COMMENTS AND OPINIONS

Delayed EPPER Syndrome

Rueda et al[1] recently reported that 17% of women receiving radiotherapy for internal cancer developed pruritic eruptions (ie, acral excoriations, erythematous papules, vesicles, and bullae) that favored the lower extremities. Histologically, a superficial and deep perivascular lymphohistiocytic infiltrate with eosinophils was present. These eruptions suggested the denomination *eosinophilic, polymorphic, and pruritic eruption associated with radiotherapy* (EPPER). We report a case with clinical, histologic, and immunofluorescent findings characteristic of EPPER. In the series reported by Rueda et al,[1] the eruptions appeared during radiotherapy. In our case, however, the eruption was delayed by many months.

Report of a Case. A 51-year-old woman presented with an 8-week history of escalating generalized pruritus and eruption involving the lower extremities. Examination findings revealed red plaques and large tense bullae (**Figure 1**). Her medical history was remarkable for a stage IC, International Federation of Gynecology and Obstetrics grade 2 endometrial carcinoma. She underwent a total abdominal hysterectomy followed by postoperative pelvis irradiation (45 Gy) and high-dose vaginal cuff boost with radium implants (20 Gy). The patient completed radiation therapy 9½ months prior to presentation. She had not used any medication in the 6 months prior to the eruption and was otherwise healthy.

Results of a complete blood cell count were within normal limits with a normal differential. Results from a punch biopsy of the edge of a bullous lesion showed a subepidermal bulla and an inflammatory infiltrate rich in eosinophils (**Figure 2** and **Figure 3**). Both direct immunofluorescence from perilesional skin and indirect immunofluorescence with monkey esophagus failed to reveal immunoreactants along the dermoepidermal junction. The eruption resolved with a 2-week course of 0.05% clobetasol propionate ointment twice daily and cetirizine hydrochloride at 10 mg/d.

Comment. Our case shares many features typical of the series of EPPER in the article by Rueda et al.[1] As in all the latter cases, the pruritus was generalized and the lesions affected the lower extremities. Also, our patient received a total radiation dose of 65 Gy. Rueda et al state that most patients developed EPPER when receiving a radiation dose between 26 and 67 Gy. Our patient showed histologic features typical for bullous pemphigoid, and Rueda et al describe histopathologic features indistinguishable from bullous pemphigoid in 8 of 18 patients. Our patient did not demonstrate immunofluorescent findings to support the diagnosis of bullous pemphigoid, and in the series by Rueda et al, all patients with tense subepidermal bullae suggestive of bullous pemphigoid likewise failed to show

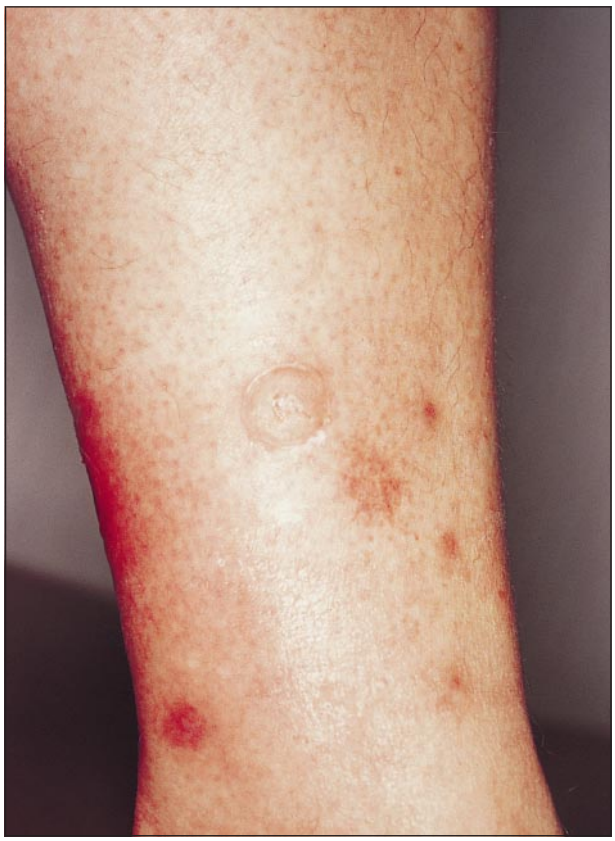

Figure 1. *Intact tense bulla (center) along with erythematous patches, plaques, and superimposed vesiculopapules on the leg.*

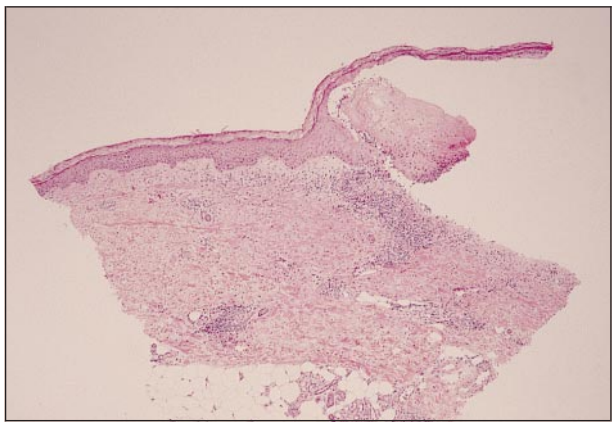

Figure 2. *Subepidermal bulla with an inflammatory infiltrate rich in eosinophils (original low magnification ×4).*

