An elastin immunostain shows greater clarity than an EVG stain to distinguish a benign nevus associated with a melanoma.

**Background:** Melanocytic nevi that occur within a malignant melanoma are a common histopathologic encounter. Although some cases will demonstrate readily evident cytologic differences between the benign nevus and malignant melanoma, other cases are more challenging. The authors previously utilized a histochemical elastic van Gieson stain (EVG) to distinguish between dermal nevus cells and melanoma. In this current paper, they report their results with an elastin immunostain.

**Objective:** To compare the elastic fiber patterns of EVG to an elastin immunostain in cases of melanomas associated with nevi.

**Design:** Retrospective study.

**Methods:** Elastin immunostain and EVG stain were performed in 30 cases of invasive melanomas associated with nevi. Controls included 12 melanocytic nevi and 14 invasive melanomas. Desmoplastic and lentigo maligna melanomas were excluded.

**Results:** The elastic fibers were preserved around the control nevus cells and around the nevus cells in the melanomas, oriented perpendicular to the skin surface, and described as a candelabra or forked appearance. In areas of invasive melanoma, the elastic fibers were decreased to absent. In melanomas associated with a nevus, the advancing melanoma component next to the nevus compressed the elastic fibers and showed a decrease to absence of elastic fibers within the melanoma cells. The nevus cells maintained elastic fibers around the nevus cells. In all cases, the elastin immunostain and EVG stained elastic fibers but the elastin immunostain distinguished the melanoma cells from the nevus with greater clarity, specifically identifying thin, small, and branching fibers.

**Conclusions:** Elastic fibers have a distinct morphological difference in melanomas associated with nevi. The elastin immunostain demonstrates these differences with greater clarity than the EVG stain.

**Reviewer's Comments:** This paper addresses a vexing problem confronting all histopathologists dealing with melanomas. While there are other papers that attempt to utilize antibodies directed against proliferation markers or oncogenes, this paper relies upon the architectural changes that occur within this histopathologic setting. This was a qualitative study with no statistical analysis or grading of the elastin stain or EVG stain. An elastin immunostain is not commonly performed in histopathological laboratories and thus any laboratory must balance the cost-benefit of adding a costly immunostain over a histochemical stain such as the EVG. However, since the accurate determination of the depth of a melanoma is of such paramount importance for prognostic and therapeutic decisions, the cost may be justified in a laboratory that deals with many pigmented lesions. (Reviewer-Paul K. Shitabata, MD).

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Keywords: Melanoma, Melanocytic Nevus, Immunohistochemistry, Elastin, Elastic van Gieson

Print Tag: Refer to original journal article
Truncal melanomas were associated with distant cutaneous metastases, while melanomas of the lower extremities presented more commonly with satellites or in-transit metastases.

**Objective:** To review the records of 4865 patients with cutaneous melanoma at a single institution. In particular, the authors investigated the incidence and pattern of skin metastases in these patients.

**Discussion:** Complete information was available for 4030 patients with melanoma stage IA to IIC. The first site of cutaneous relapse was defined as (1) locoregional, in the presence of satellites or in-transit metastases, and (2) distant, in the presence of skin lesions beyond the regional lymph nodes. Cutaneous metastases occurred in 733 (18.2%) patients. Overall, 80% of cutaneous metastases were locoregional and 20% distant. Locoregional disease was more frequent when the skin was the first site of metastasis (89%). In contrast, distant cutaneous metastases were rarely the initial site of metastases (10%) and occurred mostly after visceral involvement (65%). Patients with melanomas of the lower extremities tended to have more locoregional disease, whereas those with truncal melanomas had higher incidence of distant cutaneous metastases. Also, patients with locoregional disease had a shorter disease-free survival of 1.3 years but took longer to progress to visceral involvement (5 years). In contrast, patients with distant cutaneous disease had a longer disease-free survival (2.9 years) but progressed more rapidly to visceral disease (18 months).

