

# 25 Melanoma in children

The current understanding of childhood melanoma is derived from the collective experience of many institutions and from data obtained from state and national registries, since no single institution has a large experience with this rare condition.

Different definitions of 'childhood' have been made. Studies reporting the experiences of individual centres have tended to merge all ages of young patients, often labelling those up to 20 years of age as 'childhood' cases. However, it seems more appropriate to separate the prepubertal cases from the postpubertal or adolescent ones, since melanoma incidence rises sharply around the time of puberty. Defining puberty is itself fraught with difficulty, particularly because of the rather indistinct transition to puberty in boys. A further problem is that most reports of childhood melanoma rely on data from registries, whether they be population-based or from hospitals, which almost invariably use age groups of 1–4, 5–9, 10–14 and 15–19 years. Thus 'puberty' is most likely to occur some time in the 10–14 year age group, after which age there is a sharp rise in incidence. To illustrate this point, melanoma before the age of 10 years occurred in only seven cases (all girls) registered in Australia in 2001 by the Australian Institute of Health and Welfare.<sup>1</sup> In the 10–14 year age group, six girls and six boys were registered. This rose to 38 girls and 39 boys in the 15–19 age group. In New Zealand between 1995 and 2006, 20 melanomas were diagnosed in children under the age of 15 years and 105 diagnosed in adolescents aged 15–19 years.<sup>2</sup>

## 25.1 Diagnosis

Transplacental transmission of melanoma, an exceedingly rare condition, was first reported in 1949<sup>3</sup> and there had been less than a dozen recorded cases up until 2005.<sup>4,5</sup> This rarity is due to the fact that even within the small subset of women with placental involvement of metastatic melanoma, the risk of transmission to the foetus is only about 17%. Nearly all affected infants died within 18 months. Primary melanoma may also very rarely arise within a giant congenital melanocytic naevus, present in approximately 1 in 20,000 newborns.<sup>4</sup> The lifetime risk of malignant transformation in these giant naevi is between 2 and 20%.<sup>6</sup>

There is general agreement that because of the difficulty in differentiating benign from malignant melanocytic lesions in young adults, all histological slides should be reviewed by histopathologists highly experienced in the diagnosis of such lesions. Some melanocytic lesions are misdiagnosed as benign and only recognised as malignant when they recur. This was often the case in the past. More recently, on the other hand, there has been a tendency to over-diagnose prepubertal lesions as melanoma, thus ascribing malignancy to some lesions which have no malignant potential.<sup>7</sup> Nearly 60 years have elapsed since Sophie Spitz<sup>8</sup> reported a series of melanocytic lesions which behaved in benign manner but which shared many histological features with melanoma. Nevertheless, there are still no criteria that will definitively separate the two lesions, since each can simulate the other. Crotty et al<sup>9</sup> suggested that in some cases it may not be possible to give an unequivocal diagnosis. In such cases, the presence of deep and/or atypical mitoses is a strong indicator

of malignancy, as is positive staining with HMB45 (especially in the deep component). Even in these cases, a definite diagnosis may still not be possible and there is need to consider the balance of features in favour and against a diagnosis of melanoma. These cases should be completely excised and the patient carefully followed-up. Recently, attempts have been made to illustrate the problems associated with making this difficult diagnosis and criteria to differentiate benign from malignant lesions have been proposed.<sup>10–12</sup> Most pathologists claim that the histological features of melanoma in children are similar to those in adults. The only reports to the contrary, citing architectural and cytopathological differences, emanate from specialist referral centres where slides have been examined after the development of metastases<sup>13</sup> or in cases of advanced localised disease.<sup>14</sup> This underscores the problems associated with comparing results from population-based data with those from individual referral centres.

Evidence summary	Level	References
The differential diagnosis between Spitz naevi and spitzoid melanomas is a difficult one. Several attempts have been made to assist histopathologists make this distinction	IV	8–12

Recommendation	Grade
1. The pathology slides of all Spitz-like lesions in children suspected of being malignant be referred to histopathologists who are highly experienced in the differential diagnosis of such lesions	C

## 25.2 Treatment and survival

Irrespective of whether the source of data is population-based or from individual referral centres, the mainstay of treatment is surgical, as in adults. There is a need to integrate recent advances in the management of adult patients into the paediatric population, recognising that the relative rarity of melanoma in childhood precludes prospective trials of treatment and survival in children. Once the diagnosis of melanoma is established, whether it arises in a giant naevus, a small congenital melanocytic naevus, a dysplastic naevus or de novo, surgical excision should be performed with the same excision margins recommended for adults with melanomas of similar thickness.

The largest number of children surveyed to date comes from the National Cancer Data Base in the United States, which draws its cases from hospital registries. Their most recent publication described the demographics and clinical presentation of melanoma in 3158 young patients aged 1–19 years between 1985 and 2003, and reports a high rate of metastatic disease in 289 children aged 1–9 years.<sup>15</sup> The possible explanations given for this are either (a) a delay in diagnosis due to a low awareness of the possibility of melanoma in such young patients, or (b) age-related differences in biological behaviour not yet understood, or (c) an overrepresentation of patients with more advanced disease in their hospital-based population.

This high metastatic rate and an advanced stage at first presentation has been reported by others, but most reports have emanated from specialist referral centres<sup>16,17</sup> rather than registries.<sup>18–20</sup> Nonetheless, the consensus is that despite this more common presentation of advanced disease, ultimate survival is similar to that of adults,<sup>15–17,20</sup> and it is generally agreed that sentinel node biopsy is warranted, no matter what age, in children with melanomas of appropriate thickness.<sup>21–23</sup> Although the number of children reported to have undergone sentinel node biopsy is so far quite small, rates of positivity range from 25% to over 60%.<sup>21–26</sup> This could be regarded as an extension into early childhood of the well-accepted fact that younger adult patients have a higher incidence of sentinel node positivity than adult patients.<sup>22,25,27,28</sup>

Additionally, in all series, surprisingly good survivals have been recorded following a positive sentinel node biopsy in children. For example, five-year disease-free survival of 83% after a positive sentinel node biopsy has been reported. This again reflects the paradoxical situation in which overall survival in adults is poorer than in younger patients despite a higher sentinel node positivity rate.

Authors are divided on the value of completion lymph node dissection in children, despite the harvesting of the occasional positive non-sentinel node, but generally there is agreement that such surgery should not be avoided in young children and the indications should be the same as in adults.

Thus in sum, sentinel node biopsy for children with intermediate- to high-risk disease is a useful adjunct in the treatment of melanoma in a paediatric population with frequently apprehensive parents. The use in children of high-dose interferon alpha-2b therapy has been described as being well-tolerated with less associated toxicity, both after resected high-risk melanoma<sup>29,30</sup> and after positive sentinel node biopsy.<sup>26</sup> However, the efficacy of high-dose interferon as an adjuvant therapy in children is poorly documented, since in most drug trials subjects < 18 years of age are excluded from participation.

Evidence summary	Level	References
Surgical excision of the primary melanoma should be performed with excision margins similar to those in an adult with equivalent disease. Sentinel node biopsy, completion lymph node dissection, or adjuvant therapy with high-dose interferon are all well tolerated by children. The indications for these therapies should be the same as in adults	IV	21–26
Survival in children with advanced disease is better than in adults with comparable disease	IV	15–17

### Recommendation

	Grade
2. All facets of melanoma treatment and follow-up in adults may be integrated into the treatment and follow-up of children. Parents may be assured that survival in children is at least equivalent and probably better than it is in adults with the same stage of disease	<b>C</b>

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