COMMENTS AND OPINIONS

The Appropriateness of Curettage and Electrodesiccation for the Treatment of Basal Cell Carcinomas

In the article by Thissen et al[1] in the October issue of the *Archives of Dermatology*, published data from our institution were quoted. The article compared the recurrence rates of basal cell carcinomas (BCCs) following different treatment modalities, including Mohs micrographic surgery, surgical excision, and curettage and electrodesiccation (C&E). They presented subsets of the C&E data from a 1977 study by Kopf et al[2] from our institution as 3 separate studies. The highest rate of 18.8% cumulative recurrence at 5 years corresponded to C&E performed by resident physicians-in-training at the Skin and Cancer Unit of New York University Medical Center, New York. NY, from 1958 to 1962. Because of this finding, a greater effort was made to teach and supervise residents in this operative procedure. As a result, the cumulative recurrence rate of BCC at 5 years following C&E by resident physicians dropped to 9.6% as measured in 1970. The lowest 5-year cumulative recurrence rate in this study of 5.7% corresponded to C&E procedures performed by a fully trained dermatologist in his private practice from 1962 to 1973 (A.W.K.). In addition, they presented a 5-year cumulative recurrence rate of BCC following C&E of 13.2% from a 1991 study by Silverman et al[3] performed by resident physicians-in-training at the Skin and Cancer Unit of New York University Medical Center from 1955 to 1982.

This presentation of the data led the authors to the erroneous conclusion that "for smaller BCCs of the nodular and superficial types, surgical excision remains the first treatment of choice."[1] On the contrary, if one compares the data of C&E by a fully trained dermatologist to the other modalities, one finds that the C&E recurrence rate of 5.7% is very similar to the 5.3% recurrence rate for surgical excision.

Macrene Alexiades-Armenakas, MD, PhD
The Ronald O. Perelman Department of Dermatology
New York University School of Medicine
550 1st Ave
New York, NY 10016
David Ramsay, MD
Alfred W. Kopf, MD
New York

1. Thissen MR, Neumann MH, Schouten LJ. A systematic review of treatment modalities for primary basal cell carcinomas. *Arch Dermatol*. 1999;135:1177-1183.
2. Kopf AW, Bart RS, Schrager D, Lazar M, Popkin G. Curettage-electrodesiccation treatment of basal cell carcinomas. *Arch Dermatol*. 1977;113:439-443.
3. Silverman MK, Kopf AW, Grin CM, Bart RS, Levenstein MJ. Recurrence rates of treated basal cell carcinomas, II: curettage-electrodesiccation. *J Dermatol Surg Oncol*. 1991;17:720-726.

VIGNETTES

Accuracy of Diagnosis of Seborrheic Keratoses in a Dermatology Clinic

Seborrheic keratoses (SKs) are common benign lesions with which patients often present to clinics designed for the early detection of melanoma.[1,2] The ability to clinically recognize SKs is essential. This prospective study examined diagnostic accuracy in recognizing SKs.

Patients and Methods. The patients included were all those referred consecutively to dermatology outpatient clinics primarily regarding a lesion or lesions that were clinically diagnosed as SKs. Incidental lesions that were not the presenting complaint were excluded. Lesions thought possibly to be SKs but that would normally have biopsy specimens taken were also excluded.

A biopsy was offered to all patients. The histopathologic database was examined to ascertain how many lesions histologically diagnosed as SKs but not included in the study had been referred from our clinic over the same period.

Results. Over a 7-month period, 115 patients were offered a biopsy; 103 agreed and were included in the study. Histologic analysis confirmed the clinical diagnosis of SK in 101 specimens; 1 was reported as a squamous cell carcinoma in situ, and 1 consisted only of keratin. When this inadequate specimen was excluded, the diagnostic accuracy was assessed as 101 of 102, or greater than 99% accuracy.

During this period, 6 lesions not clinically diagnosed as SKs were diagnosed histopathologically as SKs. The tabulation below shows the clinical diagnoses made in these 6 patients and whether SK was considered among the differential diagnoses.

Clinical Diagnosis	SK Status
Benign nevus	Listed
Basal cell carcinoma	Not listed
Bowen disease	Not listed
Fibroepithelial polyp	Not listed
Viral wart	Not listed
SK but differential diagnosis included atypical nevus	Not applicable

Comment. When a clinical diagnosis of SK is made with confidence, the lesion is often left untreated or a destructive method of removal is used. Therefore, it is imperative that clinical diagnostic accuracy is of a sufficiently high level to justify such practices, which do not yield material for histopathologic confirmation of diagnosis. In this study we changed our usual management for the duration of the study in that histopathologic specimens were obtained from all patients.

This diagnostic accuracy of greater than 99% is higher than that found for dermatologists in other studies. An American and a British study showed a diagnostic accuracy for dermatologists in recognizing SKs of 61% and 66%, respectively.[3,4] However, this difference can be explained because these studies were retrospective and based on an audit of pathologic specimens. Thus those lesions diagnosed and not treated or on which a destructive method of treatment was used were excluded. As a consequence, overall diagnostic accuracy was not measured.

In our study a squamous cell carcinoma in situ was wrongly clinically diagnosed as SK. In a recent study of the 577 specimens diagnosed clinically and submitted for histologic examination as SKs, 37 (6.4%) were subsequently diagnosed as malignant tumors.[5] It is important, therefore, to emphasize that in all cases of diagnostic doubt, histopathologic analysis should be performed.

This was a prospective study and represents overall diagnostic accuracy rather than that culled from a histologic database. The extremely high diagnostic accuracy of greater than 99% justifies common clinical practice. However, a biopsy should be performed in all cases of diagnostic doubt.

Michelle Murphy, MB, MRCPI
Department of Dermatology
South Cleveland Hospital
Marton Road
Middlesbrough, TS4 3BW England
Rosemarie Watson, MD, FRCPI
Eamon C. Sweeney, MD, FRCPI, FRCPath
Louise Barnes, MB, FRCPI
Dublin, Ireland

1. Rivers JK, Gallagher RP. Public education projects in skin cancer. *Cancer*. 1995; 75(suppl):661-666.
2. Harris DWS, Benton EC, Hunter JAA. The changing face of dermatology outpatient referrals in the south-east of Scotland. *Br J Dermatol*. 1990;123:745-750.
3. Sowden JW, Lewis-Jones MS, Williams RB. Who best manages seborrhoeic keratoses? *Br J Dermatol*. 1996;135(suppl 47):47-49.
4. Stern RS, Bourdreaux C, Arndt KA. Diagnostic accuracy and appropriateness of care for seborrheic keratoses. *JAMA* 1991;265:74-77.
5. Eads TJ, Hood AF, Farmer ER. The diagnostic yield of histologic examination of seborrheic keratoses. *Arch Dermatol*. 1997;133:1417-1420.

Preliminary Evidence for an Association of Measles Virus With Recurrent Aphthous Ulceration

The etiology of recurrent aphthous ulceration (RAU), a common disease of the oral mucosa, is still obscure. Local, microbial, viral, systemic, nutritional, and genetic factors have been suggested as underlying the pathogenesis of RAUs.[1] The viruses considered as causative agents include herpes simplex, varicella zoster, and Epstein-Barr, none of which can, however, be directly isolated from RAU lesions.[2] We have noted an increased prevalence of aphthous ulcerations among patients with measles,[3] raising the possibility that RAU may be directly related to measles infection. Previously, an association was noted between measles virus infection and Crohn disease, which is characterized by ulceration of the intestinal mucosa.[4] Both Crohn disease and RAU are considered to be immunologically mediated. The purpose of the present study was to investigate whether RAU was associated with the measles virus by determining the expression of measles viral antigens in the oral mucosa of individuals with RAU, and whether any change in the expression of CD46, the receptor for measles virus,[5] could be detected in the oral mucosa of individuals with RAU compared with controls.

