American Academy of Pediatrics
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CLINICAL REPORT

Health Supervision for Children With Neurofibromatosis

Guidance for the Clinician in Rendering Pediatric Care

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ABSTRACT

Neurofibromatosis 1 is a multisystem disorder that primarily involves the skin and nervous system. Its population prevalence is 1 in 3500. The condition usually is recognized in early childhood, when cutaneous manifestations are apparent. Although neurofibromatosis 1 is associated with marked clinical variability, most affected children do well from the standpoint of their growth and development. Some features of neurofibromatosis 1 are present at birth, and others are age-related abnormalities of tissue proliferation, which necessitate periodic monitoring to address ongoing health and developmental needs and to minimize the risk of serious medical complications. This clinical report provides a review of the clinical criteria needed to establish a diagnosis, the inheritance pattern of neurofibromatosis 1, its major clinical and developmental manifestations, and guidelines for monitoring and providing intervention to maximize the growth, development, and health of an affected child.

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Key Words
neurofibromatosis, neurofibromatosis 1, cafe-au-lait spots, neurofibroma, optic glioma

Abbreviations
NF1—neurofibromatosis type 1
NF2—neurofibromatosis type 2
NIH—National Institutes of Health
CLS— cafe-au-lait spot
UBO— unidentified bright object

INTRODUCTION

This clinical report was designed to assist the pediatrician in caring for the child in whom the diagnosis of neurofibromatosis has been made. The pediatrician's first contact with the child is usually during infancy. However, neurofibromatosis occasionally is diagnosed in the fetus during pregnancy, and the parents are referred for advice. Therefore, guidance is also offered for the pediatrician in advising expectant parents whose fetus is affected by neurofibromatosis.

At least 2 distinct types of neurofibromatosis are recognized: neurofibromatosis 1 (NF1 [previously known as von Recklinghausen disease or generalized neurofibromatosis]) and neurofibromatosis 2 (NF2 [previously known as either central or bilateral acoustic neurofibromatosis]). Only issues concerning the diagnosis and management of NF1 are addressed in this clinical report.[1–10]

NF1 is a multisystem disorder in which some features may be present at birth and others are age-related manifestations. It affects approximately 1 in 3500 individuals.[11,12] A National Institutes of Health (NIH) Consensus Development Conference[9,13,14] regarding NF1 demarcated the following 7 features, of which 2 or more are required to establish the diagnosis of NF1:

1. six or more cafe-au-lait spots (CLSs) equal to or greater than 5 mm in longest diameter in prepubertal patients and 15 mm in longest diameter in postpubertal patients;
2. two or more neurofibromas of any type or 1 plexiform neurofibroma;
3. freckling in the axillary or inguinal regions;
4. optic glioma (optic pathway glioma);
5. two or more Lisch nodules (iris hamartomas);
6. a distinctive osseous lesion, such as sphenoid wing dysplasia or cortical thinning of the cortex of long bones, with or without pseudoarthrosis; and
7. a first-degree relative (parent, sibling, or child) with NF1 according to the aforementioned criteria.

In addition, although areas of increased T2 signal intensity are commonly identified on MRI of the brain, they do not represent an obligatory feature of NF1 and do not have any clinical significance. Therefore, the NIH Consensus Development Conference did not recommend routine neuroimaging of the brain as a means of establishing a diagnosis of NF1.[13,14]

