caused by a change in the NF1 gene resulting in decreased function of its protein product which is called **neurofibromin.** In about half of all patients with NF1 the genetic variant (mutation or other type of DNA damage) is inherited from a parent with NF1. Then there is the other half who do not have a family history of NF1. How do you get a genetic disorder if no one in your family has it? Spontaneous DNA changes are fairly common, and the NF1 gene is more prone to these spontaneous changes than most genes. If a spontaneous variation occurs in an NF1 gene in the sperm or egg that ultimately creates them, then that individual will have NF1, and potentially can pass it to their children. Most of this discussion refers to NF1.

There are other types of neurofibromatosis: NF2 and schwannomatosis. These are separate conditions, caused by mutations in other genes. They share a partial resemblance to NF1 because of the presence of benign nerve tumors, but they are separate and distinct from NF1. Many of the other features of NF1 do not occur in these other forms. There is no interconversion from NF1 to NF2.

COMMON MEDICAL PROBLEMS IN NF1

NF1 alters the development of some normal cells and tissues, especially nerve cells in the brain and peripheral nerves, also in the nerve-insulating schwann cells, and in skin, bones, and some other tissues. It also causes tumors to form, which are usually benign. Often the first things noticed in young children are multiple birthmarks (**café au lait macules**), and a tendency for excessive freckling. These tend to get more obvious throughout childhood. Although they may be easy to see, these features have little impact on overall health.

Although tumors are some of the more concerning problems, most are benign and grow extremely slowly. Some children are born with soft tumors **(plexiform neurofibromas)** although these are not always visible. Some are large and can affect appearance or can press on vital structures, thus requiring special monitoring and treatment. Benign nerve tumors in the skin **(cutaneous neurofibromas)** are less common in children and become more apparent in the teens, but some children may develop them. More important in children is the tendency for tumors to form on the nerves for vision **(optic nerve gliomas).** These can be very serious, but many of these do not cause any symptoms and do not need treatment. This is why your doctor will recommend at least annual eye exams.

Developmental problems like delays in reaching early milestones are common in NF1. Delayed motor and speech development are examples of this. Difficulty in school is also common. Learning disability (LD) especially related to reading is fairly common. ADHD like behaviors are common, affecting up to half of children with NF1. Altered bone development **(bone dysplasia)** is another important feature and sometimes the leg bones or the base of the skull behind the eyes are not well formed. Curvature of the spine **(scoliosis)** can be another manifestation of poor bone development, but can also occur due to tumors near the spine. **High blood pressure,** which is extremely rare in children, is a little more common in children with NF1. Children with NF1 should have their blood pressure checked at all appointments. There are other complications in children with NF1 but those tend to be rare.

As a person with NF1 goes through the teens and into early adult life, the type of problems change. Problems with development tend to reach a plateau, although problems like LD may linger. The risk of tumors and the types of tumors change, with optic nerve tumors rarely occurring after the mid-teens, but the risk of transformation of plexiform neurofibromas into more serious cancers increases. The risk of other cancers, for example breast cancer, or rare hormone producing tumors **(pheochromocytoma)** goes up also. About 10-20% of adults with NF1 will experience one or more of these various tumors and cancers. High blood pressure and blood vessel irregularities raise the risk of strokes to a higher level than in the general population. These are some of the ways in which NF1-related problems vary from infants to children, to teens, to adults. Therefore, the recommendations for monitoring adults with NF1 are different than monitoring in children.

Now back to the suspected or newly diagnosed NF1 patient….the initial evaluation is to determine whether it is actually NF1. There are some other conditions that cause brown spots and mimic NF1. Once the diagnosis is established, the next step is to determine which NF1-related problems exist and whether there are any urgent ones that could worsen to produce serious or permanent damage. It does take a careful assessment by an experienced clinician who is knowledgeable about NF to make those determinations. Fortunately, for many patients there are no urgent conditions that represent an immediate threat to health, and the initial focus is on learning about NF1 and developing a plan to monitor, often yearly, for new problems.