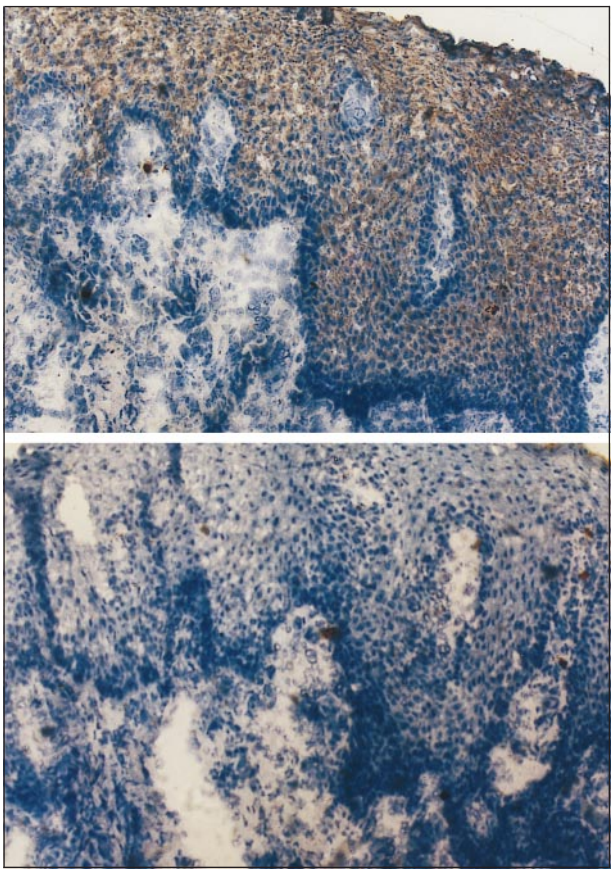
Patients, Materials, and Methods. Specimens of oral mucosa were obtained from 3 healthy men, aged 18 to 19 years, with recurrent minor aphthous ulcerations occurring about twice a month over the course of more than 2 years. All individuals received a routine public health vaccination for measles; the last injection was given at age 10 years. Biopsy specimens were taken from the oral cavity with informed consent during the early stages of the aphthous ulcer eruptions. Healthy mucosa specimens obtained during elective surgical interventions from 4 healthy young individuals served as controls. All the specimens were frozen immediately in liquid nitrogen and kept at −70°C. Fixed cryostat sections were treated with periodate, followed by normal heat-inactivated rabbit serum. Sections were incubated for 30 minutes at 37°C with the following monoclonal antibodies (mAbs): anti-measles virus mAb (ViroStat, Portland, Me) anti–herpes simplex virus mAb (NCL-HSV1; Novocastra, England [1:125 dilution]), and anti-CD46 mAb (Immunotech, Marseille, France [1:50 to 1:1000 dilution]). After rinsing, the slides were incubated for 10 minutes with affinity-purified biotinylated rabbit anti-mouse IgG antibody (Jackson Immuno-Research Laboratories, West Grove, Pa) at a 1:500 dilution and washed and incubated for 5 minutes with peroxidase-conjugated streptavidin at a 1:500 dilution. The slides were rinsed, and diamino benzidine reagent was applied, followed by hematoxylin solution.

Results. Staining with anti-measles virus mAb gave positive results in the oral mucosa of the 3 individuals tested with RAU. Twelve of the 13 sections of oral mucosa of RAU studied were clearly positive (**Table**). In some sections all the layers of epithelium were stained with anti-measles virus mAb (**Figure**, top). In other sections, the stratum spinosum layer was most obviously reactive, while the basal layer and the superficial part of the epithelium were stained weakly. The staining with anti-measles virus mAb was cytoplasmatic in nature. The RAU mucosa failed to stain with anti–herpes simplex mAb. Similarly, no staining was obtained

Immunostaining of Oral Mucosa From Normal Individuals and Individuals With Recurrent Aphthous Ulceration*

Type of Tissue Tested	No. of Sections	Primary Antibody	Results of Immunostaining		
			Positive	Negative	Unclear
RAU	13	Anti-measles virus	12	0	1
Normal	7	Anti-measles virus	0	4	3
RAU	7	Anti–herpes simplex virus	0	6	1
Normal	5	Anti–herpes simplex virus	0	5	0
RAU	8	No primary antibody	0	6	2
Normal	8	No primary antibody	0	7	1
			Strongly Positive		Weakly Positive
RAU	4	Anti-CD46 mAb	0		4
Normal	9	Anti-CD46 mAb	9		0

*RAU indicates recurrent aphthous ulceration; mAb, monoclonal antibodies. See text for detailed description of procedures.



Top, Sections of oral mucosa from individuals with recurrent aphthous ulceration were stained with monoclonal antibodies against measles virus and biotinylated rabbit anti-mouse IgG. The positive brown reaction was most obvious in the stratum spinosum layer, while the basal layer and the superficial part of the epithelium were stained weakly (original magnification ×250). Bottom, Control section of oral mucosa from an individual with recurrent aphthous ulceration exposed only to the secondary antibody, without addition of the primary antibody (original magnification ×250).

in RAU mucosa exposed to biotinylated rabbit anti-mouse IgG, without addition of the primary antibody (Figure, bottom). In contrast to the results obtained with mucosa from patients with RAU, mucosa from normal individuals was not stained by anti-measles virus mAb (Table). Normal tissue also failed to react with anti–herpes simplex virus mAb. Studies have shown that infection with measles virus can lead to down-regulation of the expression of CD46 on the surface of the infected cells.[5] While mucosa cells from normal individuals showed strong staining with anti-CD46 mAb, localized predominantly to the cell membrane, the mucosa of patients with RAU gave a very weak staining reaction with anti-CD46 mAb. Exposure of oral mucosa sections to anti-cytokeratin mAb yielded homogeneous, positive-staining reactions.

Comment. Katz et al[3] observed severe oral ulcerations in about 20% of Israeli soldiers with measles, raising the possibility that measles virus may be associated with RAU. In the present study, the oral mucosa in all the individuals with RAU reacted with antibodies against the measles virus, but failed to react with antibodies against the herpes simplex virus. In contrast, the oral mucosa of normal controls failed to react with antibodies against the measles virus. While the oral mucosa of all normal individuals showed strong reactivity with antibodies against CD46, the measles receptor, the oral mucosa of individuals with RAU showed a negligible reactivity. This observation is in line with the fact that the measles virus induces down-regulation of CD46.[5] Down-modulation of CD46 elicited by latent infection of oral mucosa with measles virus may trigger the formation of RAU lesions. Since CD46 regulates complement activation, the reduced expression of CD46 may render oral epithelial cells sensitive to lysis by complement. Activation of complement may be elicited by various other factors, explaining the observation that diverse agents may be involved in the generation of lesions of RAU.

Rakefet Czerninski, DMD
Joseph Katz, DMD
Department of Oral Diagnosis, Oral Medicine and Radiology
Faculty of Dental Medicine
Hebrew University-Hadassah Medical Faculty
Jerusalem, 91120 Israel
Michael Schlesinger, MD
Jerusalem

1. Ship J. Recurrent aphthous stomatitis. *Oral Surg.* 1966;81:141-147.
2. Pedersen A, Madsen HO, Vestergaard B, et al. Varicella-zoster virus DNA in recurrent aphthous ulcers. *Scand J Dent Res.* 1993;101:311-313.
3. Katz J, Findler M, Marmary Y, et al. Measles, Crohn's disease and recurrent aphthous stomatitis [letter]. *Lancet.* 1996;348:1250-1251.
4. Wakefield AJ, Pittilo RM, Sim R, et al. Evidence of persistent measles virus infection in Crohn's disease. *J Med Virol.* 1993;39:345-359.
5. Naniche D, Wild TF, Rabourdin-Combe C, Gerlier D. Measles virus haemagglutinin induces downregulation of gp57/67, a molecule involved in virus binding. *J Gen Virol.* 1993;74:1073-1079.