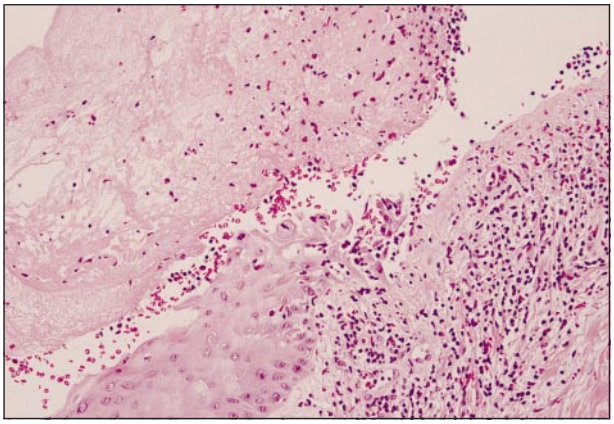

Figure 3. *Subepidermal bulla with an inflammatory infiltrate rich in eosinophils (original high magnification ×20).*

deposits along the dermoepidermal junction.

Our case differed from those of Rueda et al in 2 ways. First, most of their reported cases (27 of 32) were associated with cervical cancer, and none was associated with endometrial cancer, which was the association in our patient. Second, their cases of EPPER occurred during radiation therapy. However, in our patient the eruption was delayed, following radiotherapy by 7½ months. Although none of their original cases was delayed, some had prolonged eruptions lasting as long as 6 months. The pathogenic mechanism of EPPER is not known, and we offer no explanation for the delay in presentation.

We present a case that we believe falls within the spectrum of EPPER. Only 1 series has been reported,[1] and the full extent of this dermatosis has undoubtedly not been described. We suggest that physicians search for a history of radiotherapy in patients presenting with unusual eosinophilic eruptions.

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Neonatal and Infantile Erythrodermas

We read with interest the recent study by Pruszkowski et al[1] in the July 2000 issue of the ARCHIVES and think that the authors have made a commendable effort to determine the frequency of the various causes of erythrodermas in neonates and infants.[1] We conducted a similar study[2] in children that also included neonates and infants in the dermatology unit of Lady Hardinge Medical College and associated Kalawati Saran Children's Hospital, New Delhi, India, which is one of the largest children's hospitals in Asia having its own exclusive dermatology unit. To the best of our knowledge, our study[2] is one of the first of its kind from Asia. Subsequently, we have continued to delineate the various causes of erythrodermas in neonates and infants in a retrospective analysis (unpublished data, January 1993 to December 1999) to remediate the paucity of literature on such research from both Asian and Western countries.

As was correctly observed by Pruszkowski et al,[1] neonatal and infantile erythrodermas are rare, and their frequency is unknown; however, in our retrospective analysis we found that of the 19 000 pediatric patients treated in our unit over 6 consecutive years (1993-1999), only 20 neonates and infants had erythrodermas (an incidence of 0.11%). Although it is difficult to diagnose erythroderma, we found the following diagnostic parameters useful: congenital onset, evolution, family history of atopy, pruritus, presence of large scaling plaques, and sites of predilection after clearing.

It is not quite clear why Pruszkowski et al did not include erythrodermas involving blister formation. In their review, Hoeger and Harper[3] included neonatal erythrodermas with blister formation such as staphylococcal scalded skin syndrome, bullous ichthyosiform erythrodermas, and mastocytosis (cases not included in the study by Pruszkowski et al). We too have taken such cases into consideration. Although these erythrodermas can occasionally be excluded from the list of adult erythrodermas, we believe that they must certainly be included in the causes of neonatal and infantile erythroderma to determine the correct frequencies. Moreover, it is well known that bullous diseases can have an initial generalized erythrodermic phase that may subsequently evolve into a definite clinical entity,[4,5] and we have included only strictly erythrodermic cases of staphylococcal scalded skin syndrome.

In our analysis, the leading cause of erythroderma was infections (6 [30%] of 20 patients had staphylococcal scalded skin syndrome while 2 [10%] had candidiasis) followed by ichthyosiform erythrodermas (3 patients [15%] had nonbullous ichthyosiform erythrodermas, while 2 [10% of the total population] were collodion babies, with one case evolving into nonbullous ichthyosiform erythrodermas and the other into lamellar ichthyosis). Three patients (15%) with eczematous conditions had atopic dermatitis, and 2 (10%) had infantile seborrheic dermatitis; 2 cases (10%) were unclassified. We suspected immunodeficiency in 1 unclassified case and in 2 cases of erythrodermas due to candidiasis. Like Pruszkowski et al,[1] we observed alopecia in all 3 cases. However, owing to the lack of laboratory facilities, we could not reach a definite diagnosis. Systemic features such as lymphadenopathy, hepatosplenomegaly, and failure to thrive were absent in these patients. They were referred to hospitals with better laboratory facilities for further investigation and were subsequently lost to follow-up.

