

Diagnosis  
and Treatment  
of Early

# *Melanoma*



## *Consensus Statement*

NIH Consensus Development Conference  
January 27-29, 1992

Volume 10, Number 1

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*Diagnosis and Treatment of Early Melanoma. (Reprinted from NIH Consens Dev Conf Consens Statement 1992 Jan 27-29; 10(1).*

*This statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge on the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.*



## ***Consensus Statement***

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## Abstract

The National Institutes of Health Consensus Development Conference on Diagnosis and Treatment of Early Melanoma brought together experts in dermatology, pathology, epidemiology, public education, surveillance techniques, and potential new technologies as well as other health care professionals and the public to address (1) the clinical and histological characteristics of early melanoma; (2) the appropriate diagnosis, management, and followup of patients with early melanoma; (3) the role of dysplastic nevi and their significance; and (4) the role of education and screening in preventing melanoma morbidity and mortality. Following 2 days of presentations by experts and discussion by the audience, a consensus panel weighed the scientific evidence and prepared their consensus statement.

Among their findings, the panel recommended that (1) melanoma in situ is a distinct entity effectively treated surgically with 0.5 centimeter margins; (2) thin invasive melanoma, less than 1 millimeter thick has the potential for long-term survival in more than 90 percent of patients after surgical excision with a 1 centimeter margin; (3) elective lymph node dissections and extensive staging evaluations are not recommended in early melanoma; (4) patients with early melanoma are at low risk for relapse but may be at high risk for development of subsequent melanomas and should be followed closely; (5) some family members of patients with melanoma are at increased risk for melanoma and should be enrolled in surveillance programs; and (6) education and screening programs have the potential to decrease morbidity and mortality from melanoma.

The full text of the consensus panel's statement follows.

## Introduction

The incidence of melanoma of the skin appears to be rapidly rising. The increased incidence may be partially attributable to increased detection resulting from screening. In 1992, approximately 32,000 newly diagnosed cases and 6,700 deaths are expected in the United States. Melanoma tends to occur in adults in the prime of their family and professional lives. Detection and surgical treatment of the early stages of this malignancy are usually curative. In contrast, diagnosis and treatment in late stages often have dismal results.

Traits associated with an increased risk of developing melanoma include: multiple typical moles, atypical moles, freckling, history of severe sunburn, ease of burning, inability to tan, and light hair/blue eyes. Other factors include the presence of familial atypical mole and melanoma syndrome, disorders of DNA repair, and excessive sun exposure.

Efforts to increase public awareness of melanoma and its treatment without causing unnecessary fear presents a challenge. Public and professional education campaigns that emphasize sun protection and periodic total skin examinations for early detection of melanoma have the potential to save lives.

To resolve questions relating to the diagnosis and treatment of early melanoma, the National Cancer Institute, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the Office of Medical Applications of Research of the National Institutes of Health convened a consensus development conference January 27-29, 1992. After 2 days of presentations by experts and discussion by the audience, a consensus panel drawn from the specialties of dermatology, medical and surgical oncology, pathology, internal medicine, epidemiology, public health, biostatistics, and genetics considered the evidence and agreed on answers to the following key questions:

- What are the clinical and histological characteristics of early melanoma?
- What is the appropriate management of patients with early melanoma regarding its diagnosis and treatment?

- After treatment of early melanoma, should patients and family members be followed: Why and how?
- Do dysplastic nevi exist and what is their significance?
- What is the role of education and screening in preventing melanoma morbidity and mortality?
- What are the future directions for research, including primary prevention?