A Cycle: Recurrent Gram-negative Folliculitis With *Citrobacter diversus (koseri)* Following Eradication of Recurrent Staphylococcal Pyoderma

Gram-negative folliculitis frequently complicates long-term antibiotic therapy for acne. Follicular lesions caused by *Staphylococcus aureus* are also common, particularly in patients who chronically carry the organism. The patient in this case developed gram-negative folliculitis with *Citrobacter diversus (koseri)*, an organism that has not previously been reported to be pathogenic in this condition. He also experienced repeated episodes of *Citrobacter* and staphylococcal folliculitis in an alternating fashion because treatment directed against one organism caused a secondary infection by the other.

Report of a Case. A 28-year-old man presented with suppurative, follicular lesions on his face after having been treated for acne with minocycline hydrochloride continuously for the past 11 years. When his presumptive case of gram-negative folliculitis failed to improve with discontinuation of minocycline therapy, treatment was started with 60 mg (0.83 mg/kg) of oral isotretinoin daily. His lesions cleared rapidly, but he developed a new, very similar eruption just before completing the 5-month course. Cultures from these lesions revealed heavy growth of only 1 organism, *S aureus*. This eruption was resistant to multiple courses of oral antibiotics and 2% mupirocin calcium ointment to the anterior nares. Eradication of the carrier state was attempted with a 2-week course of oral clindamycin hydrochloride, 150 mg 4 times daily, and 600 mg of oral rifampin daily, followed by an additional 2½-month course of oral clindamycin hydrochloride, 150 mg daily.

Despite their quick resolution, suppurative lesions returned only 1 week after completion of this regimen. Multiple culture findings then revealed heavy growth of a single organism, *C diversus (koseri)*. The patient experienced complete clearing of the lesions during several 6-week courses of 800 mg of oral sulfamethoxazole, and 160 mg of trimethoprim twice daily. Since the lesions would return following each antibiotic course, isotretinoin was again administered and was successful in eliminating the *Citrobacter* folliculitis. However, the cycle continued: the patient developed staphylococcal folliculitis after each isotretinoin course for the treatment of *Citrobacter* folliculitis, followed again with another case of *Citrobacter* folliculitis due to attempts to eradicate the staphylococcal carrier state. The patient's condition continues to cycle despite oral antimicrobial therapy when needed as guided by culture and sensitivity results.

Comment. Although gram-negative folliculitis may be effectively treated with isotretinoin, this drug is associated with staphylococcal carriage in the nasal mucosa and intertriginous areas. Eradication of the *S aureus* carrier state has been accomplished by the administration of rifampin in combination with various antistaphylococcal antibiotics, as well as by clindamycin monotherapy. The use of these drugs in combination for this purpose has not been described but was very effective in this patient. However, their poor activity against most gram-negative rods may explain the return of his gram-negative folliculitis, though the full reason for the presence of the unusual organism is not clear.

Citrobacter belongs to the Enterobacter family of aerobic, nonsporulating, gram-negative bacilli, which normally inhabit the human intestines. The genus *Citrobacter* is divided into the following three species: *C freundii*, *C diversus* (also known as *C koseri*), and *C amalonaticus*. These organisms are rarely pathogenic but have been reported to cause clinically significant disease, most commonly urinary tract infections, septicemia, and neonatal meningitis. Three reported cases of *C freundii* septicemia were associated with clinically significant skin findings: gangrenous ulceration in one patient,[1] papulopustules and blisters in a second patient,[2] and cellulitis in another.[3] *Citrobacter freundii* has been reported to cause gram-negative folliculitis[4] as well as infectious diarrhea in association with urticaria.[5]

Citrobacter diversus is also an extremely rare cause of cutaneous disease. This species was the infectious agent in 2 reported patients with cellulitis,[6,7] but has never previously been noted to cause gram-negative folliculitis. In contrast to the suppressive effect of sulfamethoxazole/trimethoprim, isotretinoin effectively eradicated this patient's *Citrobacter* folliculitis but also perpetuated the cycle by inducing new staphylococcal lesions.

Mark A. Chastain, MD
Tulane University School of Medicine
Department of Dermatology, TB-36
1430 Tulane Ave
New Orleans, LA 70112
(e-mail: chastain@mailhost.tcs.tulane.edu)

1. Grant MD, Horowitz HI, Lorian V. Gangrenous ulcer and septicemia due to *Citrobacter*. *N Engl J Med.* 1969;280:1286-1287.
2. Schlossberg D, Ricci JA, Fugate JS. Dermatologic manifestations of *Citrobacter* septicemia. *J Am Acad Dermatol.* 1981;5:613-615.
3. Hicks CB, Chulay JD. Bacteremic *Citrobacter freundii* cellulitis associated with tub immersion in a patient with the nephrotic syndrome. *Mil Med.* 1988;153:400-401.
4. Mostafa WZ. *Citrobacter freundii* in gram-negative folliculitis. *J Am Acad Dermatol.* 1989;20:504-505.
5. Fisher DA. A most memorable case [editorial]. *Cutis.* 1989;43:132.
6. Shukla PC. Plantar cellulitis. *Pediatr Emerg Care.* 1994;10:23-25.
7. Bishara J, Gabay B, Samra Z, Hodak E, Pitlik S. Cellulitis caused by *Citrobacter diversus* in a patient with multiple myeloma. *Cutis.* 1998;61:158-159.

Candida parapsilosis Chondritis Successfully Treated With Oral Fluconazole

Candida parapsilosis infection can occur in any surgical setting. We present, to our knowledge, the first case of auricular *C parapsilosis* chondritis following Mohs micrographic surgery that was successfully treated with an oral antifungal agent (fluconazole).

Report of a Case. A basal cell carcinoma of the ear was removed from a 65-year-old man by Mohs micrographic surgery, sparing the perichondrium. Repair was performed with a split-thickness skin graft that was viable 1 week after surgery. The grafted area developed tenderness and erythema 10 days postoperatively while the patient was taking cephalexin. On the 14th postoperative day, the cartilage became exposed and dry, with erythema and edema of the surrounding skin. There were no systemic signs and symptoms. Fenestration of the cartilage with a 3-mm punch biopsy allowed both histopathologic analysis and the establishment of a vascular base for wound granulation.

Perichondrial and cartilaginous invasion by pseudohyphae were demonstrated, and the cultures grew *C parapsilosis*. Oral fluconazole treatment was initiated (200 mg/d) in addition to continued local wound care. Results of a biopsy taken after 2 weeks of fluconazole treatment showed no fungal invasion, but the wound culture remained positive for *C parapsilosis*. The oral fluconazole treatment was continued for another 2 weeks. The follow-up culture was negative and the wound healed by second intention with good cosmetic results. The donor site healed without complications. During surgery, no violation of sterility occurred. No other patients undergoing surgery in the same office by the same surgeons developed this infection. Therefore, acquiring the *C parapsilosis* infection at home during wound care was possible.