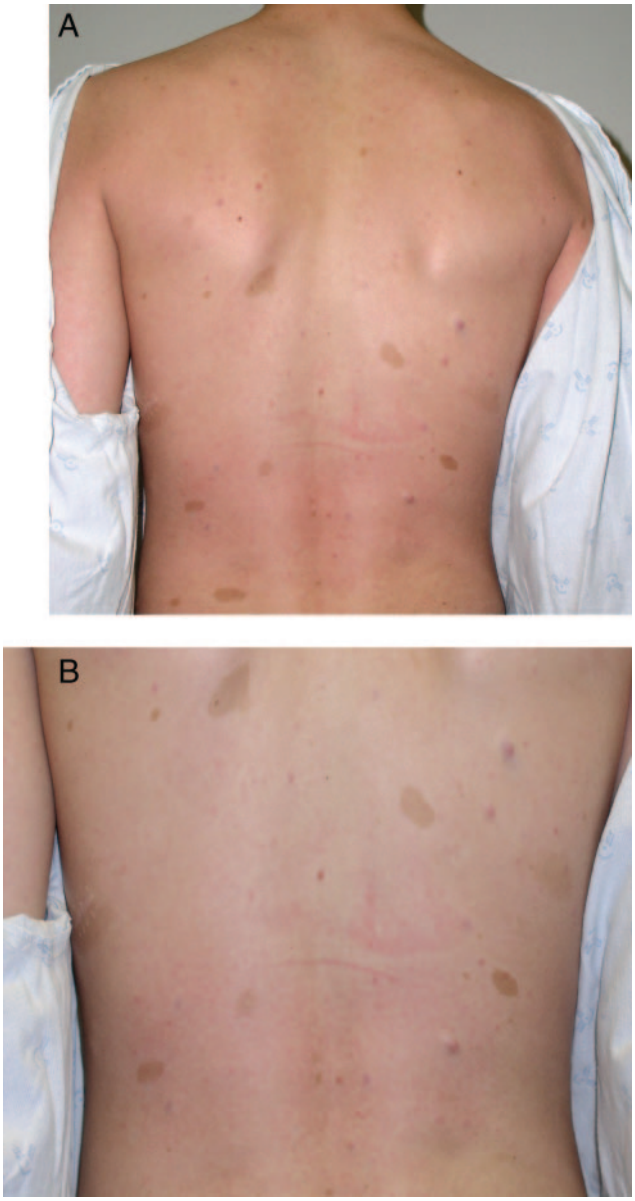

FIGURE 1
Multiple CLSs over the back. Note the dermal neurofibromas below the right scapula and right side of the lower back.

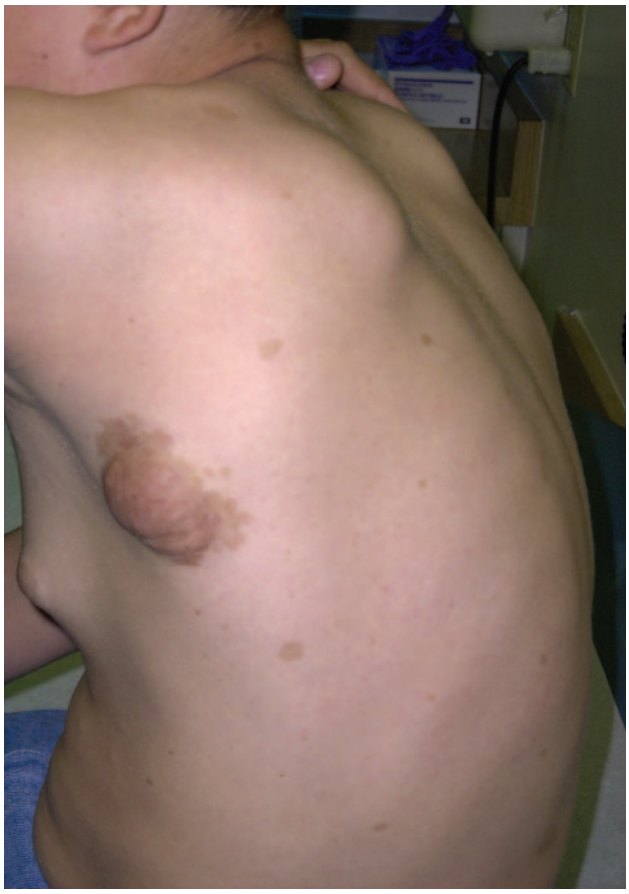

FIGURE 2
Large plexiform neurofibroma adjacent to the left axilla.

Diagnosis in nonfamilial pediatric cases, which represent 50% of those affected with NF1, may be difficult, because certain clinical features are age dependent.[15] For the same reason, the severity of NF1 in later life may be underestimated for an affected child.

CLSs usually represent the initial clinical manifestation of NF1 and may be present at birth or first appear in infancy (Fig 1). Although approximately 80% of those with NF1 will have more than 5 CLSs by 1 year of age,[12] occasionally these characteristic lesions are not present. CLSs tend to increase in number and size throughout early childhood.

Plexiform neurofibromas, which are found in at least 25% of individuals with NF1,[16] usually are congenital and, if located on the face, trunk, or extremities, can result in disfigurement (Fig 2). Early in life, the lesions may only be recognized as soft tissue enlargement or a patch of cutaneous hyperpigmentation with or without hypertrichosis. Tibial dysplasia, when present, occurs at birth and is manifested by anterolateral bowing of the lower leg (Fig 3). Its presence requires early orthopedic intervention because of the risk of fracture and development of pseudoarthrosis that results from healing, which occurs in approximately 2% to 3% of children with NF1.[12,17] Skinfold freckling (Fig 4) that develops in early childhood, typically between the ages of 3 and 5 years, usually is the second feature noted in children with NF1 and is present in three fourths of affected individuals.[15] Dermal neurofibromata usually first appear in the prepubertal period but may develop at a much earlier age and are present in virtually all affected individuals by adulthood (Fig 5). They become evident as skin nodules or tags located in cutaneous or subcutaneous tissues, as depressions in the skin with overlying purplish discoloration, or as firm nodules or cords in the deeper subcutaneous tissue. Increase in size and number of dermal neurofibromas coincide with puberty and pregnancy, but intermittent growth can persist throughout the life of an individual with NF1.[12] Plexiform neurofibromas may present as subcutaneous masses that involve deep tissues. These lesions can be found in all

