Prevention and Detection of Melanoma in the Primary Care Setting

Case Study and Commentary, Susan M. Swetter, MD, and Alan C. Geller, MPH, RN

In the United States, melanoma incidence rates are rising faster than for all other preventable or “early detectable” cancers. Early recognition and treatment of thin cutaneous melanoma have contributed to a decreased case-fatality rate over the past 50 years, but many at-risk Americans have yet to be screened. Primary prevention is directed to educating the public and health care providers to raise awareness of melanoma and change risk behavior, namely, excessive exposure to ultraviolet radiation. The goal of secondary prevention is to reduce morbidity and mortality through early detection strategies, including skin self-examination and skin screening. As yet, the only proposed measure for melanoma prevention is sun protection in childhood and adolescence, which may reduce the number of melanocytic nevi developing as an adult. Preventing adverse sun exposure in later years would likely be protective against melanoma, particularly the more ultraviolet radiation–related subtypes. Chemoprevention for melanoma is a developing field that may allow individuals at high risk for new primary melanoma to be targeted for intervention, although no oral or topical agent has yet been identified with proven efficacy in preventing melanoma.

Approximately 59,580 Americans are expected to develop invasive cutaneous melanoma in 2005, with an estimated additional 40,000 or more cases of intraepithelial melanoma in situ. The current lifetime risk for developing invasive melanoma is 1 in 65 Americans, a 20-fold increase since 1930 [1,2]. If noninvasive melanoma in situ is included, the lifetime risk rises to 1 in 37 Americans. It has been suggested that the increased incidence is largely the result of increased diagnostic scrutiny rather than a true increase in the incidence of disease [3,4]. However, the reported increase in both thick and thin melanoma in the United States and Australia would seem to refute this [5,6]. Over 7700 individuals will die from metastatic disease within the next year. More frequent recreational sun exposure (in the absence of...
sun protection) is the most likely explanation for the increased incidence of melanoma over the past 50 years, although earlier detection and treatment of thinner lesions have contributed to improved patient survival, particularly in younger individuals [7,8]. The most striking differences in melanoma incidence and mortality occur in individuals older than age 50 years; therefore, they should be a primary target for secondary melanoma prevention, including early detection and screening.

**CASE STUDY**

**Initial Presentation**

A 64-year-old married white man presents to a dermatologist with a 2-year history of a pigmented lesion on the right arm.

**History**

He reports that he first noted the lesion as a “dark spot” near the site of an influenza vaccination in the right upper arm. The lesion gradually increased in size and elevation, with onset of intermittent bleeding following minor trauma to the site. No change in color was noted, and the lesion did not exhibit asymmetry or border irregularity. He states that his other physicians examined the lesion periodically, but that he was only recently referred by his primary care physician for dermatologic evaluation.

The patient lives with his wife in a rural area and is a retired truck driver with 4 grown children. His past medical history is significant for coronary artery disease (CAD) with coronary artery bypass grafting 5 years prior. The patient reports that he had experienced crushing chest pain with radiation to the left arm for months prior to his diagnosis of CAD, and that a public message regarding symptoms of angina televised at a truck stop prompted him to seek care. Hypercholesterolemia and hypertension were diagnosed at the time of CAD. The patient has no known family history of cancer.

**Physician Examination**

Clinical examination reveals an 8-mm brown-black nodule with superficial erosion (Figure). There is no local or regional lymphadenopathy.

- What is the differential diagnosis?

  The clinical features of the lesion strongly suggest the diagnosis of cutaneous melanoma; an irritated seborrheic keratosis may mimic melanoma but tends to appear more “stuck on” and wart-like and does not typically exhibit bleeding.

**Diagnosis and Treatment**

An excisional skin biopsy is performed and reveals a nodular melanoma, 2.7 mm Breslow depth, Clark level IV with ulceration, transected peripherally and at the deep margin. No definite angiolymphatic or perineural invasion are identified; the mitotic rate measures up to 2 mitoses/mm². The patient undergoes wide local excision with 2-cm clinical margins around the biopsy scar. Sentinel lymph node dissection is performed following preoperative lymphoscintigraphy and is negative in 1 identified node in the right axilla. The re-excision skin specimen shows no residual cutaneous melanoma. Chest radiograph, liver function tests, and lactate dehydrogenase levels are within normal limits. The patient’s disease is pathologic stage IIB melanoma (T3aN0M0), with an estimated 63% 5-year survival.

- What are the major risk factors for cutaneous melanoma?

