

Watchful Waiting Best With Neurofibromatosis

BY DOUG BRUNK
San Diego Bureau

LA JOLLA, CALIF. — The way Dr. Lynne M. Bird sees it, the \$1,500 gene sequencing test for neurofibromatosis type 1 in children is rarely necessary because it usually does not change clinical management.

She favors a watchful waiting approach in children who present with the hallmark symptom of at least six café au lait macules that are at least 5 mm in size, “and [I] wait for the second criterion to appear,” she said at a meeting sponsored by Rady Children’s Hospital and the American Academy of Pediatrics. “I follow these children as if I already knew they had NF1, monitoring them for potential complications without doing gene testing.”

The prevalence of neurofibromatosis type 1 (NF1) is 1:3,000, making it the most common neurocutaneous disorder in children. Diagnosis is made if the child meets two of seven criteria: café au lait macules; axillary or inguinal freckling; two or more neurofibromas or one plexiform neurofibroma; optic nerve glioma; two or more Lisch nodules of the iris; a distinctive osseous lesion such as pseudarthrosis or sphenoid wing dysplasia; or a family history of the disease.

About half of cases with no family history meet criteria for the disorder by 1 year of age; 97% meet the criteria by 8 years of age.

NF1 is an autosomal, dominantly inherited disorder due to mutations in a gene on chromosome 17, which encodes the protein neurofibromin, a tumor suppressor. “Finding a mutation of the gene would also allow you to make this diagnosis,” said Dr. Bird of the division of genetics and dysmorphology at Rady Children’s Hospital, San Diego.

“If you have a parent with NF1 and you can determine their mutation through genetic testing, then you can offer them prenatal diagnosis. In my experience, most parents aren’t concerned enough about passing NF1 on to their children that they would consider interrupting a pregnancy. But there are some families that have experienced major complications associated with NF1, and they are very interested in not passing the gene on to their children,” she said.

A study of nearly 1,900 patients with NF1 found that the features of the disease typically appear in a characteristic order, beginning with café au lait macules (Pediatrics 2000;105:608-14).

Sometimes macules are present at birth “but others will appear in the first few months of life and certainly by the first couple of years of age,” Dr. Bird said. “Typically the next feature is axillary freckling, which is usually evident in the school-age child. Lisch nodules will appear gradually after that, followed by neurofibromas as a sign that the child is entering puberty.”

Another clue is the presence of the Riccardi sign, a tuft of hair along the back near the spine. “This sign will often be present at birth and may be there before any of the café au lait macules show up, so you will look really smart if you make a tentative diagnosis upon seeing this,” Dr. Bird said.

Optic glioma almost always appears by 3 years of age “and certainly by 6 years of age,” she said. “In addition, there is frequent thickening of the optic nerves, which is asymptomatic and doesn’t cause disease.”

A rare feature of NF1 is juvenile xanthogranuloma, which occurs in 1%-2% of cases. This skin lesion usually resolves spontaneously but is associated with an increased incidence of juvenile myeloid leukemia (JML). “When you see this you want to at least do a complete blood count and be thinking about JML, and maybe contact your local oncologist to see if they have further recommendations for monitoring,” she advised.

In most cases, the diagnosis of NF1 is made on clinical exam, including a careful evaluation of both parents. “This condition is present in 1 in 3,000 in the general population, but I don’t see anywhere near the equivalent number of kids in my clinic,” Dr. Bird said. “That tells me there is a lot of undiagnosed NF1 out there. Most parents [with NF1] are healthy; they just have spots and a few lumps on their skin.”

The best way to follow children with NF1 is to see them regularly for a complete physical examination and review of systems. There is no way to screen for every single complication of NF1 except by talking to families, said Dr. Bird. “Families should be told that symptoms which are not self-limited need to be brought to your attention,” she said. “If there is a symptom that hangs on, that’s nagging and doesn’t go away in a reasonable amount of time, they need to come in so we can explore whether it is related to NF1 or not.”

Basic follow-up tests should include checking blood pressure and monitoring for scoliosis as well as an ophthalmology evaluation and an assessment of developmental skills. “Learning disabilities are common,” she said. “Expressive language delay is the area of development most commonly affected.”



Café au lait macules are usually the first sign of neurofibromatosis type 1.



The next sign, axillary freckling, is often evident in the school-aged child.



The Riccardi sign, a tuft of hair near the spine, may be present at birth and can even appear before macules.

PHOTOS COURTESY DR. LYNNE M. BIRD AND DR. MARILYN C. JONES

Many parents ask Dr. Bird if an MRI of the brain and optic nerves is needed in children who present with multiple café au lait macules. “There is probably no correct answer to that question,” she said. “There is no evidence that detecting optic gliomas before they’re symptomatic translates into better outcome. So you could argue that doing an MRI, which requires anesthesia, is not worth the money or the risk.”

NF1 patients with neurofibromas have a 10% lifetime risk of developing a malignant peripheral nerve sheath tumor within one of the lesions. Signs of malignant degeneration include persistent pain, a change in texture, a rapid increase in size, or development of a neurologic deficit associated with the neurofibroma.

Dr. Bird had no relevant conflicts to disclose. ■

Answering Parents’ Questions About DEET, ‘Natural’ Repellents

BY DAMIAN McNAMARA
Miami Bureau

MIAMI BEACH — Children’s insect repellent products that contain alternative ingredients marketed as “natural” are becoming more widely available, and parents have plenty of questions about their use, Dr. Elizabeth Connelly said at the annual Masters of Pediatrics conference sponsored by the University of Miami.

Efficacy varies among insect repellents that do not contain N,N-diethyl-m-toluamide (DEET). Soybean oil, citronella oil, vanillin, oil of eucalyptus, and picaridin are examples of the active ingredients found in natural products.

The marketing of alternative insect repellents continues to expand. Even Disney

has entered the market for children’s dermatologic products, she said. Disney’s Gentle Naturals product line contains a DEET-free bug repellent.

Dermatologists are likely to get more questions about products they recommend now that DEET-free formulations are available at drugstores, Target, and Wal-Mart.

“I am constantly bombarded with questions by parents about insect repellents, sunscreens, and sun protection products,” said Dr. Connelly, a pediatric dermatologist at the University of Miami.

Remember “not all ‘natural’ repellents are safe,” she said. Oil of eucalyptus, for example, should be used only in children 3 years and older.

Picaridin, which comes from black pep-

per, is odorless, and physicians could recommend it to parents and children who do not like the smell of traditional repellents, but is it not as effective as DEET. Of all the Off! brands, only the Clean Feel repellent contains picaridin. “All other formulations of Off! contain DEET,” said Dr. Connelly, who said she has no financial interest in any of the products mentioned in her talk.

“You might be asking: Do these natural oils work? Citronella, patchouli, and clove, especially, work almost as well as DEET,” Dr. Connelly said. Patchouli oil is derived from mint.

Apply all insect repellents sparingly, and avoid use under clothing or near open wounds, Dr. Connelly said. Avoid use of combination repellent/sunscreen products. Also, beware of wipes that contain

DEET because the DEET gets on the child’s hands and fingers go in the mouth or around eyes. “I recommend children wash off DEET before bedtime,” Dr. Connelly added.

Products with DEET “should not be applied more than once a day. I don’t think that is something parents know,” Dr. Connelly said. Parents may be confused because the label advises application every 4 hours for adults. DEET should not be used in infants younger than 2 months. This and other recommendations from the American Academy of Pediatrics 2003 guidelines on use of DEET insect repellents are still valid, she added.

The Food and Drug Administration also provides guidelines at www.fda.gov/cder/emergency/repellants.htm. ■