Tissue Shrinkage in Skin Excisions Occurs Immediately After Excision

Shrinkage of Cutaneous Specimens: Formalin or Other Factors Involved?
Kerns MJJ, Darst MA, et al:
J Cutan Pathol; 35 (December): 1093-1096

Formalin-fixed skin excisions show less shrinkage with advancing age and increasing solar elastosis.

**Background:** Controversy exists over the degree of shrinkage that occurs with formalin-fixed skin excisions.

**Objective:** To examine the degree of tissue shrinkage with formalin-fixed skin excisions and determine other variables that may account for shrinkage.

**Design:** Prospective study.

**Participants:** Skin excisions from 97 lesions on 97 patients were obtained over a 4-month period.

**Methods:** Diseases known to have sclerotic, infiltrative, or nodular histopathology were excluded. The majority of cases were skin carcinomas with an accompanying previous biopsy site scar. Length and width measurements of the excisions were taken prior to the excision, 1 minute after removal, and 24 to 48 hours after formalin fixation. The area of shrinkage was calculated, and in excisions with >35% or <7% shrinkage, an elastic stain was performed. The site of the excision and age of the patient were recorded.

**Results:** The majority of the shrinkage occurred immediately after excision and prior to formalin fixation, with the length and width of the specimens decreased by 20.6% and 12%, respectively and total area decreased by 16%. After formalin fixation, the tissue sections slightly re-expanded in some cases. Shrinkage decreased 0.3% per year of increasing age. Head and neck excisions had slightly less shrinkage than trunk excisions. Solar elastosis was graded normal to severe, and severe solar elastosis correlated with decreased shrinkage.

**Conclusions:** Tissue shrinkage in skin excisions occurs immediately after excision. Formalin fixation contributes little to the overall shrinkage and is more dependent upon the younger age of the patient, less solar elastosis, and body site.

**Reviewer’s Comments:** The literature on the variables that may contribute to shrinkage of tissue specimens gives conflicting results. This issue is increasingly important to resolve potential discrepancies between the surgeon's record and the final pathology record. This current study finds that shrinkage of skin excisions is unrelated to formalin fixation and depends upon the intrinsic contractile properties of the skin, related to age, solar elastosis, and site of excision. While this study is a good analysis of some of the variables, it excluded excisions of tumors that may have significantly altered the contractile properties of the skin and it did not comment on the types of skin cancers. Since earlier studies have found differential shrinkage associated with benign versus malignant tumors, this study does not resolve this issue. This study also did not address any measurement discrepancies between the initial excision and potential changes that may occur with later tissue processing and paraffin embedding. Since many measurements of tumors and surgical margins are made on these slide sections, this information would be critical to determine whether this last tissue processing step contributes significantly to tissue shrinkage.

**Additional Keywords:** Shrinkage

**print tag:** () Refer to original journal article.
Adjuvant IFN Therapy for High-Risk Melanoma

**Randomized Phase III Study of 1 Month Versus 1 Year of Adjuvant High-Dose Interferon Alfa-2b in Patients With Resected High-Risk Melanoma.**

Pectasides D, Dafni U, et al:  
*J Clin Oncol*: (January 12): epub ahead of print

High-dose interferon therapy for 1 month is as effective as continued treatment for 1 year.

**Objective:** To determine if high-dose interferon (IFN) therapy given as IV infusion for 4 weeks is as effective as treatment for 1 year.

**Design:** Multicenter study from Greece.

**Participants/Methods:** The authors report on 353 patients with stages IIB, IIC, and III malignant melanoma who were randomly allocated to receive IV infusion of high dose-interferon (IFN)-α-2b 15 x 10⁶ U/m² x 5 days per week for 4 weeks versus the same infusion followed by IFN-α-2b 10 x 10⁶ U (flat dose) given subcutaneously 3 times/week for 48 weeks. The primary outcome was relapse-free survival (RFS) in the intent-to-treat population, and the secondary outcomes were overall survival (OS), distant metastases-free survival, and safety.

**Results:** There were no significant differences between treatment groups in terms of sex, age, melanoma location, or Breslow depth. Also, there were no significant differences in RFS (24 vs 27 months), 3-year recurrence rate (57% in both arms), OS (64 vs 65 months), distant-metastasis-free survival (44 vs 36 months), development of metastases (98 vs 101 patients), or deaths (78 vs 79 patients).