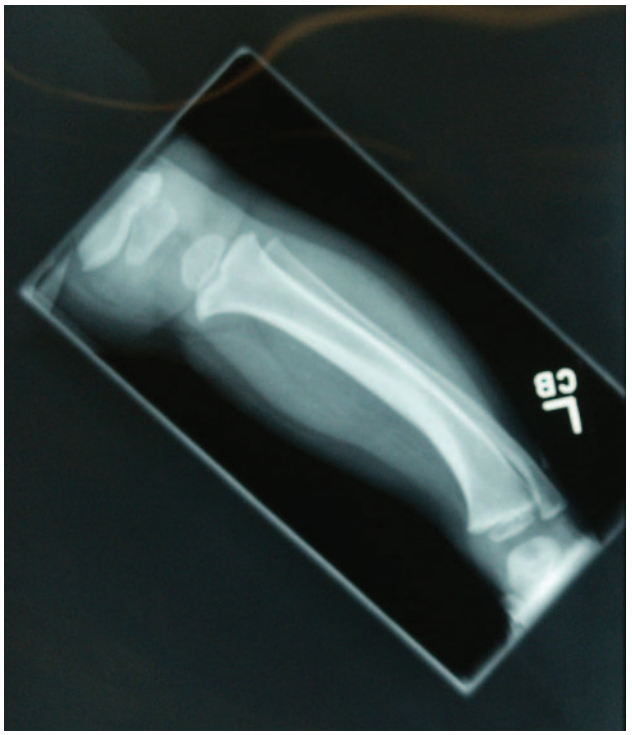

FIGURE 3
Anterior bowing of the left tibia.

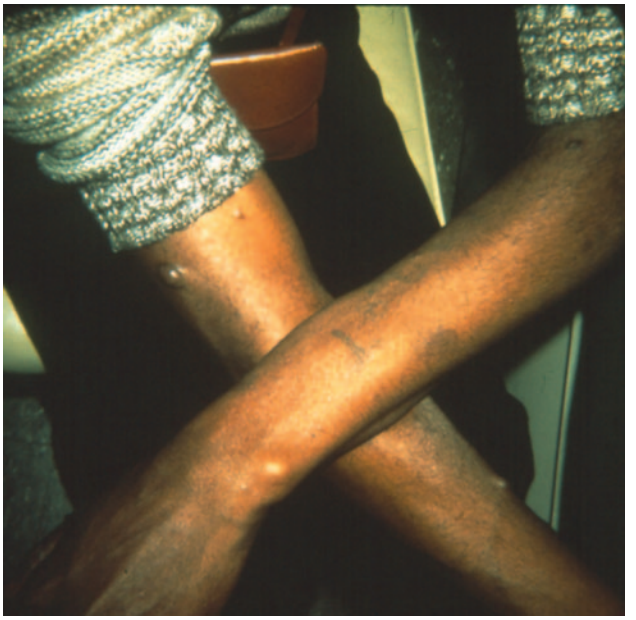

FIGURE 5
Dermal neurofibromas over both arms.

organ systems, giving rise to specific symptoms depending on size, location, and degree of encroachment on surrounding tissues. Marked growth of these lesions can occur anytime in childhood, followed by long periods of quiescence.[12] Optic pathway gliomas are present in up to 15% of children with NF1 and represent the most common central nervous system tumor related to this disorder (Fig 6). They develop in children younger than 6 years. Although their natural history is often indolent, in approximately one third of patients with NF1, optic pathway tumors become symptomatic, and in approximately 5% of cases, the lesion results in visual loss, severe proptosis, and/or hydrocephalus.[18–20] Precocious puberty also can be an occasional complication when the

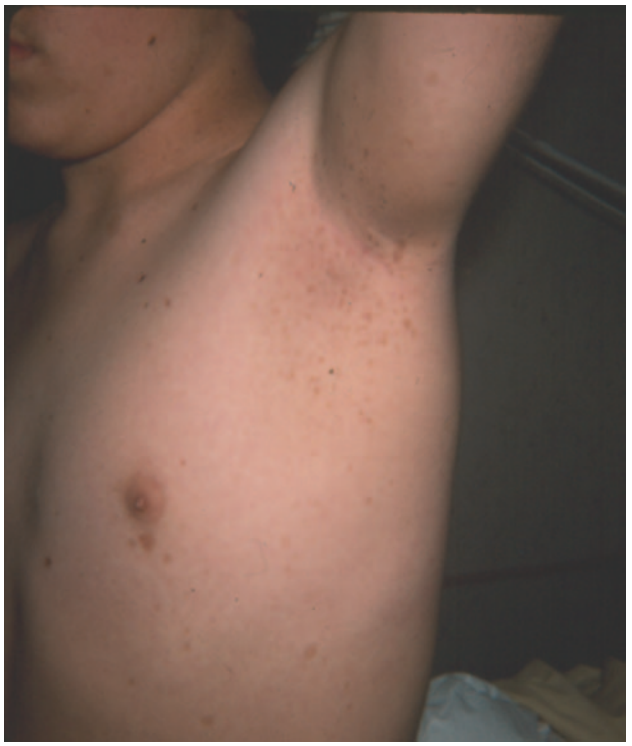

FIGURE 4
Axillary freckling.