# What Are the Clinical and Histological Characteristics of Early Melanoma?

## Clinical Features

Cutaneous melanoma is a distinct clinical and histologic entity. Clinical features of de novo pigmented lesions suggestive of melanoma include Asymmetry, Border irregularity, Color variegation, and Diameter greater than 6 millimeters (the ABCD's of melanoma). An asymmetric lesion is one that is not regularly round or oval. Border irregularity refers to notching, scalloping, or poorly defined lesion margins. Color variegation refers to a lesion with shades of brown, tan, red, white, or blue/black, or combinations thereof. Although a high level of suspicion exists for a lesion greater than 6 millimeters in diameter, early melanomas may be diagnosed at a smaller size. Earliest lesions are flat or macular and may have altered skin markings. However, a palpable lesion with uniform or irregular surface features or benign-appearing pigmented and nonpigmented lesions that change rapidly can represent early melanoma.

Melanoma has classically been divided into subtypes:

- Superficial spreading melanoma (SSM) is the most common subtype, located on any anatomic site, and with the above typical clinical features described for melanoma.
- Nodular melanoma (NM) presents as an elevated or polypoid lesion on any anatomic site. It may be uniform in pigmentation and frequently shows ulceration when advanced.
- Lentigo maligna melanoma (LMM) occurs as a macular lesion on sun-exposed skin (head, neck), often in elderly patients.
- Acral lentiginous melanoma (ALM) presents as a darkly pigmented, flat to nodular lesion on palms, soles, and subungually.

## Histologic Features

Fully developed melanoma has cohesive clusters and single atypical melanocytes at the dermal-epidermal junction. Single melanocytes and clusters of melanocytes are dispersed through the full thickness of the epidermis. The invasive component forms an asymmetric lesion in the dermis, composed of atypical epithelioid and/or spindled melanocytes with an increased nuclear/cytoplasmic ratio; pleomorphic nuclei showing prominent nucleoli and mitoses, sometimes atypical;

and abundant eosinophilic cytoplasm. There is no evidence of maturation from the superficial to deep component of the lesion. An associated inflammatory response, including tumor-infiltrating lymphocytes, is often present. Occasionally, angiolymphatic invasion and/or satellite nodules can be identified. Features of regression, including the presence of melanophages, lymphocytes, fibrosis, and vascular ectasia, with absence or degeneration of melanocytes in the papillary dermis, sometimes with no overlying intraepidermal component, may be present.

## **Prognostic Features**

A number of clinical and histologic prognostic indicators affecting survival of patients have been evaluated. The single most predictive factor for recurrence and prognosis of melanoma is the depth of invasion of the original lesion, measured in millimeters from the top of the granular cell layer to the deepest point of tumor extension. Other prognostic factors may include ulceration, regression, level of invasion (Clark), anatomical location, radial versus vertical growth phase of the lesion, and patient gender. The most significant of these may be ulceration. The clinical/histologic subtype (SSM, NM, LMM, ALM) does not appear to provide additional prognostic information when depth of invasion is taken into consideration. Regression needs to be better defined and quantitated before its prognostic significance can be assessed accurately.

## **Early Melanoma**

For the purpose of this discussion, early melanoma includes melanoma in situ and thin invasive lesions less than 1 millimeter in depth. Data currently available suggest a greater than 99 percent long-term, disease-free survival for patients with melanoma in situ and greater than 90 percent long-term overall survival for patients with lesions less than 1 millimeter; patients with intermediate (1.0-4.0 mm) and high-risk (> 4.0 mm) melanomas have a greater risk of recurrence and/or death.

## **Melanoma In Situ**

Melanoma in situ is a specific diagnosis for flat or elevated lesions with histologic features identical to those described for melanoma but confined to the full thickness of the epidermis and adnexal epithelium. Descriptive clinical/pathological terms that have been used for melanoma in situ include lentigo maligna, atypical melanocytic proliferation, and pagetoid



melanocytic proliferation. Melanoma in situ is a lesion of uncertain natural history, but it can be treated effectively with conservative surgery. Once the lesion is totally removed, melanoma in situ should have *no* impact on a patient's longevity or insurability.