Scalp involvement with or without alopecia occurred in 10 (50%) of our 20 patients with erythroderma, and Pruszkowski et al[1] have rightfully pointed out that immunodeficiency should be suspected when diagnosing the conditions of such patients. Eosinophilia also occurred in 10 patients (50%), which can be attributed to an underlying hypersensitivity or allergic phenomenon.[4] Our histopathological findings were in concor-

dance with Pruszkowski et al and were specific in only 7 patients (35%); in the other 13 patients, the changes were nonspecific, showing either chronic dermatitic or psoriasiform changes. It may be necessary to follow up for several months to let the true clinical and histopathological picture emerge and confirm the diagnosis.

We concur with the views of Hoeger and Harper[3] that although neonatal and infantile erythrodermas are life-threatening conditions, careful management including meticulous monitoring of vital signs and electrolyte levels; adequate oral or parenteral fluid intake; and topical application of emollients or antifungals, wet dressings, or steroids may go a long way toward reducing the mortality.

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Multiple Interpretations of Cancer Risks From Body Mole Counts in Preventive Care

Mikkilineni and Weinstock[1] gave an excellent review of the usefulness of mole self-counting by patients. It would seem that this is especially useful when done by individuals in their second to fourth decades of life. However, the risk for melanoma of any patient must be considered within the context of the patient's genetic heritage, which offers an entry point into the patient's kindred for preventive cancer care.

From this inheritance perspective, the total-body mole count can have multiple interpretations of cancer risks depending on different histories of cancer in kindreds. After establishing that the patient (proband) has an abnormally high total-body mole count, the next steps in the kindred investigation include obtaining medical histories of (1) the presence or absence of atypical nevi in the proband, including previously removed moles; (2) the occurrence of any melanoma in the proband, including intraocular melanoma; (3) the occurrences of the 3 cutaneous phenotypes (atypical nevi, abnormally high mole counts, and melanomas) in first- and second-degree relatives; and (4) the presence of other primary systemic cancer phenotypes in the kindred. Depending on the collected data, a small pedigree may need investigation beyond second-degree relatives. It is imperative that the presence or absence of pertinent phenotypes be documented (by medical records and pathology and/or autopsy reports). Any cancer occurrence should be recorded with a specific cancer diagnosis and the pedigree position, sex, and age of the patient at recognition of the cancer.

Findings of a survey of dermatologists indicated that in-depth familial investigations of these patients are not done routinely.[2] With sufficient information of cancer occurrences in a kindred, an informatics analysis of the kindred could identify, along with appropriate surveillance and preventive cancer care options, 3 categories of cancer risks: (1) hereditary high lifetime; (2) familial increased empirical; and (3) sporadic general population.[3,4] Monitoring of the hereditary group requires guidelines for intensive periodic screening for specific cancer syndromes and specific preventive care procedures. The familial group has modified American Cancer Society surveillance guidelines for suspected cancer risks (although periodic updating of new primary cancer occurrences in the kindred is necessary to identify specific hereditary syndromes). The sporadic category has American Cancer Society general population surveillance guidelines for cancer detection and prevention.

After the presence of a hereditary cancer syndrome with significant melanoma occurrences is established, a high mole count in a member of that kindred indicates an increased risk for melanoma. The absence of cutaneous phenotypes of high mole count and atypical nevi in other members of a familial atypical multiple mole melanoma (FAMMM) kindred does not indicate an absence of risk for melanoma, even in an albino member.[4] The presence of other primary systemic cancers in the FAMMM kindred indicates additional primary cancer risks and different surveillance strategies.[4] The dermatologist, as the clinical investigator of the kindred's health history, can be instrumental in initiating the first preventive cancer care for a kindred with a cancer-associated genodermatosis.[5]

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Arsenic Therapy

In the December 2000 issue of the *Archives*, Dr Mark Bernhardt[1] cites a case from a century ago of what would now presumably be called mycosis fungoides, and its treatment at that time with the arsenical preparation known as Fowler's solution (arsenic trioxide dissolved in potassium bicarbonate). The therapeutic effect in that case was not noted in Dr Bernhardt's update (af-

ter 3 months there was no improvement), but he goes on to remark on the irony that this treatment poisoned many people (before its toxicity was fully appreciated), and on the recent recognition in Bangladesh that wells sunk in the 1970s to provide safe drinking water were contaminated with high levels of arsenic.

There is another irony about arsenic, namely, that this ancient remedy not only remains in the therapeutic armamentarium but is finding new uses. The organic arsenical melarsoprol is said to be the current treatment of choice for African trypanosomiasis.[2] In the form of arsenic trioxide injection, it has recently been approved by the Food and Drug Administration as a treatment for acute promyelocytic leukemia refractory to retinoid and anthracycline chemotherapy. Moreover, it may prove useful in other leukemias and lymphomas.[3]

At mid century, arsenic had not yet been abandoned as a treatment for mycosis fungoides, being regarded by Bluefarb[4] as a useful agent. If it finds a place in the "modern" therapy of mycosis fungoides, that indeed would be ironic.

