

# Evaluation and Management of Melanocytic Nevi in Children

Children with melanocytic nevi require proper counseling to discuss the risk for melanoma.

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**M**elanocytic nevi, commonly referred to as moles, are very common in children, and the overwhelming majority of melanocytic nevi in children are benign. Given the increased general awareness of melanoma, however, caregivers often express concerns about the development or appearance of their child's moles. An understanding of the more common types of melanocytic nevi seen in children and of the associated risk for the development of melanoma is essential in order to properly counsel caregivers and patients about management recommendations.

## CLASSIFICATION OF MELANOCYTIC NEVI

Melanocytic nevi may be congenital or acquired. Congenital melanocytic nevi (CMN) are generally present at birth, although in a minority of cases they may not be clinically apparent until one to two years of age (tardive congenital nevus). Acquired melanocytic nevi (AMN) may develop at any age but most commonly develop after the age of two years and increase in number with age during childhood and early adulthood.

*Congenital melanocytic nevi.* CMN are noted in approximately one percent of newborns. Congenital melanocytic nevi may be further classified on the basis of their size in

adulthood; this final size may be predicted during childhood. Small CMN are less than 1.5cm in greatest diameter, intermediate CMN are between 1.5–10cm in greatest diameter, and large CMN are greater than 20cm in greatest diameter; a fourth classification, the giant CMN, is sometimes used to indicate a CMN that is greater than 50cm in diameter. Large and giant CMN on the torso are often referred to as “bathing trunk nevi” on the basis of their distribution. Some patients with large or giant CMN may also have one or more smaller CMN on the head, trunk, and extremities; these are referred to as satellite nevi. Rarely, a patient may have multiple small or intermediate CMN without a large or giant CMN; this is referred to as multiple CMN (MCMN).

The risk of malignant degeneration in small and intermediate CMN appears to be exceedingly small, and melanoma arising within a small or intermediate CMN is seen predominantly in adults. The prophylactic excision of all CMN is therefore unwarranted. Those that are clinically atypical or located in areas that preclude routine examination by caregivers or by self-examination may be considered candidates for excision, but the vast majority can be followed clinically with monthly self-examination with the assistance of a caregiver, if appropriate. In contrast, the risk of melanoma arising in large and giant CMN has been well-studied, with estimates of two to five percent over lifetime; a significant risk for the development of



Fig. 1. Banal acquired melanocytic nevus.

melanoma is present in the first decade of life, and therefore children with a large or giant CMN should be referred to an experienced dermatologist and a pediatric surgeon at birth for close follow-up and discussion of the risks and benefits of surgical intervention.<sup>1</sup>

Children with large or giant CMN involving the torso, in particular when associated with multiple satellite nevi, are also at risk for neurocutaneous melanosis (NCM), in which there is an abnormal proliferation of melanocytes within the central nervous system, including the brain parenchyma and leptomeninges.<sup>1</sup> Although it appears as though many patients with limited NCM may remain clinically asymptomatic, patients with extensive NCM are at high risk for neurologic complications, which often develop within the first few years of life and which include seizures, hydrocephalus, and neurodevelopmental delays. Symptomatic patients are also at risk for the development of primary central nervous system malignant melanoma, which is invariably fatal. Infants at risk for NCM should undergo appropriate neuroradiologic screening with MRI of the brain and spine, and those with evidence of NCM should be referred to an experienced dermatologist, pediatric neurologist, and pediatric neurosurgeon for further evaluation.

*Acquired melanocytic nevi.* Risk factors for the development of AMN include fair skin type (often with red hair, blue eyes, and inability to tan), propensity to sunburn, freckling, and sun exposure.<sup>2</sup> Acquired melanocytic nevi may be flat (junctional melanocytic nevus) or raised (compound and dermal melanocytic nevus) and are usually less than 6mm in diameter. AMN are usually of uniform color, which may range from light brown to dark brown, and symmetric in appearance (Fig. 1). Children of darker skin types often make more darkly pigmented moles. Often,



Fig. 2. Halo nevus phenomenon.

the majority of moles observed on a particular child will have a similar appearance, the so-called “signature” mole. Evaluation of acquired melanocytic nevi should take into consideration the “ABCDE” mnemonic: Asymmetry, irregular Border; multiple Colors; Diameter >6mm; and Enlarging or Evolving over time. In adults, additional concerning features include observations that the nevus is Elevated; Firm; and/or Growing, but in children, these features are often observed in benign moles and therefore are not as helpful in identifying those that are concerning.