**Reviewer's Comments:** The authors propose that the pattern of cutaneous dissemination in melanoma is closely related to the location of tumor. Truncal melanomas were associated with distant cutaneous metastases, while melanomas of the lower extremities presented more commonly with satellites or in-transit metastases. These results also suggest that local therapies such as isolated limb perfusion may be the first choice for patients with locoregional skin metastases, while a more aggressive systemic therapeutic approach should be selected for patients with distant cutaneous disease, as the latter usually represents a late event and is associated with a faster progression. Previous published studies show that locoregional melanoma recurrence appears to be highly predictable in the presence of histopathological signs of lymphatic invasion and that this finding is more common in melanomas of the lower extremities. Therefore, lymphatic invasion is an important prognostic parameter and should be included as a stratification criterion when selecting patients for adjuvant therapy. (Reviewer-Carlos Garcia, MD).

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Keywords: Melanoma Metastases, Incidence, Pattern

Print Tag: Refer to original journal article
What Does Presence of Telangiectasias Tell You About Systemic Sclerosis?

Clinical and Laboratory Features of Japanese Patients With Scleroderma and Telangiectasia.

Ashida R, Ihn H, et al:

Clin Exp Dermatol 2009; 34 (October): 781-783

The presence of telangiectasias in patients with systemic sclerosis suggests esophageal involvement, calcinosis, shortening of the sublingual frenulum, pitting scars, and decreased lung capacity to diffuse carbon monoxide.

Objective: To perform a retrospective review of 211 Japanese patients with systemic sclerosis.

Participants/Methods: Patients were evaluated clinically and by laboratory data for gastrointestinal, pulmonary, cardiac, and renal involvement. The presence or absence of telangiectasias was recorded. There were 192 females and 19 males, ranging in age from 12 to 83 years (mean, 51 years).

Results/Conclusions: Of the 211 patients, 115 had limited cutaneous systemic sclerosis (formerly known as CREST syndrome) and 96 had diffuse cutaneous systemic sclerosis. The mean disease duration was 7.4 years. Telangiectasias were found in 56% of patients. There were no significant differences between patients with and without telangiectasias regarding gender, age, duration of disease, auto-antibodies, kidney disease, Raynaud phenomenon, or percentage of cases with limited cutaneous versus diffuse cutaneous systemic sclerosis. However, patients with telangiectasias had significantly more esophageal involvement, calcinosis, shortening of the sublingual frenulum, and pitting scars, and decreased lung capacity to diffuse carbon monoxide.

Reviewer's Comments: This paper is interesting because it attempts to explain the meaning of telangiectasias in a specific population of patients with scleroderma. Although others have indicated that telangiectasias reflect the degree of vascular involvement, few if any studies have correlated the presence or site of telangiectasias with clinical features. Unfortunately, the authors of this paper failed to describe the type, size, and location of telangiectasias and the meaning of their findings is unclear. Having said so, it seems reasonable to postulate that Japanese patients with systemic sclerosis (limited and diffuse) and telangiectasias of the face, trunk, or upper extremities may have a decreased lung carbon monoxide diffusing capacity and increased incidence of calcinosis, pitting scars, shortening of the sublingual frenulum, and esophageal involvement. Whether this is applicable to our patient population is still unknown but seems worthy of investigation because other clinical features of scleroderma have been found useful to predict prognosis or internal involvement. For example, male patients with early onset systemic sclerosis, more severe skin fibrosis, impaired lung carbon monoxide diffusing capacity, and anti-topo I are more likely to exhibit prior or current digital ulcers. Also, the presence of phalangeal contractures is a marker of esophageal involvement, pulmonary fibrosis, and heart involvement. Finally, anticentromere antibodies are associated with telangiectasias and calcinosis. (Reviewer-Carlos Garcia, MD).

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Keywords: Systemic Sclerosis, Telangiectasias

Print Tag: Refer to original journal article
Mohs surgery may be more cost-effective than traditional excision in eradicating nonmelanoma skin cancer.

**Background:** Past studies have shown Mohs surgery to be more cost-effective than traditional excision surgery. However, a study in 2006 by Essers et al, came to a different conclusion.

**Methods:** This was a computer-simulation, probabilistic, decision model to perform a cost-effectiveness analysis, with each patient serving as his or her own control. Outcomes were measured in quality-adjusted life years, cost, and cost-effectiveness.

**Results:** Mohs surgery was $292 less expensive than traditional excision. This was 0.056 incremental quality-adjusted life years or 3 weeks more optimal quality of life than excision.