**Risk Factors for Melanoma**

Risk factors for melanoma (Table 1) have been intensively studied and include the genodermatoses xeroderma pigmentosum and familial atypical mole-melanoma (FAMM) syndrome, the presence of atypical (or dysplastic) nevi, large (or giant) congenital nevi, numerous common nevi, prior melanoma, immunosuppression, sun-sensitive phenotype, history of excessive sun exposure/severe childhood sunburns, melanoma in a first-degree relative (without FAMM syndrome), and importantly, older age (≥ 50 years) and male gender.
Biopsy of Suspected Melanoma

Proper biopsy of a suspicious pigmented lesion is essential for accurate diagnosis and histologic microstaging. Complete excision of the tumor will allow for the most precise estimates of prognosis based on histologic features, including Breslow depth, ulceration, lymphovascular invasion, Clark level, mitotic rate, and host response. Tumor thickness

- How is cutaneous melanoma diagnosed and staged?

**Table 1. Major Melanoma Risk Factors**

<table>
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<tr>
<th>Risk Factor</th>
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<tr>
<td>Xeroderma pigmentosum</td>
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<tr>
<td>Familial atypical mole-melanoma syndrome</td>
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<tr>
<td>Atypical/dysplastic nevi (particularly &gt; 5–10)</td>
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<tr>
<td>Numerous (&gt; 100) common nevi</td>
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<tr>
<td>Large (giant) congenital nevi (&gt; 20 cm diameter in an adult)</td>
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<tr>
<td>Previous melanoma</td>
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<tr>
<td>Sun sensitivity/history of excessive sun exposure or severe childhood sunburns</td>
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<tr>
<td>Prior nonmelanoma skin cancer (basal cell and squamous cell carcinoma)</td>
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<tr>
<td>Melanoma in first-degree relative(s)</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>Age &gt; 50 years</td>
</tr>
<tr>
<td>Artificial sources of ultraviolet light (PUVA and tanning beds)</td>
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</table>

PUVA = psoralen and ultraviolet A.

has been confirmed as the most important determinant of prognosis, followed by the presence or absence of histologic ulceration, features that should be reported by the interpreting pathologist in cases of invasive cutaneous melanoma. Clark level, which measures anatomic level of invasion, is also relevant for primary tumors of less than or equal to 1 mm in thickness.

Narrow excisional biopsy, with 1-mm to 3-mm margins around the visible borders of the lesion and into the subcutaneous fat, should be performed when possible. Wider margins (> 1–2 cm) may disrupt afferent cutaneous lymphatic flow and affect the ability to accurately identify the sentinel node(s) in patients eligible for this procedure. For the same reason, orientation of the excisional biopsy should be parallel to lymphatic drainage (ie, longitudinally on the extremities).

Superficial shave biopsies of suspected melanomas are discouraged, as partial removal of the primary tumor may preclude accurate measurement of Breslow depth. Multiple punch biopsies are appropriate for large lesions, such as lentigo maligna and acral lentiginous subtypes, and should include the most suspicious areas (darkly pigmented, hypopigmented/regressed, or nodular). Wood’s lamp examination using ultraviolet light (365 nm) is extremely useful in delineating clinical borders of lentigo maligna and superficial spreading subtypes by identifying hypopigmented areas of regression that may be contiguous with the pigmented portion of the cutaneous melanoma.

**Sentinel Lymph Node Biopsy**

Sentinel lymph node biopsy for cutaneous melanoma was developed in the early 1990s to allow a selective approach to identifying individuals with occult regional nodal metastasis through localization of the first draining or “sentinel” node.
MELANOMA

[27]. The success of the technique is based on the concept that cutaneous lymphatic flow is well delineated in melanoma and that the histology of the sentinel node is characteristic of the entire lymph node basin (ie, a negative sentinel node obviates the need for further lymph node dissection). Both of these concepts were borne out in the initial studies of the staging technique [27,28]. The sentinel node is typically identified via preoperative lymphatic mapping with the use of lymphoscintigraphy involving a radiolabeled sulfur colloid as well as injection of a vital blue dye around the primary melanoma site to localize the sentinel node. An intraoperative gamma probe is used to detect and remove “hot” nodes, which are then microscopically examined with serial sections and immunohistochemical stains to confirm whether the node is positive or negative for micrometastasis.