Comment. Localized and systemic infections with *C parapsilosis* can occur in several surgical settings, mostly after extensive burns and in the immunocompromised patient. *Candida* species were isolated from the hands of 29% of hospital personnel working in an intensive care unit, with *C parapsilosis* being one of the most frequently recovered isolates.[1] There is a probability of glove tears with subsequent transmission of the pathogen to patients in any surgical setting.[2] *Candida parapsilosis* is sensitive in vitro to amphotericin B, 5-fluorocytosine, fluconazole, ketoconazole, and itraconazole.[3]

The auricular cartilage is vulnerable because of its avascular nature, the lack of subcutaneous tissue, and the exposed position of the ear. As a rule, the onset of chondritis is insidious, and usually manifests 3 to 5 weeks after the injury. The therapy for chondritis ranges from topical application of antibiotics to the surgical removal of all involved cartilage. Extensive chondritis can lead to disfigurement of the ear.[4] The cartilage of the ear is frequently exposed during Mohs micrographic surgery, and the postoperative course may involve complications if the cartilage is stripped of its perichondrium.

We suggest that when chondritis following auricular surgery is nonresponsive to antibiotic therapy, tissue samples be analyzed for histopathologic characteristics, and routine fungal cultures be considered. These will allow the evaluation for invasive *Candida* species and other fungi in the setting of nonbacterial infectious chondritis.

Zoltan Trizna, MD, PhD
The University of Texas Medical Branch at Galveston
Department of Dermatology, Rte 0783
301 University Blvd
Galveston, TX 77555-0783
(e-mail: ztrizna@pol.net)
San-Hwan Chen, MD
Susanne Lockhart, MD
Kurt F. Lundquist, MD
Edgar B. Smith, MD
Richard F. Wagner, MD
Galveston

Presented at the Eighth European Association of Dermatology and Venerology, Amsterdam, the Netherlands, September 29-October 3, 1999.

1. Huang YC, Lin TY, Leu HSW, Wu JL, Wu JH. Yeast carriage on hands of hospital personnel working in intensive care units. *J Hosp Infect*. 1998;39:47-51.
2. Diekema DJ, Messer SA, Hollis RJ, Wenzel RP, Pfaller MA. An outbreak of *Candida parapsilosis* prosthetic valve endocarditis. *Diagn Microbiol Infect Dis*. 1997;29:147-153.
3. Araj GF, Daher NK, Tabbarah ZA. Antifungal susceptibility of *Candida* isolates at the American University of Beirut Medical Center. *Int J Antimicrob Agents*. 1998;10:291-296.
4. Skedros DK, Goldfarb IW, Slater H, Rocco B. Chondritis of the burned ear: a review. *Ear Nose Throat J*. 1992;71:359-362.

Nutria Itch

In south Louisiana, a dermatitis has been recognized called "nutria itch," "marsh itch," or "creeping eruption." The possible link between the large number of nutrias and the occurrence of a severe pruriginous rash hours after people have been in water or close to a swamp has been noted.[1-3]

A 12-year-old boy and his 68-year-old grandfather developed diarrhea and an intensely pruritic rash on their trunks and extremities after working in mud next to a marsh populated with nutrias. After 2 weeks of severe pruritus and no improvement, they sought medical attention. Results of their physical examination showed a maculopapular erythematous rash that involved the chest and extremities, but the grandfather's rash was more severe (**Figure 1** and **Figure 2**).

Their white blood cell counts were normal except for mild eosinophilia, 0.03 and 0.06, in the child and the grandfather, respectively. Stool samples were not obtained for ova and parasites. Results of a skin biopsy on the grandfather's lesion revealed an inflammatory infiltrate consisting of eosinophils and mast cells. No microorganisms or larvae were identified.

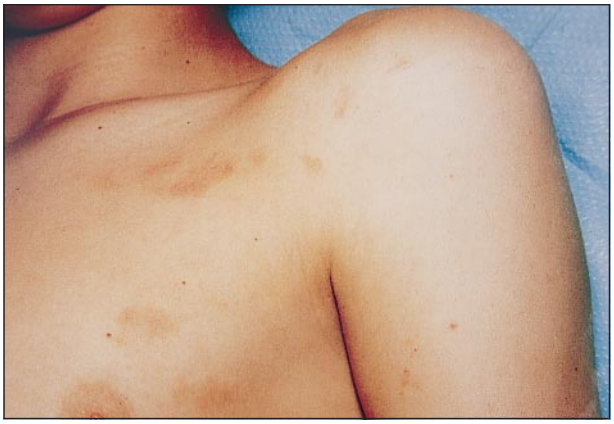


Figure 1. *Rash on the boy's chest.*

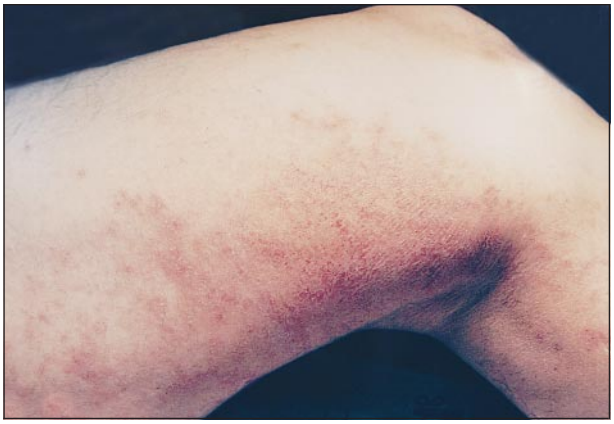


Figure 2. *Rash on the grandfather's leg.*

Serum samples were sent to the Centers for Disease Control and Prevention, Atlanta, Ga, for an enzyme immunoassay test (EIA) for *Strongyloides*. The child's results were negative for *Strongyloides*, but the grandfather's were strongly positive (71%; positive, >8%). Both patients were treated for 5 days with albendazole, with improvement of the itching, diarrhea, and skin rash.

In 1959, Burks and Jung[1] reported 4 cases of "nutria itch." These 4 patients had been in a swamp before the rash appeared. A parasite was not identified, either in the stools or the tissue.

Strongyloides myopotami and *Strongyloides procyonis* found in nutrias have been postulated as possible agents causing this condition.[1-3] Approximately 85% of nutrias in Louisiana carry *S myoptami* in the gastrointestinal tract.[4] Feces from nutrias are found in marshes they inhabit.[1]

Similar rash has been reproduced in volunteers after exposure to these *Strongyloides*.[3] We presume that the infection was acquired through skin contact with soil or water contaminated with the larvae of *Strongyloides*. Diagnosis of *Strongyloides* infection is based on visualization of the larva,[4] isolation of the larva, polymerase chain reaction, or antibody titers by EIA.[5] The sensitivity of the EIA test is 90% and the specificity, 83%. False-positive reactions have occurred in patients with hookworm, filaria, *Paragonimus*, and *Echinococcus*, but coinfection with *Strongyloides* could not be excluded (Mariana Wilson, PhD, Centers for Disease Control and Prevention, unpublished data, 1999). The grandfather had a strongly positive titer by EIA for *Strongyloides*, possibly related to a larger inoculum or a prior infestation with other species of *Strongyloides* or other helminths.

Although this condition seems to be self-limited, the use of antihistaminics[1] or albendazole accelerated the resolution of the itch and rash (R.S.). *Strongyloides* from nutrias should be considered in patients with pruritic rash from an area with a substantial population of nutrias. However, other parasitic infestations (*Strongyloides stercoralis*, *Ancylostoma*, *Necator*, and *Schistosoma*) should be considered.[1]

Hector F. Bonilla, MD
Louisiana State University/Washington St Tammany Medical Center
400 Memphis St
PO Box 40
Bogalusa, LA 70427
(e-mail: Hbonil@POL.net)
Diane H. Blanchard, MD
Baton Rouge, La
Richard Sanders, MD
Creole, La

We would like to thank Mariana Wilson, PhD, at the Centers for Disease Control and Prevention, Atlanta, Ga; Alfredo Suarez, MD, Louisiana State University, Baton Rouge; and Carol Kauffman, MD, University of Michigan, Ann Arbor.