A not uncommon phenomenon that may develop in association with AMN in children is the halo phenomenon, in which a depigmented “halo” develops around the periphery of one or more nevi (Fig. 2). Over time, the nevus itself may partially or completely depigment and regress. This phenomenon results from localized autoimmune destruction of melanocytes and is often seen in association with vitiligo, although it is not clear if the pathogenesis is the same. It is considered a benign process in children and unless the involved melanocytic nevus appears clinically atypical, the nevus does not need to be biopsied or excised. The halo phenomenon may also occur in association with congenital melanocytic nevi, but much less commonly.

Several distinct variants of AMN that are distinguished on the basis of clinical and histological features may be seen in children, including the dysplastic nevus and the Spitz nevus.

*Dysplastic nevi.* Dysplastic nevi are distinguished on the basis of characteristic clinical and histological features.<sup>3</sup> They are usually greater than 6mm in diameter and often have a “fried egg” appearance, with a combination of flat and raised components (Fig. 3). The edges may appear fuzzy or indistinct, and there are often multiple colors



Fig. 3. Dysplastic nevus.

present, ranging from pink to tan to dark brown. Cytologic and architectural atypia define the histologic characteristics of dysplastic nevi. Dysplastic nevi are considered to be a marker for an increased overall risk for the development of melanoma, although the majority of dysplastic nevi never develop into melanoma. Small epidemiologic studies in children suggest that the development of dysplastic nevi in children is not common, and the majority appear to develop in adults.<sup>4</sup> The development of multiple dysplastic nevi may be familial, however, in particular in families with the familial atypical multiple mole melanoma (FAMMM) syndrome associated with germline mutations in *CDKN2A/p16* gene; in affected families, development of dysplastic nevi begins in childhood and adolescence.<sup>5</sup>

Although most experts do not recommend biopsy or excision of all clinically dysplastic nevi, biopsy of individual dysplastic nevi is often recommended if the nevus has undergone progressive changes in appearance, if the nevus appears clinically different than the majority of the other nevi noted on the patient (the so-called “ugly duckling” mole), or if there are risk factors such as immunosuppression or family history of melanoma. Melanocytic nevi on the scalp often manifest many of the clinical and histological features of dysplastic nevi, but prophylactic excision is not generally recommended due to the low risk of malignant degeneration.<sup>6</sup> Excision of scalp nevi in children may be considered for very large or atypical melanocytic nevi, in children with a family history of melanoma or other risk factors such as immunosuppression, or in younger children if the child requires anesthesia for another indication and the excision can be easily performed at the same time.

*Spitz nevi.* Spitz nevi are a peculiar variant of the acquired melanocytic nevus with characteristic clinic and histologi-



Fig. 4. Classic Spitz nevus.

cal features.<sup>7</sup> Most Spitz nevi are acquired, although rarely they can be present at birth. Unfortunately, when first described in the literature in 1956, the Spitz nevus was also called “benign juvenile melanoma,” creating confusion as to the natural history and ontogeny of these nevi. The classic Spitz nevus presents in a child as a small pink to red-brown papule on the face (Fig. 4).

Spitz nevi are considered benign, yet excision of Spitz nevi is controversial, with some experts arguing that as they are benign, they do not need to be prophylactically excised. However, a minority of Spitz nevi may exhibit clinical and/or histological atypia with one or more features worrisome for melanoma; these “atypical Spitz tumors” (AST) are among the most controversial among melanoma experts, and optimal management has yet to be defined, although at a minimum complete excision of the nevus is recommended.<sup>7</sup> Some experts recommend sentinel lymph node mapping and biopsy in order to assess risk for malignant potential, metastatic disease and possible need for adjuvant therapy, although this is highly controversial. In general, AST are >1cm in diameter, may ulcerate, and demonstrate histological features suggestive of malignant melanoma, although some atypical Spitz nevi as well as some melanomas with Spitzoid features are clinically indistinguishable from benign Spitz nevi.<sup>7</sup> On the basis of this ambiguity in diagnosis and treatment, biopsy of all clinically suspected Spitz nevi is recommended by some experts. Children diagnosed with an atypical Spitz nevus should be referred to a dermatologist and oncologist with expertise in pigmented lesions for further evaluation and management.