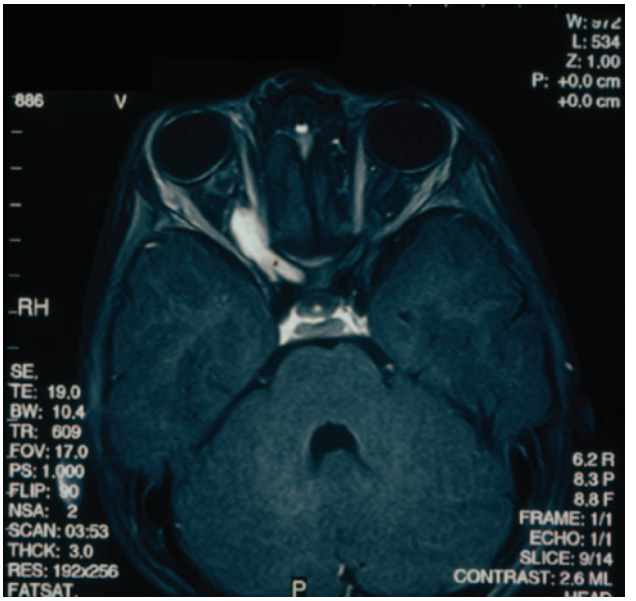

FIGURE 6
Optic glioma affecting the left optic pathway.

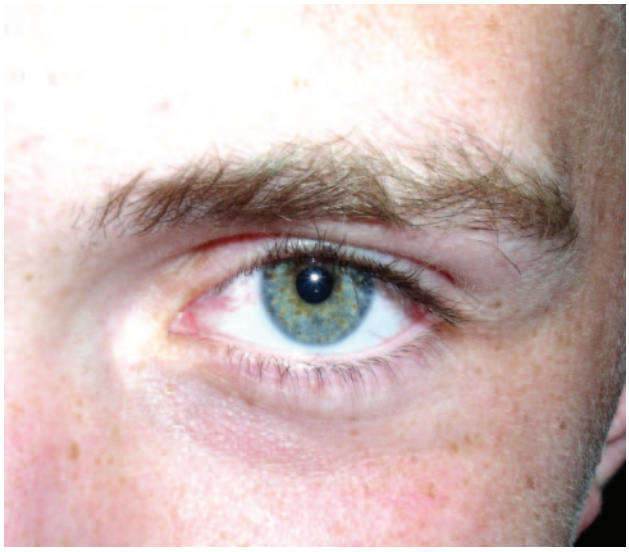

FIGURE 7
Multiple Lisch nodules.

optic pathway tumor involves the optic chiasm.[20,21] In the small proportion of symptomatic tumors in which clinically significant growth or progressive visual loss develops, treatment is necessary.[22] Treatment with carboplatin and vincristine sulfate has been effective in preventing further increase in tumor size and preserving remaining vision.[23] On the basis of the natural history of optic pathway tumors, the National Neurofibromatosis Foundation Optic Pathway Task Force previously has recommended against routine neuroimaging for all children with NF1; rather, yearly eye examination by either a pediatric ophthalmologist or an ophthalmologist who is knowledgeable of the ocular manifestations of NF1 has been advocated for all young children with NF1.[19,23] Lisch nodules (iris hamartomas)[12] usually develop in early adolescence, but they do not have any clinical significance (Fig 7). The sphenoid bones comprise multiple ossification centers that fuse to become the essential components of the orbits. Approximately 5% of individuals with NF1 have sphenoid wing dysplasia, which is usually unilateral. The abnormality can lead to proptosis, and approximately one half of patients with NF1 with sphenoid wing dysplasia will develop ipsilateral temporal-orbital plexiform neurofibroma.[12]