1. Burks JW, Jung RC. A new type of water dermatitis in Louisiana. *South Med J.* 1960;53:716-719.
2. Crawford A. Nutria itch: scourge of the marsh. *Louisiana Conservationist.* 1996; May/June:21-24.
3. Little MD. Dermatitis in a human volunteer infected with *Strongyloides* of nutria and raccoon. *Am J Trop Med Hyg.* 1965;14:1007-1009.
4. Schacher JF. *Final Report on Parasites of Louisiana Mammals With Emphasis on Nutria* (Myopotamus coypus) *and Otter* (Lutra canadensis *ssp*). Bogalusa, La: Louisiana Wildlife & Fisheries Commission; 1956.
5. Sato Y, Koba Y, Shiroma Y. Serodiagnosis of strongyloidiasis: the applications and significance. *Rev Inst Med Trop Sao Paulo.* 1995;37:35-41.

Genetic Mosaicism in an Acquired Inflammatory Dermatosis Following the Lines of Blaschko

Congenital, nevoid, and acquired skin diseases may follow lines of Blaschko, which are thought to reflect cell migration and clonal expansion during embryogenesis of the skin.[1] This concept greatly relies on the hypothesis that disorders following Blaschko lines are caused by genetic mosaicism. The genetic mosaicism that manifests along Blaschko lines may result from Lyonization (random inactivation of 1 of the two X chromosomes in women) or somatic postzygotic mosaicism.[2] Authentic genetic mosaicism was proved in only a few cases of Blaschko-linear nevoid or X-linked diseases.[1,3,4] It is less obvious how the clonal hypothesis of Blaschko lines deals with acquired inflammatory diseases along the lines of Blaschko. The latter include, among others, such different diseases as lichen striatus, lichen planus, psoriasis, and lupus erythematosus. In this report, we were able to demonstrate for the first time genetic mosaicism in a Blaschko-linear inflammatory dermatosis.

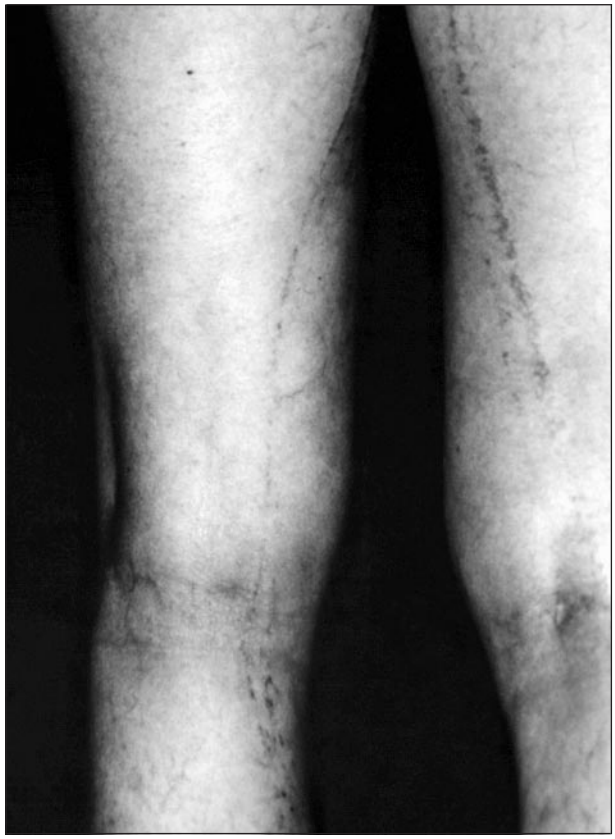


Figure 1. *Linear eruption following the lines of Blaschko in a 38-year-old woman.*

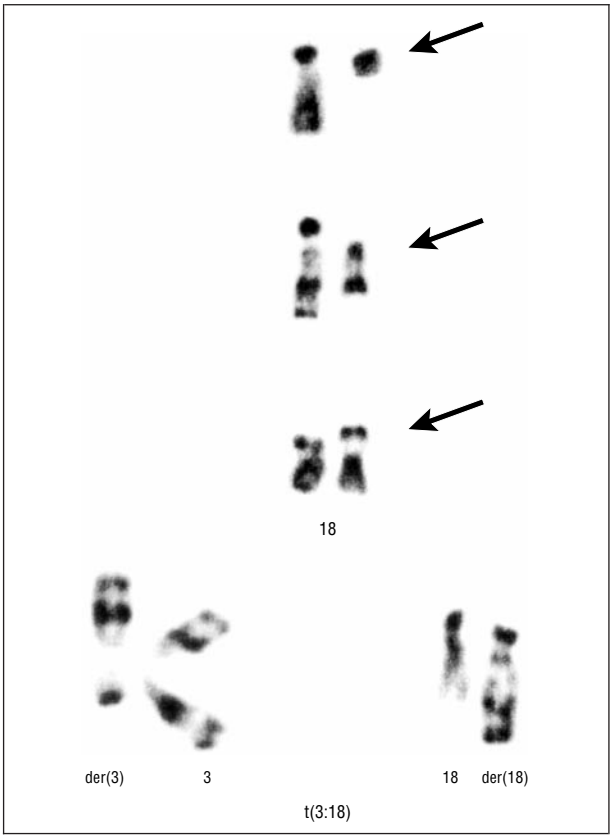


Figure 2. *Karyotype analysis of dermal fibroblasts showing abnormalities including chromosome 18 in lesional skin but not in normal-appearing skin. Arrows indicate abnormal chromosomes 18 compared with their normal counterparts at the left. The 2 pairs of chromosomes at the bottom show a 3:18 translocation. A monosomy of chromosome 18, which was also present, is not shown here; der(3) and der(18) indicate the chromosomes that contain the translocation.*

Patient, Methods, and Results. A 38-year-old woman developed an extensive, Blaschko-linear, inflammatory dermatitis involving the face, the 4 limbs, and the trunk (**Figure 1**). The eruption consisted of a 5-mm-wide, linear, slightly scaling erythema, which became more patchy on the buttocks. Results of a cutaneous biopsy showed a lymphocytic upper dermal infiltrate, acanthosis, and mild spongiosis. We performed additional cutaneous biopsies within diseased skin and at adjacent normal-appearing skin for cell culture and chromosome analysis using standard methods.[4] Chromosomal analysis was also performed on peripheral blood lymphocytes. Findings of cytogenetic studies revealed a normal 46, XX karyotype on 98 mitoses in normal-appearing skin, while an abnormality including chromosome 18 was found in 5 of 100 mitoses in diseased skin. There was 1 complete deletion of chromosome 18, a partial deletion of chromosome 18, a translocation (3:18), a ring chromosome 18, and a chromosome 18 with a modified centromeral index (**Figure 2**). Chromosome analysis of peripheral blood lymphocytes showed a normal 46, XX karyotype. The eruption lasted 4 months and then regressed totally, leaving only discrete postinflammatory hyperpigmentation, which disappeared completely within 6 months.

Comment. This patient had "Blaschkitis," which was first described by one of us (E.G.) in 1990.[5] It is an autonomous entity that corresponds neither to a known inflammatory dermatitis in Blaschko-linear distribution nor to a hamartoma or X-linked disease. For the first time, we were able to demonstrate a genetic mosaicism in an acquired Blaschko-linear inflammatory dermatosis. The mechanisms through which genetic mosaicism can lead to such a linear inflammatory dermatosis still remain hypothetical. This genetic mosaicism could be responsible for cutaneous antigenic mosaicism, the expression of which might be induced by a viral infection, for example. This viral infection could then trigger an inflammatory T-cell response in a Blaschko-linear fashion. Although the exact pathophysiologic characteristics of acquired inflammatory Blaschko-linear diseases remain largely unknown, the presence of genetic mosaicism is certainly of primary importance in their occurrence. The demonstration of genetic mosaicism in an acquired inflammatory Blaschko-linear dermatosis strongly supports the clonal hypothesis of Blaschko lines.