**Reviewer's Comments:** Based on this trial, there is no significant difference between the 1-month and the 1-year high dose-IFN treatments. These results seem to be valid, not only because of the well-designed and randomized nature of the study and its report of results on an intention-to-treat basis, but also because the figures reported here are in agreement with previous data regarding IFN treatment of high-risk melanoma as reported in Eastern Cooperation Oncology Group (ECOG) trial 1684 and ECOG trial 1694. Having said so, it is good to remember that adjuvant IFN therapy for melanoma is still under careful and intense study. A recent meta-analysis of 12 IFN trials reported in *Cancer Treatment Reviews* 2003 showed no OS benefit and a 17% reduction in recurrences, but only if given for 2 years. Only 2 trials (E1684 and E1694) have shown a 20% to 30% RFS as well as a 10% to 20% OS benefit.

**Additional Keywords:** High-Dose Interferon-α-2b

**print tag:** () Refer to original journal article.
ER Expression Patterns Offer Clues to Growth Potential of Malignant Melanomas

Estrogen Receptor Expression in Cutaneous Melanoma: A Real-Time Reverse Transcriptase-Polymerase Chain Reaction and Immunohistochemical Study.

de Giorgi V, Mavilia C, et al:
Arch Dermatol; 145 (January): 30-36

ERa and ERb expression may play a role or provide clues in the growth patterns of malignant melanomas.

Background: Estrogen receptor (ER) expression has been suspected to play a role in melanocytic lesions with multiple anecdotal reports of melanocytic nevi changing during pregnancy, and a few reports suggesting deeper melanomas in pregnant patients compared with nonpregnant patients. However, literature reviews and the lack of efficacy of anti-estrogens in metastatic melanoma do not demonstrate a clear link between estrogens and melanoma. ERs are part of the nuclear hormone receptor superfamily that can lead to profound changes in gene expression. ER-alpha (ERa) is an ER that is the target of anti-estrogen cancer therapy (ie, tamoxifen), and is hypothesized to be stimulatory for cell growth in breast and ovarian cancer. ER-beta (ERb) is another ER that may play a role in suppressing cell growth, and loss of ERb expression has been found in certain cancers.

Objective: To evaluate the expression of ERa and ERb in melanoma.

Methods: The authors studied the ER messenger RNA (mRNA) and protein expression in 14 patients with 12 cutaneous melanomas and 2 melanocytic nevi (7 males and 7 females), as well as from each patient's surrounding healthy skin.

Results: The authors found ERa and ERb mRNA expression in all melanocytic lesions, and that levels of ERa did not differ between benign and malignant melanocytic lesions. ERb expression was similar between benign melanocytic tissue and healthy surrounding skin. ERb levels were higher in melanoma cells than the surrounding healthy skin in 8 of 11 melanoma patients, and in the other 3 melanoma patients, ERb expression was very low in the melanoma cells but higher in the surrounding normal skin. These 3 patients had nodal metastasis at the time of evaluation, while the other 8 had no evidence of metastatic disease. When dividing the melanoma cases into 2 groups for Breslow thickness, (1 mm in 6 cases and >1 mm in 6 cases), ERa and ERb mRNA expression was high in the thin melanoma group and low in the thick melanoma group. The 12th patient, who had melanoma metastasis in transit, showed very low levels of ERb in both melanoma cells and in the surrounding healthy skin.

Conclusions: The authors hypothesized that expression of ERs, especially ERb, is markedly decreased in the metastatic phase of melanoma.

Reviewer's Comments: The biology of melanomas is very difficult to discern. This is a very small study that is trying to look into differences in gene expression in order to provide insight into tumor biology. The findings here are interesting, but further and more large-scale studies are needed to further understand which genes are turned on or off that allow certain tumors to progress, and perhaps provide targeted therapeutic options in the future.

Additional Keywords: Estrogen Receptor Expression

print tag: () Refer to original journal article.
Malignancy Risks and Rates in Patients With EB


Fine J-D, Johnson LB, et al:

J Am Acad Dermatol; 60 (February): 203-211

JEB and RDEB patients have a high risk of developing SCCs, and RDEB patients may have an increased risk of childhood melanomas.

