original publications assumed the UV-A energy exposure from commercial nail polish drying devices would fall within the estimated range determined to be potentially carcinogenic. However, considering the low UV-A energy exposure in an average manicure visit, multiple visits would be required to reach the threshold for potential DNA damage. Although the in vivo risk from multiple manicure visits remains untested, our data suggest that, even with numerous exposures, the risk for carcinogenesis remains small. That said, we concur with previous authors in recommending use of physical blocking sunscreens or UV-A protective gloves to limit the risk of carcinogenesis and photoaging.

Lyndsay R. Shipp, MD
Catherine A. Warner, MD
Frederick A. Rueggeberg, DDS, MS
Loretta S. Davis, MD

Author Affiliations: Division of Dermatology, Department of Medicine, Medical College of Georgia and College of Dental Medicine at Georgia Regents University, Augusta.

Corresponding Author: Lyndsay R. Shipp, MD, Division of Dermatology, Department of Medicine, Medical College of Georgia at Georgia Regents University, 1004 Chafee Ave, FH-100, Augusta, GA 30904 (lshipp@gru.edu).

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Author Contributions: Dr Shipp had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Table. Number of Nail Salon Visits and the Risk for DNA Damagea

<table>
<thead>
<tr>
<th>Light Source No.</th>
<th>UV-A Irradiance, Median, mW/cm²</th>
<th>UV-A Energy Dosage Exposure for Single Visit (8 min) (J/cm²)b</th>
<th>Months to Attain DNA Damage Threshold, No. (60 J/cm²)c</th>
<th>Visits Needed to be Exposed to Threshold Value for DNA Damage, No. (60 J/cm²)d</th>
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The median UV-A irradiance for each nail polish drying device was used to determine the energy dosage a client would receive per visit. This energy was then compared with the energy known to cause DNA damage to determine the number of visits and months required for a potential risk of carcinogenesis.

Conflict of Interest Disclosures: None reported.

Correction: This article was corrected online June 19, 2014, for errors in the Table.


Alectocolumab Therapy for Leukemic Cutaneous T-Cell Lymphoma: Diffuse Erythema as a Positive Predictor of Complete Remission

Low-dose alectocolumab (LDA) therapy is highly effective and generally well tolerated for refractory cutaneous T-cell lymphoma (CTCL) with peripheral blood disease. Treatment with LDA is effective in patients with blood involvement (leukemic
disease) but ineffective in mycosis fungoides (MF), reflecting the fact that these lymphomas derive from distinct T-cell subsets. Malignant T cells in patients with blood disease have the phenotype of CCR7+/L-selectin+ central memory cells (T_{CM}) (migratory cells that recirculate between skin, blood, and lymph nodes), while MF T cells are derived from nonmigratory skin resident memory T cells (T_{RM}). Because the mechanism of T-cell depletion with LDA requires neutrophils and/or natural killer cells (cells common in blood but rare in skin), LDA kills T cells in blood but not in skin. In patients with blood disease, LDA depletes all circulating T cells and purges the skin over time of recirculating malignant T cells, leading to complete and

Figure 1. Diffuse Cutaneous Erythema and a Lack of Discrete Plaques and/or Tumors Associated With Excellent Clinical Responses to Treatment With Low-Dose Alemtuzumab (LDA)

A, Clinical images of 3 patients who achieved complete remission after LDA therapy. B, Clinical images at presentation of 2 patients who achieved clearance of blood disease but incomplete clearing or worsening of skin disease after LDA treatment. Discrete patches, plaques, or tumors on presentation were associated with incomplete response to LDA therapy.

Figure 2. Patients Who Have Circulating Malignant T Cells With a Phenotype of CCR7+/L-Selectin+ Central Memory Cells (T_{CM}) Have Better Responses to Low-Dose Alemtuzumab (LDA) Therapy