Dan Lipsker, MD
Clinique Dermatologique
1, Place de l'Hôpital, F-67091 Strasbourg Cedex, France
(e-mail: dlipsker@cybercable.fr)
Bernard Cribier, MD, PhD
Françoise Girard-Lemaire, MD
Elisabeth Flori, MD
Edouard Grosshans, MD
Strasbourg

1. Bologna JL,Orlow SJ, Glick SA. Lines of Blaschko. *J Am Acad Dermatol.* 1994; 31:157-190.
2. Happle R. Mosaicism in human skin: understanding the patterns and mechanisms. *Arch Dermatol.* 1993;129:1460-1470.
3. Paller AS, Syder AJ, Chan YM, et al. Genetic and clinical mosaicism in a type of epidermal nevus. *N Engl J Med.* 1994;331:1408-1415.
4. Moss C, Larkins S, Stacey M, Blight A, Farndon PA, Davison EV. *J Med Genet.* 1993;30:752-755.
5. Grosshans E, Marot L. Blaschkite de l'adulte. *Ann Dermatol Venereol.* 1990; 117:9-15.

Double-blind, Right/Left Comparison of Calcipotriol Ointment and Betamethasone Ointment in the Treatment of Prurigo Nodularis

Prurigo nodularis (PN) is a disease characterized by chronic, intense, itchy nodules in the distal extremities of the limbs.[1,2] Although topical steroids have been widely used to treat PN, there have been no controlled trials evaluating their efficacy. Topical vitamin D_3 (tacalcitol) has been reported effective for PN in an open study,[3] but our preliminary report is the first prospective, randomized, double-blind, right/left comparative study evaluating the therapeutic efficacy and tolerability of 50 µg/g calcipotriol ointment (Leo Pharmaceutical Products, Ballerup, Denmark) with that of 0.1% betamethasone valerate ointment in the treatment of PN.

Patients and Methods. Ten patients (5 male, 5 female; aged 8-55 years) with chronic persistent nodules of more than 0.5 cm in diameter, symmetrically located on the lower legs, were enrolled in the study after providing written informed consent. The study was approved by the ethics committee of the National Skin Centre of Singapore. There were 8 Chinese, 1 Malayan, and 1 Indian. The mean duration of disease was 3.4 years (range 1-8 years). One (11%) of 9 patients had a history of allergic rhinitis. No patients had atopic dermatitis. All patients had used potent topical steroid creams and 5 (56%) of 9 patients had received intralesional steroid injection previously. All topical and systemic therapies were stopped 1 month before entry. Exclusion criteria included pregnancy, calcium supplements, and known steroid and calcipotriol allergy. Treatment with calcipotriol or 0.1% betamethasone valerate ointment was randomly assigned to nodules on opposite sides of the legs, twice daily, according to computer-generated random numbers, after the 4-week washout period during which aqueous cream was used as an emollient. Calcipotriol ointment (50 µg/g) was applied twice a day to nodules on one side of the leg while 0.1% betamethasone valerate ointment (1 mg/g) (Dermasone ICM, Singapore, Singapore), which was similar in appearance and texture to the calcipotriol ointment, was applied twice daily to nodules on the opposite side. Both drugs (up to 50 g/wk) were applied without occlusion to the nodules. The right hand was used to apply the ointment to the left side and vice versa. Patients were assessed at weeks 0, 2, 4, and 8 of treatment. The total number of palpable nodules on each leg was counted, and the mean diameter of the 3 largest nodules on each leg was used to represent the mean size of the nodules. The overall response to treatment was scored at week 8 of treatment for each leg separately, using a 6-point scale (–1, worse; 0, no change; 1, slight improvement; 2, moderate improvement; 3, marked improvement; and 4, no lesions). Adverse effects were recorded at each clinic visit. Hemoglobin and serum calcium levels were obtained before and at the end of the study. A comparison of the efficacy of treatment was based on changes in the total number and mean size of nodules from baseline value within subjects, using the Wilcoxon matched paired signed rank test. Comparisons between the number and mean size of nodules on both calcipotriol- and betamethasone valerate–treated sides were also made.

Results. The total number and mean size of the nodules were comparable at baseline. One patient withdrew from the study after 2 weeks because of noncompliance. Statistically significant ($P<.05$) reduction in the total number of nodules was attained after 2 weeks for the calcipotriol-treated side, whereas improvement did not occur until week 8 for the betamethasone valerate–treated side ($P<.05$). The percent change from baseline between the 2 treatments was statistically significant in favor of calcipotriol at week 4 and week 8 ($P<.05$). Statistically significant reduction in the size of nodules was attained after 2 weeks for both the calcipotriol-treated side ($P<.01$) and the betamethasone valerate–treated side ($P<.05$), but the percent change from baseline between the 2 treatments showed that calcipotriol was more effective at week 4 and week 8 ($P<.05$). After 8 weeks of calcipotriol treatment, the reduction in the number and size of nodules was 49% and 56%, respectively, compared with 18% and 25% for the betamethasone valerate (**Table**). At the end of treatment, both in-

Clinical Evaluation During the 8 Weeks of Randomized Treatment (n = 9)*

	No. of Nodules			Size of Nodules, cm		
	Calcipotriol	0.1% Betamethasone Valerate	*P*	Calcipotriol	0.1% Betamethasone Valerate	*P*
Baseline	19.4 (14.1)	23.3 (10.4)	.4	1.0 (0.4)	0.9 (0.2)	.2
2 Weeks	14.7 (10.8)†	23.1 (10.5)		0.8 (0.4)‡	0.8 (0.2)†	
Change from baseline, %	27.2 (18.6)	2.4 (4.0)	.12	21.6 (20.2)	7.9 (7.6)	.05
4 Weeks	11.8 (7.9)†	21.1 (8.9)		0.6 (0.4)‡	0.8 (0.2)†	
Change from baseline, %	37.4 (22.4)	5.5 (9.1)	.02	44.8 (28.6)	11.5 (13.4)	.02
8 Weeks	9.2 (5.2)‡	18.9 (9.1)†		0.5 (0.5)‡	0.7 (0.2)†	
Change from baseline, %	49.1 (20.0)	18.1 (16.4)	.02	56.1 (30.8)	25.0 (16.5)	.02

**Unless otherwise indicated, data are expressed as mean ± SD.*
†P<*.05.*
‡P<*.01.*

vestigator and patients gave better global scores for the calcipotriol- than for the betamethasone valerate–treated side, although the cohort was too small for statistical analysis. Mild perilesional skin irritation was observed in 4 patients (44%) treated with calcipotriol ointment within the first 2 weeks, which resolved spontaneously. Serum calcium levels were normal before and after treatment. After the completion of the 8-week trial, all 9 patients were treated with the betamethasone valerate ointment in the morning and calcipotriol ointment at night and after a further 2 months, 3 had complete remission; 6 required maintenance treatment with calcipotriol ointment.

Comment. Our data indicate that calcipotriol ointment is more effective than 0.1% betamethasone valerate ointment in the treatment of PN. We found that calcipotriol ointment cleared prurigo nodules more rapidly than the betamethasone valerate ointment. Although none of our patients had atopic dermatitis, the presence or absence of background atopic dermatitis did not seem to influence the outcome of calcipotriol treatment in PN.[3] Calcipotriol has proven effective in the treatment of psoriasis and other disorders of abnormal epidermal growth and differentiation, including ichthyosis, epidermal nevus, pityriasis rubra pilaris, and palmoplantar keratoderma,[4] supporting the concept that calcipotriol has an effect on epidermal differentiation and/or proliferation. Although the pathogenesis of PN is still unknown, PN shares some histologic features (epidermal proliferation) with psoriasis and ichthyosis.[1,2] In addition, tacalcitol analogs interfere with cutaneous inflammation, keratinization, and epidermal proliferation; they also exert immunomodulating effect on lymphoid cells.[5,6] Any combination of these effects may have played a role in the beneficial outcome of calcipotriol therapy in our patients with PN.