Sentinel node status is the most important prognostic factor for recurrence and the most powerful predictor of survival in melanoma patients. In a study of 612 patients with cutaneous melanoma (stage I/II), sentinel lymph node–negative biopsy was associated with a nearly 60% increase in 3-year disease-free survival compared with sentinel lymph node–positive biopsy [29]. Furthermore, determination of regional lymph node status may affect entry into clinical trials and/or early initiation of adjuvant therapy [30]. While it remains unclear whether removal of microscopically involved, clinically occult, regional lymph nodes has an effect on overall survival (ie, a therapeutic benefit), there is no question that the sentinel lymph node biopsy offers valuable staging and prognostic information for patients with cutaneous melanoma. The 2002 melanoma staging guidelines adopted by the American Joint Committee on Cancer (AJCC) and its European counterpart promote pathologic staging of the regional lymph nodes for cutaneous melanoma with greater than 1-mm depth, along with microstaging of the primary melanoma, as the most complete means of staging [23,24].

• What is the significance of melanoma subtypes?

Histogenetic Subtypes of Melanoma

There are 4 major clinical-pathologic subtypes (or growth patterns) of primary cutaneous melanoma: superficial spreading melanoma (SSM), nodular melanoma (NM), lentigo maligna melanoma (LMM), and acral lentiginous melanoma (ALM). Distinction among subtypes is largely based on anatomic site, and it remains controversial whether melanoma subtype affects overall prognosis, although molecular analysis has demonstrated different patterns of cell death, oncogene expression [31], gene amplification [32] and BRAF mutation frequency [33] among the 4 main histogenetic types. With the exception of nodular melanoma, all growth patterns are characterized by a preceding in situ (radial growth) phase that lacks the biologic potential to metastasize and may last from months to years before dermal invasion occurs. While all in situ melanoma may not necessarily progress to invasive melanoma, complete excision is recommended to prevent invasion and effect cure [22,24].

Superficial Spreading Melanoma

SSM is the most common subtype of melanoma, accounting for about 70% of all cases, particularly among patients aged 30 to 50 years [35]. It occurs most frequently on the upper back of men and women as well as the lower extremities of women. The clinical lesion typically shows irregular, asymmetric borders with color variegation, and size is generally greater than 6 to 8 mm. A history of gradual or recent change is frequently reported.

The most common melanoma simulants are seborrheic keratoses (benign keratinocytic proliferations) and traumatized nevi, which often present as a “bleeding mole.” Common nevi may also be clinical mimics, particularly during puberty or pregnancy when hormonally induced benign growth or darkening tends to occur. In addition, a mole showing severely atypical features may be clinically indistinguishable from early melanoma. SSM is the most likely subtype to be associated with a preexisting nevus [21,36], although again, the majority of cutaneous melanomas arise de novo.

Nodular Melanoma

NM is the second most common subtype of melanoma, occurring in 15% to 30% of patients [35]. In the most recent Surveillance Epidemiology and End Results (SEER) analysis, NM comprised 9% of all lesions but 32% of all lesions greater than 2 mm [5]. Like SSM, legs and trunk are the most frequent sites of involvement. However, rapid growth over weeks to months is a hallmark of NM and corresponds to its lack of a preceding in situ phase. Clinically, the lesion presents as a raised dark brown to black papule or nodule, and ulceration and bleeding are common.

Lentigo Maligna Melanoma

LMM is linked to cumulative rather than intermittent sun exposure. The precursor in situ lesion, lentigo maligna, is usually present for over 5 to 20 years and often attains large
size (> 3 cm diameter) before progression to LMM (invasive melanoma) occurs. Lentigo maligna appears as a tan to brown macule or patch with variation in pigment or areas of regression that appear hypopigmented clinically. Only 5% to 8% of lentigo maligna is estimated to evolve to invasive melanoma [38], and this event is characterized by nodule development within the flat precursor lesion.

**Acral Lentiginous Melanoma**

ALM is the least common subtype, representing only 2% to 8% of melanoma in whites, although it accounts for 29% to 72% of melanoma in dark-complexioned individuals (African Americans, Asians, and Hispanics) [35,39]. Delay in the diagnosis of this subtype is believed to contribute to advanced presentation and poorer prognosis for cutaneous melanoma in African Americans [1,40]. ALM typically occurs on the palms or soles or beneath the nail plate (subungual variant). Irregular pigmentation, large size (≥ 3 cm diameter), and plantar location are characteristic features. Subungual melanoma occurs most commonly on the great toe or thumb and is characterized by the rapid onset of diffuse nail discoloration or a longitudinal pigmented band within the nail plate. Longitudinal pigmented banding of the nails (melanonychia striata) is common in darker-skinned people and typically involves multiple nails. Single nail involvement and/or extension of pigmentation onto the proximal or lateral nail folds (Hutchinson’s sign) strongly suggests subungual melanoma and warrants biopsy of the nail matrix, from which these melanomas arise. Subungual melanoma may be confused with a benign junctional nevus, pyogenic granuloma, infectious process (bacterial or fungal), Bowen’s disease (squamous cell carcinoma in situ, particularly if clinically amelanotic), or subungual hematoma. If subungual hematoma is suspected, a history of trauma should be elicited, and the lesion followed to ensure resolution with continued growth of the nail plate.