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VIGNETTES

Use of the 308-nm Excimer Laser for Postresurfacing Leukoderma

Leukoderma is a common, late complication of carbon dioxide laser resurfacing[1] and is usually very distressing to patients. Grimes et al[2] recently reported a pilot study in which topical psoralen plus UV-A therapy induced moderate to excellent repigmentation in 71% of patients with postresurfacing hypopigmentation. Immunohistochemical staining with Fontana-Masson and Mel-5 revealed evidence of residual melanocytes and epidermal melanin.[2]

The 308-nm excimer laser (XTRAC; Photomedex, Radnor, Pa) has recently proven effective for the treatment of psoriasis[3] and is currently being investigated for other UV-responsive dermatoses, including repigmentation for patients with vitiligo. Narrow-band UV-B therapy is an effective and rapid therapeutic option for patients with vitiligo with fewer adverse effects than topical psoralen plus UV-A therapy.[4] Lotti et al[5] recently demonstrated that UV-B radiation microphototherapy produced a greater than 50% repigmentation in 7 of 8 patients treated for 6 months. Encouraged by these studies, we sought to determine the efficacy and safety of 308-nm excimer laser radiation in the treatment of leukoderma secondary to resurfacing.

Report of Cases. After internal review board approval, 2 patients with Fitzpatrick skin phototype III and a 5-year or longer history of leukoderma secondary to carbon dioxide resurfacing were treated with the 308-nm excimer laser. Minimal erythema doses ranging from 100 to 350 mJ/cm^2 were administered, and erythema occurred after 24 hours. The patients were initially treated at suberythemogenic doses (minimal erythema dose minus 50 mJ/cm^2). If erythema was not seen 24 hours after treatment, the dose was increased by 50 mJ/cm^2 until erythema occurred. Patients were treated using a clear plastic template twice a week for a maximum of 10 treatments or until greater than 75% repigmentation had occurred. Patients were instructed on the importance of a broad-spectrum sunscreen after the treatment sessions. Repigmentation was assessed by 3 blinded observers on a quartile scale by standardized photography.

The initial treatment dose ranged from 100 to 150 mJ/cm^2. Erythema occurred after treatment doses of 150 to 200 mJ/cm^2. A greater than 75% improvement in pigmentation was noted in the first patient after 8 treatment sessions, 4 weeks after the initiation of treatment (**Figure 1**). The second patient demonstrated a 50% to

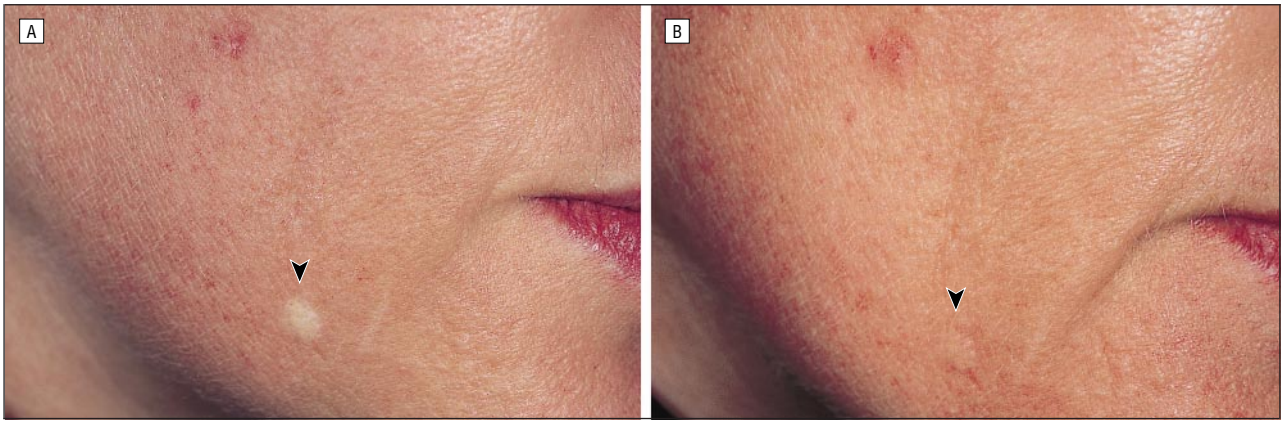

Figure 1. *A, Leukoderma of the right jaw (arrowhead) caused by carbon dioxide resurfacing of an intradermal nevus in 1994. B, Seventy-five percent repigmentation (arrowhead) after 8 treatment sessions.*