## **Pathology Reporting**

After appropriate biopsy of a suspicious lesion, complete and accurate pathology reports can be issued based on permanent sections. Frozen section evaluation is not recommended for primary diagnosis. Pathology reports should include certain essential data to assess prognosis and guide subsequent management and followup. The pathology report should reflect the diagnosis and histologic characteristics but need not provide recommendations for treatment.

- Essential to the report:
  - Diagnosis
  - Measured thickness (in millimeters)
  - Margins
- Suggested additional information:
  - Subtype (SSM, NM, LMM, ALM, melanoma in situ)
  - Level (Clark I-V)
- Ulceration (present/absent)
- Regression (present/absent)
- Precursor lesion (present/absent; type)
- Satellitosis (present/absent)
- Angiolymphatic invasion (present/absent)
- Mitotic activity
- Host response (lymphocytic infiltrate)
- Radial versus vertical growth phase

# What Is the Appropriate Management of Patients With Early Melanoma Regarding Its Diagnosis and Treatment?

## Diagnostic Techniques

A properly performed biopsy is critical in establishing the diagnosis of melanoma. The histologic interpretation of the biopsy will determine the prognosis and plan of therapy. An excisional biopsy with a narrow margin of normal-appearing skin is recommended for any suspicious lesion. The use of Wood's lamp may be helpful in delineating the borders of suspicious lesions. The excisional biopsy (including punch, saucerization, or elliptical excision) should include a portion of underlying subcutaneous fat for accurate microstaging. Removal of a suspicious lesion by shaving or curettage is not recommended. For large lesions where an excisional biopsy would represent a formidable procedure, an incisional biopsy can be performed. This should entail removal of an ellipse or core of full-thickness of skin and subcutaneous tissue at the most raised and irregular site, or, if this is not apparent, at an area of dark pigmentation. The diagnosis and microstaging of the suspicious lesion should be performed on fixed histological specimens.

## Patient Evaluation

The initial evaluation of a patient with a suspected melanoma includes a personal history, a family history, and an appropriate physical examination that includes a total body skin examination and palpation of the regional lymph nodes. The focus of this evaluation is to identify risk factors, signs or symptoms of metastases, atypical moles, and additional melanomas.

## Surgical Therapy

Standard therapy for melanoma is surgical excision. For melanoma in situ, excision of the lesion or biopsy site with a 0.5 centimeter border of clinically normal skin and layer of the subcutaneous tissue is sufficient. This should be curative.

Previously, the therapy for invasive melanoma was to excise lesions with up to 5 centimeter margin of normal skin, often necessitating skin grafting procedures for reconstruction. Recent clinical trials suggest that thin melanomas can be excised with narrower margins. For melanomas less than 1 millimeter thick, a 1-centimeter margin of clinically normal

skin and underlying subcutaneous tissue down to fascia is recommended as an appropriate excision. The surgical margin should be histologically uninvolved by tumor. This excision often can be performed with a primary closure of the surgical defect without the need for reconstructive procedures. The use of this narrower margin has allowed better cosmetic and functional results apparently without compromising survival. There are no studies indicating that the removal of underlying fascia enhances survival or decreases the risk of local recurrences.

Currently, there is not enough clinical experience utilizing microscopically controlled excision (Mohs surgery) for the treatment of primary melanomas to recommend it as an alternative approach. Mohs surgery may prove a useful technique for certain types and locations of melanoma, but more data are needed.

The results of a 1-centimeter margin of excision for early melanoma (less than 1 millimeter thick) are excellent, with approximately 95 percent 8-year survival. Elective (i.e., prophylactic) regional lymph node dissection is not indicated in this group of patients. Extensive diagnostic studies (CT, MRI, and nuclear scans) are not indicated, are economically wasteful, and should not be performed in staging asymptomatic patients. There are no data to support the practice of obtaining chest x-rays and liver function studies, although many physicians still believe they should be performed as a baseline.