One of the most important differences between subtypes is that nodular melanoma tends to lack the typical ABCD warning signs (Table 2) and thus may elude early detection. Desmoplastic melanoma is a rare variant that also lacks these features. Most SSM, ALM, and LMM display asymmetry (A), border irregularity (B), color variation (C), and/or diameter greater than 6 mm (D) [41]. NM, on the other hand, is characterized by elevation and clinical ulceration with onset of easy bleeding [42] and may be amelanotic (ie, lacking brown pigmentation). As such, amelanotic NM may be impossible to distinguish from other nonmelanoma skin cancers (basal cell and squamous cell carcinoma) or from benign processes such as dermatofibroma or a ruptured follicle (ie, “pimple”). It has been recommended that the term “evolving” (E) be added to the ABCD criteria to enhance the ability of physicians and the public to recognize “lesion change over time” as crucial to early diagnosis of some melanoma subtypes, regardless of whether the classic ABCD clinical signs are met [43]. Again, while the prognosis for NM is not worse when compared with SSM of similar thickness, NM accounts for the majority of thick cutaneous melanomas, particularly in older individuals [5,6,44]. In terms of lesion size, the Norwegian Melanoma Project recently found that the frequency of small diameter melanomas (< 7 mm) was 11.4% but argued that the current ABCD rule (with the 6-mm diameter guideline) remains a practical tool for early recognition of melanoma despite its limitations [45].

### One Month Following Definitive Surgery

The patient is evaluated in a multidisciplinary melanoma tumor board for discussion of systemic adjuvant therapy. Examination reveals a well-appearing, normotensive, moderately obese man with a well-healed linear scar on the right bicep region. Total body skin examination reveals less than 20 nevi, all of which are clinically banal. No lymphadenopathy or hepatosplenomegaly are present. The patient is clinically disease-free. While eligible for a cooperative group trial involving randomization to 1 month of high-dose interferon, he is considered a poor candidate due to his history of CAD; systemic adjuvant therapy with 1 year of high-dose interferon is not offered on the basis of his primary tumor depth of 4 mm or less and node-negative status. Likewise, the patient is not interested in receiving any therapy with significant associated toxicity, as he wants to enjoy

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<th>Table 2. Clinical Warning Signs for Cutaneous Melanoma</th>
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<td><strong>ABCDE Criteria</strong></td>
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<td>A “Asymmetry”—one half of lesion does not match the other</td>
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<tr>
<td>B “Border” irregularity—edges are ragged, notched, or blurred</td>
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<tr>
<td>C “Color” variegation—pigmentation not uniform, may display shades of tan, brown, or black; white, reddish, or blue discoloration of particular concern</td>
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<td>D “Diameter”—diameter &gt; 6 mm, although any growth in a nevus warrants evaluation</td>
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<tr>
<td>E “Evolving”—lesion has changed over time—critical for nodular or amelanotic melanoma which may not exhibit classic criteria above; any “changing mole” should be evaluated by a skin specialist or otherwise considered for biopsy</td>
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Common nevi are generally small, round, brown or pink colored, flat or elevated, and number up to 50 in whites by age 40 years. Dysplastic nevi share some clinical features with melanoma but are best considered as markers for increased melanoma risk. Patients with numerous dysplastic nevi or the “atypical mole syndrome” (> 100 nevi with at least 1, and typically more than 5, demonstrating clinical atypia and size > 8 mm diameter) warrant regular examination (self and provider) and excisional biopsy for onset of suspicious clinical change.
his retirement. He opts for continued close observation with the melanoma tumor board and his local physicians (primary care and dermatologist providers), and remains disease-free 9 months following diagnosis and treatment.

• What are the options for adjuvant therapy for stage IIB melanoma?