COMPLICATIONS

Although most individuals with NF1 are mildly affected, a risk of significant morbidity and life-threatening problems exists and cannot be predicted on the basis of findings in childhood. Serious complications of NF1 can result from direct involvement of multiple organ systems by plexiform neurofibromas. In addition, the lifelong risk of malignancy in affected individuals is increased. Malignant peripheral nerve sheath tumors represent the most common neoplasm, occurring in approximately 5% to 10% of individuals with NF1.[12,24] They usually develop in adulthood and are heralded by the presence of pain or rapid growth of a plexiform or deep nodular neurofibroma; however, similar manifestations can occur with a benign lesion. Other malignancies occur less frequently in patients with NF1, including pheochromocytoma, rhabdomyosarcoma, leukemia, and brain tumors other than optic gliomas.[12,25,26] Other associations exist with NF1, such as vascular changes. Macrocephaly affects most individuals with NF1.[27] Short stature occurs in one third of individuals with NF1 and does not seem to be related to disease severity. Height-growth velocity is normal for both genders during childhood, but the pubertal growth spurt is slightly reduced.[27] Growth charts made specifically for children with NF1 are available.[27,28] Neurofibromas develop in the gastrointestinal tract in a small proportion of patients with NF1 and usually present after early childhood. They may cause bleeding and anemia or signs of functional or mechanical obstruction. Rare forms of intraabdominal secretory or nonsecretory neoplasms also represent low-frequency associations. Evaluation for gastrointestinal complications should be pursued in the presence of unexplained anemia or weight loss, abdominal bloating, sudden or persistent abdominal pain, chronic diarrhea, signs of malabsorption, gastrointestinal bleeding, or recurrent emesis.[29,30] Seizures occur in 6% to 7% of cases.[12] Although electroencephalographic abnormalities are commonly reported, electroencephalography is not routinely recommended. If seizures are present, an intracranial tumor must be excluded, although usually no etiology is found. Nonossifying fibromas of the long bones and especially the distal femur and proximal tibia, on occasion, occur in adolescence or adulthood and can result in fracture. Therefore, a screening radiograph of both knees may be considered in early adolescence to provide appropriate intervention for individuals in whom lesions are detected.[31] Scoliosis is present in 10% to 30% of NF1 cases. Both idiopathic and dystrophic forms occur[12] and can lead to diminished pulmonary function. Variability in progression, however, makes it difficult to determine the prognosis once scoliosis is detected, and close monitoring is necessary after it has been discovered. An increased risk for osteoporosis in adulthood also exists.[32] Hypertension affects approximately 4% of individuals with NF1. Although essential hypertension is the most common cause of hypertension, in NF1 it can also result from renovascular disease, tumors that secrete vasoactive compounds, and coarctation of the aorta.[12] Therefore, monitoring blood pressure on a yearly basis is indicated, and if hypertension is found, additional evaluation and treatment or referral to an appropriate specialist for management is indicated.

NF1 is associated with an increased incidence of mental retardation (4%–8%)[33]; however, in most instances, intellectual abilities are in the average to low-average range. In contrast, specific learning disabilities are observed in as many as 40% to 60% of affected children,[12,34] and impaired performance on at least 1 test of academic achievement is present in 65% of children with NF1.[33] Deficits in visual-spatial-perceptual skills can result in reading and spelling difficulties. Poor fine-motor coordination can lead to problems with handwriting. Attention-deficit/hyperactivity disorder also occurs

more frequently in children with NF1. Children with NF1 have a higher likelihood of being hypotonic and of having subtle neurologic abnormalities that affect balance and gait.[33,35,36] Speech problems also may occur, and an association with velopharyngeal insufficiency exists.[37]

The reported incidence of complications in NF1 varies from study to study, mostly because of biased patient selection by age and specialty referral but also because of inconsistent diagnostic criteria and variable use of imaging techniques. Generally, complications are overestimated, because most studies involve patients in hospitals or referral clinics.[38] Approximately one third of patients with NF1 develop serious complications, and approximately one half are mildly affected. However, because of the extreme degree of variability even within a family and the progressive nature of NF1, it is not possible to determine the prognosis after establishing a diagnosis, especially at a young age.

GENETICS

NF1 is inherited in an autosomal dominant fashion. In approximately one half of patients, the condition is caused by a new mutation in that conception. In such instances, neither parent has any clinical features of NF1, and risk for recurrence of NF1 is likely not to exceed 1%. Rare instances of recurrence from phenotypically unaffected parents are attributed to germ-line or somatic mosaicism. However, individuals with NF1 caused by a new mutation are at a 50% risk of transmitting the gene to each of their offspring. The NF1 gene has a high penetrance rate; therefore, an individual who carries the mutation can be expected to have clinical manifestations of the disorder. Some individuals are mosaic for an NF1 mutation and may have localized signs, referred to as "segmental neurofibromatosis." These individuals may be at risk of transmitting the mutant gene to their offspring if the germ line includes cells with the mutation, which results in an increased risk of NF1 in their offspring.

The NF1 gene is located on the long arm of chromosome 17 at band q11.2.[39–41] Neurofibromin, the protein product of the normal gene, acts as a tumor suppressor by downregulating another cell protein, Ras, that enhances cell growth and proliferation.[12,42,43] A wide variety of mutations have been identified within the NF1 gene, which give rise to diminished function of neurofibromin in affected persons. Detection of mutations in the NF1 gene by DNA analysis has proven to be complex because of the gene's large size, presence of pseudogenes, and great variety of possible abnormalities. Molecular technology that is capable of detecting 95% of mutations in NF1 is now available,[44] but it is typically not indicated because a diagnosis of NF1 in 95% of cases can be established on the basis of clinical findings alone by 11 years of age.[28] However, when there is uncertainty regarding a definitive diagnosis, for instance, in the presence of some of the clinical manifestations of NF1, such as only CLSs, but not enough to establish a clinical diagnosis, consideration should be given to seeking genetic consultation and determining whether genetic testing is indicated at that time to expedite a diagnosis. Molecular testing also may represent an option in those instances when a couple in which one person has NF1 is seeking prenatal diagnosis. Although establishing a diagnosis is achievable when a mutation has been detected in an affected partner, determining its possible clinical effects after establishing a diagnosis in utero is not.