# After Treatment of Early Melanoma, Should Patients and Family Members Be Followed? Why and How?

## Assessment of Risk for Relapse and Development of Subsequent Melanomas

The prognosis for long-term survival for patients with early invasive melanoma is excellent. Life-threatening metastases following complete removal of early melanoma are rare. Patients with relapse tend to do so at local or regional sites that may still be amenable to surgical therapy.

Overall, there is an increased incidence of second primary melanomas in affected patients (a minimum of 3 percent will develop second melanomas within 3 years). The risk may be higher in patients with associated atypical moles and is particularly high in affected members of melanoma-prone families (approximately 33 percent will develop second melanomas within 5 years). Thus, patients need close followup for the development of subsequent primary melanomas. Studies show that subsequent melanomas diagnosed in a surveillance program are thinner than the initial melanoma.

Familiar patterns of melanoma exist. Persons with atypical moles and a positive family history of melanoma (at least one other affected family member) are at unusually high risk of developing melanoma. Thus, it is extremely important to identify affected kindreds so that these patients may be closely followed. Patients with xeroderma pigmentosum, a rare genetic disorder, have a high incidence of melanoma.

## Recommendations for Followup After Surgical Therapy

- Patients should be followed with serial examinations of the skin and palpation of the excision site and regional lymph nodes. Because the occurrence of distant metastases in patients with early melanoma is unusual, it is not necessary to perform routine screening for occult visceral lesions. Choice of interval between examinations is arbitrary. An appropriate interval may be 6 months for patients without atypical moles and without a family history of melanoma. If patients have not shown evidence of recurrence or a second primary melanoma by the second anniversary after diagnosis, the interval between examinations can be extended to 1 year.

For patients with atypical moles, a positive family history of melanoma or atypical moles, or any of the poor prognostic factors for recurrence, a shorter interval between examinations, such as 3 to 6 months, should be considered. Baseline photographs may be useful in following atypical moles. The decision to extend the interval and the choice of interval between evaluations after a 2-year observation period should be based on the stability and characteristics of the atypical moles.

There appears to be little risk of relapse for patients with melanoma in situ. There are few data available on the risk for subsequent melanomas in patients with melanoma in situ who do not have atypical moles. However, it seems prudent to follow these patients with serial skin examinations, including the excision site, at regular intervals.

- Patients can assist in their management by performing monthly self-examination of the skin. In addition, patients should be counseled to avoid excessive sun exposure and to use protective clothing and sunscreens. The use of oral contraceptives and development of subsequent pregnancies do not appear to influence the recurrence rate in average risk patients; the effects of these variables are still being evaluated in high-risk cohorts.
- Obtaining a detailed family history from a patient with melanoma is critical in establishing whether the patient belongs to a melanoma-prone family. However, history alone may not be sufficient to establish this risk factor. The presence of atypical moles in the patient may be an important clue in this regard. If a patient has a positive family history of melanoma or has atypical moles, it is recommended that first-degree family members be evaluated for the presence of atypical moles and melanoma. Family members with atypical moles should be enrolled into a regular screening program.

Because family history of melanoma is an important risk factor for the development of melanoma, it may be worthwhile to perform initial screening in first-degree family members of all patients with melanoma.

# Do Dysplastic Nevi Exist and What Is Their Significance?

## Atypical Moles

Atypical moles (dysplastic nevi) are acquired pigmented lesions of the skin whose clinical and histologic appearances are different from typical common moles (common nevi). Neither the clinical nor the histologic features of atypical moles that occur in families differ from those of sporadic atypical moles. Atypical moles vary in size and are often larger than common moles. Atypical moles have macular and/or papular components and have borders that usually are irregular and frequently are ill-defined. Their color is variegated, ranging from tan to dark brown often on a pink background. While these atypical moles may appear anywhere on the body, they especially occur on the trunk.

## Familial Atypical Mole and Melanoma Syndrome

Some families are affected with an inherited familial atypical mole and melanoma (FAM-M) syndrome. This syndrome is defined by (1) occurrence of melanoma in one or more first or second degree relatives, (2) large numbers of moles (often greater than 50) some of which are atypical and often variable in size, and (3) moles that demonstrate certain distinct histologic features.