Numerous adjuvant therapies have been investigated for the treatment of localized cutaneous melanoma following complete surgical removal. No survival benefit has been demonstrated for adjuvant therapies involving chemotherapy [46], passive (nonspecific) immunotherapy [47], vitamin therapy [48], or retinoids [49]. Interferon (IFN) alfa-2b therapy is the only U.S. Food and Drug Administration–approved adjuvant therapy for high-risk melanoma (defined as stages IIB, IIC, III), which is associated with a 40% to 80% chance of relapse and death [23,50]. The exact anticancer mechanism of IFN alfa remains unknown, although it is believed to diminish proliferation of tumor cells, induce apoptosis, and potentiate the immune response by increasing the numbers and activity of natural killer cells and cytotoxic T lymphocytes [51].

The efficacy of high-dose IFN alfa-2b (HDI) in patients with stage IIB (> 4 mm thickness, node negative pre-2002 AJCC staging) and stage III (node-positive) melanoma has been studied in 3 randomized, controlled Eastern Cooperative Oncology Group (ECOG)/Intergroup trials [52–54]. In these high-risk subgroups, 1 year of HDI produced substantial to significant reductions in disease-free survival. Assessment of overall survival benefit in the study population produced variable results, with only 2 studies demonstrating a statistically significant benefit of HDI [52,54]. Data regarding HDI efficacy for tumors 4 mm depth or less with or without histologic ulceration (stages IIB and IIA, respectively, per current 2002 AJCC melanoma staging guidelines) are lacking. Pooled analysis of the 3 cooperative group trials, with median follow-up ranging from 2.1 to 12.6 years, has revealed strong evidence for improved relapse-free survival but not overall survival for patients treated with HDI compared with observation [55]. However, the potential benefits of HDI must be weighed against its substantial tolerability and toxicity issues, including year-long duration of therapy, commonly associated flu-like symptoms, and potential for significant adverse reactions (eg, severe neuropsychiatric, autoimmune, ischemic, and infectious disorders) [56].

Numerous vaccines are under investigation to provide active specific immunotherapy for the treatment of melanoma. Vaccine therapy is designed to elicit a host immune response to known or unknown tumor-associated antigens and is generally associated with minimal toxicity (eg, injection site reactions). There are many clinical trials of melanoma vaccines in progress, but as yet, no large phase III randomized trial has demonstrated a survival advantage [57]. In addition, most of the current trials are restricted to individuals with advanced melanoma (nodal and visceral disease) and may require certain human leukocyte antigen haplotypes (eg, A2 positivity for peptide vaccines), which are not prevalent in certain ethnicities [58].

• What is the value of baseline and surveillance studies for patients with asymptomatic cutaneous melanoma?

Baseline Staging and Surveillance

Careful history taking, review of systems, and physical examination are the most important aspects of initial workup for patients with cutaneous melanoma, with sentinel lymph node biopsy for pathologic staging of the regional nodal basin for primary tumors 1-mm or greater depth [59]. Additional laboratory, chest radiography, or further imaging studies should generally be symptom- and exam-directed (ie, performed if physical findings [lymphadenopathy, hepatomegaly, cutaneous metastasis] or review of systems [eg, unanticipated weight loss, headache, diplopia, bone pain, change in bowel habits] suggest metastatic disease or if the patient has documented nodal metastasis from sentinel lymph node biopsy). Recently published data have shown that baseline and surveillance laboratory studies, chest radiographs, and other imaging studies (eg, positron emission tomography, computed tomography, bone scans, brain magnetic resonance imaging) are not typically beneficial in stage I and II (cutaneous) melanoma patients without clinical signs or symptoms of metastasis or disease recurrence [60–62]. In a study of 224 melanoma patients with localized invasive melanoma who prospectively underwent baseline chest radiography and serum lactate dehydrogenase (LDH) testing following melanoma diagnosis, no true-positive chest radiograph or LDH findings were noted, and those with sentinel lymph node–positive disease showed no correlation with either abnormal chest radiograph or LDH [62]. Many melanoma specialists believe that chest radiograph and LDH should no longer be accepted into the routine clinical follow-up of melanoma patients in the absence of data supporting their use [63].

In general, current clinical practice guidelines developed by the National Comprehensive Cancer Network (NCCN) recommend that baseline or surveillance chest radiograph and LDH be performed on an “optional” basis every 3 to 12 months at the discretion of the clinician. Further imaging studies (computed tomography, positron
emission tomography, magnetic resonance imaging) are also deemed unnecessary, but should be obtained as clinically indicated for documentation or suspicion of metastasis [64]. Since an estimated 5% of patients with a history of melanoma will develop new primary melanoma (generally within the first 3 years following diagnosis) [65], the NCCN guidelines promote annual skin examinations for life.