CLINICAL MANAGEMENT

The multiorgan occurrence of neurofibromas and their complications often requires care from a variety of medical subspecialists and surgical specialists. The medical home has the opportunity and responsibility to coordinate such care. In addition, patients with more than minimal manifestations of NF1 may benefit from referral to a multidisciplinary neurofibromatosis clinic for primary or specialty care or to a physician with expertise in the care of individuals with NF1. Such clinics and/or physicians are valuable consultation resources for medical homes that care for affected patients.

Longitudinal care for NF1 is aimed at the early detection and symptomatic treatment of complications as they occur. Some of the medical problems, such as hypertension resulting from renal artery stenosis, can be managed successfully if detected early. Enlarging plexiform neurofibromas may be managed surgically, although regrowth may occur. In addition, surgical removal of a plexiform neurofibroma, especially when it compromises an essential organ system, may not be possible because of an inaccessible site or infiltration into surrounding tissue. In most instances, management of most malignancies including leukemia is the same as for children without NF1. On the other hand, outcome of treatment of malignant peripheral nerve sheath tumors is poor. Therefore, early suspicion that there may be malignant degeneration of a plexiform neurofibroma is critical from a prognostic standpoint.

In providing medical supervision to a child with NF1, general clinical evaluation through the medical home should be provided regularly, but the frequency should increase to address disease complications. Therefore, recommendations for ongoing assessment and periodic review throughout life (Table 1), including the following:

1. Evaluate the child for new neurofibromas and progression of lesions. Examine the skin carefully for signs of plexiform neurofibromas that may impinge on or infiltrate underlying structures.
2. Check the child's blood pressure yearly to determine if there is evidence of hypertension, which occurs more frequently with NF1 and could be secondary to renal artery stenosis, aortic stenosis, and pheochromocytoma, the latter being more common in adults. A variety of vascular hypertrophic lesions may be found.
3. Evaluate neurodevelopmental progress of an affected child.
4. Obtain a formal ophthalmologic evaluation yearly.
5. Evaluate the child for skeletal changes. Look for scoliosis, vertebral angulation, and limb abnormalities,

TABLE 1 Health Supervision Guidelines for Children With Neurofibromatosis

	Prenatal	Infancy (1 mo to 1 y)					Early Childhood (1 to 5 y)						Late Childhood (5 to 13 y), Annual[a]	Adolescence (13 to 21 y), Annual[a]
		Neonatal	2 mo	4 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	3 y[a]	4 y[a]		
Diagnosis														
DNA analysis	X[b]													
Phenotype review	X[c]	X												
Genetic counseling	X[c]	X												X[d]
Reproductive options for parents														
Adoption/termination	X													
Future reproductive planning		X					X			X			X[d]	
Anticipatory guidance														
Family support	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Support groups	X	X	X				X						X[d]	X[d]
Long-term planning	X	X					X						X[d]	X[d]
Sexual and reproductive issues													X[d]	X
Medical evaluation and treatment[e]														
Growth		O	O	O	O	O	O	O	O	O	O	O	O	O
Blood pressure		O	O	O	O	O	O	O	O	O	O	O	O	O
Skin examination		O	O	O	O	O	O	O	O	O	O	O	O	O
Bone examination/scoliosis		O	O	O	O	O	O	O	O	O	O	O	O	O
Neurologic examination		O	O	O	O	O	O	O	O	O	O	O	O	O
Vision screening		S/O	S/O	S/O	S/O	S/O	S/O[f]	S	S	S/O[f]	S/O[f]	S/O[f]	S/O[f]	S/O[f]
Hearing screening		S	S	S	S	S	S/O[f]	S	S	S	S	S/O[f]	S/O	S/O
Sexual maturation													O	O
Diagnostic imaging examinations[e]														
Psychosocial evaluation														
Development and behavior		S/O	S/O	S/O	S/O	S/O	S/O	S/O	S/O	S/O	S/O	S/O[f]	S/O	S/O
Preschool program											S	S		
School placement/performance													S/O	S/O
Psychological/social adjustment							S	S	S	S	S	S	S	S
Intrafamily relationships		S			S		S	S	S	S	S	S	S	S

X indicates to be performed; S, subjective, by history; O, objective, by a standard testing method.

[a] Advise semiannual visits, as indicated.

[b] See "Discussion."

[c] Or at the time of diagnosis.

[d] Once in this time period.

[e] As needed for significant abnormalities and/or new signs.

[f] Refer to subspecialist.

particularly tibial dysplasia. Sometimes localized hypertrophy of a leg, arm, or other part of the body results from plexiform neurofibromata. Nonossifying fibromas of the long bones infrequently occur in adolescence or adulthood and have been associated with fracture; although a screening radiograph of the knees in adolescence has been suggested as a routine study, evidence is not sufficient to support routine screening at this time.

