PERIODIC SYNOPSIS

This report reflects the best data available at the time the report was prepared, but caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations set forth in this report.

Malignant melanoma

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Writing a periodic synopsis on melanoma is a difficult task. New data, especially relating to diagnostic techniques and advances in the area of therapy, tend to make any reference on the topic outdated by the time the material is published. The articles below represent the seminal references on melanoma published through 2002. Several important studies, especially pertaining to the therapeutics (e.g., the role of sentinel lymph node dissection as a therapeutic procedure) are currently ongoing, and data are not available to present at this time. While we have emphasized references published in the past 5 years, we thought that a few key earlier publications deserve to be included because of their continued importance in the field of melanoma.

GENERAL REFERENCES

PRECURSOR LESIONS
Acquired melanocytic nevi

Dysplastic nevi

Key points
1. Patients with an increased number of clinically benign (also termed “common acquired”) nevi have an increased risk of melanoma.
2. The critical number at which point the relative risk becomes significant depends not only on the number on nevi, but also on other factors such as family history, environmental sun exposure, etc.
3. Caucasians may exhibit up to 50 moles by age 40; greater numbers imply an increased mole count.
4. The relative risk of melanoma developing in patients with an increased mole count is difficult to discern from the current literature. Estimates have ranged from a 3- to 10-fold increased relative risk in patients with 100 or more clinically banal nevi.

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Key points

1. Dysplastic nevi occur in both familial and sporadic settings. The risk of melanoma developing in these patients is dependent on several factors, including the total number of nevi present (both dysplastic and common acquired) and a positive family history of dysplastic moles.

2. In individuals with familial atypical mole-melanoma (FAMM) syndrome, melanoma risk is estimated to be 500-fold greater in the setting of a previous melanoma compared with 150-fold greater in patients with atypical moles but no prior melanoma.

3. The lifetime melanoma risk in individuals with FAMM syndrome approaches 100% by the age of 70.

4. Patients with dysplastic nevi outside of the familial melanoma setting are thought to have an increased melanoma risk, but at a much lower rate. Relative risk of developing melanoma in the nonfamilial setting ranges from 2-3 to 12-14 in various studies, depending on dysplastic nevus count.

5. Prophylactic removal of dysplastic nevi does not eliminate the risk of subsequent melanoma formation, as dysplastic nevi more commonly represent a “marker” for increased melanoma risk rather than precursors to melanoma. Removal should be considered for clinical signs of severe atypia/early melanoma within dysplastic moles or in the setting of suspect clinical change.

Congenital nevi


Key points

1. Melanoma risk in congenital nevi is both location and size dependent. The lifetime risk of malignant transformation in patients with large congenital melanocytic nevi (>20 cm diameter adult size) has been estimated to be between 5% and 15%.

2. Approximately 60% of melanomas that develop in giant congenital nevi do so during the first decade of life, and the majority arise subcutaneously, rather than from the dermal junction.

3. Patients with large congenital melanocytic nevi (LCMN) in a posterior axial location, especially when associated with multiple satellite melanocytic nevi, are at greater risk for the development of neurocutaneous melanosis.

4. Approximately 40% to 50% of patients with symptomatic central nervous system melanosis (usually manifest by age 2) progress to leptomeningeal melanoma, which is uniformly fatal.

5. The vast majority of melanomas arising within small congenital nevi originate from the dermal junction.

6. The incidence of malignant degeneration of small (<2 cm) and medium-sized (2-20 cm diameter) congenital nevi is extremely low and may be no greater than that of common acquired nevi. Unlike LCMN, malignant transformation of small and medium-sized congenital nevi is a postpubertal phenomenon.

7. Prophylactic removal of clinically stable, small and medium-sized congenital nevi is generally not indicated.

STAGING/PROGNOSIS


Buzaid AC, Ross MI, Balch CM, Soong S-J, McCarthy WH, Benjamin RS, et al. Critical analysis of the current American Joint Committee

Key points

1. The Breslow depth is the most important prognostic indicator in primary cutaneous melanomas, with stratification cutoffs of <1, 1.01-2, 2.01-4, and >4 mm in the revised 2002 American Joint Committee on Cancer (AJCC) melanoma staging system.
2. Microscopic ulceration is the next most important adverse prognostic pathologic feature, and its presence or absence has been incorporated into the revised AJCC staging so that ulceration “upstages” individuals into the next worst prognostic level.
3. The number of regional lymph nodes involved is a more powerful predictor of survival than the size of involved nodes.
4. Sentinel lymph node status is the most important prognostic factor for recurrence and the most powerful predictor of survival for melanoma patients and has also been incorporated into the 2002 staging system as microscopic (vs macroscopic) nodal disease.
5. The therapeutic benefit of sentinel lymph node biopsy/dissection remains unclear. Several studies are in progress to answer this question.

LABORATORY TESTING/DIAGNOSTIC IMAGING

Rinne D, Baum RP, Hor G, Kaufmann R. Primary staging and follow-up of high risk melanoma patients with whole-body 18F-fluorodeoxyglucose positron emission tomography: results of a prospective study of 100 patients. Cancer 1998;82:1664-71.
Swetter SM, Carroll LA, Johnson DL, Segall GM. Positron emission tomography (PET) is superior to computed tomography (CT) for metastatic detection in melanoma patients. Ann Surg Oncol 2002;9:646-53.

Key points

1. Routine blood work analysis and chest x-rays have limited value in postoperative follow up of patients with resected intermediate- and high-risk cutaneous melanomas.
2. Serum lactate dehydrogenase levels may indicate metastasis, but their specificity and sensitivity are low; however, lactate dehydrogenase assessment is useful in the management of patients with stage IV (disseminated) disease.
3. Careful history and physical examination detects the vast majority of melanoma recurrences and should be used to direct further laboratory and imaging studies.
4. Total body computed tomographic scans as well as directed liver, brain, or bone imaging do not appear to be useful for detecting occult melanoma metastasis in asymptomatic patients with primary melanoma.
5. Newer techniques, such as whole-body positron emission tomography are currently being investigated and may eventually supplement or replace current laboratory and imaging tests.

SURGICAL TREATMENT


Key points
1. Surgical margins of 5 mm are recommended for melanoma in situ and margins of 1 cm for melanomas up to 2 mm depth.
2. Randomized, prospective studies show that 2-cm margins are appropriate for tumors in the intermediate-thickness group (1-4 mm), although 1-cm margins have been shown to have no adverse effects on survival for tumors 1 to 2 mm in depth.
3. Although no prospective data exist regarding appropriate margins for melanomas thicker than 4 mm, one recent retrospective study concluded that margins greater than 2 cm had no effect on local recurrence, disease-free relapse, or overall survival and thus 2-cm margins are appropriate in this high-risk subgroup.
4. Wider margins may be necessary to achieve local control for melanomas on the head, neck, hands, and feet compared with those on the trunk or proximal extremities. However, adequate surgical margins are often difficult to obtain in these locations because of cosmetic and functional considerations.

ADJUVANT THERAPY