Background: Epidermolysis bullosa (EB) is a genetic disorder of the basement membrane that is subdivided into 3 main categories (simplex, junctional, and dystrophic), with many subtypes within each category.

Design/Participants: To look at the rates of cutaneous malignancies, complications, and causes of death in 3280 patients enrolled consecutively in the National EB Registry (NEBR) from September 1986 to April 2002, with follow-up through 2006. Of the 3280 patients in the registry, 2745 had data that allowed classification of EB type and statistical analysis of cancer deaths.

Results: The frequency of skin cancer development was 1% in EB simplex (EBS) patients and 0.7% in dominant dystrophic epidermolysis bullosa (DDEB), which is not dissimilar from expected norms. Increased frequencies were noted in junctional EB-Herlitz (JEB-H) (4.5%), recessive dystrophic EB-Hallopeau Siemens (RDEB-HS) (23%), RDEB, non-HP (RDEB-nHS) (9.9%), and RDEB-inversa (RDEB-I) (17.7%). All squamous cell carcinomas (SCCs) in EBS patients were in sun-exposed sites, but in RDEB, the most common sites were in wounds and scars. Tumors were primarily excised with wide local excision, and a few were removed with Mohs surgery, with no differences in recurrence rates. Most EBS patients had SCCs later in life (>65 years old). In JEB, the cumulative risk of SCC development was 18.2% by age 25. In RDEB-HS, the cumulative risk of developing 1 SCC was 7.5%, 67.8%, and 90.1% by ages 20, 35, and 55 years, respectively. Similar but lower curves were seen in other RDEB subtypes. No SCC deaths occurred in patients with EBS, DDEB, or JEB. Metastatic SCC was the most common cause of death during adulthood in RDEB patients, with the earliest occurrence in RDEB-HS. In RDEB-HS patients with at least 1 SCC, the cumulative risk of death from any SCC was 12.7% by age 20 and 87.3% by age 45. BCCs were primarily seen in patients with EBS-Dowling-Meara (EBS-DM) and only 2 (0.8%) occurred in patients with RDEB. The cumulative risk of BCC development was 43.6% by age 55 years for EBS-DM and very low for other EBS subtypes and DDEB. No BCCs developed in scars or wounds. Malignant melanomas (MM) arose in 0.4% to 0.5%, 1.2%, and 2.1% of patients with EBS, DDEB, and RDEB-HS, respectively. MM arose only in childhood in RDEB-HS patients, occurring in 3 patients at ages 2.8, 6.5, and 12 years, respectively. MM did not develop in scars, nevi, or wounds, and the cumulative risk of MM development was 2.5% in RDEB-HS by 12 years of age. No deaths from melanomas occurred.

Reviewer's Comments: This review confirms the high risk of SCC deaths in RDEB patients. What is interesting is the increased risk of BCC carcinoma development in EBS-DM and childhood melanomas in RDEB-HS patients. Vigilant surveillance for not only SCCs, but also MM as well, is required for RDEB patients.

Additional Keywords: Life-Threatening Cancers

print tag: () Refer to original journal article.
Topical Tretinoin Said to Increase Death Rate

Topical Tretinoin Therapy and All-Cause Mortality.

Weinstock MA, Bingham SF, et al:
Arch Dermatol; 145 (January): 18-24

This study involves older patients for whom the indication for tretinoin is possible cancer chemoprophylaxis.

Background: The Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) Trial Group investigated the potential of topical 0.1% tretinoin in the prevention of keratinocyte carcinomas, that is, basal cell and squamous cell carcinoma of the skin. This trial was an anticipated 6-year trial launched in 1998. During the trial, another trial with systemic isotretinoin was observed to be associated with an unexpected increased mortality among smokers and decreased mortality among never smokers.

Objective: To determine excess mortality occurring in the topical retinoid study.

Design: Retrospective review.

Participants: 1131 United States military veterans, mostly men, with a mean age of 71 years, excluding any patients with a very high estimated short-term risk of death were included. The patients had been randomized to receive tretinoin, 0.1%, or vehicle control cream applied twice daily to the face and ears. The primary outcome in this particular report was death.