HOW TO GET EXPERT MEDICAL ADVICE

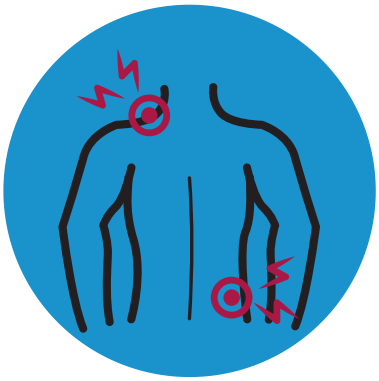
Few primary care providers, such as the pediatrician or family doctor, have seen many NF patients. But they all will have seen quite a few patients with rare or unusual disorders. They also will have an expert working knowledge of normal development (weight, height, head size, major milestones, etc). Even if they know only a little about NF, they can provide expert advice on what is normal, what is a serious or urgent problem, and how to direct consultations with experts in the field who are familiar with NF. The role of the primary care team remains very important for maintaining overall health measures such as vaccinations and screening for routine health issues. Make sure to get their help and advice and stay in close contact with them. You can also help them learn the special things related to NF for your child.

- The pediatrician / primary care doctor is essential to getting good health care for patients with rare disorders like NF.
- Evaluation by doctor with understanding and experience with NF is also very important.
- It takes a team of experts to care for most patients with NF.

SERIOUS PROBLEMS & RED FLAGS

Most of the NF1 related tumors are benign and very slow growing. Vision problems like blurriness in one or both eyes, or double vision should lead to an evaluation. Progressive headaches or headaches with nausea and vomiting, new or progressive numbness, weakness, or progressive pain complaints, especially back pain, should be evaluated. The “red flag” your doctors will watch for in these types of symptoms largely stems from their “progressive” character. A single headache is rarely a serious problem, but headaches that occur progressively more and more often can signify a serious problem. Progressive pains are another “red flag” because they can reflect nerve or tissue injury from a growing tumor. In NF there are also pains that are not tumor related, like back pain from scoliosis. Passing out spells or seizure-like events also require evaluation.

Remember, common things are common, even in individuals with NF1. Most patients with NF1 who have headaches or constipation or back pain or upset stomach will not have complications related to NF1, but rather more routine causes that can occur in anyone. However, for NF1 patients if symptoms progress and do not respond to usual treatments, then further evaluation is needed.



- NF1 patients can have common health issues like anyone.
- Some problems, especially progressively worse ones, may need more detailed testing for patients with NF1.
- Learn the “red flags” to watch for from your NF specialist.

MOST HELPFUL INITIAL TESTS

The most helpful evaluation is a good history and physical exam by a doctor knowledgeable about NF1. If enough of the textbook features are present, then NF1 gene (DNA) testing is not needed to confirm the diagnosis. There may be other reasons to consider gene testing. For example, if there are other family members who might have NF1 and should be screened. At present gene testing does not provide very much information about which features of NF1 will occur in an individual as time goes by. There are a few exceptions to this, and as more NF research is done it is expected that predictions from DNA testing will improve. Genetic testing may also be needed if family planning is desired.

Other tests depend on what problems or symptoms are present. Brain and body MRI scans are not necessary unless there is a symptom or problem that warrants them. When needed, they are safe and do not involve any radiation. Still they can be hard for young children and for some adults too, and may require sedation to get good results. Minimizing exposure to x-rays is important since x-ray radiation can damage DNA. Fortunately, there are no x-rays or radiation in an MRI. Bone X-rays and CT scans are best avoided unless there is a strong reason like scoliosis or bone deformity.

A detailed eye/ophthalmology exam by a doctor knowledgeable about NF1 is very important starting at about 18 months, and should be repeated yearly. The main reason is to evaluate vision in each eye since optic gliomas can reduce vision, and when progressive can affect other brain structures. These tumors are found in about 15% of young children with NF1. The most common eye finding is not optic glioma, but small raised dots on the iris called Lisch nodules. Almost everyone with NF1 has at least a few Lisch nodules. Fortunately, they almost never have any impact on vision.

No specific blood testing is done routinely for NF1. No x-rays or CT or MRI scans are recommended for every patient. X-rays and scans are commonly needed, but only when a specific concern is raised on the history and physical exam.

- Taking a medical history and physical exam on a regular basis is the most important "test" to monitor for NF1 related health issues.
- Monitoring regularly for the most frequent NF1-related complications: visual loss, scoliosis, high blood pressure, developmental and growth parameters is the cornerstone of NF care.
- DNA/gene testing is not always needed but can be very helpful in certain instances.
- More detailed imaging, like MRI scanning, and special blood testing is generally done to analyze specific symptoms or problems.
- Guidelines for monitoring patients with NF1 are updated and published every few years and have changed as more is learned about it.