Following surgical resection, regular clinical follow-up should be initiated to detect local, regional, and distant disease metastasis. Physical examination should include total cutaneous examination to exclude local melanoma recurrence or new primary melanoma, examination of regional and distant lymph node basins for adenopathy, and examination of the abdomen for hepatosplenomegaly. Patients should also be educated regarding warning signs of local, regional, or distant melanoma recurrence to assist with early detection of metastatic disease, including change in the melanoma excision site (new induration, nodule development, pigment change in or around the scar), development of in-transit or regional adenopathy, or alteration in review of systems as described above. Early detection of metastasis may improve survival in individuals with limited resectable disease [66], although there is no known survival benefit for presymptomatic detection of distant metastatic disease, largely related to the lack of effective therapy for advanced melanoma at present [62,67].

- How can melanoma be diagnosed early and who should be targeted for education and early detection messages?

Role of the Primary Care Provider

Primary care physicians are uniquely positioned to examine their patients for atypical moles and early melanoma. Physicians can play 1 of 3 roles: screen their high-risk patients themselves, provide training opportunities for nurses and physician assistants in order to enable them to do screening, or refer these patients to specialists. Patients with many moles or at least a few (≥ 5) atypical moles found in a baseline examination can subsequently be followed by dermatologists. Fewer than 20% of Americans have a dermatologist, whereas approximately 85% see a physician every 2 years (most commonly, a primary care physician in the office setting) [68]. In 1 study, physician-detected melanoma, compared with patient or family detection, was associated with an increase in the probability of detecting thinner (≤ 0.75 mm) melanomas (relative risk, 4.2 [95% confidence interval [CI], 1.4–11.1]; P = 0.01) with higher likelihood for cure [69]. Brady et al also found that physicians were 3.6 times more likely to detect thin lesions (≤ 0.75 mm) compared with non-physician detectors (95% CI, 2.1–6.5; P < 0.001) [70].

As an external tumor, melanoma should be more readily discovered than other types of cancer, and it has been stated that “melanoma writes its message in the skin with its own ink and is there for all to see” [71]. Education can alert patients on ways to recognize melanoma, especially stressing the ABCDE rule [41,43]. Publicity in the physician office could promote awareness of risk factors, prompt medical attention for suspect lesions, and increase skin self-examination rates for high-risk persons. Increasingly, skin self-examinations have been improved through the use of photo books given to high-risk patients in busy dermatology referral sites [72]. Because patients may be unaware of melanoma on the back and other areas that are difficult for self-inspection, visual examinations by physicians and nurses could aid in early detection. Professional education can be facilitated by melanoma’s unique visual nature and teaching through pictorial displays, atlases, and Web-based education.

In general, the most efficient screening programs target individuals at high risk for developing or dying from the disease. Screening that targets high-risk individuals, such as those with fair skin, tendency to sunburn, increased mole count and/or dysplastic nevi, and family history of melanoma, may be more useful and lead to a higher yield than routine screening of all patients.

It is well documented that men, particularly those aged 50 years and older, have higher incidence and mortality rates for melanoma [73–76]. Of particular relevance to mortality rates, during the past decade the U.S. incidence of thick tumors (> 4 mm) increased significantly only in males aged 60 years and older [77]. Nearly 50% of all melanoma deaths in the United States are in white men aged 50 years and older [78]. A U.S. study of mass screening for melanoma found a high yield by targeting middle-aged and older men, with the greatest utility in men aged 50 years or older [79]. The yield among men aged at or above 50 years was 2.63, a factor of 1.8 greater than among men younger than age 50, 2.8 times greater than among women younger than aged 50 and 2.4 times greater than among women aged 50 years and older. Among middle-aged and older men, the yield of confirmed melanoma was even higher if they reported a changing mole (4.60/1000) or skin type I/II (3.80/1000). When both risk factors were present, the yield was 6.63 per 1000 screenings. Thus, middle-aged and older men accounted for a disproportionately high number of detected melanomas while representing only a small fraction of total screened individuals.

This suggests that in order to optimize benefit from mass skin cancer screening and public education, publicity campaigns should expand outreach to men aged 50 years and above. Marketing strategies might also include specially crafted messages to encourage middle-aged and older men to ask their physicians for a skin cancer check. Primary care
physicians can also play another important prevention role by counseling their melanoma patients to make sure that their adult first-degree family members are screened and that their children use full sun protection when outdoors.