Persons with this syndrome have a markedly increased risk of developing melanoma. Their lifetime risk may be as high as 100 percent. Intensive surveillance, necessary for diagnosis and treatment of early melanoma in these patients, has been successful in preventing life-threatening complications. This regimen requires monthly self-examination by the patient and physician examination initially at 4- to 6-month intervals. Baseline high-quality total body photographs may aid such examinations, as may other enhanced optical techniques such as epiluminescence microscopy. These techniques need further research to validate their effectiveness.

## Risk Factors for Melanoma in FAM-M Syndrome

The role of nongenetic factors in this syndrome is not fully understood. The role of oral contraceptives and pregnancy in regard to the development of melanomas in women with FAM-M syndrome has not been determined but is under study. Further research is necessary to define the role of sun exposure, UVB and UVA, in promoting the development of melanomas in

individuals with the FAM-M syndrome. Broad spectrum sunscreens and/or physical blockers should be used when sun exposure is anticipated.

### **Skin Examination and Biopsy**

In examining patients, physicians should biopsy moles that have developed or shown change in any of the following characteristics: asymmetry, border irregularity, color, diameter, or erythema. Detection of lesions may be enhanced by Wood's light examination. Lesions that develop de novo may be monitored for 6 months to 1 year, but they should be biopsied if there is a suspicion of melanoma or rapid changes occur. To permit adequate diagnosis, the biopsy should be a total removal by punch, saucerization, or elliptical excision to include a portion of underlying subcutaneous fat.

### **Histologic Criteria**

The term "dysplastic nevus" has been used by various investigators in significantly different ways thereby generating a great deal of controversy, and should be avoided. This confusion has resulted in a tenfold difference in estimates of the frequency of these lesions. The lesion is generally diagnosed using histologic criteria of architectural disorder with asymmetry, subepidermal fibroplasia (concentric eosinophilic and/or lamellar), and lentiginous melanocytic hyperplasia with spindle or epithelioid melanocytes aggregating in nests of variable size and fusing with adjacent rete ridges to form bridges. Frequently there is a variable dermal lymphocyte infiltration. Also helpful in the identification of these nevi is the presence of a "shouldering" phenomenon in which the intraepidermal melanocytes extend singly or in nests beyond the main dermal component.

The essence of the problem in defining the significance of nevi with architectural disorder seems to rest in the degree of melanocyte nuclear atypia in the lesion required for the histologic diagnosis. At one end of the spectrum are nevi with the architectural disorder described above, usually recognizable with the low power or scanning microscope objective. Atypical melanocytes may be absent or scant and randomly scattered through the lesion. At the other end of the spectrum is a lesion with extensive and severe melanocytic atypia that may pose a difficult differential diagnosis from melanoma in situ. Because of the controversy surrounding use of the term "dysplastic nevus," it seems appropriate to discontinue use of that diagnosis and to describe these lesions as "nevus with architectural

disorder” with a statement as to the presence and degree of melanocytic atypia. It is strongly recommended and essential that dermatologists, pathologists, and dermatopathologists formulate a reproducible schema for diagnosing and reporting these nevi. In providing the histologic interpretation of a nevus with architectural disorder with varying degrees of melanocytic atypia, the pathologist should note whether the margins of the specimen are involved by the process. If re-excision is indicated, margins of 0.2 to 0.5 centimeter are appropriate.

### **Nonfamilial Atypical Moles**

There is a continuum of clinically and histologically atypical moles in the population. Atypical moles clearly do occur in individuals with no family history of melanoma or without an increased number of moles that are clinically atypical in appearance. The clinical significance of the histologic diagnosis of nevus with architectural disorder must be evaluated separately for each case. For those individuals having atypical moles without a family history of melanoma, the risk of developing a melanoma is clearly different from that in someone with FAM-M syndrome. The increased relative risk for an individual with nonfamilial atypical moles to develop melanoma compared with that of general population may range from two to eight. Epidemiologic studies of patients with nonfamilial atypical moles could clarify further the needed interval to be used for continued surveillance of such individuals.