### MELANOMA

Melanoma in children is exceedingly rare, although recent data from the SEER database indicate that the incidence

appears to be increasing, in particular in white, male adolescents and young adults.<sup>8</sup> About 300-400 cases of malignant melanoma are diagnosed in children and adolescents every year in the United States. Overall mortality due to melanoma in children, however, appears to be declining.<sup>9</sup> Although some of this observed increase in incidence may be attributed to better surveillance, earlier diagnosis, and/or over-diagnosis, it is believed that the increase in pediatric melanoma also mirrors the increase in melanoma seen in adults believed to be directly related to factors such as increased exposure to ultraviolet light. A family history of melanoma, in particular in association with familial mutations in the CDKN2A/p16 gene, accounts for only a small minority of cases of pediatric melanoma, and genetic testing in the absence of a family history is not generally recommended. Other risk factors include chronic immunosuppression, prior history of pediatric cancer with chemotherapy and/or radiation therapy, primary immunodeficiency, and other genetic predisposition syndromes, including xeroderma pigmentosum.

### MANAGEMENT OF MELANOCYTIC NEVI BY THE PEDIATRICIAN

Questions sometimes arise about the role of the dermatologist in verifying diagnoses and/or educating pediatricians about pediatric melanocytic nevi. The majority of children with melanocytic nevi do not need to be referred to a dermatologist. However, all children and caregivers should receive education on sun safety, including sun avoidance and use of sunscreen and sun protective clothing from the pediatrician and his/her staff. This is true of children being followed by the dermatologist as well. In addition, children and caregivers should be instructed on the use of the ABCDE criteria for melanoma detection and on the importance of routine skin examination with the assistance of a caregiver, which should ideally be performed on a monthly basis. For most children, the skin examination is best performed before or after bathing, as the child is already undressed. Examination of the scalp and genitalia should be included. A complete skin examination should be part of every well-child evaluation by the primary care provider, and any melanocytic nevi of note should be documented in the medical record with a complete description of the location, color, and size of the nevus and notation of any color variation, raised component, or other notable features.

If a melanocytic nevus develops worrisome changes such as focal change in pigmentation (either darker or lighter), asymmetry, an irregular border, a focal raised component, or symptoms such as pain, itching, crusting, or bleeding, further evaluation is warranted. However, in the majority

of cases these changes are not suggestive of melanoma or significant dysplasia and often no biopsies are warranted. Clinical photodocumentation with appropriate image resolution, lighting, and color balance is immensely helpful in serial clinical follow-up of melanocytic nevi and should be available with the dermatologist. Pediatricians should be advised that referral to a dermatologist for a total body skin examination and documentation of any atypical melanocytic nevi should be considered for children at risk for dysplastic nevi and melanoma, including those with a family history of melanoma or dysplastic nevi, in particular in a first-degree relative; or children with a history of malignancy, chronic immunosuppression, or immunodeficiency.

### SUNSCREEN

Education on sunscreen use as well as on other sun safety measures should be part of the pediatrician's well-child visit starting in infancy. Use of sunscreen is recommended for infants age six months and older; infants less than six months of age in general should avoid sun exposure, although sunscreen should be used in younger infants if sun avoidance is not possible.