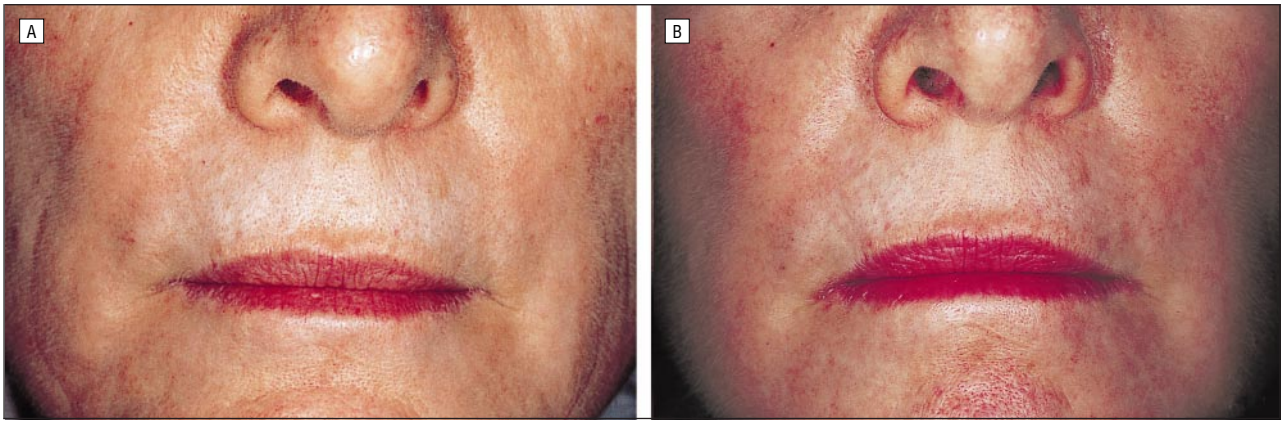

Figure 2. *A, Perioral leukoderma secondary to carbon dioxide resurfacing performed in 1995. B, Fifty percent repigmentation after 10 treatment sessions.*

75% improvement in pigmentation after 10 treatment sessions, 5 weeks after the initiation of treatment (**Figure 2**). The average cumulative UV-B dose was 1750 mJ/cm^2, and there was no evidence of hyperpigmentation or blistering at these treatment parameters. Patient questionnaires confirmed a 50% to 75% improvement or greater in the leukoderma, with patients reporting a steady darkening and less striking areas of hypopigmentation. There was no loss of the repigmentation at the 4-week follow-up.

Conclusions. In summary, our preliminary results suggest that the 308-nm excimer laser offers a rapid and effective treatment for stimulating residual melanocytes in patients with resurfacing-induced leukoderma at a relatively low cumulative UV-B dose. The mechanism of UV-B repigmentation is probably related to the stimulation of melanocyte migration and proliferation by the release of cytokines and inflammatory mediators in the skin. We are currently performing a larger, prospective clinical trial with histologic evaluation and longer follow-up to further support our findings.

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The Historical and Geomedical Immunogenetics of Pemphigus Among the Descendants of Sephardic Jews in New Mexico

The prevalence of pemphigus vulgaris (PV) among Hispanic New Mexicans is approximately 4 times higher than that among non-Hispanics generally and approaches that among Ashkenazi Jews. One explanation for this is suggested by studies revealing the existence of so-called crypto-Jewish populations in the Southwestern United States,[1] whose ancestors fled the Inquisition in 15th- and 16th-century Spain and Portugal and came to Mexico and then to the present-day Southwestern United States. In the present study, we examined the cultural practices, heritage, and immunogenetics of New Mexican Hispanic patients with PV to determine whether their PV is associated with Sephardic Jewish ancestry.

Patients and Methods. A total of 17 patients in the state of New Mexico were diagnosed as having PV by routine clinical histologic characteristics and/or direct immunofluorescence findings. Consenting patients underwent interviews regarding their genealogy, religious practices, dietary habits, mourning customs, and circumcision practices. Human leukocyte antigen typing was performed by standard serological methods using both GenTrak (GenTrak Inc, Plymouth Meeting, Pa) and Biotest (Biotest Diagnostics, Denville, NJ) trays. High-resolution identification of *DRB1* and *DQB1* alleles was performed with sequence-specific polymerase chain reaction and direct DNA sequencing of polymerase chain reaction products.[2] The Fisher exact test was used for statistical analysis.

Results. Forty percent of the population of New Mexico is Hispanic, while 12 of 17 New Mexico patients with PV (71%) identified themselves as Hispanic. This represents a prevalence of PV at approximately 2 per 100 000 for Hispanics and 0.5 per 100 000 for non-Hispanics (difference in prevalence significant [$P<.05$] at 95% confidence intervals).

Interviews regarding possible Sephardic Jewish ancestry were obtained from 6 consenting Hispanic patients with PV. Three patients were not available for interview, 2 refused to be interviewed, and 1 could not provide reliable informa-

Ancestry and Immunogenetics of Hispanic Patients With Pemphigus Vulgaris†

Patient No.	Sephardic Ancestry	Class II Antigens		Class II High-Resolution Analysis Findings	
		DR	DQ	*HLA-DRB1*	*HLA-DQB1*
1	Confirmed‡	6	3		
2	Confirmed‡	3,4	2,3	*0404	*0302
3	Suggestive	4	3	*0402 *0412	*0302
4	Suggestive	4,8	3	*0404	*0302
5	Suggestive	4,6	1,3	*0402	*0302
6	Suggestive	4,14	1,3	ND	ND
7	Refused interview	8,14(6)	1		
8	Refused interview	4,11	3	*0402	*0302
9	Not interviewed	4,8	3	*0402	*0302
10	Not interviewed	1,4	1,3	*0402	*0302
11	Not interviewed	4,6	1,3	ND	ND
12	Not interviewed	14(6)	1		

†*ND indicates testing not done.*
‡*Patient or patient's family indicated a consciousness of Sephardic ancestry.*

tion because of a chronic mental illness. Two patients reported their ethnicity as Sephardic Jewish. Four others, although unaware of any Judaic heritage, offered histories highly suggestive of Sephardic Jewish ancestry.