6. If any unexplained complications occur or if cutaneous lesions appear to be growing rapidly, refer the patient to the appropriate subspecialist for further evaluation.
7. Refer to the review of NF1 at www.genetests.org to obtain rapid access to updated clinical information on the condition.
8. Recommend available resources for patients with NF1 (eg, neurofibromatosis clinics, support groups, and families of children with NF1). Books, pamphlets, and Web-site addresses can be obtained from the Children's Tumor Foundation (www.ctf.org). The Children's Tumor Foundation can also provide additional information and clinic locations.

THE PRENATAL VISIT

At times, the pediatrician may be asked to counsel a family when one of the parents-to-be is affected and the fetus is at risk or has been diagnosed prenatally to have NF1 by DNA testing. In this situation, the family most likely already has been counseled about the disorder and its inheritance pattern. However, the pediatrician may be called on to review the information and assist the family in the decision-making process. When appropriate, pediatricians who have experience in the care of individuals with NF1 may wish to have a discussion with the family, or those with less experience may seek consultation from a geneticist to provide more in-depth information to:

1. review the results of the prenatal diagnostic study;
2. explain the mechanism for occurrence of the disorder in the fetus and the risk of recurrence;
3. review the clinical manifestations, variability, progressive nature, and prognosis of the disorder;
4. review the various forms of treatment and intervention that are currently available, including their efficacy, complications, and adverse effects;
5. discuss the options available to the family for management and rearing of the child (in cases of early prenatal diagnosis, this may include discussion of available options after in utero diagnosis, including continuation of the pregnancy or its termination, and discussion of appropriate management strategies and options for child rearing after delivery);
6. when appropriate, consider referral to a clinical geneticist for a more in-depth discussion of clinical findings, recurrence risk, future reproductive options, and evaluation of risks of disease for other family members; and
7. inform the family that, in many parts of the country, there are specialty neurofibromatosis clinics that are available for guidance, therapy, and consultation.

HEALTH SUPERVISION FROM BIRTH TO 1 MONTH: NEWBORN INFANTS

Examination

1. Confirm the diagnosis by the presence of cutaneous manifestations. CLSs may be present, and in 10% to 15% of neonates, a plexiform neurofibroma will be recognized. However, the clinician must be aware that a normal examination at this age does not exclude the diagnosis of NF1.
2. All first-degree relatives should be advised to have a physical examination, including a slit-lamp examination to look for Lisch nodules, which are found in >90% of adults with this disorder but are uncommon in children younger than 5 years.
3. Some specialists recommend an initial MRI study to determine if an optic glioma is present when the diagnosis of NF1 is made.[1,18] In addition to being able to identify an optic pathway glioma, if present at this age, areas of increased signal intensity on T2-weighted images, also known as unidentified bright objects (UBOs), which are present in approximately 60% of affected children, also can be detected. These lesions are well circumscribed and nonenhancing, and they are located in the brainstem, cerebellum, basal ganglia, and thalamus. An association between UBOs and learning disabilities or cognitive deficits may exist. The lesions are not space occupying and tend to disappear in adulthood. Although potentially helpful in establishing an early diagnosis when clinical findings are equivocal, because of the lack of specificity and the inability to consistently identify UBOs, the benign nature of most optic gliomas, and the need to sedate the child, neuroimaging of the brain may not be warranted. Therefore, the NIH Consensus Development Conference[13] did not recommend computed tomography or MRI studies for asymptomatic patients with NF1 and generally recommended special studies only when they were clinically indicated. Neuroimaging of the brain, on the other hand, would seem to be indicated for a small percentage of the NF1 population for whom a deletion of the entire NF1 gene and flanking DNA is found.[40,45] Affected individuals have a distinct phenotype, including facial dysmorphism, a large number of neurofibromas, severe cognitive impairment, and, frequently, evidence of structural brain anomalies.

Anticipatory Guidance

1. Review the natural history and genetics of NF1.
2. Advise the parents to report any unusual or new symptoms.

3. Stress the need for regularly scheduled visits, including careful cutaneous, skeletal, and neurologic examinations and evaluation of blood pressure.
4. Emphasize the need for a yearly ophthalmologic evaluation.

HEALTH SUPERVISION FROM 1 MONTH TO 1 YEAR: INFANCY

Examination

1. Compare the infant's growth and development with figures on growth charts.[27,28] As a group, children with NF1 are shorter than average but have a larger head size. Rarely, aqueductal stenosis can cause obstructive hydrocephalus, but in most children with NF1, the basis for macrocephaly is likely to be increased brain volume.
2. Examine the patient for the presence of CLSs. Inform the family that new ones may appear, and preexisting CLSs often increase in size. Reassure the family that CLSs have no functional significance.
3. Check for proptosis, a rapidly increasing head size, and focal neurologic signs.
4. Perform a careful physical examination and look for skeletal abnormalities, especially in the spine and legs. This is particularly important before the child begins to bear weight because of the risk of cortical thinning of the long bones, which increases the likelihood of fracture.
5. Refer the infant for formal ophthalmologic evaluation and to other appropriate specialists and subspecialists, as indicated.
6. Check the infant's neurodevelopmental progress at each visit.