We have demonstrated that calcipotriol is safe and more effective than betamethasone valerate. Calcipotriol represents a therapeutic advance in the management of PN because it is free of the cutaneous and systemic adverse effects of chronic steroid therapy. Further large-scale studies are necessary to confirm its therapeutic role in PN, but the use of combination or sequential topical calcipotriol with topical steroid might maximize the benefits and decrease the potential adverse effects of both drugs. Whether this strategy will further enhance treatment efficacy for this chronic, recalcitrant skin disorder awaits further studies.

Sai-Siong Wong, MB, BCh, MRCP(UK)
Evangel Hospital
222 Argyle St
Kowloon, Hong Kong
Chee Leok Goh, MD, FRCP(Edin)
Singapore, Singapore

1. Rowland-Payne CME, Wilkinson JD, McKee PH. Nodular prurigo: a clinical pathological study of 46 patients. *Br J Dermatol.* 1985;113:431-439.
2. Jorizo JL, Gatti S, Smith EB. Prurigo: a clinical review. *J Am Acad Dermatol.* 1981;4:723-728.
3. Katayama I, Miyazaki Y, Nishioka K. Topical vitamin D3 (tacalcitol) for steroid-resistant prurigo. *Br J Dermatol.* 1996;135:237-240.
4. Van de Kerkhof PCM, Wittenhorst M, Gerritsen MJP, de Jong EMGJ, Luker GPH, Steylen PM. Possible indications for vitamin D3 analogues in conditions other than psoriasis vulgaris. *J Derm Treat.* 1996;7:195-198.
5. Bikle DD, Gee E, Pillai S. Regulation of keratinocyte growth, differentiation, and vitamin D metabolism by analogs of 1,25-dihydroxy vitamin D. *J Invest Dermatol.* 1993;101:713-718.
6. Bagot M, Charue D, Lescs MC, Paphile RP, Revuz J. Immunosuppressive effects of 1,25-dihydroxyvitamin D3 and its analogue calcipotriol on epidermal cells. *Br J Dermatol.* 1994;30:424-431.

Comparison of Urinary 8-Hydroxy-2′-deoxyguanosine in Patients Treated With Topical Corticosteroids, UV-B, and Psoralen UV-A Therapies

Photochemotherapy combines the use of a photosensitivity drug and long-wave UV-A light (320-400 nm). The topical application and oral administration of the selected psoralen, mostly 8-methoxypsoralen followed by UV-A irradiation (PUVA) have been proven to be very effective in the treatment of psoriasis, vitiligo, and cutaneous T-cell lymphoma.[1] However, a statistically significant increase in the incidence of squamous cell carcinoma as well as malignant melanoma has been demonstrated in patients undergoing PUVA treatment.[2,3] Skin cancers may arise as a result of the mutagenic psoralen photoadducts (and their mismatch or lack of repair) formed in keratinocytes during photochemotherapy. Other types of DNA damage may also contribute to the carcinogenicity of PUVA. Besides the direct interaction of psoralens with DNA, the role of reactive oxygen species (ROS) such as the superoxide anion (O_2^-), the hydroxyl radical ($HO^\bullet$), and singlet oxygen ($^1O_2$) in PUVA-induced cytotoxicity has been proposed.[4] These ROS may cause oxidative damage to macromolecules such as DNA if not timely scavenged. Oxidative DNA damage has been known to be associated with gene mutations, carcinogenesis, and age-related disorders. 8-Hydroxy-2′-deoxyguanosine (8-OHdG), a widely used biomarker of oxidative DNA damage, has been implicated in several carcinogenic processes, including skin cancer, and is used as an indicator of overall oxidative DNA damage in vivo.

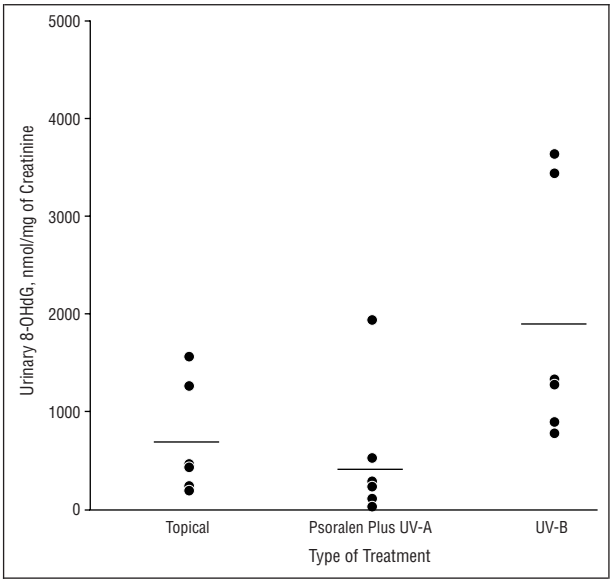
Because PUVA treatments can generate reactive oxygen species, which subsequently cause oxidative DNA damage, we hypothesized that PUVA treatments may result in higher levels of oxidized DNA base in this group of patients, which may be responsible, at least in part, for increased incidence of skin cancer. It is known that oxidatively modified DNA bases can be removed by endogenous repairing enzymes and excreted through urine.[5] Therefore, the levels of urinary 8-OHdG can reflect the total load of oxidized DNA bases in the body. Our prediction was that the patients receiving PUVA would produce the highest level of 8-OHdG owing to the link to oxidative stress by PUVA therapy.

Patients, Methods, and Materials. Twenty spot urine samples were collected from patients being treated at the dermatology clinic at Mount Sinai Hospital, New York, NY. Subjects were selected and divided into 3 groups, based on the treatment for their psoriasis or cutaneous T-cell lymphoma (topical corticosteroids [sham radiation control], PUVA, and UV-B therapy). All patients in

Summary of Patient Information and the Level of Urinary 8-OHdG*

Patient No./ Sex/Age, y	Diagnosis	8-OHdG, nmol/mL	Urine Creatinine, mg/mL	Normalized 8-OHdG, nmol/mg of Creatinine
Topical Treatment Group (n = 6), Mean (SEM) Normalized 8-OHdG, 341.1 (92.7) nmol/mL				
1/F/40	Psoriasis	1271.2	2.87	442.9
2/M/67	Psoriasis	468.9	1.59	294.9
3/M/54	Psoriasis	1566.2	2.88	543.3
4/F/28	Psoriasis	182.0	0.87	214.9
5/F/38	Psoriasis	239.1	1.88	127.2
6/M/44	Psoriasis	427.1	0.93	459.3
PUVA Treatment Group (n = 8), Mean (SEM) Normalized 8-OHdG, 314.4 (85.2) nmol/mL				
7/F/42	CTCL	141.9	0.84	168.9
8/F/42	CTCL	539.6	1.99	270.6
9/M/72	Psoriasis	242.2	0.56	439.2
10/M/61	CTCL	45.1	1.69	26.8
11/M/80	CTCL	1962.0	3.72	527.4
12/M/44	Psoriasis	305.8	0.41	742.3
13/M/80	CTCL	29.0	0.38	77.3
14/M/38	Psoriasis	314.0	1.19	263.8
UV-B Treatment Group (n = 6), Mean (SEM) Normalized 8-OHdG, 2233.8 (349.9) nmol/mL				
15/F/41	Psoriasis	3668.1	1.01	3617.5
16/M/71	Psoriasis	1350.2	0.77	1751.2
17/M/73	Psoriasis	1566.2	1.19	2921.9
18/M/51	Psoriasis	1306.8	0.64	2035.5
19/F/71	Psoriasis	898.0	0.53	1687.9
20/F/23	Psoriasis	809.6	0.583	1388.7

**8-OHdG indicates 8-hydroxy-2'-deoxyguanosine; PUVA, psoralen plus UV-A; and CTCL, cutaneous T-cell lymphoma.*



Comparison of urinary 8-hydroxy-2' -deoxyguanosine in (8-OHdG) patients undergoing different treatment modalities.

the study were white and signed consent forms. The group as a whole consisted of 8 women, 12 men, and 2 smokers (patients 9 and 14). Their ages ranged from 23 to 80 years, with a mean age of 52 years (**Table**).