Pemphigus vulgaris was associated with DR4,DQ3 in 9 (75%) of 12 Hispanic patients and 5 (83%) of 6 of the Hispanic patients with known or presumed Sephardic Jewish ancestry (**Table**). The DRB1*0402 subtype was found in 5 of 7 of the DR4/DQ3 Hispanic patients and 2 of 4 of the DR4/DQ3 Hispanic patients with confirmed or presumed Sephardic Jewish ancestry. By contrast, DRB1*0402 was found in 24 (92.39%) of 26 Ashkenazi Jews with PV.[3] Consistent with our findings, Gonzalez-Escribano et al[4] have also found HLA-DRB1*0402 in 81% of Spaniards with PV, and commented on the possible contribution of a "historical Spanish-Jewish admixture" to the current Spanish HLA pool. In contrast, the DRB1*0402/DQB1*0302 haplotype comprises only 1.6% of DR4/DQ3 haplotypes in nonaffected Hispanic New Mexican controls.[5]

Comment. The interviews and immunogenetic data imply that many of the Hispanic patients with PV in New Mexico are descended from Spanish crypto-Jewish populations. In light of this finding, it becomes important now to ask whether New Mexico Hispanics are also at increased risk for other genetic diseases that are more prevalent in Sephardic or Ashkenazi Jewish populations.

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Malignant Melanomas: Search for Human Papillomaviruses

Little is known about the etiological factors involved in cutaneous malignant melanomas. Ultraviolet radiation, total number of nevi, skin type, and hereditary predisposition have been identified as risk factors for (1) superficial spreading nodular and (2) lentigo maligna melanomas, but these factors have no proven association with the development of, eg, acral lentiginous and mucosal melanomas.[1]

Specific types of human papillomaviruses (HPVs) have been identified as causal factors in malignant tumors of the genital tract.[2] A number of investigations have also demonstrated the presence of HPV DNA in nonmelanoma skin cancer in both immunosuppressed and immunocompetent patients.[3] However, large epidemiological studies and in vitro studies demonstrating the role of HPVs in the etiology of these tumors are still lacking. The detection of a broad spectrum of HPV types in 35% of normal skin biopsy specimens,[4] and up to 90% of swab-surface scrapings from normal skin[5] points to the wide distribution of these viruses in all human populations.

Since HPV-38 has been isolated from a cutaneous malignant melanoma,[6] only a few studies have attempted to identify papillomaviruses in cutaneous malignant melanomas, and these used small sample sizes.[4] We examined 54 samples of melanomas from immuno-

competent patients from Africa and Italy (28 women and 26 men; mean age, 42 years) for the presence of HPV DNA using polymerase chain reaction primers that detect most known and putative new HPV types.[4] The cases included 45 acral lentigi nous malignant melanomas of the sole (25 level IV and 20 level V melanomas), 4 nodular melanomas (level IV), 4 lentigo maligna melanoma–type lesions, and 1 sample from a superficial spreading conjunctival malignant melanoma. Samples of normal skin from the same patients were not available. All polymerase chain reaction products were cloned and sequenced.

Human papillomavirus DNA sequences were identified in 4 (7.4%) of the 54 cases: HPV-16, HPV-18, and DL436 (HPV-17 related) were identified in a lentigo maligna melanoma on the cheek of an African patient, and HPV-SCI was found in an acral lentiginous melanoma sample from Italy. Human papillomavirus 24 was present in an acral lentiginous malignant melanoma and in the conjunctival melanoma that also harbored DL284 DNA (HPV-20 related). The putative new HPV-type DL284 was previously found in a melanoma sample of another study.[4] In that study, 2 of 15 melanoma samples harbored HPV DNA, one, the DL284; the other, DL297 (HPV5 related). The distribution of these putative new HPV types and their association with disease have yet to be determined by large studies. Despite the low incidence of HPV DNA in our series as well as in other reports, the presence of papillomaviruses in a number of cases should stimulate future studies to investigate whether HPVs are casually present or play an etiologic role in the molecular mechanism of melanoma development.

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Successful Treatment of an Intractable Case of Hereditary Basal Cell Carcinoma Syndrome With Paclitaxel

Hereditary nevoid basal cell carcinoma (BCC) syndrome, known as Gorlin syndrome is a rare autosomal dominant familial tumor syndrome characterized by more than 30 congenital malformations.[1] Affected individuals often present with recurrent BCCs that slowly progress and cause severe disfigurement despite treatment with surgery, curettage and electrodesiccation, cryosurgery, dermabrasion, laser vaporization, intralesional interferon, and topical fluorouracil. We describe a patient with Gorlin syndrome for whom systemic therapy was needed to arrest the progression of aggressive BCCs.