# What Is the Role of Education and Screening in Preventing Melanoma Morbidity and Mortality?

## Primary Prevention

To reduce morbidity and mortality from melanoma, efforts should be undertaken aimed at both primary (risk reduction) and secondary (early detection) prevention. Different approaches are needed for these two types of prevention.

Ongoing public education is the major, currently available means of achieving primary prevention of melanoma. There are several ways to accomplish this: mass media campaigns; educational campaigns in schools, worksites, and other community settings; and patient education by physicians and other health care providers.

Evidence for the potential effectiveness of such campaigns is available in the area of skin cancer prevention as well as the prevention of other conditions, such as coronary heart disease and stroke. Public educational campaigns in other countries aimed at skin cancer prevention through risk factor reduction have resulted in decreased outdoor sun exposure among targeted populations as well as increased use of sunscreens.

Two strategies are needed for these educational activities: a high-risk strategy and a population-based strategy. The high-risk strategy should target individuals at increased risk due to the presence of one or more of the following risk factors: (1) large number of typical moles; (2) presence of atypical moles; (3) family history of melanoma; (4) prior melanoma; and (5) history of repeated severe sunburns, ease of burning, freckling, or inability to tan. Individuals who have these characteristics should be educated concerning the fact that they are at increased risk of developing melanoma. They should be strongly encouraged to minimize their future risk through reducing exposure to UV radiation.

Recommendations for accomplishing this should include avoiding exposure to sunlight unless protected by clothing, hats, and/or application of broad spectrum sunscreens of SPF 15 or higher and avoiding exposure to midday sunlight and tanning parlors. Strict avoidance of sunburning should be strongly recommended to this group.

The general population should also be encouraged to minimize exposure to UV radiation. The educational campaign for primary prevention should use multiple sources, including television, radio, newspapers, posters, and magazines. The messages should be clear, simple, and focused. They should also include additional reasons for avoiding sun exposure that may provide more incentive to many people, in particular that of avoiding premature skin wrinkles. Given the importance of childhood sun exposure to subsequent risk of developing melanoma, as well as the fact that childhood lifestyle behaviors often persist into adulthood, educational programs beginning in elementary school should be a major focus of these campaigns.

Physicians and nurses involved in primary care specialties (pediatrics, internal medicine, family practice, and obstetrics/gynecology) are important in transmitting information to patients and their families. They should provide brief educational messages concerning melanoma, should learn to identify members of high-risk groups, and should stress protective measures.

## **Secondary Prevention**

There is sufficient evidence to warrant screening programs for melanoma in the United States. Melanoma meets most of the criteria for initiating screening. The condition represents an important public health problem in terms of morbidity and mortality. There is a reliable screening test (visual inspection), which is safe, relatively inexpensive, and acceptable to the public. There is a latent, asymptomatic phase to the disease during which screening can be accomplished. A safe, effective treatment (surgical excision) exists, which favorably affects subsequent morbidity and mortality.

Two other criteria for screening, which ideally should also be present before initiating screening programs, are not met. The primary care medical community is not yet adequately prepared for undertaking or responding to patient-screening programs. A randomized trial of screening versus no screening has not been done. Preliminary evidence from uncontrolled trials in countries such as Scotland, however, suggests that screening programs may favorably influence morbidity and mortality rates within several years of inception. These trials have shown that it is feasible to teach primary care physicians how to perform skin examinations and to attract the public into these screening efforts.