Anticipatory Guidance

1. Review the family's psychological support and intrafamilial relationships.
2. Advise the parents to use sunscreen after the child reaches 6 months of age. Sun exposure deepens pigment in CLSs. Although this is usually of cosmetic significance only, melanoma and basal cell carcinoma have been reported in adults with NF1; however, the risk for developing these malignancies is not known to be increased for patients with NF1.[25]
3. If appropriate, review future pregnancy planning with the affected infant's parents.

HEALTH SUPERVISION FROM 1 TO 5 YEARS: EARLY CHILDHOOD

Examination

1. Examine the child for neurofibromata and the presence of skinfold freckling, which can appear in any intertriginous area. Assure parents that CLSs and freckling only have cosmetic significance.
2. Consider taking photographs to document lesion size for future reference.
3. Evaluate the child's vision and recommend that the child undergo an ophthalmologic examination annually throughout childhood.
4. If there are visual changes, persistent headaches, seizures, marked increase in head size, or a plexiform neurofibroma of the head, obtain a brain MRI.
5. Assess the child's speech and motor skills for deficits that require further assessment. Hypernasal speech attributable to velopharyngeal insufficiency can be present, and there may be delayed expressive language development.
6. Monitor blood pressure yearly.

Anticipatory Guidance

1. Review the child's preschool program.
2. Obtain appropriate developmental evaluations of the child for assessment of learning, speech/language, and motor abilities if developmental concerns are raised. The child may benefit from preschool services, speech/language and/or motor therapy, and special education programming to address delays. With NF1, the risk of hearing impairments is not increased appreciably.
3. Discuss indications for surgery, as appropriate. If there is a change in the size of superficial neurofibromata or evidence of a space-occupying internal lesion, refer the child to a neurofibromatosis clinic or other appropriate subspecialists.
4. Pruritus can occur in young children and may be found to be associated with cutaneous neurofibromata. However, antipruritic medications are not helpful in relieving symptoms.

HEALTH SUPERVISION FROM 5 TO 13 YEARS: LATE CHILDHOOD

Examination

1. Examine the child for skin tumors causing disfigurement and obtain a consultation with a specialist if surgery is desired to improve appearance or function. Severe cosmetic disfigurement is seen more often in adults than in children.
2. Evaluate the child for signs of puberty. Premature onset of sexual maturation or delayed puberty may occur. If sexual precocity is present, evaluate the child for the presence of an optic glioma or hypothalamic lesion.[18,21]
3. Check for signs of learning disabilities and attention-deficit/hyperactivity disorder.
4. Review the child's social adjustment.
5. Monitor the child's ophthalmologic status yearly under 8 years of age, followed by complete eye examination every 2 years.[23]

6. Monitor blood pressure yearly.

Anticipatory Guidance

1. Review the child's development and appropriateness of school placement.
2. Refer the child to a clinical psychologist or child psychiatrist for further evaluation and therapy should problems with self-esteem related to his or her physical findings or developmental problems exist.
3. Review the effects of puberty on the disease.
4. Discuss the possibility of the growth of neurofibromata during adolescence and pregnancy.
5. Counsel the parents about how and when to discuss the diagnosis with their child.

HEALTH SUPERVISION FROM 13 TO 21 YEARS OR OLDER: ADOLESCENCE TO EARLY ADULTHOOD

Examination

1. Examine the adolescent for signs of abnormal pubertal development.
2. Perform a thorough skin examination to evaluate for and determine the status of plexiform neurofibromata and a complete neurologic examination to check for findings that might suggest the presence of deep plexiform neurofibromata.
3. Obtain a surgical consultation with a specialist if signs of pressure on deep structures are found.
4. Continue monitoring blood pressure yearly.
5. Continue opthalmological examination every 2 years until 18 years of age.[23]

Anticipatory Guidance

1. Discuss the genetics of NF1 or refer the adolescent for genetic counseling.
2. Discuss sexuality.
3. Discuss birth control, including the risks and benefits of birth control pills, and reproductive options.
4. Discuss the effect of pregnancy on NF1, if appropriate. Women with NF1 may have complications during pregnancy because of enlargement of the neurofibromata[46,47] and, not uncommonly, eruption of more dermal neurofibromas.
5. Review prenatal diagnosis by using available molecular DNA studies and discuss its applicability to the patient with NF1 or refer the patient to a geneticist for further discussion of diagnostic options.
6. Facilitate transition to adult medical care.

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RESOURCES

For further information please contact the Children's Tumor Foundation, 95 Pine St, 16th Floor, New York, NY 10005; telephone: 800-323-7938 or 212-344-6633; Web sites: www.ctf.org or www.genetests.com.