In all histograms, numbers in the corners specify the percentage represented by the given quadrant. A, Clinical presentation before therapy and the T-cell phenotype of a representative treatment-responsive patient with greater than 80% T_{CM} malignant T cells. In the graphs, the black dots represent nonclonal T cells. Malignant T cells (shown in red) were identified by their expression of a clonal T-cell receptor (TCR) Vβ subunit; the percentage of malignant CCR7+/L-selectin+ T_{CM} was determined by flow cytometry. This patient achieved a complete remission on LDA. B, Clinical presentations before and after treatment and the phenotype of a representative treatment-resistant patient with less than 80% T_{CM} circulating malignant T cells. In the graphs, the black dots represent nonclonal T cells. Only 16% of circulating malignant T cells (shown in red) had a T_{CM} phenotype. Clinically, diffuse erythema cleared in this patient after LDA therapy, but discrete lesions remained. C, In 2 patients, diffuse erythema cleared after LDA therapy, but localized skin lesions clinically worsened despite reduction of the malignant clone in the skin. In the graphs, the black dots represent nonclonal T cells; malignant T cells are shown in red. Skin biopsies demonstrated that the malignant clone had been reduced from 50% before LDA therapy to 9% afterwards. Worsening skin lesions were infiltrated by highly activated interferon-γ (IFNγ)-producing nonclonal CD8+ T cells, suggesting that inflammation was mediated by activation of benign reactive T cells. Histograms on the right are gated to show only CD8+ T cells.
often durable remissions in 50% of patients while sparing benign T cells in skin.1 We present herein our findings that clinical appearance can be used to differentiate patients likely to experience a complete remission following LDA from those who will have persistent and/or worsening skin disease.

Methods | Work was performed according to the ethical principles set out in the Declaration of Helsinki and was approved by the Dana-Farber Cancer Institute institutional review board. All patients provided written informed consent. T cells isolated from skin2 or blood were stained with directly conjugated monoclonal antibodies and analyzed on a Becton-Dickinson FACSCanto using FACSĐiva software (version 5.1).

Results | Diffuse Cutaneous Erythema Without Discrete Plaques and/or Tumors Associated With Complete Remission After LDA Therapy. Twenty-three patients with peripheral blood disease (eTable 1 in the Supplement) were treated with LDA (10 mg subcutaneously, 3 times a week). Of these, 17 patients presented with diffuse erythema without superimposed plaques or tumors (Figure 1A). Thirteen patients experienced complete remission following LDA treatment, and the remaining 4 had residual or emergent skin disease controllable by skin-directed therapy alone (eTable 1 in the Supplement). In contrast, of 6 patients presenting with discrete patches, plaques, or tumors with or without background diffuse erythema (Figure 1B), none experienced full remission after LDA; 1 responded fully to subsequent electron beam therapy, and 5 had recurrent and/or progressive disease, including 2 patients who developed large cell transformation.

Circulating Malignant T Cells With a T Cm phenotype Correlation With LDA Responsiveness. In 19 patients, we measured the proportion of malignant T cells with T Cm markers (CCR7+/L-selectin−). Of 10 patients with greater than 80% T Cm, 8 experienced full remission with LDA alone (Figure 2A), and 2 after subsequent skin-directed therapies (eTable 1 in the Supplement). Of 9 patients with less than 80% T Cm, 3 cleared after LDA therapy alone, and 6 had persistent and/or progressive disease (Figure 2B). The proportion of malignant T Cm in skin could be measured in 12 patients; in 4 of 6 patients with greater than 80% T Cm in skin, disease cleared with LDA therapy alone; in 1 of 6 it cleared with LDA plus skin-directed therapy; and in 1 of 6, the disease progressed. Two patients with different clones in the blood and skin did not experience complete clearance with LDA therapy alone but experienced full remission after additional skin-based therapies (eTable 1 in the Supplement). In 2 patients with worsening skin disease during or after LDA therapy, biopsies showed large numbers of nonclonal, activated, interferon-γ-producing CD8+ T cells, suggesting that inflammation was mediated by benign T cells (Figure 2C).

Discussion | All patients treated with LDA had clearance of peripheral blood disease, but only patients presenting with diffuse erythema without superimposed plaques or tumors also had complete and long-lasting clearance of skin disease. Initial clinical presentation was more predictive of response than was complex cellular phenotyping of T cells from blood and skin. In other words, the eyes of a well-trained dermatologist were more powerful than a comprehensive translational research program in identifying complete responders to LDA therapy. On a scientific level, diffuse erythema is likely caused by migrating T cells, and only T cells that migrate into blood are cleared by LDA. Fixed skin lesions are more likely to be caused by T RM, cells that escape LDA clearance by remaining long-term in skin. Based on our clinical and scientific findings, we recommend the use of LDA with or without adjuvant skin-directed therapy in patients with diffuse cutaneous erythema, but we caution against its use in patients with preexisting plaques and/or tumors.