Secondary prevention programs should include both high-risk and population-based components. They should incorporate both public and professional elements. The public efforts should aim at education concerning the need for periodic screening for melanoma. The public should be encouraged to ask their primary care physicians and nurses for periodic skin examinations when seeing them for other purposes, for example, a physical examination. They also should be taught warning signs concerning melanoma, that is, the ABCD signs, and told to see their physicians if such signs appear. Mass media campaigns, educational posters, and brochures should all be utilized to disseminate information about the importance of regular self- and professional-initiated skin examinations. These brochures should also stress the need for high-risk individuals to receive such examinations more frequently. The brochures should include information on how to perform total-body self-examination of the skin.

Health professional-based screening programs should be encouraged. These can take place in the community at large. However, the major source for such screening should be as part of routine primary care. Because of the lack of skills in dermatologic diagnosis in primary care specialties, professional education programs should be mounted. Enhancement of health professional skills can be accomplished through both continuing education courses and self-instruction brochures. Training concerning these issues should be routinely incorporated into medical school curricula and residency training programs.

## **Evaluation**

Following the institution of primary and secondary prevention programs, evaluation should be initiated to assess program effectiveness. These evaluations should include assessment of changes in public behavior, reliability of primary care health professional dermatologic examinations, and changes in incidence and mortality rates from melanoma.

# What Are the Future Directions For Research, Including Primary Prevention?

## Clinical

- Determine the optimal margins for primary melanomas deeper than 1 millimeter.
- Determine the efficacy of elective lymph node dissection in patients with intermediate depth melanomas.
- Develop specific serologic tests and tissue tests (e.g., in situ probes, monoclonal antibodies, DNA ploidy by image cytometry on tissue sections) for invasive early melanoma to better characterize radial and vertical growth phases of the lesion.
- Determine the significance of histological regression in melanoma.
- Examine alternative therapies for primary melanomas where normal tissue conservation is critical (e.g., Mohs micrographic surgery and cryosurgery).
- Determine the genetic basis of the FAM-M syndrome and the clinical significance of sporadic atypical moles.
- Determine the role of optical and computer technology for the following of patients with atypical moles.
- Perform overview of margins and risk of relapse.

## Biological

- Determine the effect of UV radiation on the formation and progression of melanoma and on the immune system by:
  - determining the effect of UV-induced immune suppression on melanoma.
  - contrasting the effect of high-dose intermittent ultraviolet B light on human melanocytes with chronic UVB exposure.
- Define the basic biology of melanoma by:
  - determining the cellular characteristics associated with malignancy, invasion, and metastases, including growth factors, growth factor receptors, gangliosides, and karyotypic analysis.
  - developing cell lines for melanoma of different biological potential.

- developing new markers for early stages of melanocytic neoplasia.
- studying the relationship between melanocytes and the cells of moles.
- investigating the mechanisms of melanocyte migration in fetal life and in metastases.
- determining the roles of tumor suppressor genes and oncogenes in melanoma progression.
- understanding the role of DNA repair defects in melanocytes.
- detecting and determining the significance of melanoma tumor antigens.
- developing transgenic mouse models for melanoma.

### **Public Health**

- Determine the characteristics of those who neglect changing skin lesions so educational campaigns may be improved.
- Determine the optimum frequency of skin screening for individuals of varying risk for melanoma.
- Develop better means to determine population-based incidence and prevalence data for melanoma.
- Determine the effect of primary and secondary prevention measures on melanoma incidence and mortality.