Report of a Case. A 54-year-old white man with no family history of skin disorders had developed multiple BCCs at age 13 years. The first lesions developed on his scalp followed by appearance on his face, trunk, back, upper extremities, and to a lesser extent the lower extremities. Most of these lesions were treated with excision and skin grafting. By age 15 years, he had all his teeth extracted because of multiple jaw cysts. He was treated with systemic retinoids with initial improvement, but the disease recurred.

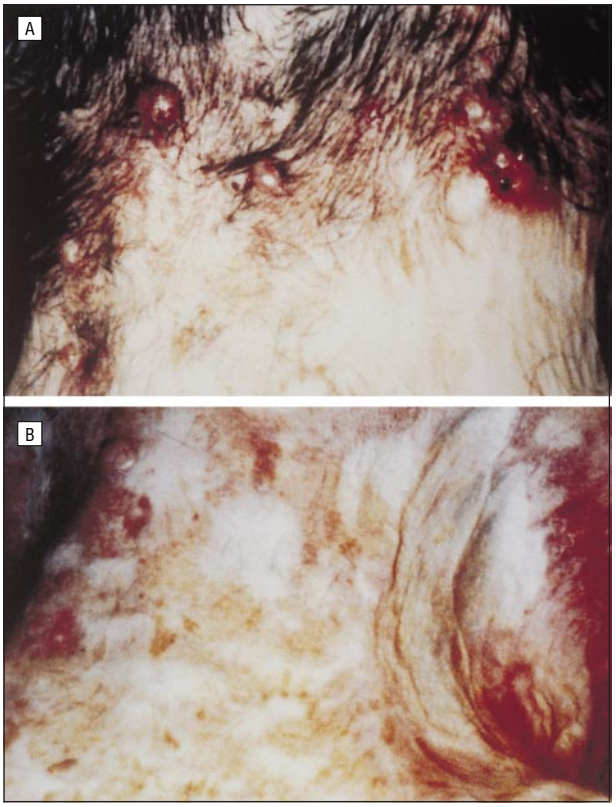
He was treated with phenylbutyrate by intravenous (IV) continuous infusion for 10 cycles at a dose of 250 mg/kg of ideal body weight during the period from May 22 through October 19, 1995. However, because of repeated central line infections, this therapy was stopped.

Chemotherapy was begun when his lesions began to ulcerate and bleed. He was treated with single-agent cisplatin in July 1997 at a dose of 100 mg/m^2 IV and experienced an initial positive response. By the fourth cycle, however, the dose was reduced by 25% because of nephrotoxic effects. After the sixth cycle, his lesions recurred, and he developed a large basal cell carcinoma in the inner canthus of his left eye that threatened his eyesight. The resultant cicatricial ectropion and the aggressive nature of his other tumors made his treatment challenging.

In July 1998, treatment with paclitaxel (Taxol; Bristol-Myers Squibb, Princeton, NJ), a chemotherapeutic agent active against a variety of tumors,[2,3] was started. It was administered at 175 mg/m^2 as a 3-hour infusion every 3 weeks. Also, 480 µg of granulocyte colony–stimulating factor was administered subcutaneously for 10 days of each cycle to minimize the period of neutropenia. A premedication regimen of 20 mg of IV dexamethasone sodium phosphate, 50 mg of IV diphenhydramine hydrochloride, and 50 mg of IV ranitidine hydrochloride was administered prior to the paclitaxel. A total of 19 cycles were administered and were well tolerated, with no clinically significant toxic effects.

Over a period of follow-up exceeding 16 months, most of the preexisting lesions healed without scarring. The remaining lesions continue to involute, and there is no evidence of development of any new lesion (**Figure**).

While other agents have been used to treat BCCs,[4,5] paclitaxel seems to offer a promising alternative for the



A, Multiple basal cell carcinomas on the patient's neck before treatment with paclitaxel. B, After treatment, most of the lesions have healed.

treatment of multiple aggressive BCCs, especially in cases such as ours where the location, size, and aggressive nature of the tumors were particularly challenging. To our knowledge, paclitaxel has not been previously used in patients with Gorlin syndrome. Further studies are needed to define its role in this condition.