Rei Watanabe, MD, PhD
Jessica E. Teague, PhD
David C. Fisher, MD
Thomas S. Kupper, MD
Rachael A. Clark, MD, PhD

Author Affiliations: Harvard Skin Disease Research Center, Department of Dermatology, Brigham and Women’s Hospital, Boston, Massachusetts (Watanabe, Teague, Kupper, Clark); Cutaneous Lymphoma Program, Dana-Farber Brigham and Women’s Cancer Center, Boston, Massachusetts (Fisher, Kupper).

Corresponding Author: Rachael A. Clark, MD, PhD, Department of Dermatology, Brigham and Women’s Hospital, 221 Longwood Ave, Room 505A, Boston, MA 02115 (rclark1@partners.org).

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Author Contributions: Dr Clark had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Watanabe, Fisher, Kupper, Clark.
Acquisition of data: Watanabe, Teague, Fisher, Kupper.
Analysis and interpretation of data: Watanabe, Teague, Kupper, Clark.
Drafting of the manuscript: Clark.
Critical revision of the manuscript for important intellectual content: Watanabe, Teague, Fisher, Kupper, Clark.
Statistical analysis: Kupper.
Obtained funding: Kupper, Clark.
Administrative, technical, or material support: Teague, Fisher, Kupper.
Study supervision: Fisher, Clark.

Conflict of Interest Disclosures: Drs Kupper and Clark previously had an equity interest in TremRX, a start-up company that seeks as a long-term business plan to improve vaccine formulation and delivery. During the period Drs Kupper and Clark held the equity, the interest was deemed to create a financial conflict of interest (as defined by the specific Public Health Service regulations) with the research discussed in this article. To resolve this matter, Drs Kupper and Clark divested themselves of the equity interest in this company, so this financial conflict of interest no longer exists. Dr Clark has served as a Scientific Advisor for Novartis and Stiefel Laboratories and received honoraria for these services. No other disclosures are reported.

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Additional Contributions: We are indebted to the patients who made this work possible, both for entrusting us with their clinical care and for donating skin and blood samples.


OBSERVATION

True Leukonychia in Crohn Disease Induced by Selenium Deficiency

Leukonychia is divided into 2 major types: **true leukonychia**, which involves the nail plate, and **apparent leukonychia**, which involves the nail bed.1 Herein, we present the first case to our knowledge of true leukonychia successfully treated with selenium substitution.

Report of a Case | A man in his 30s presented with an 18-year history of Crohn disease and had undergone partial resections of both small and large bowel 6 times. In recent years, the patient had been maintained on total parenteral nutrition, taking enteral nutritional products because of short-bowel syndrome. He was referred to our outpatient clinic with a 2-week history of nail color changes.

On physical examination, we found that the proximal halves of the affected nails of his fingers and toes were whitish; the distal halves were normal; and the 2 color zones were sharply demarcated (Figure, A). Routine laboratory examination for patients on total parenteral nutrition revealed a significantly low serum selenium level (2.0 μg/dL; reference level, 10.6-17.4 μg/dL). After treatment with 100 μg/d of selenium for 8 weeks to improve the selenium deficiency, interestingly, the proximal part of the nails at the nail base gradually turned normal, and the whitish part moved toward the distal direction without changing in appearance or size (Figure, B). Consequently, the whitish part regressed completely, and the nail conditions turned normal in 14 weeks (Figure, C).

Discussion | The present patient presented with true leukonychia in association with Crohn disease as well as selenium deficiency. Although there have been some reports about associations of leukonychia, Crohn disease, and selenium deficiency, all 3 conditions have not been discussed together. An association of Crohn disease with half-and-half nails has been reported in at least 1 case,2 but the serum selenium levels were not estimated in that case. Furthermore, Crohn disease has been associated with selenium deficiency,3 but the nail conditions were not described in detail in those reports. Therefore, we believe this case to be the first providing evidence that true leukonychia is caused in part, if not wholly, by selenium deficiency in Crohn disease and is curable with selenium substitution. However, care must be taken with adverse effects,4 and selenium levels must be carefully monitored to avoid toxic effects.

Leukonychia is caused by the abnormality of either nail bed or nail plate. In half-and-half nails, Lindsay5 has suggested that the whitish part of the nails stayed at the same portion and remained unchanged while the nail grew toward the distal portion, implying that the cause of color change begins in the nail bed rather than the nail plate. On the other hand, our true leukonychia case showed an interesting clinical course during the improvement of nail color in which the whitish part moved toward the distal portion during the nail growth after selenium substitution, suggesting that the primary pathologic site was not in the nail bed but in the nail plate.

In addition, little is known about specific physiological roles of selenium in the formation and/or maintenance of the nail apparatus. Selenium is a component of the antioxidant en-