## Conclusions and Recommendations

- The diagnosis of early melanoma (melanoma in situ and invasive melanoma less than 1 millimeter thick) is important, because:
  - melanoma in situ is a distinct diagnostic entity effectively treated surgically with 0.5 centimeter margins. There have been no reported deaths from adequately excised melanoma in situ.
  - thin invasive melanoma, less than 1 millimeter in measured thickness, has the potential for long-term survival in more than 90 percent of patients after surgical excision with a 1 centimeter margin.
- Minimal criteria for an acceptable pathology report for melanoma include diagnosis, depth of invasion (thickness) in melanoma, and status of margins.
- Elective lymph node dissections and extensive staging evaluations are not recommended in early melanoma.
- Patients with early melanoma are at low risk for relapse but may be at high risk for development of subsequent melanomas and should be followed closely.
- Some family members of patients with melanoma are at increased risk for melanoma and should be enrolled in surveillance programs.
- The use of "dysplastic nevus" as a clinical and histologic diagnosis is discouraged. The clinical lesions should be described as "atypical moles." Lesions with the appropriate constellation of microscopic features should be reported as "nevi with architectural disorder" accompanied by a statement describing the presence and degree of melanocytic atypia. The biologic significance of these nevi as indicators of melanoma risk must be determined by the clinical features and family history of each case.
- The familial atypical mole and melanoma syndrome (FAM-M) is clinically recognizable. Individuals with this syndrome have a greatly increased risk of developing melanoma. Careful surveillance of these patients is necessary.

- Education and screening programs have the potential to decrease morbidity and mortality from melanoma.
- The public should be made aware of: (1) the increased risk of melanoma related to excessive sun-exposure, particularly in childhood; (2) the clinical appearance of early melanoma; (3) the excellent prognosis associated with detection and treatment of early melanoma; and (4) the need for regular skin examinations by themselves and by their health professionals.

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**A. Bernard Ackerman, M.D.**

"Critique of Report"  
and "Dysplastic Nevi"

**Charles M. Balch, M.D.,  
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"Diagnosis and Treatment  
of Early Melanoma"

**Natale Cascinelli, M.D.**

(presentation given by  
Charles M. Balch)

"One Centimeter Free  
Margins Excision Is the  
Treatment of Choice for  
Patients With Stage I  
Melanoma Not Thicker  
Than Two Millimeters"

**Wallace H. Clark, M.D.**

"Workshop Without Walls  
Report"

**Evan R. Farmer, M.D.**

"Summary of Workshop  
Without Walls Report"

**DuPont Guerry IV, M.D.**

"Tumor Progression in  
Melanocytic Neoplasia:  
Lessons for the Clinic"

**Alan N. Houghton, M.D.**

"Prevention of Melanoma—  
A Realistic Goal"

**Howard K. Koh, M.D., F.A.C.P.**

"Population Screening and  
Education for Melanoma"

**Alfred W. Kopf, M.D.**

"What Is Early Melanoma"

**Kenneth H. Kraemer, M.D.**

"Genetics/Host Factors, UV"

**Rona M. MacKie, M.D.,  
F.R.C.P., F.R.C.Path., F.R.S.E.**

"Educational Activities Aimed  
at Earlier Diagnosis of Malignant  
Melanoma and Their Evaluation"

**John C. Maize, M.D.**

"Regressing Melanoma"

**Frank L. Meyskens, Jr., M.D.**

"Evaluation of the Patient  
With Early Melanoma"

**Douglas A. Perednia, M.D.**

"Developing Uses for Digital  
Imaging in the Diagnosis and  
Treatment of Melanoma"

**Michael W. Piepkorn, M.D.,  
Ph.D.**

"Problems in Histologic  
Diagnosis of the  
Dysplastic Nevus"

**Darrell S. Rigel, M.D., M.S.**

"Dysplastic Nevus Syndrome—  
Clinical Significance"

**Gary S. Rogers, M.D.**

"Followup Studies: Second  
Primary Melanoma"

**Richard W. Sagebiel, M.D.**

"A Mole By Any Other Name...  
The Presence of Precursor  
Moles in Association With  
Primary Malignant Melanoma"

**Arthur J. Sober, M.D.**

"Clinical Studies—Overview"

**Margaret A. Tucker, M.D.**

"Risk of Melanoma in Members  
of Melanoma-Prone Families"

**Mark R. Wick, M.D.**

"Overview of Histopathology"

**John J. Zone, M.D.**

"Family Studies of Malignant Melanoma and Dysplastic Nevus Syndrome"

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