Results: There were a statistically significant excess number of deaths in the treated group (82 in the treated group vs 53 in the control group). A retrospective analysis showed only minor randomization imbalances in age, comorbidities, and smoking status. Although all were important predictors of death, after adjusting for them, the difference in mortality between the randomized groups remained statistically significant.

Conclusions: For this reason, intervention was terminated 6 months early. The authors concluded that they found an association of topical tretinoin therapy with death, but would not infer a causal association, stating that current evidence suggests causality is unlikely. That evidence, however, is primarily a lack of a similar observation particularly in young people and the absence of any plausible explanation.

Reviewer’s Comments: If the question arises, my plan is to simply tell my patients that this was a study that is controversial, limited to elderly patients, and there is no suggestion that the use of tretinoin in younger people has any risk associated with it. For the rare oldster, it is probably worth bringing up in anticipation of what otherwise might be a phone call from a concerned son or daughter. For the prescribing physician, until the question is resolved, it is certainly reasonable to consider the ramifications from a medical-legal perspective of prescribing tretinoin to individuals carrying a high risk of death from all causes in the short term.

Additional Keywords: All-Cause Mortality

print tag: () Refer to original journal article.
Folic Acids Helps Reduce Hepatic Adverse Effects of Methotrexate Tx

Effect of Folic or Folinic Acid Supplementation on Methotrexate-Associated Safety and Efficacy in Inflammatory Disease: A Systematic Review.

Prey S, Paul C:
Br J Dermatol; 160 (March): 622-628

A 38% reduction in hepatic toxicity can be observed in patients managed with folic acid and methotrexate.

Background: Dermatologists are generally very comfortable using methotrexate for the treatment of inflammatory skin disorders such as psoriasis and bullous pemphigoid. Lately, most of us are prescribing folic acid supplementation along with the methotrexate. Our sense in doing this is that folic acid may limit the toxicity of methotrexate on the bone marrow, gastrointestinal tract, and liver. How valid is that assumption?

Objective: To ascertain the effect of folic or folinic acid supplementation on methotrexate-associated safety and efficacy.

Design: Literature review.

Methods: Cochrane and MEDLINE databases were searched. The authors pulled randomized controlled trials in patients treated with methotrexate for rheumatoid arthritis, psoriasis, and psoriatic arthritis. They specifically selected double-blind, randomized, placebo-controlled trials. They analyzed each subgroup for the prevalence of gastrointestinal, mucocutaneous, hematologic, or hepatic side effects.

Results: The authors found 6 randomized controlled trials with a total of 648 patients, including 257 patients in the placebo group, 198 patients treated with folic acid, and 193 patients treated with folinic acid. There was a significant reduction of 35.8% of hepatic side-effects induced by methotrexate for patients with supplementation with folic or folinic acid. There was a trend in favor of supplementation for mucocutaneous and gastrointestinal side-effects although it was not statistically significant. The incidence of bone marrow side-effects was too low to draw conclusions. The authors were unable to answer the question of reduction in efficacy because of variations in assessment between subgroups.

Conclusions: Supplementation with folic acid is an effective measure to reduce hepatic adverse effects associated with methotrexate treatment. There is no difference between folinic acid and folic acid.

Reviewer's Comments: In Great Britain, approximately 30% of dermatologists use combination folic acid and methotrexate. By the way, a perk is that patients with severe psoriasis often have folic acid depletion and any consequential hyperhomocysteinaemia could increase their cardiovascular risk, which we all know is a problem in psoriasis. So, folate supplementation may mitigate some of that risk. Regarding any reduction in methotrexate efficacy, there are 2 ways methotrexate might work in psoriasis. The first is by inhibition of dihydrofolic acid reductase, for which folic acid is an antidote. Most gurus believe that the primary effect in psoriasis, however, is by inhibition of aminomimidazole carboxamide ribonucleotide transformylase, inducing the accumulation of T-cell controlling adenosine. This enzyme is not influenced significantly by folic acid. Recently, some authors have challenged the relative unimportance of the dihydrofolate reductase pathway in psoriasis, and have suggested that folic acid may increase the necessary methotrexate therapeutic dosage. The answer to that open question was not found in this study.