Sunscreen agents may be classified as physical agents such as zinc oxide and titanium dioxide, which physically reflect or scatter ultraviolet light, and chemical agents, which absorb ultraviolet light. Chemical sunscreen agents typically are further classified into those that absorb UVA light (such as avobenzone), those that absorb UVB light (such as homosalate), and those that are broad-spectrum and absorb both UVA and UVB light (such as oxybenzone). Physical sunscreen agents are considered broad-spectrum. UVB light includes ultraviolet light in the range of 290-320nm and contributes to sunburn; UVA light includes ultraviolet light in the range of 320-400nm (UVA1 includes 340-400nm and UVAII includes 320-340nm) and contributes predominantly to photodamage and photoaging. Both UVA and UVB contribute to the development of melanoma and non-melanoma skin cancer. Sunscreens have historically been labeled with an SPF (sun protection factor) that indicates the degree of protection offered against UVB irradiation and sunburn. Sunscreen with an SPF of 15 filters out 93 percent of UVB exposure, while sunscreen with an SPF of 30 filters out 97 percent of UVB exposure. Use of sunscreen with a higher SPF affords more protection against UVB-induced sunburn by allowing longer periods of exposure. In theory, someone who normally burns after 10 minutes of sun exposure could tolerate a maximum of 150 minutes of sun exposure with use of an SPF 15 sunscreen. The additional protection afforded by sunscreen with an SPF greater than 50, however, is negligible. Use of a broad spectrum, water-resistant sunscreen of at least

**TABLE 1. SUN SAFETY RECOMMENDATIONS FOR PARENTS AND CHILDREN****Sun Safety Tips**

- Avoid being in the sun from 10:00 AM to 4:00 PM, when the sun's rays are strongest.
- Have your child wear sun protective clothing (broad-brim hats, long-sleeve shirts) and sunglasses when outdoors.
- When swimming, have your child wear swimwear that is sun protective (rated UPF 50) and ideally has long sleeves and covers his or her entire chest and back.
- Use a sunscreen that is labeled "water-resistant" and broad-spectrum with an SPF of at least 30
- Use sunscreen consistently and regularly, even on cloudy days.
- Use enough sunscreen! You should use about ½ - 1 ounce of sunscreen, depending on the size of your child.
- Don't forget to apply sunscreen to the scalp (if exposed), ears, neck, and feet!
- Reapply sunscreen every 2 hours or after swimming or sweating.
- Apply sunscreen at least 15 minutes before going outside.
- Have your child apply a lip balm with an SPF of at least 30 regularly.
- Use caution with medications that can make your child more sun sensitive.
  - Ibuprofen
  - Tretinoin, adapalene, tazarotene (topical acne medications)
  - Isotretinoin
  - Cetirizine
  - Methotrexate
  - Doxycycline
- Encourage your teen to avoid indoor tanning.

SPF 30 is recommended. Chemical sunscreen agents have the potential to cause more irritation and, rarely, allergic contact dermatitis; therefore, sunscreen that contains only physical sunscreen agents is often recommended for infants and young children and those children with sensitive skin. FDA-approved sunscreen agents are considered to be safe and effective. Concerns regarding systemic absorption of zinc oxide and titanium dioxide nanoparticles appear to be largely unfounded, as are concerns regarding the potential for oxybenzone to act as a hormone disruptor.

In 2012, new labeling of sunscreen products sold in the United States was to be introduced, but implementation

has been delayed. Only sunscreens that are water-resistant and provide broad-spectrum coverage with an SPF of at least 15 will be able to claim that they reduce the development of skin cancer; those that do not meet these three requirements will be labeled "This product has been shown only to help prevent sunburn, not skin cancer or early skin aging." In addition, the use of the terms "waterproof" and "sweatproof" will be eliminated; instead, the term "water-resistant" will be used to indicate that the sunscreen continues to provide the stated SPF after either 40 minutes or 80 minutes of water exposure.

Sunscreens are available as lotions, creams, gels, sticks, and aerosols, and different vehicles may be easier to apply to different areas. Most people under-apply sunscreen; the recommended amount to apply per application for an average-sized adult is one ounce for a creamy product. Additional recommendations for the use of sunscreen are provided in Table 1.

**CONCLUSIONS**

The majority of melanocytic nevi in children and adolescents can be managed conservatively by serial clinical examinations by the primary care provider and caregivers. Fortunately, the incidence of melanoma in children is very low, although it appears to be increasing due to a number of factors. Children with clinically atypical melanocytic nevi and those children with a history of immunosuppression or other risk factors for the development of melanoma should be referred to a dermatologist for further evaluation. All children and their caregivers should receive appropriate education on sun protection, including the use of sunscreens, as well as on the ABCDE features of melanocytic nevi that warrant further evaluation. ■

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