LOOKING AHEAD: WHAT TO EXPECT

One of the most common recommendations is that every child should have regular NF1-related checkups. For children less than 5 years of age these are done every 6 months. In older children and adults exams are usually done yearly. These monitoring exams focus on the following issues:

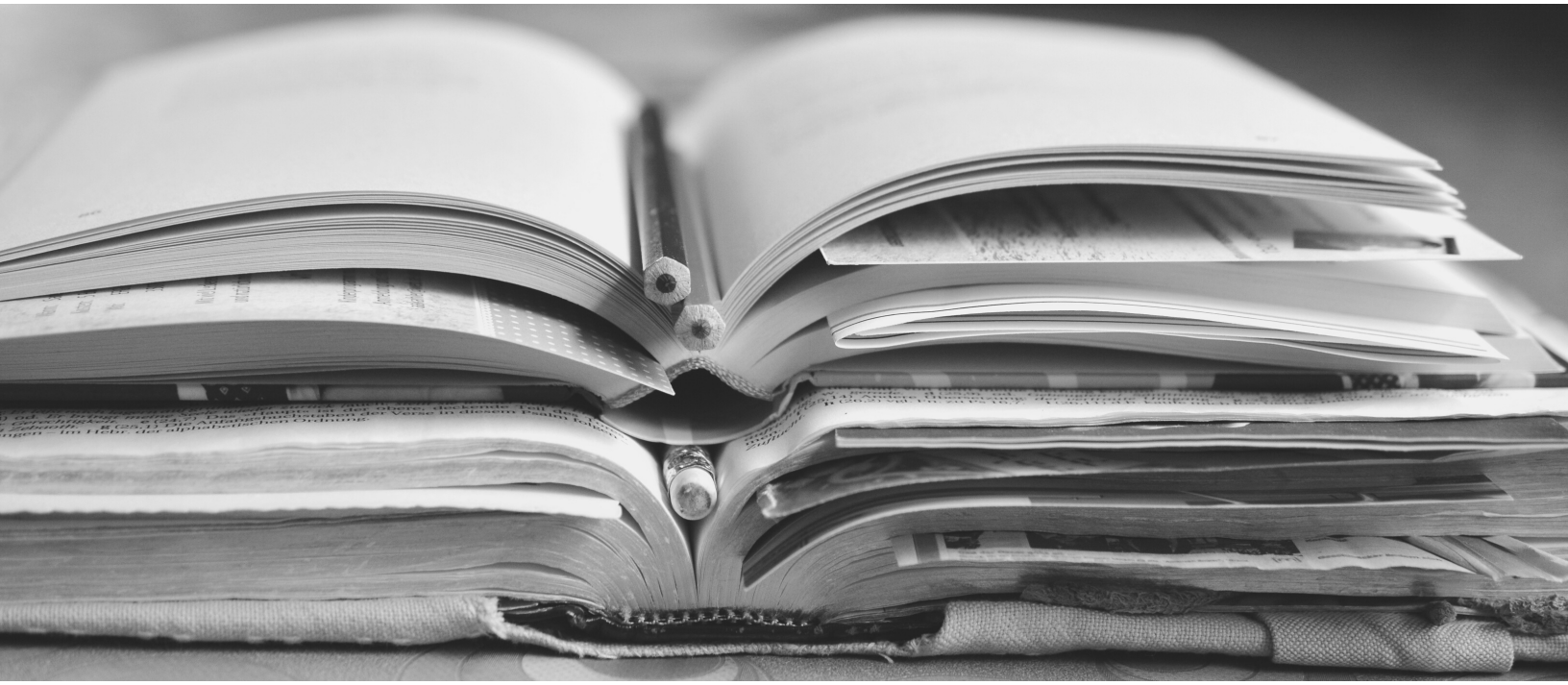
- History and Physical exam by a physician who knows about NF including:
  - Assessment for any tumors
  - Skin exams
  - Blood pressure check
  - Scoliosis check
  - Developmental assessment
- Eye exam by an ophthalmologist knowledgeable about NF at least through the mid-teens
- Assessment of academic performance and need for structured accommodations (Individualized Education Program or IEP, or 504 Plan)
- Red Flags: problems that require careful attention, sometimes reflects urgent underlying conditions.
  - New or progressive pains or headaches
  - New visual loss, double vision
  - Numbness, weakness, poor balance, or difficulty walking
  - Passing out spells or seizures
  - Visible tumors that are growing bigger over a few weeks or months
  - Unexplained problems with breathing, nausea, lower GI symptoms, weight loss

HOW MANY DOCTORS WILL IT TAKE?