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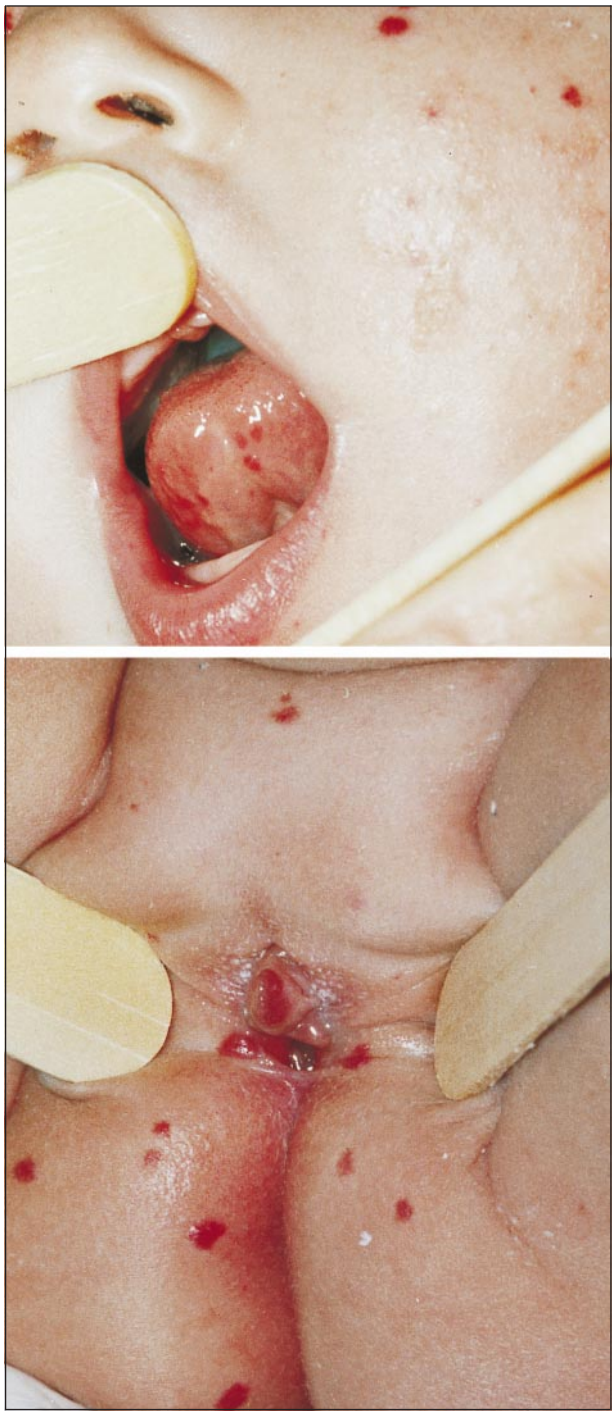
Benign Neonatal Hemangiomatosis With Mucosal Involvement

Benign neonatal hemangiomatosis (BNH) is a rare, self-limited disease where multiple capillary hemangiomas occur exclusively in the skin and lips. It must be distinguished from diffuse neonatal hemangiomatosis (DNH), a severe condition with asimilar cutaneous presentation but with the presence of life-threatening visceral hemangiomas. The presence of mu-



Multiple capillary hemangiomas scattered over the skin and mucous membranes.

cosal lesions in oral, genital, and conjunctival areas is considered a clinical clue in diagnosing the diffuse form of neonatal hemangiomatosis. We report the first case of multiple mucosal lesions associated with BNH.

Report of a Case. A female infant was referred to us at age 5 months, presenting with multiple 0.5- to 6.0-mm hemangiomas scattered over the scalp, face, trunk, extremities (including palms and soles), vaginal and oral mucous membranes, lips, and tongue (**Figure**). The lesions appeared after the child was 45 days old as multiple pinpoint erythematous lesions that increased rapidly in number and size.

She had normal heart and pulmonary sounds, absence of hepatomegaly and splenomegaly, and no evidence of hepatic bruit or pulsation. Findings of funduscopic examination were normal, and no lesions affected the conjunctivae.

The following laboratory results were normal or negative: complete blood cell count, platelet count, urinalysis, serum electrolytes, and stool guaiac. Other complementary examination findings included a normal electrocardiogram, a normal chest radiogram, and normal computed tomography of the brain, chest, and abdomen, with no signs of brain or visceral hemangiomata. A biopsy specimen of an abdominal lesion demonstrated a capillary hemangioma.

Comment. Benign neonatal hemangiomatosis is a nonheritable disorder in which multiple cutaneous capillary hemangiomas appear in an eruptive manner during the neonatal period.[1-3] They increase rapidly in number and size (reaching up to 2 cm in diameter) during the first few months and follow a benign course with spontaneous regression, usually within the first 4 months after their appearance. In previously reported cases,[2] there was no oral, genital, and conjunctival mucous membrane involvement. Generally, visceral involvement is absent or unremarkable. Histologically, lesions are typical capillary hemangiomas. Treatment is usually not required because spontaneous resolution occurs with excellent cosmetic appearance.[1]

However, DNH is a systemic presentation of neonatal hemangiomatosis characterized by cutaneous and visceral hemangiomas that may involve any organ but with clear predilection for the liver.[1-3] Oral, conjunctival, and genital lesions frequently occur.[3,4] Internal involvement causes severe clinical complications leading to mortality rates that range from 60% to 95% of patients.[1,5] Early therapy is indicated, and treatment options are systemic corticosteroids, partial liver resection, hepatic artery ligation or embolization, radiation therapy, and subcutaneous injection of interferon.

Because the cutaneous presentations of BNH and DNH are similar, it is of fundamental importance to determine the presence and extent of visceral involvement. The investigation must include clinical, laboratory, and imaging findings.[5]

The presence of multiple mucosal lesions is always associated with visceral hemangiomas, exclusive of DNH. We suggest, however, that they might also occur in cases of BNH.

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