Additional Keywords: Folic/Folinic Acid Supplementation

print tag: () Refer to original journal article.
Surgery Complications Same in Smokers and Nonsmokers

Prospective Study of Skin Surgery in Smokers vs. Nonsmokers.
Dixon AJ, Dixon MP, et al:
Br J Dermatol; 160 (February): 365-367

Advice regarding the cessation of smoking after surgery to improve outcomes may not be necessary.

Background: Previously, smoking has been associated with higher incidence of complications in those undergoing surgical procedures. Subsequently, many of us are very careful to tell our patients not to smoke prior to or after surgery.

Methods: This was a 5-year prospective trial of 7224 excisional surgery wounds in 4197 patients. Patients were not instructed to do anything different regarding smoking prior to surgery. Complications were recorded.

Results: Of the 4197 enrolled patients, 439 were smokers. The smokers had 646 procedures performed. Smokers were found to be younger (mean, 55 years) versus nonsmokers (mean, 66 years). Incidence of infection, bleeding, flap tip necrosis, and wound dehiscence were not significantly different. Scar contour distortion was significantly worse in smokers. Age-matched comparisons of the above end points did not lead to significantly different outcomes between smokers and nonsmokers.

Conclusions: Smokers and nonsmokers suffer similar complication rates. Advice regarding the cessation of smoking after surgery to improve outcomes may not be necessary.

Reviewer’s Comments: This is another wonderful example of science contradicting surgical dogma. Other studies have shown higher complication rates for patients who smoke for other types of surgeries. The espoused hypothesis for this is vasoconstriction caused by nicotine. With the exception of scar contour distortion, there were no differences in complications between smokers and nonsmokers. Scar contour deformity was not defined by the authors and one wonders how reproducible this outcome measure is. In my personal experience, I have not seen higher rates of complications in smokers over that of nonsmokers. However, I will continue to encourage my patients to quit smoking as this is an excellent opportunity to make a difference in the long-term health of our patients. I will often prescribe Zyban or Chantix to these patients and have been modestly successful at getting my patients to permanently quit.

Additional Keywords: Complications in Smokers

print tag: () Refer to original journal article.
Lenalidomide Helpful for Resistant DLE

Lenalidomide for the Treatment of Resistant Discoid Lupus Erythematosus.

Shah A, Albrecht J, et al:
Arch Dermatol; 145 (March): 303-306

Lenalidomide requires careful monitoring as it carries a black box warning for neutropenia and can also cause venous thrombosis.

Background: Discoid lupus erythematosus (DLE) is characterized by scarring, prominent pigmentary changes, and permanent hair loss, and is therefore often disfiguring. First-line treatment with anti-malarials and local corticosteroids is ineffective in a significant fraction of patients. Thalidomide is a remarkably effective therapy for these resistant cases, but long-term treatment is often limited by side effects of neuropathy, sedation, and teratogenicity. Lenalidomide is a thalidomide analog approved for treatment of multiple myeloma with a lower frequency of neuropathy and sedation and increased inhibition of tumor necrosis factor (TNF) relative to thalidomide.

Objective: To investigate if lenalidomide may have potential use in treatment-resistant DLE.

Participants: 2 patients with chronic, severe DLE unresponsive to conventional treatments were included.

Results: The first subject had a 9-year history of generalized DLE associated with systemic lupus erythematosus (SLE). She had failed to respond to topical corticosteroids, several antimalarial agents, dapsone, methotrexate, mycophenolate mofetil, rituximab, IV immunoglobulin, and azathioprine. The patient had previously responded to thalidomide, but the drug was discontinued because of neuropathy. Lenalidomide was started at a dosage of 5 mg/day and clinical improvement was seen 1 month after starting the drug. By 2 months, the Cutaneous Lupus Erythematosus Severity Index (CLASI) activity score was approximately 50% the starting level. The patient's corticosteroid dose was then tapered from 60 mg/day to 5 to 10 mg/day, with a slight worsening of the CLASI score. Notably, the patient did not experience the neuropathy that had caused discontinuation of her thalidomide. Lenalidomide was increased to 10 mg/day, but was later decreased back to 5 mg/day because of mild neutropenia. The second patient also presented with generalized DLE associated with SLE; however, unlike the first subject, this patient did not respond to a previous course of thalidomide. Unfortunately, this patient showed no clinical response despite treatment with lenalidomide for 6 months.