Most NF1 patients will need a team of doctors including a primary care physician, an NF specialist, an ophthalmologist, and often other specialists depending on specific needs. High on the list of other specialists are neurologists, neurosurgeons, orthopedic surgeons, plastic surgeons, oncologists, and endocrinologists. For a few children a psychologist, psychiatrist, or expert in Developmental Medicine will play an important role. For a few children the team might include therapists such as speech, occupational and physical therapists. It is rare that a person needs all of these caregivers, but the main point here is that it takes a team.

TEACHING THE TEACHER

Children with NF1 commonly have trouble with reading or other skills that are important in school. Learning disabilities are found in 30-50%, and so many children with NF1 should be considered for testing to see if an Individualized Education Plan or other plan for accommodations like a 504 plan would be helpful. School systems are required by law to do this if the need is demonstrated or requested. Physicians can be helpful in initiating this, so be sure to ask them about it. These plans also include reassessments that can be very worthwhile. Behavior issues like ADHD also are found in 30-50% of children with NF1, and awareness and effective treatment can make a big difference in school performance. These issues are common enough that there is a lot of expertise in the NF community and that has led to the preparation of booklets and online information for teachers.



SOMETHING UNEXPECTED

Annual checkups, even with the most experienced physicians, do not always detect every NF-related problem, and so sometimes medical issues arise unexpectedly. Good communication with the providers, which is based in part on conscientiously keeping routine monitoring visits, and attention to red flags is important. Having emergency contact numbers and being able to contact your provider via email for non-urgent problems is helpful. Having the pediatrician or primary care provider as the first contact is often a way to get on the right track quickly. They can provide advice and also serve as an advocate to move things forward quickly if an emergency comes up.

DOES EVERY RELATIVE NEED TO BE CHECKED?

This question needs to be asked whenever a new diagnosis of NF1 is made. Parents and siblings should have some screening for obvious features like birthmarks. Also trying hard to get a complete family medical history helps a lot. NF1 does not skip generations, but there are a few people with mild versions of NF1 who are not diagnosed as children. The diagnosis only comes to light when they have a child with NF1. There are a lot of children, about 50% of newly diagnosed children, for whom the family history is negative, and most of these instances are attributed to spontaneous mutations in the NF1 gene. In some instances, doing gene testing for an NF1 gene abnormality makes it very easy to accurately test other family members who might also have inherited NF1. Since gene testing is highly accurate, it can provide a good guide to whether anyone else in the family needs regular monitoring.

WHERE CAN I LEARN MORE?

For the parents of a child with newly diagnosed NF1, figuring out what it all means can be very difficult. Any important medical problem in a child comes with a lot of anxiety and stress. The ripples that travel through a family initially, and over time as years go by, have many ramifications. The more you can learn about the important features of NF1 for your loved one, and the better you can get connected to a medical team, the better the likelihood of moving through this successfully. Also, it is important to know that NF1 is the topic of a lot of research and as years go by new treatments for many of the various NF1-related problems will emerge. So learning more and keeping up with new developments can really make a big difference.

The Children's Tumor Foundation and the Neurofibromatosis Network both provide valuable materials developed by NF experts to teach us and keep us updated. Click here for more information:

https://www.ctf.org/understanding-nf/newly-diagnosed
Educational Materials - Neurofibromatosis Network (nfnetwork.org)

ACKNOWLEDGEMENTS

We hope this information helps you develop good ways to think and learn about NF1 as you get started. We also hope it can serve as a "living document" to allow others to learn from your experience and insights. If you have important observations that can help others navigate the challenges of dealing with newly diagnosed NF1, please send us your comments to add to this document with the aim of growing the collective wisdom of our NF community.

Special thanks to Dr. Jennifer Brault, M.D. for her detailed review and excellent comments. Special thanks to Ms. Elizabeth Wright for expert editorial assistance.

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March 27, 2021

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