**Conclusions:** Mohs surgery may be more cost-effective than standard excision. More studies on this matter are suggested.

**Reviewer's Comments:** With imminent changes to our health care system likely and outcomes and costs becoming more paramount, studies of this nature are likely to be mandated to justify procedures and treatments we perform in the future. The issue of cost-effectiveness of Mohs largely depends on what recurrence rates are used, which vary from study to study, and what is done when one encounters a positive margin with traditional surgical excision. In this model, the authors reached conclusions based upon using Mohs to treat any positive margins encountered with traditional surgical excision. If traditional surgical excision was used to treat positive margins, then Mohs was found to be slightly less cost-effective than traditional surgery. Other methods of treatment, such as imiquimod, and electrodessication and curettage were not considered, but likely would have been even more cost-effective. Of course, these other treatment modalities have their own drawbacks, even if they are more cost-effective. The difference in findings between this study and that of Essers et al, is likely due to the shorter follow-up time of their study. (Reviewer-Daniel Eisen, MD).
More education is necessary on the appropriate application of sunscreen.

**Background:** Sunscreens are commonly advocated by dermatologists for use against photoaging and skin cancers. It was previously unknown what type of basic knowledge the public possessed regarding sunscreen use.

**Methods:** Members of the public attending health care seminars in New Jersey were asked to complete a 22-question survey regarding sunscreen use.

**Results:** 423 individuals completed the survey, of which 86% of respondents knew sunscreen could prevent sunburns and 70% stated that sunscreen could prevent skin cancers. Only 32.1% of respondents knew that sunscreen should be applied 30 minutes prior to sun exposure, and only 18.0% knew that 1 ounce of sunscreen is recommended to cover the entire body.

**Conclusions:** More education is necessary on the appropriate application of sunscreen.

**Reviewer's Comments:** I found the premise of this study interesting. Unfortunately, I don't think the study population queried represents that of the public at large. Nevertheless, the public clearly needs better instructions on when to apply sunscreen and how much to apply. Most people apply only half to one fourth as much sunscreen as is recommended. In general, a handful of sunscreen (1 ounce) is the appropriate amount to cover the entire body. Technically, the number is 2 mg/cm². It should be reapplied every 2 hours to maintain its protection. Interestingly, proof that sunscreen prevents skin cancers is far from convincing. Of the 15 case-control studies that have thus far been performed, 3 have shown benefit to using sunscreen, 4 have shown no effect, and 8 have shown greater incidence of skin cancers with its use. Despite these findings, most would argue that advocating sunscreen use is the prudent thing to do in order to prevent photoaging and reduce chances of skin cancers, even if the evidence isn't entirely convincing yet. (Reviewer-Daniel Eisen, MD).

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Keywords: Sunscreen, Skin Cancer, Photoaging

Print Tag: Refer to original journal article
About one third of patients with moderate-to-severe atopic dermatitis have osteopenia or osteoporosis, and that finding is independent of physical activity, lifestyle, or the cumulative dose of topical and oral corticosteroids used within 5 years prior to this study.

**Background:** There may be an association between atopic dermatitis and the risk of osteoporosis. This potential association is an obvious one given the common use of topical and even systemic glucocorticosteroids for this condition.

**Objective:** To measure the prevalence of osteoporosis and osteopenia in adult patients with moderate-to-severe atopic dermatitis via bone mineral density (BMD). Also, to measure any associations between corticosteroid use and BMD and between disease severity and BMD as well as other risk factors for osteopenia.

**Participants:** 125 adult patients, ages 16 to 82 years, with moderate-to-severe atopic dermatitis.

**Methods:** The authors measured BMD at the lumbar spine and hips in subjects using dual-energy X-ray absorptiometry. In addition, they measured a number of biochemical parameters of bone metabolism and vitamin D levels. The cumulative dose of topical and oral corticosteroids was found by review of pharmacy prescription records of 5 years prior to the study, and a lifestyle questionnaire was used to get a handle on physical activity.

**Results:** The authors found that osteoporosis and osteopenia were common. Six patients had osteoporosis (4.8%) and 41 patients had osteopenia (32.8%). Men were more likely to be affected (43.8%) than women (16.4%). There was no significant association between low BMD or biochemical parameters of bone metabolism and the cumulative dose of topical and oral corticosteroids. Nor was there any difference between patients with low bone density and normal bone density in alcohol, coffee and dairy products intake, smoking, exercise, sunlight exposure, use of contraceptives, or menopausal status.