Conclusions: Lenalidomide shows promise for treatment of resistant DLE in patients who cannot tolerate thalidomide.

Reviewer’s Comments: In my experience, thalidomide works great for cutaneous lupus, but neuropathy has forced me to discontinue thalidomide in the majority of patients in which I have used the drug. This series of 2 patients suggests that lenalidomide may have potential for treating resistant DLE patients who have to discontinue thalidomide because of neuropathy. However, lenalidomide requires careful monitoring as it carries a black box warning for neutropenia and can also cause venous thrombosis. Obstacles associated with both lenalidomide and thalidomide include their high cost and cumbersome manufacturer sponsored monitoring programs.

Additional Keywords: Lenalidomide

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**Complex Aphthae Respond Well to Treatment**

*Successful Treatment of Complex Aphthosis With Colchicine and Dapsone.*

Lynde CB, Bruce AJ, Rogers RS III:

*Arch Dermatol;* 145 (March): 273-276

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**Background:** Complex aphthosis is defined as the prolonged presence of multiple painful oral or genital ulcers in the absence of Behcet's syndrome. There is some overlap between complex aphthosis and Behcet's as some of these patients progress to Behcet's. Because of the pain associated with complex aphthosis, the disease can be debilitating. Drugs used to treat aphthosis include thalidomide, colchicine, dapsone, and corticosteroids.

**Objective:** The authors of this paper have an extensive experience treating patients with colchicine and then adding dapsone if needed.

**Methods:** Most patients were started on colchicine at 0.6 mg, administered each evening for 1 week. If a patient had no significant gastrointestinal tract upset during this therapy after 1 week, the dose was increased to 1.2 mg with ingestion of both tablets in the evening preferred to reduce gastrointestinal tract intolerance. Some patients were eventually increased to 1.8 mg/day if tolerated. Dapsone was given in a stepwise manner by increasing the dose every 3 days until reaching a final dose of 125 to 150 mg per day. Patients with low hemoglobin were limited to 100 mg/day of dapsone. Treatment success was defined as a >50% reduction in aphthae.

**Design:** Chart review.

**Participants:** 55 patients with complex aphthosis treated at the authors’ institution between 1988 and 2007 were included; 45 patients with oral aphthae only, while the remaining 10 patients had both oral and genital aphthae.

**Results:** 52 of the 55 patients started treatment with colchicine. Of these 52 patients, 60% reached therapeutic success with colchicine alone. However, only 3% experienced complete clearing of all aphthae. Fourteen patients received a combination of colchicines and dapsone. Twelve of the 14 received the combination treatment because they did not adequately respond to colchicines alone and 2 received the combination as initial treatment because of the severity of their disease; 71% of these patients reached treatment success and 20% reached complete clearing. Five patients were treated with dapsone alone because of intolerance to colchicine. Four of these 5 patients reached treatment success. There were no serious adverse events with either drug.

**Conclusions:** Colchicine and dapsone are effective treatments for complex aphthosis and the 2 can be combined for resistant cases.

**Reviewer's Comments:** Both colchicine and dapsone are generally well tolerated agents that most dermatologists are comfortable using. Colchicine requires relatively little laboratory monitoring, so it is a good first choice. Dapsone commonly causes hemolytic anemia, but most patients tolerate the drop in hemoglobin well and remain on the drug. Although combining partially effective agents is an intriguing idea, it remains unclear from this paper if the combination of colchicine and dapsone is better than dapsone alone.

**Additional Keywords:** Dapsone & Colchicine

**print tag:** () Refer to original journal article.
Can Systemic Retinoids Improve Nails With Psoriasis?

_Evaluation of the Efficacy of Acitretin Therapy for Nail Psoriasis._
Tosti A, Ricotti C, et al:
_Arch Dermatol;_ 145 (March): 269-271

Low-dose acitretin improves isolated nail psoriasis by approximately 50%.

**Background:** Nail changes are common in psoriasis and in some instances, nail disease is the only manifestation of psoriasis. Unfortunately, nail psoriasis is unresponsive to topical therapies. Systemic therapies are thought to be effective for nails, but their usefulness is poorly documented. Among the systemic agents, acitretin (a retinoid) is commonly thought to have a favorable side effect profile compared to immunosuppressive agents.