• How can I screen high-risk patients in a time-efficient manner?

Time burdens, while onerous, do not have to be insurmountable. Screening examinations can be brief and woven into the routine physical examination, with particular emphasis on hard-to-see areas such as the back (where at least a third of melanomas are found in men) and the legs of women [80]. Many middle-aged and older patients have 5 to 10 physician visits per year [68], and skin cancer screening can be incorporated into at least 1 of these visits. Screening prompts and chart reminders, successfully used in other health promotion counseling [81], should be studied as ways to augment skin cancer screening in the primary care setting.

Dermatologists in many countries have been trained in the use of dermoscopy, a noninvasive imaging technique that increases the ability to distinguish accurately between suspicious moles and other pigmented lesions using skin surface microscopy. Primary care physicians in Australia have also been trained in dermoscopy. In a recent analysis, 4 standard dermoscopy algorithms (pattern analysis, the 7-point checklist, the ABCD rule, and the Menzies’ method) were assessed following training in a “nonexpert” setting involving 61 medical practitioners, mainly primary care physicians in Australia. Participant assessment of clinical and dermoscopic images of 40 melanocytic skin lesions was undertaken and revealed high rates of diagnostic accuracy (73%–81%) following self-guided training with all 4 algorithms [82]. Dermoscopy use has not been as widespread in the United States, either among practicing dermatologists or primary care providers, largely due to lack of sufficient training [83].

• What is the cost-effectiveness of melanoma screening?

Economic savings might represent yet another reason for conducting skin cancer examinations. Tsao et al [84] provided a baseline estimate of melanoma related costs in the United States. The annual direct cost of treating newly diagnosed melanoma in 1997 was estimated to be $563 million. Stages I and II disease each comprised about 5% of the total cost whereas stages III and IV disease consumed 34% and 55% of the total cost, respectively. About 90% of the total annual direct cost of treating melanoma in 1997 was attributable to less than 20% of patients with advanced disease [84].

An Australian study of the cost-effectiveness of every 5-year screening for melanoma by family practice physicians for men over age 50 found a cost-effectiveness of $6900 per year of life saved for men (Australian dollars). Available data suggest that the cost-effectiveness of such screenings is comparable with that of other cancer screenings, including breast cancer [85]. Freedberg et al found that American Academy of Dermatology skin cancer screening increased both life expectancy and quality-adjusted life expectancy [86]. Although the Academy screen could not be directly compared with other cancer screening cost-effectiveness studies, a 1-time skin cancer screening was generally comparable in cost-effectiveness with screening for breast cancer in women aged 55 to 65 years [86]. Strong benefits to screening were observed for men aged 50 years and older.

• What type of skin cancer training programs are available to practicing physicians?

Skin Cancer Training for Primary Care Providers

In a randomized trial, Gerbert and colleagues [87] tested a brief multicomponent educational intervention designed to improve the skin cancer diagnosis and evaluation planning of primary care residents to a level equivalent to that of dermatologists. The intervention consisted of face-to-face individualized feedback sessions, an interactive seminar, and provision of educational materials and tools. Results showed that primary care residents who participated in the intervention performed significantly better than the control group on overall diagnosis and evaluation planning of all 3 cancerous lesion categories. The findings suggest that a targeted and multicomponent educational intervention aimed at primary care residents could result in proficient triage of cancerous lesions. The authors recommended development of other less labor-intensive teaching tools to train residents in evaluating skin lesions, such as computer-based applications. Further evaluation of the cost-effectiveness and feasibility of this type of training is warranted.

Primary care providers are able to deliver preventive health care services to the majority of the general population. Early detection of skin cancer may reduce mortality, but many primary care providers do not participate in skin cancer control activities due to lack of training and confidence. A 2-hour Basic Skin Cancer Triage curriculum was tested with a convenience sample of 28 primary care providers [88]. Assessments included skills (evaluated by a 20-item slide quiz), confidence, knowledge, and attitudes measured pre- and post-training. Provider ability to accurately diagnose and triage lesions significantly improved (from 46% to 64%
[P < 0.001] and 61% to 71% [P < 0.001], respectively). The greatest improvement in triage ability occurred in providers’ ability to appropriately reassure patients about lesions (from 49% to 70%; P < 0.001). There were also significant improvements in both knowledge of skin cancer control practices (from 68% to 74% correct answers; P = 0.026) and confidence in ability to provide skin cancer preventive services (from 2.95 to 4.13 on a scale from 1 to 5; P < 0.001) [88].