**Conclusions:** About one third of patients with moderate-to-severe atopic dermatitis had osteopenia or osteoporosis, and that finding was independent of physical activity, lifestyle, or the cumulative dose of topical and oral corticosteroids used within 5 years prior to this study. Male sex was an independent risk factor in this group.

**Reviewer’s Comments:** Chronic inflammation is by itself a risk factor for osteopenia, as is commonly seen in, for example, rheumatoid arthritis. One shortcoming is the question of whether there was a difference in corticosteroid use beyond 5 years prior to the study. I think it may be of value to point out to patients the importance of bone health and perhaps screening, just as many of us are now mentioning cardiovascular health to our psoriasis patients. This may be especially true in male atopic patients, for whom primary care physicians may not be as aggressively approaching bone health. (Reviewer-David L. Swanson, MD).

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Keywords: Atopic Dermatitis, Osteoporosis, Osteopenia

Print Tag: Refer to original journal article
MAL PDT Effective for Nodular Basal Cell Cancer

Photodynamic Therapy With Methyl Aminolevulinate for Primary Nodular Basal Cell Carcinoma: Results of Two Randomized Studies.

Foley P, Freeman M, et al:

Int J Dermatol 2009; 48 (November): 1236-1245

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PDT—Is Red or Blue Light Better?

**Background:** Blue light photodynamic therapy (PDT) with aminolevulinic (ALA) acid is being used for superficial basal cell carcinomas, but is said to not work as well for nodular lesions because of poor penetration of ALA. Topical methyl aminolevulinate, with the more manageable moniker MAL PDT, has been reported effective in nodular lesions; the basis for the use of MAL PDT is greater depth of penetration.

**Objective:** To investigate the use of MAL PDT as part of an ongoing study of this therapy for the indication of basal cell carcinoma.

**Design:** Double-blind placebo-controlled trial of MAL or placebo, plus light.

**Participants:** 131 patients with 150 nodular basal cell cancers that were ≤5 mm in depth. Exclusions were morpheaform or sclerosing patterns, high-risk locations, and large diameter lesions.

**Methods:** Patients were equally randomized to treatment with MAL cream 160 mg/g or placebo cream. After light curettage, the cream was applied for 3 hours under occlusion with Tegaderm followed by illumination with broad-spectrum noncoherent red light (75 J/cm², 570 to 670 nm). The treatment was repeated 7 days later. Patients with a partial response of ≥50% reduction in greatest diameter at 3 months were re-treated (21%). Treatment sites were excised at 3 months for clinical nonresponders, defined as <50% reduction, or 6 months for clinical responders after their last treatment.

**Results:** Complete responses occurred in 73% of patients, with 89% clearing in patients with facial lesions. The placebo response was 27%. Cosmetic outcome was good or excellent in 98% of evaluable completely responding lesions. There were mild-to-moderate local adverse events that usually resolved within 1 day, except for lesion destruction effects.

**Conclusions:** This study supports prior work suggesting that there is potential for topical MAL PDT as a noninvasive treatment alternative for nodular basal cell cancer.

**Reviewer's Comments:** This study was funded by PhotoCure ASA, Oslo, Norway. A number of the authors reported conflicts of interest. The high placebo effect was felt by the authors to be most likely due to the mild curettage that preceded the use of the PDT. I think that those of us already using blue light PDT, and that number is rising, will ultimately find ourselves switching to MAL red light PDT for basal cell cancers. Because of shorter incubation times and ease of use, I suspect blue light PDT will continue to be favored for actinic keratoses and some superficial basal and squamous cell cancers. (Reviewer-David L. Swanson, MD).

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Keywords: Basal Cell Cancer, Photodynamic Therapy, MAL PDT

Print Tag: Refer to original journal article
A subset of lesions that fit accepted histology criteria for melanoma are slow growing and show little structural change over time.

**Background:** Recent epidemiologic data have shown a large increase in the incidence of thin melanomas in recent decades with relatively little change in incidence of thick melanomas or melanoma mortality. It has been suggested that many of these thin melanomas may represent a less aggressive sub-type of the disease.