**Objective:** To quantitatively document nail improvement during and after treatment with low-dose acitretin.

**Design:** Uncontrolled, open-label study.

**Participants:** 36 patients with moderate to severe nail psoriasis and no skin involvement.

**Methods:** Patients were placed on low-dose acitretin (0.2 to 0.3 mg/kg per day) for 6 months. Disease severity was quantified using the Nail Psoriasis Severity Index (NAPSI) or a modified NAPSI designed to measure involvement of a pre-determined single index nail. Patients were assessed every 2 months during treatment and 6 months following discontinuation of the drug.

**Results:** After 6 months on acitretin, the average decline in NAPSI and modified NAPSI was 41% and 50%, respectively. Approximately 25% of the patients were judged to exhibit complete or almost complete clearing. However, most of this improvement was lost by 6 months after discontinuing the drug. No patient had to discontinue acitretin because of adverse effects. However, 1 patient developed multiple pyogenic granulomas that resolved after lowering the dose of acitretin.

**Conclusions:** The authors suggest that acitretin is useful in isolated nail psoriasis.

**Reviewer's Comments:** Nail improvement with acitretin in this study is roughly comparable to that already reported with anti-tumor necrosis factor biologic agents. Although previous studies have documented nail improvement with systemic retinoids, this study documented the improvement with an objective rating scale. Moreover, this study was limited to patients with isolated nail psoriasis. Apart from its teratogenic effects, acitretin appears safe in the short term. However, the drug can have adverse effects on blood lipids and may be associated with increased cardiovascular death in psoriasis patients. As with any drug, potential benefits must be weighed against risks.

**Additional Keywords:** Acitretin Tx

print tag: () Refer to original journal article.
Histologic Features Have Prognostic Value

Merkel Cell Carcinoma: Histologic Features and Prognosis.
Andea AA, Coit DG, et al:
Cancer; 113 (November 1): 2549-2558

Tumor stage, thickness, lymphovascular invasion, and tumor growth pattern are significant predictors of survival for patients with Merkel cell carcinoma.

Objective: To determine prognostic features of primary cutaneous Merkel cell carcinoma (MCC).

Design: Retrospective single-institutional study.

Participants: The authors identified 156 patients with a diagnosis of MCC from 1989 to 2005. The median follow-up for the cohort was 51 months. The authors evaluated potential prognostic factors including tumor thickness, tumor size, deepest microanatomic compartment, lymphovascular invasion, tumor-infiltrating lymphocytes, tumor necrosis, ulceration, and solar elastosis. The primary outcome was disease-specific survival.

Results: The most common primary site was the extremity area (42%), followed by head and neck (37%), buttocks (16%), and trunk (4.5%). The median patient age was 69.5 years. The cohort included more men than women (56% vs 44%). Most patients (52%) presented with stage I disease; 19% had stage II, 23% had stage III, and 6% had stage IV disease. The mean tumor thickness was 12.3 mm and mean size was 20.1 mm. On multivariate analysis, higher stage, tumor growth pattern (infiltrative vs nodular), and the presence of lymphovascular invasion were significantly associated with worse disease-free survival. When tumor growth pattern was excluded from the model (because it could be evaluated for only 108 patients), tumor thickness was a significant predictor of survival. The 5-year survival rates for patients with stage I and II disease were 86% and 82.5%, respectively. For patients without lymph node metastases, tumor growth pattern, anatomic compartment, lymphovascular invasion, and tumor infiltrating lymphocytes were significant prognostic factors.

Conclusions: In addition to tumor stage, specific histologic features (tumor thickness, lymphovascular invasion, and tumor growth pattern) are significantly associated with disease-free survival for patients with MCC.

Reviewer’s Comments: MCC is a difficult disease to treat because it is rare, the patients are often elderly, and approximately 25% of patients have lymph node metastases at diagnosis. The histological features associated with worse prognosis in this study may be used to identify patients for sentinel lymph node staging and potentially adjuvant therapy. Nevertheless, the benefits of lymphadenectomy and systemic adjuvant therapy are not known.

Additional Keywords: Histology/Prognosis

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