• When should patients be referred to a dermatologist?

Many Americans at risk for melanoma have never been fully screened for melanoma nor seen a dermatologist for an expert skin cancer examination. Adding a question regarding past history of a full skin cancer screen would be a useful adjunct to the medical intake form. Referrals to dermatologists should be considered for any patient who has any of risk factors in Table 3.

CONCLUSION

Screening and early detection programs could save many lives otherwise lost to melanoma [89]. This cancer is external and visible, risk factors are well documented, and screening tests are safe and acceptable to the public. Furthermore, early melanoma can usually be cured by simple surgical excision. Compared with colorectal, prostate, and breast cancer, melanoma is the only early detectable cancer where death rates are rising, but the number of screened individuals has changed very little or even diminished over the past decade [90]. Targeted efforts to reach high-risk, previously unscreened individuals would be a welcome first step. Men older than 50 years or persons with fair skin, many moles, or a family history of melanoma, particularly in first-degree relatives, should be referred to a dermatologist for a full-body examination and counseling.

Table 3. Primary Care Triage Considerations for Dermatology Referral

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<tr>
<th>Patients with many moles—common nevi and/or clinically dysplastic</th>
<th>Patients with at least a few (≥5) atypical/dysplastic moles</th>
<th>Patients with a history of cutaneous melanoma</th>
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<tbody>
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<td>Patients with a history of nonmelanoma skin cancer (basal cell carcinoma, squamous cell carcinoma) who have not seen a dermatologist in the past year</td>
<td>Patients with fair skin who burn easily or who have numerous actinic keratoses (sun-induced pre-cancers)</td>
<td>Patients with a strong family history of melanoma, particularly in first-degree relatives</td>
</tr>
</tbody>
</table>

REFERENCES

49. Sondak VK, Liu PY, Flaherty LE, et al. Phase II evaluation of all-trans-retinoic acid plus interferon alfa-2a in stage IV


CME EVALUATION: Prevention and Detection of Melanoma in the Primary Care Setting

DIRECTIONS: Each of the questions below is followed by 4 possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. Mortality rates for melanoma are increasing most rapidly in:
   (A) Men younger than 50 years of age
   (B) Men older than 50 years of age
   (C) Women younger than 50 years of age
   (D) Women older than 50 years of age

2. Thin cutaneous melanoma is most likely to be detected by
   (A) The patient
   (B) The patient’s significant other
   (C) The patient’s physician or other health care provider
   (D) The patient’s other family members (parent, sibling, son/daughter)

3. Which of the following is NOT a risk factor for melanoma?
   (A) Age younger than 15 years
   (B) Numerous common and/or dysplastic moles
   (C) History of severe childhood sunburns/excessive sun exposure
   (D) Male gender

4. The ABCD clinical warning signs may NOT apply for which of the following melanoma subtypes?
   (A) Superficial spreading melanoma
   (B) Acral lentiginous melanoma
   (C) Lentigo maligna melanoma
   (D) Nodular and desmoplastic melanoma

5. Baseline and surveillance laboratory and radiographic studies for primary cutaneous melanoma have the greatest utility when
   (A) The primary melanoma is less than 1-mm depth
   (B) The primary melanoma is ulcerated
   (C) Signs or symptoms suggest metastatic disease or melanoma recurrence
   (D) The primary melanoma is greater than 4-mm depth
EVALUATION FORM: Prevention and Detection of Melanoma in the Primary Care Setting

Participants may earn up to 1 hour of category 1 credit by reading the article named above and correctly answering at least 70% of the accompanying test questions. A certificate of credit and the correct answers will be mailed within 6 weeks of receipt of this page to those who successfully complete the test.

Circle your answer to the CME questions below:

1. A B C D
2. A B C D
3. A B C D
4. A B C D
5. A B C D

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   __ Excellent __ Good __ Fair __ Poor

2. This article was fair, balanced, free of commercial bias, and fully supported by scientific evidence.
   __ Yes __ No

3. Please rate the clarity of the material presented in the article.
   __ Very clear __ Somewhat clear __ Not at all clear

4. How helpful to your clinical practice was this article?
   __ Very helpful __ Somewhat helpful __ Not at all helpful

5. What changes will you make in your practice as a result of reading this article?

   _______________________________________________________

   _______________________________________________________

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6. What topics would you like to see presented in the future?

   _______________________________________________________

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