**Objective:** To examine serial clinical and dermoscopic features of melanomas that were examined by dermoscopy at least 1 year prior to excision.

**Design:** Multicenter retrospective study.

**Methods:** Lesions excised at an average of 20 months after initial consultation were evaluated. The authors compared dermoscopic images obtained at first consultation with images obtained just prior to excision.

**Results:** 103 melanomas that were examined by dermoscopy at least 1 year prior to excision were identified. Lesions on the head were excluded. The reason that lesions were not excised at the first visit ranged from benign appearance to patient's refusal of biopsy. Some lesions were eventually biopsied due to subtle changes noticeable only by comparison with the previous dermoscopic image. Histology showed an average Breslow thickness of 0.48 mm. Most lesions were in situ or early invasive. When dermoscopy at first visit was compared to dermoscopy just prior to excision, 58% of melanomas were characterized as showing only minor to moderate changes over the observation period, meaning the lesions showed <2 mm increase in size without development of new melanoma-specific dermoscopic criteria. Remarkably, 6 of 103 melanomas showed no detectable changes in size, structure, or melanoma-specific dermoscopic criteria over the >12-month observation period.

**Conclusions:** A subset of lesions that fit accepted histology criteria for melanoma are slow growing and show little structural change over time.

**Reviewer's Comments:** This article supports growing evidence that melanoma is a heterogeneous disease. The more malignant end of the spectrum is characterized by lesions that grow rapidly and metastasize within months. At the more benign end of the spectrum is lentigo maligna, and, as identified in this paper, a subgroup of thin melanomas that occur in areas of intermittent sun exposure. These lesions present with a reticular dermoscopic pattern characterized by moderate asymmetry and areas of regression. Less aggressive melanomas may account for much of the increase in melanoma incidence over the past few decades. If many of these lesions fail to progress to malignant disease in a patient's lifetime, these slow-growing melanoma may help explain the discrepancy between melanoma incidence and mortality. This paper supports the utility of serial digital dermoscopy to differentiate these lesions from benign nevi. (Reviewer-Michael S. Kolodney, MD, PhD).

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Keywords: Melanoma, Slow Growing, Sub-Type

Print Tag: Refer to original journal article
LAHS is a relatively common cause of non-scarring alopecia in young girls with sparse or fine hair.

**Background:** When encountering non-scarring alopecia in a young child, the diagnosis of Loose anagen hair syndrome (LAHS) should be considered along with alopecia areata, telogen effluvium, trichotillomania, and tinea capitis. LAHS is a sporadic or autosomal dominant disorder that mainly manifests in light-haired female children and improves with age. It frequently presents as hair shedding, thinning, patchy alopecia, or the failure of hair to grow long enough to get a haircut. The texture of hair is often described as sticky, dry, or rough.

**Objective:** To better characterize the clinical features of LAHS.

**Design:** Retrospective chart review.

**Participants:** 347 children referred to an academic pediatric dermatology practice for alopecia.

**Results:** LAHS was diagnosed in 33 of 347 children with alopecia. LAHS began at a mean age of 2.8 years compared with 7.1 years for other forms of alopecia. All but 1 of the children with LAHS were female. The clinical history noted sparse or fine hair in 20 of 33 patients; frizzy, unmanageable, or unruly hair in 7 of the children; slow-growing hair in 8 patients; and hair shedding in 10. None of the LAHS patients had nail changes or abnormalities in thyroid function. All of the LAHS patients had blond or light brown hair. Loose anagen hairs exhibited misshapen bulbs, ruffled cuticles, and absent inner root sheaths. Thirty-two of the 33 patients showed >50% loose anagen hairs on microscopic examination of plucked hairs (trichogram).

**Conclusions:** LAHS is a relatively common cause of non-scarring alopecia in young girls with sparse or fine hair. A trichogram should be performed prior to any laboratory work-up. LAHS was first described in 1984 and reflects a structural defect in the internal root sheath, resulting in easily pluckable hairs. Although less common than alopecia areata, telogen effluvium, and trichotillomania, LAHS should be considered one of the more common causes of non-inflammatory alopecia in light-haired preschool girls. Rapid recognition of this easily diagnosed disorder may avoid an unnecessary work-up. The 10% of all children with alopecia that were diagnosed with LAHS at this study seems somewhat high and likely reflects the referral-based population at this specialty clinic. (Reviewer-Michael S. Kolodney, MD, PhD).