Urine samples were collected and immediately frozen at –20°C. Urine samples were prepared as described by Erhola et al[5] with a slight modification. Briefly, 0.01 mL of ammonium hydroxide was added to 1.0 mL of urine and centrifuged for 5 minutes. The supernatant was removed and placed in a clean tube to which 0.01 mL of acetic acid was added and mixed well. One milliliter of the prepared sample was loaded to a 3-mL C-18 SEP-PAK column (Waters, Watford, England) preconditioned with 3 mL of methanol and 10 mL of distilled water. The eluant was discarded and the column washed with 10 mL of distilled water followed by 1 mL of 15% methanol. The fraction containing 8-OHdG as the nucleoside was then eluted with 1 mL of 15% aqueous methanol.

Analysis of prepared 8-OHdG urine was done using high-pressure liquid chromatography device (model 510 Waters), as described.[5] All levels of urinary 8-OHdG were expressed relative to creatinine corrected for differences in urine dilutions.

Results. The **Figure** compares the urinary 8-OHdG levels in patients receiving different treatment modalities. After normalization of the samples based on the urine creatinine levels, the amount of 8-OHdG elaborated was significantly elevated in the UV-B treatment group with a mean value of 2233.8 nmol/mL when compared with PUVA and topical steroid therapies ($P = .007$). However, there was no statistically significant difference in the levels of 8-OHdG between the PUVA and topical corticosteroid groups, with the similar means of 314.4 and 347.1 nmol/mg of creatinine, respectively (Table and Figure).

Comment. Oxidative DNA damage has been implicated in several carcinogenic processes, including skin cancer. Oxidation of DNA bases can be induced by exposure to ionizing radiation and UV light. It is known that PUVA therapy is capable of generating ROS. Therefore, we postulated that PUVA therapy could increase the formation of 8-OHdG in genomic DNA, thereby resulting in the elevation of urinary excretion of 8-OHdG. The present study indicated that UV-B (290-320 nm) significantly increased the urinary 8-OHdG, whereas PUVA had no effect on the urinary excretion of 8-OHdG compared with topical steroid therapy. These results contradict our hypothesis that PUVA would generate the most oxidative DNA damage because it is associated with the generation of ROS and an increased incidence of skin cancer.

A possible explanation may lie in the different mechanisms of action of PUVA and UV-B. PUVA has 2 mechanisms of action. The type 1 reaction does not require oxygen and involves cellular DNA. It involves forming monofunctional adducts with pyrimidine bases on 1 DNA strand. After absorption of a second photon, a bifunctional adduct is formed with pyrimidine bases on opposing strands, which causes crosslinking of the double helix. This crosslinking inhibits DNA synthesis and cell division, thereby providing therapeutic action on psoriasis and cutaneous T-cell lymphoma. The type 2 reaction requires oxygen and involves the transfer of energy from the excited triplet state of psoralen to molecular oxygen forming ROS and free radicals. Irradiation of DNA

with different adenine-thymine (AT)–guanine-cytosine ratios showed that the yield of 8-OHdG varied in proportion to AT content, suggesting that AT base pairs in DNA enhance generation of the oxidizing species and subsequent oxidation of deoxyguanosine. It was also shown that UV-induced 8-OHdG was proportionally correlated with AT content of DNA not present in free deoxyguanosine. Perhaps the crosslinks formed as the result of the type 1 reaction of PUVA lead to a decrease in the AT base pairs. If this is the case, it would explain the relatively low production of 8-OHdG in the PUVA group. The proposed mechanism of action for UV-B involves the synthesis of DNA, RNA, and the release of inflammatory mediators. Perhaps the alterations in DNA do not involve a crosslink or different crosslinks, which permits the preservation of AT. If AT base pairs in DNA are preserved after UV-B therapy, then the amount of 8-OHdG formed would be greater, because the 2 are directly proportional. Thus, the level of 8-OHdG remains a good indicator of oxidative DNA damage due to UV-B.

Another explanation is that extensive formation of photoadducts by PUVA impedes the excision of 8-OHdG by endogenous DNA-repairing enzymes, eg, formaminopyrimidine DNA glycosylase. Psoralen UV-A treatment substantially increases the formation of 8-OHdG in cellular or genomic DNA. However, our study showed that urinary 8-OHdG in patients undergoing PUVA remained unchanged, probably due to the compromised repairing enzymes. In this scenario, 8-OHdG may be accumulated in the genomic DNA and lead to the potential risk of mutagenicity or carcinogenicity. This may also explain the fact that PUVA results in more risk of skin cancer than UV-B therapy in the treatment of psoriasis because UV-B–induced oxidative DNA damage is more readily repaired and excised by endogenous nuclease than that caused by PUVA.

In conclusion, urinary 8-OHdG levels were increased in the patients undergoing UV-B therapy, but not in the patients having PUVA therapy. Our findings should be considered preliminary, given the differences in the treatment groups' clinical characteristics. Because PUVA treatment is known to increase the formation of 8-OHdG in purified DNA and cultured cells, the unchanged level of urinary 8-OHdG in the patients undergoing PUVA treatment suggests that the formation of photoadducts by PUVA either compromises the formation of 8-OHdG or impedes the excision of 8-OHdG from DNA by endogenous DNA-repairing systems. Moreover, because dermatologists will continue to use both PUVA and UV-B for the treatment of psoriasis, cutaneous T-cell lymphoma, and vitiligo, further studies need to be conducted in these areas.

Amy E. Goldstein, DO
Bronx, New York, NY
Mark Lebwohl, MD
Huachen Wei, MD, PhD
Department of Dermatology
PO Box 1047
Mount Sinai Medical Center
1425 Madison Ave
New York, NY 10029
(e-mail: weih01@doc.mssm.edu)

1. Parrish JA, Fitzpatrick TB, Tanenbaum L, Pathak MA. Photochemotherapy of psoriasis with oral methoxsalen and long-wave ultraviolet light. *N Engl J Med.* 1974;291:1207-1211.
2. Stern RS, Lange R. Non-melanoma skin cancer occurring in patients treated with PUVA five to ten years after first treatment. *J Invest Dermatol.* 1988;91:120-124.
3. Stern RS, Nichols KT, Vakeva LH. Malignant melanoma in patients treated for psoriasis with methoxsalen (psoralen) and ultraviolet A radiation (PUVA). *N Engl J Med.* 1997;336:1041-1045.
4. Pathak MA, Joshi PC. Production of active oxygen species by psoralen and ultraviolet-radiation (320-400 nm). *Biochim Biophys Acta.* 1984;798:115-126.
5. Erhola M, Toyokuni S, Okada K, et al. Biomarker evidence of DNA oxidation in lung cancer patients: association of urinary 8-hydroxy-2'-deoxyguanosine excretion with radiotherapy, chemotherapy, and response to treatment. *FEBS Lett.* 1997;409:287-291.