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**Keywords:** Loose Anagen Alopecia, Guidelines, Evaluation

**Print Tag:** Refer to original journal article
Legius syndrome often presents as café au lait spots and axillary freckling but typically lacks internal manifestations of NF1.

**Background:** The combination of ≥6 café au lait macules with axillary freckling or a family history of neurofibromatosis type 1 (NF1) is sufficient to satisfy the National Institutes of Health (NIH) criteria for diagnosis for NF1. Although clinically useful, individuals with disorders other than NF1 may also meet these criteria. A new syndrome termed NF1-like syndrome shares the pigmentary features of NF1, and individuals with this syndrome may meet NIH criteria for NF1. To prevent confusion with NF1, this syndrome has more recently been designated as Legius syndrome. Both diseases are transmitted in an autosomal dominant fashion by genes involved in the RAS signaling pathway, but Legius syndrome is due to a mutation in SPRED1 rather than the NF1 gene.

**Objective:** To better characterize the clinical characteristics of Legius syndrome in a large cohort of patients and to determine the degree of overlap with NF1.

**Design:** This was a cross-sectional study of a clinical cohort of 23 families carrying the SPRED1 mutation and a second cross-sectional study of 1318 anonymous genomic samples from individuals with some clinical characteristics of NF1.

**Methods:** The authors determined aggregated clinical features of SPROUTY1 mutated individuals from the 23 families and 1318 genomic samples.

**Results:** 42 individuals with SPRED1 mutations were identified from the 23 affected families. About half of these subjects met criteria for NF1 due to the presence of café au lait macules, axillary freckling, and family history. None of these subjects exhibited neurofibromas, osseous lesions, or optic gliomas. In the anonymous genetic samples, 27 were found to have pathogenic SPROUTY1 mutations. About 2% of those individuals from the anonymous genomic samples that met NIH criteria for NF1 were found to have SPROUTY1 mutations. Ninety-four of the anonymous donors were noted to have familial café au lait macules with or without axillary freckling but no other features of NF1. Of these 94 individuals, 69 had pathogenic mutations in NF1, while 18 had SPROUTY1 mutations.

**Conclusions:** A significant fraction of families with autosomal dominant café au lait macules but without NF1 mutations have Legius syndrome. This syndrome does not appear to be associated with non-pigmentary features of NF1.

**Reviewer's Comments:** The similar pigmentary manifestations of NF1 and Legius syndrome present a diagnostic difficulty in individuals without a personal or family history of neurofibromas, osseous lesions, or optic gliomas. It is important to differentiate the 2 diseases, as Legius syndrome is primarily a pigmentary disorder while the neural tumors of NF can have serious consequences. This study emphasizes the importance of genetic testing in establishing the diagnosis of NF1 in the setting of clinical uncertainty. (Reviewer-Michael S. Kolodney, MD, PhD).

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Keywords: NF1, Cafe Au Lait, Legius Syndrome

Print Tag: Refer to original journal article
Is Molecular Analysis of SLNs More Sensitive Than Pathologic Examination?

**Highly Sensitive Multivariable Assay Detection of Melanocytic Differentiation Antigens and Angiogenesis Biomarkers in Sentinel Lymph Nodes With Melanoma Micrometastases.**

Vitoux D, Mourah S, et al:

Arch Dermatol 2009; 145 (October): 1105-1113

Quantitative assessment of tyrosinase mRNA in sentinel nodes in combination with histologic analysis better predicts outcome than histologic analysis alone.

**Background:** Sentinel lymph node (SLN) mapping involves identifying and removing the first node draining a tumor. The node is serially sectioned and immunostained for melanoma-specific antigens. If micrometastases are seen in the sentinel node, the entire lymph node basin is dissected. Although the usefulness of SLN mapping for improving outcome in melanoma patients is controversial, the technique clearly provides prognostic information. Patients with a positive sentinel node have a 5-year relapse-free survival of 53%, while those with negative sentinel nodes have a 5-year relapse-free survival of 86%. However, about 20% of patients with a negative sentinel node will develop recurrent disease, suggesting that node metastases are missed, or alternatively, these melanomas may metastasize without involving the sentinel node.

**Objective:** To determine if molecular analysis of SLNs predicts clinical outcome.

**Participants:** 91 patients with cutaneous or mucous membrane melanomas who underwent SLN biopsies.

**Methods:** The sentinel node was bisected and half was used for histology and the other half for molecular analysis. Micrometastases were defined as clusters of ≥5 cells. Reverse transcriptase polymerase chain reaction (RT-PCR) was used to measure mRNA levels of the melanocyte differentiation markers MART-1 and tyrosinase markers. In addition to the melanoma markers, the investigators also measured levels of mRNA for angiogenesis biomarkers. mRNA levels were expressed as a ratio to a housekeeping gene mRNA (TATA box binding protein).

**Results:** 15% of patients showed positive sentinel nodes by histology. mRNA expression for the angiogenesis factor VEGF was associated with micrometastasis, but did not predict recurrence-free survival. Expression of tyrosinase mRNA at a level >27 copies/copy of TATA box binding protein mRNA independently predicted relapse or death.

**Conclusions:** Quantitative assessment of tyrosinase mRNA in sentinel nodes in combination with histologic analysis better predicts outcome than histologic analysis alone.

**Reviewer's Comments:** This well-designed study suggests that using modern molecular tools to measure biomarkers can improve analysis of sentinel lymph nodes. RT-PCR analysis has the advantage of providing quantitative analysis of biomarkers. However, the obvious disadvantage of RT-PCR is that the method does not identify which cells are the source of the marker. The sample size in this study was relatively small so these results should be considered preliminary. Moreover, even if these results can be replicated in a larger sample, the value of these data in guiding therapy remains an open question. (Reviewer-Michael S. Kolodney, MD, PhD).

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Keywords: Melanoma, SLN Mapping, Tyrosinase mRNA

Print Tag: Refer to original journal article
Research Sheds Light on Sun Exposure, Melanoma Progression

Divergent Cancer Pathways for Early-Onset and Late-Onset Cutaneous Malignant Melanoma.
Anderson WF, Pfeiffer RM, et al:
Cancer 2009; 115 (September 15): 4176-4185

Early-onset melanomas present gene-sun interactions that occur early and intermittently. Late-onset melanomas may reflect life-long sun exposure in less susceptible individuals.

Objective: To evaluate the relationship between age, site, and melanoma development.
Participants: The authors used the Surveillance, Epidemiology, and End Results (SEER) database to identify patients diagnosed with cutaneous melanoma from 1975 to 2004. Melanoma in situ was excluded. Patient and tumor characteristics were analyzed, including gender, age, histopathologic classification, race, and tumor thickness. Incidence rate ratios were calculated as relative risks in which a given factor was compared with a referent factor. Age-adjusted incidence trends by gender were plotted on a log-linear scale by six 5-year periods.

Results: 96,900 melanoma cases were identified. Melanoma was more common among men than among women. However, before age 40 years, the age-specific incidence rates were lower for men. The incidence ratios were greater among men than women for all tumor characteristics except for melanomas of the lower extremity. Melanoma was slightly more common in intermittently sun-exposed skin as compared with chronically sun-exposed skin. The most common anatomic site was the lower extremity for women and trunk for men. Most lentigo maligna melanomas developed in sun-exposed skin as compared with only 37% of superficial spreading melanoma. For both genders, the melanoma incidence rate increased during the study period. The gap between men and women widened over time. Lentigo maligna and head/neck melanoma occurred predominantly in older patients, whereas superficial spreading melanoma occurred predominantly in younger patients.

Conclusions: Early-onset melanomas represent gene-sun interactions that occur early and intermittently. In contrast, late-onset melanomas may reflect life-long sun exposure in less susceptible individuals.
Reviewer’s Comments: This is a hypothesis-generating study, but it is limited by the lack of consistent histologic typing in SEER and actual patient information regarding sun exposure. (Reviewer-Todd M. Tuttle, MD).

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Keywords: Cutaneous Malignant Melanoma, Risk Factors vs Incidence

Print Tag: Refer to original journal article